P. J. MEHTA'S

PRACTICAL MEDICINE



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20

NATIONAL

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History Taking and Symptomatology

1

History taking is an art, which a doctor learns over the years by repeated practice and experience. History is the record of medical events that have already taken place in the patient. Since every disease has a pattern of behavior, a good history combined with a sound knowledge of medicine would help the doctor to judge the likely cause(s) that may be responsible for the patient's problems. In over 80% cases the most likely diagnosis can be reached by a proper history. On clinical examination, the clinical state of the patient is determined at that given time. However, nothing is usually known of the past problems. Hence, without an appropriate history, an incorrect interpretation of the physical findings may be made. E.g. a person has brisk reflexes and extensor plantar: a recent history of transient ischemic attack would suggest recent stroke, whereas an old history of stroke a few years ago would suggest residual effect of a past stroke.

A good history must record the following information in a systematic order.

1. **Biodata of the patient:** This should include name, age, sex, address, occupation, religion and marital status of the person.
2. **Complaints of the present illness:** The complaints with which the patient has come should be recorded in chronological order and the duration should be noted.
3. **Origin, duration and progress:** Details of each symptom must be recorded separately. The mode of onset, whether sudden or gradual, the duration of each symptom and its progress and finally the present status of the symptom must be noted. Associated symptoms must also be inquired into and recorded.
4. **History of past illness:** Similar illness in the past with their time of occurrence, duration and results should be noted. Childhood illnesses (eruptive fevers, pertussis, influenza), tuberculosis, diabetes, hypertesnion, asthma, heart disease, jaundice, joint swelling, etc. must be inquired into. Past injuries, accidents, operations or hospital stay and blood transfusion history must also be noted in details.
5. **Personal history**: Patient's appetite, food habits, type of diet, bowel and micturition habits, sleep and addictions like alcohol, smoking, tobacco chewing, charas, ganja, marijuana etc., must be inquired into. Loss of appetite and weight may suggest an active disease process. Similarly improper sleep due to other symptoms would suggest that those symptoms require urgent attention. Alcohol, tobacco, smoking and other intoxicants can adversely affect many systems in the body and the role of these substances in the patient's problems can be easily judged by the history. E.g. alcohol may be responsible for liver cell failure and cirrhosis as well as acute gastritis. Heavy smoking may be responsible for precipitating coronary artery disease or hypertension in the young.
6. **Family history**: Any illness in the family must be recorded. The state of health of parents, peers and children should be noted. If any member is deceased, the cause of death should be noted. Some genetically transmitted diseases are:
   a. **X-linked recessive diseases** (e.g. Duchenne muscular dystrophy, hemophilia, G6PD deficiency, ichthyosis). Women are carriers and do not suffer from the disease, whereas males suffer from the disease. Hence, in such illnesses, the family history would suggest similar illnesses in the patient's brothers,

sister's sons, mother's brother and mother's sister's sons.

b. **Autosomal dominant disorders** (e.g. familial hyperlipidemias, polycystic kidney, Huntington's disease, neurofibromatosis, congenital spherocytosis, myotonia dystrophica). There will be a family history of similar illness in either of the parents and/or grandparents.

c. **Autosomal recessive disorders** (e.g. beta thalassemia, sickle cell anemia, spinal muscular dystrophy, phenylketonuria, cystic fibrosis, congenital adrenal hyperplasia). There is usually no history of similar illness in the parents since they may be heterozygous and hence only carriers. However, history of consanguineous marriage in the parents (marriage between cousins or brother and sister or uncle and niece) may be present and may be responsible for the homozygous state in the patient and thus the manifestation of the disease.

7. **Menstrual and obstetric history:** In females, the date of onset of menstruation, date of last menstruation and the amount of blood flow, regularity and pain during menstruation should be noted. In a woman who has conceived, details of past abortions, premature births and normal or abnormal deliveries should be noted.

Some of the common symptoms which the patients present with and their causes are given below:

1 › Weight Loss

1. Caloric malnutrition: Fasting, inappropriate diet
2. Infections (chronic): Infective endocarditis, tuberculosis, amebic liver abscess, fungal infections, H.I.V. infection, etc.
3. Acute infections: Viral hepatitis, typhoid, septicemia
4. Malignancy
5. Malabsorption syndrome
6. Endocrine diseases: Diabetes mellitus, thyrotoxicosis, panhypopituitarism, Addison's disease, etc.
7. Anorexia nervosa

2 › Weight Gain

1. **Increased water retention:** Cardiac failure, cirrhosis of liver, nephrotic syndrome, hypoproteinemia, edema states, etc.
2. **Increased tissue mass:**
   a) *Obesity*
   b) *Endocrine diseases:* Cushing's disease, hypothyroidism, acromegaly, etc.
   c) *Hypothalamic diseases:* Craniopharyngi-oma, Frohlich's syndrome, hamartoma, etc,
   d) *Drugs:* e.g. steroids

3 › Anorexia

1. **Viral hepatitis** including anicteric hepatitis
2. **Tuberculosis**
3. Carcinoma of stomach and other **malignancies**
4. **Endocrine diseases:** Addison's disease, panhypopituitarism
5. **Chronic wasting diseases:** Uremia, cirrhosis of liver, chronic alcoholism, chronic smoking etc.
6. **Drugs:** Digitalis, quinine, metronidazole, etc.

4 › Fever

(Refer Pg. 36 : Temperature)

5 › Chest Pain

1. **Cardiac:** Ischemic heart disease, pericarditis, infective endocarditis, cardiomyopathy, valvular heart disease, dissecting aneurysm of aorta, etc.
2. **Respiratory:** Pleurisy, pneumothorax, pulmonary embolism, pulmonary hypertension, malignancy
3. **Musculoskeletal:** Rib fracture, vertebral collapse, costochondritis, myositis of pectoral muscle, etc.
4. **Functional**
5. **Miscellaneous:** Herpes zoster of intercostal nerves, esophagitis, pancreatitis, peptic ulcer, cholecystitis, splenic flexure syndrome, etc.

6 › Dyspnea

1. **Physiological:** Mountaineers, exercise, hyperpyrexia, anemia
2. **Respiratory:** Airway obstruction, bronchial asthma, chronic obstructive lung disease, pulmonary infections, pulmonary edema, pulmonary embolism, bronchogenic carcinoma, pleural effusion, pneumothorax, etc.
3. **Cardiac:** Acute myocardial infarction, valvular heart disease, left ventricular failure, congenital cyanotic heart disease, etc.
4. **Metabolic:** Diabetes, uremia, hypokalemia
5. **Neurological:** Respiratory center depression as in syringobulbia, motor neuron disease, Guillain Barre syndrome, bulbar polio, myasthenia gravis
6. **Psychogenic**

(For ATS Dyspnea Scale: Refer pg. 125)

(For NYHA Classification: Refer pg. 211)

7 › Cough

1. **Respiratory:**
   a. *Laryngeal and pharyngeal* infections and neoplasms
   b. *Tracheobronchial:* Tracheobronchitis, bronchial asthma, bronchiectasis, bronchogenic carcinoma, pressure over the trachea and bronchus from outside, aspiration, etc.
   c. *Lung*: Pneumonia, tuberculosis, lung abscess, tropical eosinophilia, pulmonary edema and infarction, interstitial fibrosis, etc.
   d. *Pleural:* Pleural effusion, pneumothorax, etc.
2. Cardiac: Left ventricular failure, mitral stenosis, aneurysm of aorta, etc.
3. Mediastinum: Enlarged lymph nodes, mediastinal tumors, etc.
4. Psychogenic
5. Reflex: Wax or foreign body in the ear, subphrenic or liver abscess, etc.

8 › Hemoptysis

(Refer Pg. 382)

9 › Palpitations

1. **Physiological**: Exercise, emotional or sexual excitement, etc.
2. Excessive **tea, coffee, tobacco, alcohol** consumption
3. **Anxiety state**
4. **High output state**: Anemia, beriberi, thyrotoxicosis, A-V fistula, Paget's disease, etc.
5. **Cardiac arrhythmia:** Extrasystoles, paroxysmal tachycardia, atrial fibrillation, heart block, etc.
6. **Drugs:** Sympathomimetic agents, nitrates, overdose of digoxin or insulin
7. **Miscellaneous:** Pheochromocytoma, hypoglycemia, etc.

10 › Syncope

1. **Vasovagal syncope**
2. **Postural hypotension**
3. **Cardiac arrhythmia:** Stokes Adam's syndrome
4. **Stenotic lesions of the heart**: Aortic stenosis, hypertrophic subaortic stenosis, pulmonary and mitral stenosis, Fallot's tetrad, ball valve thrombus in left atrium.
5. **Cerebrovascular insufficiency:** Vertebrobasilar insufficiency, carotid sinus syncope, etc.
6. **Miscellaneous:** Massive myocardial infarction, pericardial tamponade, left atrial myxoma, micturition syncope, cough syncope, internal bleeding, etc.

11 › Polyuria

1. **Transient:** Excessive water drinking, diuretic therapy, cold weather, stress
2. **Persistent:**
   a. Diabetes mellitus

b. Diabetes insipidus (pituitary and nephrogenic)

c. Renal: Chronic renal failure, recovery from acute tubular necrosis, analgesic abuse nephropathy, etc.

d. Compulsive water drinking

12 › Pyuria

1. **Renal:**
   a. *Infective:* Pyelonephritis, pyonephrosis, perianal abscess, renal tuberculosis
   b. *Non-infective:* Hypersensitivity nephritis, analgesic nephropathy, hypokalemia, nephrocalcinosis, lead poisoning, radiation nephritis
2. **Lower urinary tract:**
   a. *Cystitis:* Infective, radiation, cytotoxic drugs
   b. *Urethritis*
3. **Adnexa:** Perinephric abscess, gynecological infections

13 › Frequency of Micturition and Nocturia

1. **Bladder:** Cystitis, small contracted bladder, tumors, vesicular calculus, cystocele
2. **Bladder neck:** Incomplete evacuation due to enlarged prostate or stricture of urethra, incompetent internal urethral sphincter, ectopic ureter
3. **Urethra:** Urethritis, neoplasms, balanitis, stricture of urethra, pinhole meatus, phimosis
4. **Miscellaneous:** Polyuria, psychogenic, pregnancy, pressure from surrounding structures

14 › Hesitancy and Precipitancy of Urine

1. **Cerebral:** Cerebrovascular accidents, cerebral tumors, head injuries, etc.
2. **Urinary tract disease:** Enlarged prostate, bladder neck obstruction

15 › Retention of Urine

1. **Neurological:** Spinal cord diseases (transverse and compression myelitis), cauda equina lesions, multiple sclerosis
2. **Genitourinary:**
   a. *Penis:* Phimosis
   b. *Urethra:* Posterior urethral valves, foreign body, stones, stricture, rupture, spasm of sphincter, etc.
   c. *Prostatic enlargement*
   d. *Bladder*: Atony, tumour, stone, or compression by fibroids or retroverted uterus.
   e. *Following parturition.*
3. **Drugs:** Sympathomimetic agents, salbutamol, terbutaline, anticholinergic drugs, etc.
4. **Functional**

16 › Hematuria

1. **Renal:** Glomerulonephritis, renal infarction, stones, tumors, tuberculosis, interstitial nephritis, papillary necrosis, polycystic kidneys, etc.
2. **Ureteric:** Trauma, tuberculosis, stones, neoplasms
3. **Bladder:** Trauma, tuberculosis, stones, neoplasms, cystitis, following cyclo-phosphamide therapy
4. **Urethral:** Trauma, stones, foreign body, urethritis
5. **Prostatic:** Prostitis, neoplasms
6. **Systemic diseases:** Diabetes, amyloidosis, collagen disease, DIC, etc.

17 › Anuria

1. **Renal:** Glomerulonephritis, pyelonephritis, polycystic kidney, chronic renal failure, nephrotoxic drugs, SLE etc.
2. **Pre-renal:** Diarrhea and vomiting, burns, blood loss, hypotension, septicemia, intravascular hemolysis, etc.
3. **Obstructive:** Calculi in kidney or urinary tract, blockage of ureters by malignancy or crystals, retroperitoneal fibrosis, accidental ligation during surgery, etc.

18 › Pain in the Loin

1. **Renal:** Stone, malignancy, infections (pyelonephritis, perinephric abscess, etc.), polycystic kidney, Dietl's crisis, etc.
2. **Extrarenal:** Acute pancreatitis, cholecystitis, appendicitis, porphyria, ruptured duodenal ulcer or spleen, ectopic gestation, etc.

19 › Abdominal Pain

1. **Acid peptic disease**
2. **Peritonitis**
3. **Mechanical obstruction** of hollow viscus
4. **Colic:** Intestinal, renal, biliary, etc.
5. **Vascular** disturbances producing ischemia and abdominal angina: Thromboembolism, sickle cell crisis, rupture of aneurysm, etc.
6. **Abdominal wall:** Fatty hernia through linea alba, trauma or infection of the muscle etc.
7. **Referred pain:** Pneumonia, pleurisy, ischemic heart disease, panniculitis, torsion of the testes or ovary.
8. **Metabolic:** Diabetes, uremia, porphyria, lead poisoning, Henoch Schonlein purpura
9. **Neurogenic:** Herpes zoster, tabes dorsalis, etc.
10. **Functional**

20 › Dysphagia

1. **Esophageal:** Inflammation, webs, strictures, tumors, achalasia cardia, spasm, hiatus hernia, Chagas' disease, scleroderma, radiation, etc.
2. **Upper gut:** Pharyngeal and laryngeal lesions
3. **External compression:** Cervical spondylitis, retropharyngeal abscess, goitre, enlarged left atrium, aneurysm, etc.
4. **Neurological:** Bulbar palsy, polyneuropathy, motor neuron disease, myopathies, myasthenia, dermatomyositis.

21 › Water Brash

1. Normal individuals following heavy meals
2. Incompetent lower esophageal sphincter
3. Peptic ulcer disease
4. Biliary tract disease

22 › Indigestion

1. **Upper gastrointestinal tract:** Alcohol, following heavy meals, aerophagia, hiatus hernia, gastroesophageal reflux, peptic ulcer disease, gastritis, drugs, etc.
2. **Lower gastrointestinal tract:** Parasites, Food intolerance, irritable bowel syndrome, increased intraluminal gas, etc.
3. **Hepatobiliary:** Cholecystitis, stones, pancreatitis, splenic flexure syndrome, etc.
4. **Systemic diseases:** Uremia, cardiac failure, tuberculosis, malignancy
5. **Functional**

23 › Eructation

1. **Faulty dietary habits:** Aerated water, chewing gum, mouth breathing, etc.
2. **Addiction:** Smoking, alcohol, betel nut, pan, etc.
3. **Gastrointestinal:** Gastritis, peptic ulcer, hiatus hernia, cholecystitis, stones, irritable bowel syndrome
4. **Psychogenic:** Anxiety, depression, etc.

24 › Heart Burns

1. **Organic lesions:** Reflux esophagitis, hiatus hernia, peptic ulcer, etc.
2. **Functional:** Faulty dietary habits, addictions, etc.
3. **Psychogenic:** Neurosis, repressed emotions etc.

25 › Vomiting

1. **Abdominal:**
   a. *Gastritis and Peptic ulcer*
   b. *Colic*
   c. *Acute abdominal emergencies*: Appendicitis, cholecystitis, peritonitis, pancreatitis, intestinal obstruction, etc.
2. **Cardiac:** Myocardial infarction, cardiac failure, etc.
3. **Central:** Raised intracranial tension, Meniere's disease, motion sickness, radiation, etc.
4. **Metabolic:** Diabetes, alcohol, pregnancy, hypercalcemia, Addison's disease
5. **Toxic**: Febrile illnesses (viral hepatitis), cholera, drugs (salicylates), corrosive poisons
6. **Functional**

26 › Hematemesis

(Refer Pg. 387)

27 › Constipation

1. **Acute:**
   a. *Intestinal obstruction:* Volvulus, intussusception, hernia, etc.
   b. *Acute abdomen:* Appendicitis, salpingitis, perforation, colic, etc.
   c. *General:* Septicemia
2. **Chronic:**
   a. *Faulty habits:* Laxative abuse, prolonged travel, insufficient dietary roughage, etc.
   b. *Painful anal conditions:* Piles, fissures, etc.
   c. *Organic obstruction:* Carcinoma, diverticulum, strictures, etc.
   d. *Adynamic bowel:* Scleroderma, myopathies, myotonia, etc.
   e. *Metabolic:* Hypothyroidism, hypokalemia, hypercalcemia, porphyria, lead poisoning
   f. *Drugs:* Atropine group, opium group, tricyclic antidepressants, coffee, etc.

28 › Flatulence

1. **Gastric:** Aerophagy, neurosis, gastric or biliary disease (hiatus hernia, pyloric stenosis, biliary dyspepsia), following vagotomy etc.
2. **Food intake:** Cabbage, cauliflower, peas, beans, etc.
3. **Intestinal:** Steatorrhea, intestinal obstruction, malignancy, etc.
4. **Systemic diseases:** Cardiac failure, cirrhosis, etc.

29 › Diarrhea

1. **Osmotic:** Laxative abuse, maldigestion of food
2. **Infections:** Typhoid, cholera, amebiasis, giardiasis, helminthiasis, H.I.V. infection, etc.
3 **Endocrine diseases:** Thyrotoxicosis, diabetes, Addison's disease, etc.
4. **Drugs:** Thyroxine, prostigmin, ampicillin, phenolphthalein, etc.
5. **Anxiety:** Irritable bowel syndrome, etc.
6. **Miscellaneous:** Malignant carcinoid syndrome.

30 › Bleeding Per Rectum

1. **Anal:** Fissure, fistula, foreign body, etc.
2. **Rectal:** Piles, proctitis, foreign body, neoplasms
3. **Colonic:** Bacillary and amebic dysentery, ulcerative colitis, carcinoma, polyps, diverticula, ischemia, irritant drugs, etc.
4. **Hematological**: Blood dyscrasias, anti-coagulant therapy, uremia, etc.

31 › Jaundice

(Refer Pg. 19)

32 › Epistaxis

1. **Hematological:**
   a. *Thrombocytopenia:* ITP, leukemia, aplastic anemia, etc.

b. *Qualitative platelet defects:* Glanzmann's thrombasthenia, von Willebrand's disease, etc.

c. *Coagulation disorders:* Hemophilia, afibrinogenemia, etc.

d. *Miscellaneous:* Hypersplenism, vitamin B_{12} deficiency, etc.

2. **Nasal diseases:** Trauma, tumors, rhinitis, diphtheria, sinusitis, etc.

3. **Systemic diseases:**

a. *Infective fevers:* Typhoid, malaria, measles, viral infections, etc.

b. *Hypertension*

c. *High altitude*

d. *Collagen disease:* Pseudoxanthoma elasticum, Ehlers' Danlos syndrome, etc.

33 〉 Bleeding Gums

1. **Hematological:**

a. *Thrombocytopenia:* Leukemias, aplastic anemia, ITP, etc.

b. *Qualitative platelet defect:* Glanzmann's thrombasthenia, von Willebrand's disease, giant platelet syndrome, etc.

c. *Coagulation disorders:* Hemophilia, Christmas disease, vitamin K deficiency, afibrinogenemia, anticoagulants, etc.

d. *Miscellaneous:* Hypersplenism, vitamin B_{12} deficiency, disseminated intravascular coagulation, etc.

2. **Gum diseases:** Gingivitis, periodontitis, herpes, Vincent's infection

3. **Systemic disease:**

a. Scurvy

b. Drugs: Phenytoin therapy

c. Diabetes mellitus, Cushing's syndrome

d. Pregnancy

e. Henoch-Schonlein purpura

f. Connective tissue disease: Ehlers' Danlos syndrome, etc.

34 〉 Hoarse Voice

1. **Local:** Singer's nodules, laryngitis, foreign body, tumours of larynx.

2. **Recurrent laryngeal nerve palsy**

3. **Systemic diseases:** Myxedema, angioneurotic edema, etc.

4. **Toxic:** Tobacco, alcohol

35 〉 Itching

1. **Skin disease:** Scabies, candidiasis, psoriasis, urticaria, pediculosis, allergic dermatitis, dry skin

2. **Systemic diseases:**

a. *Drug reaction*

b. *Senile purpura*

c. *Infections:* Enterobius vermicularis, hookworm, tinea infections, hydatid cyst, etc.

d. *Endocrine diseases:* Diabetes mellitus, hypothyroidism, hepatic diseases, obstructive jaundice, primary biliary cirrhosis, etc.

e. *Renal diseases:* Chronic renal failure, etc.

f. *Blood diseases:* Polycythemia vera, malignancy, Hodgkin's disease, myeloma, etc.

3. **Pregnancy**

36 〉 Hirsutism

1. **With virilization:** Arrhenoblastoma, malignant adrenal tumors, congenital adrenal hyperplasia, testicular tumors, etc.

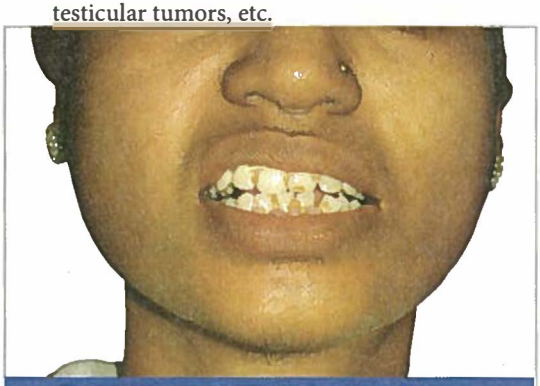


Fig. 1.1 : Hirsuitism with gum hypertrophy due to phenytoin toxicity

2. **Without virilization:**
   a. Familial
   b. Idiopathic
   c. Polycystic ovarian syndrome
   d. Acromegaly, Cushing's syndrome, HAIR-AN syndrome, congential adrenal hyperplasia
   e. Drugs: Androgens, phenytoin sodium, minoxidil

37 › Gynecomastia

1. **Physiological:** During infancy and at puberty
2. **Refeeding:** Recovery from wasting diseases
3. **Testicular:** Agenesis, orchitis, tumour, Klinefelter's syndrome, etc.
4. **Endocrine:** Acromegaly, adrenal tumors, ectopic hormone production, etc.
5. **Drugs:** Digitalis, spironolactone, phenothiazine, metoclopramide, cimetidine, etc.
6. **Miscellaneous:** Cirrhosis of liver, rheumatoid arthritis, leprosy, etc.



Fig. 1.2: Gynecomastia in a case of Klinefelter's syndrome

38 › Backache

1. **Physiological:** Faulty posture, asthenic individuals, pregnancy
2. **Trauma:** Prolapsed intervertebral disc, lumbosacral strain
3. **Infection:** Osteomyelitis, tuberculous spine (Pott's spine)
4. **Neoplastic:** Primary tumors, secondaries, multiple myeloma, etc.
5. **Metabolic:** Osteoporosis, osteomalacia, hyperparathyroidism, renal stones, etc.
6. **Congenital:** Spina bifida
7. **Arthritis:** Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, etc.
8. **Referred pain:** Pancreatitis, retroperitoneal tumors, cholecystitis, diverticulitis, retroverted uterus, uterine prolapse, etc.
9. **Spinal deformities:** Kyphosis, scoliosis and lordosis

39 › Hiccough

1. **Metabolic:** Uremia, diabetes
2. **Toxemia:** Septicemia, high fever
3. **Abdominal:** Liver abscess, peritonitis, subphrenic abscess, etc.
4. **Thoracic:** Aortic aneurysm, mediastinal glands, substernal goitre, etc.
5. **Neurological:** Encephalitis, meningitis, brain tumour, etc.
6. **Psychogenic:** Hysterical, neurosis
7. **Epidemic hiccoughs**

40 › Headache

1. **Intracranial:**
   a. *Meningeal:* Meningitis
   b. *Vascular:* Intracranial aneurysm, malignant hypertension, subarachnoid hemorrhage
   c. *Skeletal:* Metastasis, Paget's disease, etc.
   d. *Space occupying lesion:* Subdural hematoma, tumors, granulomas, abscess
   e. *Post lumbar puncture*
2. **Extracranial**
   a. *Vascular:* Migraine, cluster headache, temporal arteritis, etc.
   b. *Skeletal:* Paget's disease, torticollis, etc.

   c. *Referred pain:* Sinusitis, eyestrain, glaucoma, aural, etc.
3. **Miscellaneous:** Psychogenic, posttraumatic, alcohol, nitrates, monosodium glutamate ingestion etc.

41 › Tinnitus

1. **Auditory:**
   a. External ear: Wax, polyp, foreign body, etc.
   b. Middle ear inflammation
   c. Internal ear: Meniere's disease, labyrinthitis, acoustic neuroma
2. **Systemic:** Migraine, barotrauma, anemia, aortic regurgitation, salicylates, quinine, etc.

42 › Tingling and Numbness

1. **Peripheral neuropathy**
2. **Entrapment neuropathy:** Carpal tunnel syndrome, thoracic inlet tumor
3. **Skeletal:** Cervical spondylitis, lumbar canal stenosis, disc lesion, tumour, etc.
4. **Transient**

43 › Cramps

1. **Idiopathic**
2. **Electrolyte disturbances:** Hyponatremia, hypocalcemia, hypomagnesemia
3. **Neurological:** Amyotrophic lateral sclerosis, muscular dystrophy, myotonia, peripheral neuritis
4. **Metabolic:** Uremia, McArdle's disease
5. **Occupational:** Miners, writers, typists, tailors, telephone operators, etc.
6. **Miscellaneous:** Pregnancy, dehydration, chronic wasting diseases, overexertion.

44 › Intermittent Claudication

1. **Arterial:** Atheroma, embolism, Buerger's disease
2. **Systemic:** Diabetes mellitus, syphilis, anemia, McArdle's disease, overexertion

45 › Vertigo

1. **Cerebellar:** Cerebellitis, injury, infarction, etc.
2. **Brain Stem:** Vertebrobasilar insufficiency
3. **Vestibular:** Neuronitis, acoustic neuroma, cerebello pontine angle tumour, etc.
4. **Auditory:** Acute labyrinthitis, Meniere's disease, toxic effects of alcohol, streptomycin, salicylates, spread of disease from middle ear, Eustachian tube blockage
5. **Miscellaneous:** Migraine, aura of epilepsy, anemia, hypotension, head injury, etc.

General Examination

2

The general examination of the patient must be done systematically, noting the following:

1. Built
2. Body proportions
3. Nutrition
4. Decubitus
5. Clubbing
6. Cyanosis
7. Jaundice
8. Pallor
9. Lymphadenopathy
10. Edema
11. Skin, hair and nails
12. Vertebral column
13. Thickened nerves
14. Joints
15. Temperature
16. Pulse
17. Jugular venous pulse & pressure
18. Blood pressure
19. Respiration

1 › Built

Built is the skeletal structure in relation to age and sex of the individual as compared to a normal person.

Tall Stature

A child is considered to be tall when the height is greater than 2 standard deviations above the mean for the age. *Gigantism* is the term applied when the patient's height is greatly in excess of the normal for his age before fusion of epiphysis. There is no fixed height to constitute a giant, but in adults, it is applied for individuals with a height of more than 6½ ft.

Causes

1. ***Simple or primary gigantism:*** Racial, familial or constitutional
2. ***Endocrine:*** Hyperpituitarism, hypogonadism
3. ***Genetic:*** Klinefelter's syndrome
4. ***Metabolic:*** Marfan's syndrome, homocystinuria
5. ***Miscellaneous:*** Cerebral gigantism, etc.

Differential Diagnosis

1. ***Constitutional:*** Usually in constitutional tall stature the parents are also tall. In all children whose parents or grand parents are also tall, a suspicion of a pathological disorder must be raised. The child is otherwise normal. In boys usually no treatment is required. In girls long term estrogen could be used to suppress further growth. However, because of its side-effects, usually it is avoided unless the predicted adult height is more than 183 cms.
2. ***Gigantism (Acromegaly/Hyperpituitarism):*** In gigantism the patient is very tall but with normal body proportions. However, the features are coarse with increased heel pad thickness. There may be evidence of raised intracranial tension and bitemporal hemianopia. Pituitary tumors need surgery.
3. ***Cerebral Gigantism* (Soto's syndrome):** Children with cerebral gigantism have a large elongated head, prominent forehead, large ears and jaws, elongated chin, antimongoloid slant to the eyes and coarse facial features. They have subnormal intelligence and impaired coordination. The cause is not known.
4. ***Sexual Precocity and virilizing disorders:*** In these children, acceleration of linear growth occurs simultaneously with signs of premature sexual development or inappropriate virilization. This disorder may be due to congenital adrenal hyperplasia, adrenal tumor, gonadal tumor or premature secretion of gonadotropic hormones. The bone age is usually advanced so that the adult stature may be diminished.

Table 2.1 : Differential Diagnosis of Gigantism when Upper Segment = Lower Segment

		Constitutional	Hyperpituitarism	Cerebral gigantism
1.	Family history	+	—	—
2.	Obesity	+	—	+
3.	Mental retardation	—	—	+
4.	Other features	—	Of Gigantism	Macrocrania, large hands and feet
5.	Post-glucose growth hormone (G.H.)	N	Increased	N

Table 2.2 : Differences between Marfan's Syndrome and Homocystinuria

		Marfan's Syndrome	Homocystinuria
1.	Inheritance	Autosomal dominant	Autosomal recessive
2.	Ectopia lentis	Upward dislocation	Downward dislocation
3.	High arched palate	Present	Absent
4.	Loose jointedness	Present	Absent
5.	Arachnodactyly	Strikingly seen	Not striking
6.	Mental retardation	Absent	Present
7.	Vascular disease	Aortic	Thrombotic
8.	Urine Benedict's test	Normal	Positive
9.	Cyanide Nitroprusside test	Absent	Cystine and homocystine present
10.	Liver biopsy	Normal	Low activity of Cystathionine synthetase

5. ***Marfan's syndrome:*** These patients are tall with long limbs, narrow hands, long slender fingers (arachnodactyly), hyperextensible joints, dislocation of the lens, high arched palate, kyphoscoliosis, arm span greater than the height and the lower segmetnt more than the upper segment.
6. ***Homocystinuria:*** This condition resembles Marfan'ssyndrome. The differences are mentioned in the table.
7. ***Klinefelter's syndrome:***
   a. Lower segment more than the upper segment
   b. Gynecomastia
   c. Small, firm testes, azoospermia
   d. Chromatin (Barr) body usually present (47XXY). Some may be chromatin negative.
   e. Mental retardation may be associated.
   f. Associated with mongolism and leukemia.
   g. Chronic pulmonary disease, varicose veins and diabetes are more common

Short Stature (Dwarfism)

Dwarfism is the term applied when the patient's height is 2standard deviations less than that for his/her age and sex. Mid-parental height usually determines the final height.

Causes

1. ***Hereditary/Genetic***
2. ***Chromosomal:*** Turner's syndrome (45XO), Down's syndrome, Noonan's syndrome, etc.
3. ***Constitutional*** growth delay
4. ***Delayed puberty***
5. ***Nutritional:*** Malnutrition, malabsorption, rickets
6. ***Endocrine:*** Growth hormone deficiency, hypopituitarism, hypothyroidism, excessive androgens, Cushings syndrome, congenital adrenal hyperplasia
7. ***Skeletal:*** Achondroplasia, spinal deformities, skeletal dysplasias
8. ***Systemic diseases:*** Renal tubular acidosis, uremia,

congenital cyanotic heart disease, cirrhosis of liver, etc.

Differential Diagnosis

1. ***Hereditary***: In hereditary short stature there is no endocrine abnormality. The bone age and the dental age are normal. Although they are short, they grow at a constant rate of 4-5 cms a year and they have normal body proportions for age. This may be either genetic (if there is a family history of short stature) or primordial (if there is no family history of short stature). The latter may be due to intrauterine growth failure or postnatal growth retardation. These children require no endocrine treatment.
2. ***Constitutional growth delay and delayed puberty***: This disorder is common among adolescent boys. There is no true endocrine deficiency. They grow at a constant rate of about 4 cm a year but their bone age and dental age is delayed by about 2 years. Often there is a history of delay in growth and pubertal development in the father and other male relatives.

   If puberty does not occur spontaneously by 15 years of age, it can be induced by testosterone enanthate 250 mg IM once a month for 3 months.
3. ***Turner's syndrome (SHOX gene deficiency)***: These children are girls who have agenesis of their ovaries. The chromosomal pattern is 45XO. They have a characteristically short webbed neck, low hairline, square and shield-like chest, cubitus valgus and mental retardation. Although short, they grow at the rate of less than 4 cm each year with normal bone age and dental age but absent pubertal growth spurt, so that during adolescence, the skeletal age is delayed due to the absence of sex hormones (streak ovaries).

   Giving them oxandrolone 0.15 mg/kg/day with growth hormone from early adolescence till puberty can increase the height. After the age of 15 years cyclical estrogen replacement therapy in physiological doses is given for life. Growth hormone replacement is recommended before epiphyseal fusion.
4. ***Hypopituitarism (including Growth Hormone deficiency)***: These children have the skeletal age and the dental age delayed by more than 2 years. The growth rate is less than 4 cm/year. The ratio of the upper segment and the lower segment is normal. They have genetic defects (prop-1, pit-1 gene deficiency). MRI shows hypoplastic or aplastic pitutaries. Growth hormone replacement is necessary.
5. ***Hypothyroidism***: These children have mental, dental and skeletal retardation since birth. There would be coarse dry skin and constipation. Their body proportion is infantile i.e. upper segment is more than lower segment. Lifelong thyroxine replacement is required.
6. ***Achondroplasia***: Achondroplastic dwarfs have short limbs resulting in short stature. Hence,

Table 2.3 : Differential Diagnosis of Short Stature (Dwarfism)

	Constitutional	*Hereditary*	*Hypopituitarism*	*Hypothyroidism*	*Turner's syndrome*
1. Family history	+	+	—	—	—
2. Birth wt. and height	N	↓	N	N	↓
3. Pattern of growth	Slow from birth	Slow from birth	Slow few months	Slow from birth	Slow from birth
4. Features	Immature but later normal	Mature	Immature	Infantile	Characteristic features
5. Bone age	Slight delay	N	Progressive retardation	Marked retardation	N
6. Dentition	N	N	Delayed	Delayed	N
7. Mental status	N	N	N	Retarded	Retarded/N
8. Puberty	Later but normal eventually	N	Delayed	Marked delay	Absent

Table 2.4 :Vitamins

	Vitamin (Daily Requirement)	*Sources*	*Deficiency State*	*Therapeutic dose*
1.	**Vitamin A** (5000 IU, 8000 IU in pregnancy)	Carrot, Spinach, sweet potatoes, milk, liver and fish liver oils	Night Blindness, Bitot's spots Xerophthalmia, Keratomalacia, Imperfect enamel formation. Follicular hyperkeratosis of skin	500 IU/kg/day I.M. **Toxic effects** : Painful bone Exostosis, premature epiphyseal fusion. Pruritus, intracranial hypertension, anorexia, irritability, dry itchy skin, sparse hair
2.	**Vitamin D** (400 IU)	Milk butter, yeast, fish, liver oil, egg yolk, Synthesis in skin when it is irradiated	Tetany and rickets in children Osteomalacia in adults	500 IU/day **Toxic effect:** Anorexia, vomiting, diarrhea, lassitude, thirst, sweating and headache
3.	**Vitamin E** (200/ 400/ 600 IU/day)	Whole rice, wheat germ oil, lettuce, maize, molasses, peas and meat	In man- No symptoms In animals - habitual abortion, testicular degeneration, etc.	**Uses:** 1. Premature infants 2. Retrolental fibroplasia 3. G_6PD deficiency - to prevent hemolysis
4.	**Vitamin K** (40 mg/day)	Green vegetables, cabbage, spinach, tomatoes, egg yolk. It is also synthesised in the intestines.	Hemorrhagic diathesis	10 mg IM **Uses:** In newborn, to prevent Haemorhagic Disease of New born
5.	**Vitamin B_1** (Thiamine) (1-2mg/day)	Whole grain, cereals, yeast, beans, liver, meat, egg yolk	Anorexia and nausea, Dry & wet beriberi, Wernicke's encephalopathy. Korsakoff's psychosis	100 mg orally or IM
6.	**Riboflavin** (2 mg/day)	Germinating seeds, milk eggs, liver	Angular stomatitis, cheilosis or magenta tongue, corneal vascularisation, scrotal dermatitis	10 mg orally
7.	**Nicotinic acid** (15-20 mg)	Rice, liver, brain, eggs, meat and yeast	Erythema, Pigmentation, hyperkeratosis of skin, seborrhea around the nose, raw red tongue, diarrhea, dementia and paraplegia	500 mg orally. **Toxic effects :** itching, flushing, amblyopia, liver dysfunction and hyperuricemia
8.	**Pantothenic acid** (3-10 mg)	Whole grain, milk, eggs, liver, kidney, meat	Burning feet syndrome	4-10 mg orally
9.	**Pyridoxine/ Vitamin B_6** (1-2 mg/day)	Yeast, cereals, lettuce, spinach, milk, eggs, meat and liver	Nasolabial seborrhea, cheilosis, glossitis, peripheral neuropathy, convulsions, hypochromic microcytic anemia, lymphocytopenic and eosinophilia	50-1000 mg orally **Uses :** 1. With INH, cycloserine, oral contraceptives, hydrallazine and D-penicillamine 2. Alcoholism 3. Hyperemesis gravidarum, Motion sickness, radiation sickness 4. Sideroblastic anemia 5. Agranulocytosis 6. Infantile convulsions 7. Homocystinuria, hyperoxaluria and Hartnup's disease

Table 2.4 : Vitamins *(Contd...)*

	Vitamin (Daily Requirement)	Sources	Deficiency State	Therapeutic dose
10.	**Inositol** (not known)	Green citrus fruits, grains, yeast.	Not known in man. In animals - alopecia, dermatitis and fatty liver	
11.	**Biotin**	Liver, eggs, meat.	Not known in man	
12.	**Choline**	Egg yolk, liver, meat	Fatty liver and cirrhosis Hemorrhagic renal lesions	3-6 mgorally
13.	**Folic acid** (0.05-0.2 mg)	Yeast, fresh green vegetables, cereals, liver, kidney, meat	Pernicious anemia, Glossitis	15 mg orally
14.	**Cyanocobalamin** Vitamin B_{12} (1 mcg)	Liver, Synthesized in colon but not useful to the host as it is excreted and not absorbed	Pernicious anemia, Glossitis, Subacute combined degeneration of spinal cord.	100 mcg orally or IM
15.	**Vitamin C** (Ascorbic acid)	Green vegetables, citrus fruits, strawberries, potatoes	Scurvy **Toxic Effects:** 1. Oxalate and urate stones 2. Iron overload in iron storage disease	50-100 mg/day **Uses :** Scurvy. Wound healing, common cold, Threatened abortion, Alkalosis. Methemoglobinemia Alkaptonuria, prickly heat With iron therapy Hemorrhagic disease of newborn

the lower segment is always less than the upper segment. Their mental and dental ages are normal and so are the endocrine functions.

7. ***Systemic diseases:*** Most chronic systemic diseases can cause growth failure during childhood. These illnesses can be recognized by their own specific clinical features and growth failure is a secondary problem.

2 › Body Proportions

Normally, in adults, the height of the person is equal to the length of arm span. The upper segment (from vertex to the pubic symphysis) is equal to the lower segment (from pubic symphysis to the heel).

In infants, the upper segment is greater than the lower segment and the height is greater than the arm span. This infantile type of body proportion persists in achondroplasia, cretinism and juvenile myxedema. The reverse of infantile body proportion i.e. arm span greater than height and lower segment greater than upper segment occurs in eunuchoidism, Marfan's syndrome, homocystinuria, Klinefelter's syndrome and Frohlich's syndrome.

3 › Nutrition

A normal person is well nourished as regards proteins, fats, carbohydrates, vitamins and minerals. Certain clinical signs help to diagnose deficiency of one or more of these nutrients.

1. **Proteins:** Hypoproteinemia causes rough skin and later edema of feet and brittle hair.
2. **Fats:** Fat malnutrition leads to cachexia with hollowing of cheeks, loss of the shape of hips (due to loss of fats), flat abdomen and absent fat over the subcutaneous tissues of the elbows.
3. **Carbohydrates:** Carbohydrate malnutrition is difficult to detect clinically because there is gluconeogenesis from fats or proteins.
4. **Vitamins:** These can be fat soluble (Vitamins A, D, E, K) or water soluble (rest) and are discussed in the tables.
5. **Minerals:** Deficiency of two minerals can be diagnosed clinically. Iron deficiency causes koilonychia and pallor whereas calcium deficiency causes tetany.

4 Decubitus

Decubitus or the posture a patient adopts when lying in bed often gives a valuable diagnostic clue.

1. **Hemiplegia:** The patient lies in bed with one side immobile, the affected arm flexed and the affected leg externally rotated and extended.
2. **Meningitis and tetanus:** The patient has neck stiffness and opisthotonos.
3. **Colic:** In renal, biliary or intestinal colic, the patient is markedly restless and tossing and turning in bed in agony.
4. **Acute inflammatory abdominal disease:** The patient lies on his back quietly with legs drawn up.
5. **Cardiorespiratory embarrassment:** The patient is more comfortable in sitting-up position. This position is also assumed in abdominal distention and ascites when intra-abdominal pressure is raised.
6. **Pneumonia and pleurisy:** The patient is most comfortable lying on the affected side because the movement on the affected side is restricted.

5 Clubbing

Definition

Clubbing is bulbous enlargement of soft parts of the terminal phalanges with both transverse and longitudinal curving of the nails. The swelling of the terminal phalanges occurs due to interstitial edema and dilation of the arterioles and capillaries.

Causes

1. ***Pulmonary***
   a. Bronchogenic carcinoma, mesothelioma
   b. Lung abscess
   c. Bronchiectasis
   d. Tuberculosis with secondary infection
   e. Diffuse fibrosing alveolitis
   f. Empyema
2. ***Cardiac***
   a. Infective endocarditis
   b. Cyanotic congenital heart diseases, Eisenmenger's physiology
   c. Atrial myxoma
3. ***Alimentary***
   a. Ulcerative colitis
   b. Crohn's disease
   c. Cholangiolitic cirrhosis
   d. Biliary cirrhosis
   e. Hepato-pulmonary syndrome
4. ***Endocrine***
   a. Myxedema
   b. Thyroid acropachy (thyroid nails of hyperthyroidism e.g. in Grave's disease)
   c. Acromegaly
5. ***Miscellaneous***
   a. Hereditary
   b. Idiopathic
   c. *Unilateral:* Pancoast tumor, subclavian and innominate artery aneurysm
   d. Unidigital: Traumatic or tophi deposit in gout
   e. Only in the upper limbs in heroin addicts due to chronic obstructive phlebitis

Grades

I. Softening of nail bed
II. Obliteration of the angle of the nail bed
III. Swelling of the subcutaneous tissues over the base of the nail causing the overlying skin to become tense, shiny and wet and increasing the curvature of the nail, resulting in parrot beak or drumstick appearance (Figs. 2.1 & 2.2).
IV. Swelling of the fingers in all dimensions associated with hypertrophic pulmonary osteoarthropathy causing pain and swelling of the hand, wrist etc. and radiographic evidence of subperiosteal new bone formation (commonly seen in bronchogenic carcinoma, paraneoplastic syndromes).

Schamroth's Sign (Fig. 2.3)

Normally when two fingers are held together with nails facing each other, a diamond-shaped space is seen at the level of proximal nail fold. This is lost in case of clubbing

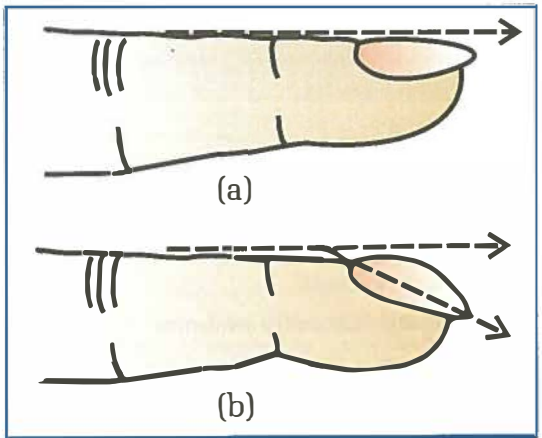


Fig. 2.1 (a) & 2.1 (b): (a): Normal nail bed; Profile angle = 180°; (b): Severe clubbing - hypertrophy of soft tissues; Profile angle > 180°



Fig. 2.2 : Clubbing Grade III - Parrot beak appearance

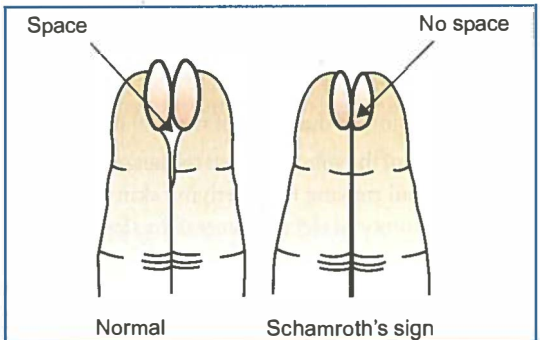


Fig. 2.3 : Left: Normal; Right: Schamroth's sign

Mechanism

1. The exact mechanism is not known. It is believed that the stimulus for clubbing is hypoxia. Hypoxia leads to opening of deep arteriovenous fistulas, which increase the blood supply of the fingers and toes causing it to hypertrophy.
2. Another hypothesis is that when reduced ferritin in venous blood escapes oxidation in the lungs and enters the systemic circulation, it causes dilation of arteriovenous anastomosis and hypertrophy of the terminal phalanx resulting in clubbing.
3. Platelet-derived growth factor causing vasodilatation.

Pseudoclubbing

In hyperparathyroidism or leprosy excessive bone resorption may result in disappearance of the terminal phalanges with telescoping of soft tissues and a 'drumstick' appearance of the fingers resembling clubbing. However, the curvature of the nail is not present.

6 › Cyanosis

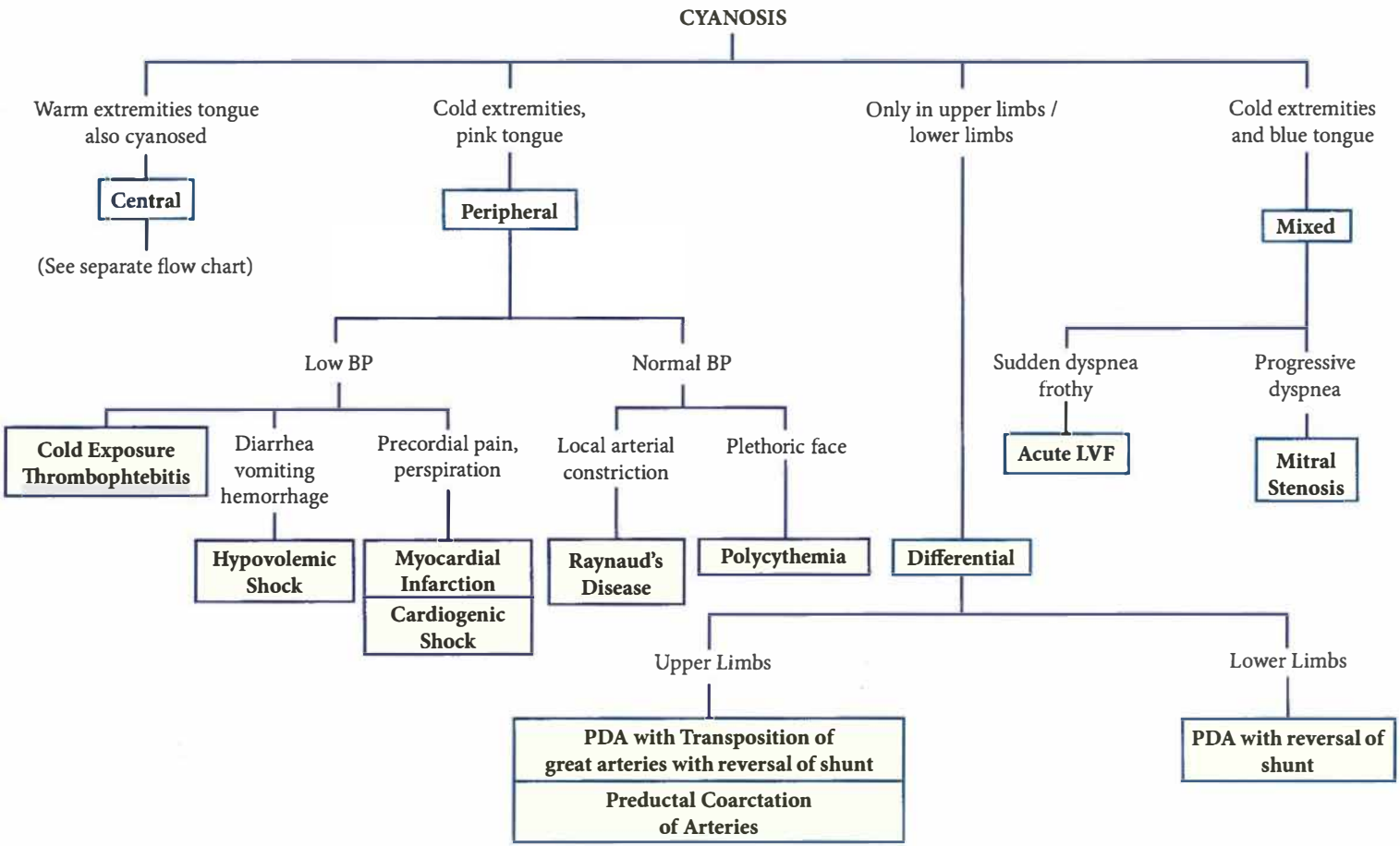
DEFINITION: Cyanosis is a bluish discoloration of the nails due to increased amount of reduced hemoglobin (more than 5 mg%) in capillary blood.

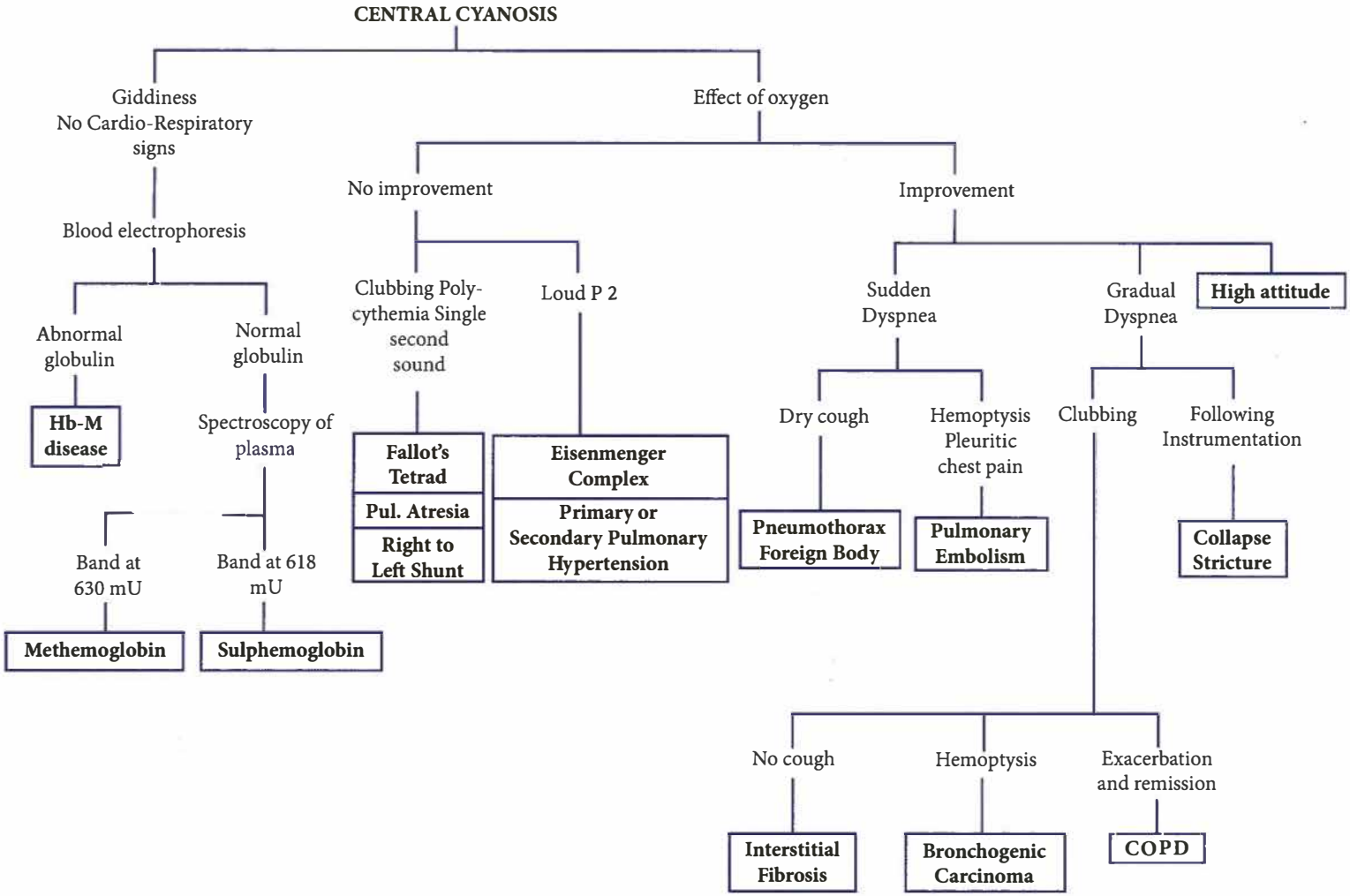
Types

I. Central
II. Peripheral
III. Cyanosis due to abnormal pigments
IV. Mixed

Table 2.5 : Differences between Central and Peripheral Cyanosis

		Central	*Peripheral*
1.	Mechanism	Diminished arterial oxygen saturation	Diminished flow of blood to the local part
2.	Sites	On skin & mucous membranes e.g. tongue, lips, cheeks etc.	On skin only
3.	Temperature of the limb	Warm	Cold
4.	Clubbing and polycythemia	Usually associated	Not associated
5.	Local heat	Cyanosis remains	Cyanosis abolished
6.	Breathing pure oxygen	Cyanosis decreases	Cyanosis persists


CYANOSIS
Warm extremities tongue also cyanosed
Central
(See separate flow chart)
Cold extremities, pink tongue
Peripheral
Only in upper limbs / lower limbs
Cold extremities and blue tongue
Mixed
Low BP
Normal BP
Sudden dyspnea frothy
Progressive dyspnea
Cold Exposure Thrombophtebitis
Diarrhea vomiting hemorrhage
Precordial pain, perspiration
Local arterial constriction
Plethoric face
Acute LVF
Mitral Stenosis
Hypovolemic Shock
Myocardial Infarction
Cardiogenic Shock
Raynaud's Disease
Polycythemia
Differential
Upper Limbs
Lower Limbs
PDA with Transposition of great arteries with reversal of shunt
Preductal Coarctation of Arteries
PDA with reversal of shunt


CENTRAL CYANOSIS
Giddiness
No Cardio-Respiratory signs
Blood electrophoresis
Abnormal globulin
Hb-M disease
Normal globulin
Spectroscopy of plasma
Band at 630 mU
Methemoglobin
Band at 618 mU
Sulphemoglobin
Effect of oxygen
No improvement
Clubbing Poly-cythemia Single second sound
Fallot's Tetrad
Pul. Atresia
Right to Left Shunt
Loud P 2
Eisenmenger Complex
Primary or Secondary Pulmonary Hypertension
Improvement
Sudden Dyspnea
Dry cough
Pneumothorax Foreign Body
Hemoptysis Pleuritic chest pain
Pulmonary Embolism
Gradual Dyspnea
High attitude
Clubbing
No cough
Interstitial Fibrosis
Hemoptysis
Bronchogenic Carcinoma
Exacerbation and remission
COPD
Following Instrumentation
Collapse Stricture

Mechanism

In an adult, on an average, there is 15 gm% of hemoglobin, 95% of which is saturated with oxygen and only 5% i.e. 0.75 gm% is reduced. Hence, in capillaries, a mean of the two i.e. only 2-3 gm% is reduced hemoglobin and the color of the skin and mucous membranes is pink.

When the amount is reduced hemoglobin exceeds 5 gm% in the capillaries, the blood appears dark, giving the tissues a bluish hue. This is seen earliest in the warm areas with increased capillary circulation e.g. palate, tongue, inner sides of the lips and conjunctiva. Peripheral cyanosis occurs due to slowing of blood, which allows more time for removal of oxygen by the tissues, so that cyanosis is visible on the tip of nose, ear lobule, tip of finger, nailbed and cheek. In mixed cyanosis there is both arterial hypoxemia and sluggish circulation.

Causes

I. **Central:**
   - A. *Cardiac*
     1. Congenital, cyanotic heart disease: Fallot's tetrad, Eisenmenger's complex etc.
     2. Congestive cardiac failure.
   - B. *Pulmonary*
     1. Chronic obstructive lung disease.
     2. Collapse and fibrosis of lung.
     3. Marked pulmonary destruction due to any cause.
     4. Pulmonary AV fistula.
   - C. Abdominal hepato-pulmonary syndrome.
   - D. *High altitude due to low partial pressure of oxygen.*

II. **Peripheral:**
   - A. Cold (local vasoconstriction)
   - B. Increased viscosity of blood
   - C. Shock
   - D. Reynaud's phenomenon

III. Mixed
   - A. Acute left ventricular failure
   - B. Mitral stenosis (left atrial failure and peripheral vasoconstriction).

IV. **Cyanosis due to abnormal pigments:**

Normal hemoglobin has iron in ferrous form. In **methemoglobinemia**, iron is in the ferric form designated as MHb. Several substances like nitrite ingestion (well water), sulfonamide or aniline dyes oxidize Hb to MHb, but this is immediately reduced back to Hb by methemoglobin reductase I or diaphorase I. If there is deficiency of diaphorase I, MHb circulates in blood, causing cyanosis.

Colour of blood is chocolate brown. The MHb levels should be > 1.5 g/dl to cause cyanosis.

Sulfhemoglobin (SHb) is an abnormal sulphur containing substance, which is not normally present but is formed by toxic action of drugs and chemicals like sulphonamides, phenacetin, and acetanilide. SHb forms an irreversible change in the Hb pigment that has no capacity to carry oxygen and causes cyanosis. SHb levels should be >0.5 g/dl to cause cyanosis.

Differential Cyanosis

I. **Only of lower limbs** — Patent ductus arteriosus (PDA) with reversal of shunt.

II. **Only of upper limbs** — PDA with reversal of shunt in a transposition of great vessels.

III. **Cyanosis of left upper limb and both lower limbs** — PDA with reversal of shunt and pre-ductal coarctation of aorta.

Conditions where Cyanosis does not Occur

1. In **severe anemia** where hemoglobin is less than 5 gm%, even if all the hemoglobin is reduced in the capillaries, it will be less than the critical level of 5 gm% and cyanosis does not occur.
2. In **carbon monoxide poisoning**, carboxy-hemoglobin prevents reduction of oxyhemoglobin and the former has a cherry red color. Hence there is no cyanosis.

7 〉 Jaundice

Definition

Jaundice is a symptom complex which is characterized

by yellow coloration of tissues and body fluids due to an increase in bile pigments. It may arise due to:

1. Increased bile pigment load to the liver.
2. Affection of bilirubin diffusion into the liver cells.
3. Defective conjugation.
4. Defective excretion.

Other Causes of Yellow Coloration of Tissues

Yellow coloration of tissues can occur due to carotenemia and mepacrine therapy.

Normal Values

Serum bilirubin: Total: 1 mg%, Direct: 0.25 mg%. Urinary bilirubin is present if direct bilirubin is greater than 0.4 mg% in serum.

Urine urobilinogen: 100-200 mg/day.

Fecal stercobilinogen: 300 mg/day

Distribution of Jaundice

Since bilirubin binds with circulating proteins, it is more evident if proteins are increased e.g. exudates. Again, bilirubin has more affinity for nervous tissue e.g. basal ganglia and elastic tissues e.g. skin, sclera and blood vessels.



Fig. 2.5: Icterus in jaundice

Etiology

I. **Hemolytic (Pre-hepatic)**

A. ***Intra-Corpuscular Defects:***

1. Hereditary spherocytosis.

Table 2.6 : Differential Diagnosis of Jaundice

		Hepatocellular	*Obstructive*	*Hemolytic*
I.	**HISTORY:**			
	1. Abdominal pain	Absent	Present	Present in crisis
	2. Pruritus	Transient	Marked	Absent
	3. Past history	a) Contact with jaundice patient b) Drugs	a) Pain (Stones) b) Weight loss (Neoplasm) c) Surgery (Stricture)	a) Of crisis b) Drugs, blood transfusion etc.
II.	**EXAMINATION:**			
	1. Tender liver	May be present	Absent	Absent
	2. Spleen	May be present	Absent	Present
	3. Gall bladder	Not palpable	Palpable if due to neoplasm	Not palpable
	4. Pallor	Absent	Present	Present
II.	**INVESTIGATIONS:**			
	1. Urine:			
	Bilirubin	Present	Present	Absent
	Urobilinogen	Present	Absent	Present
	2. Stools:			
	Sterocobilinogen	Present	Absent	Present
	3. Peripheral smear	Leucopenia in infective hepatitis	Normal	Reticulocytosis Spherocytosis
	4. L.F.T.			
	a) Bilirubin	++	++	+
	b) Alkaline phosphate	Raised	Markedly raised	Normal
	c) SGOT	Markedly raised	Raised	Normal
	5. Barium meal and cholangiography	Normal	May reveal pancreatic growth	Normal
	6. RBC survival	Normal	Normal	Decreased

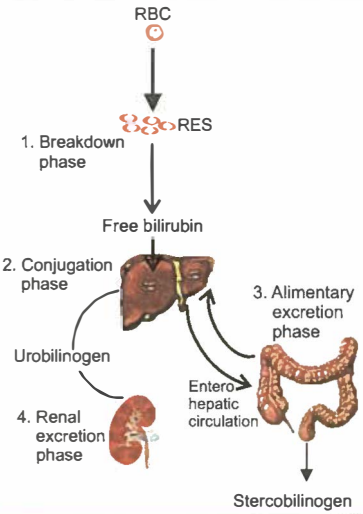
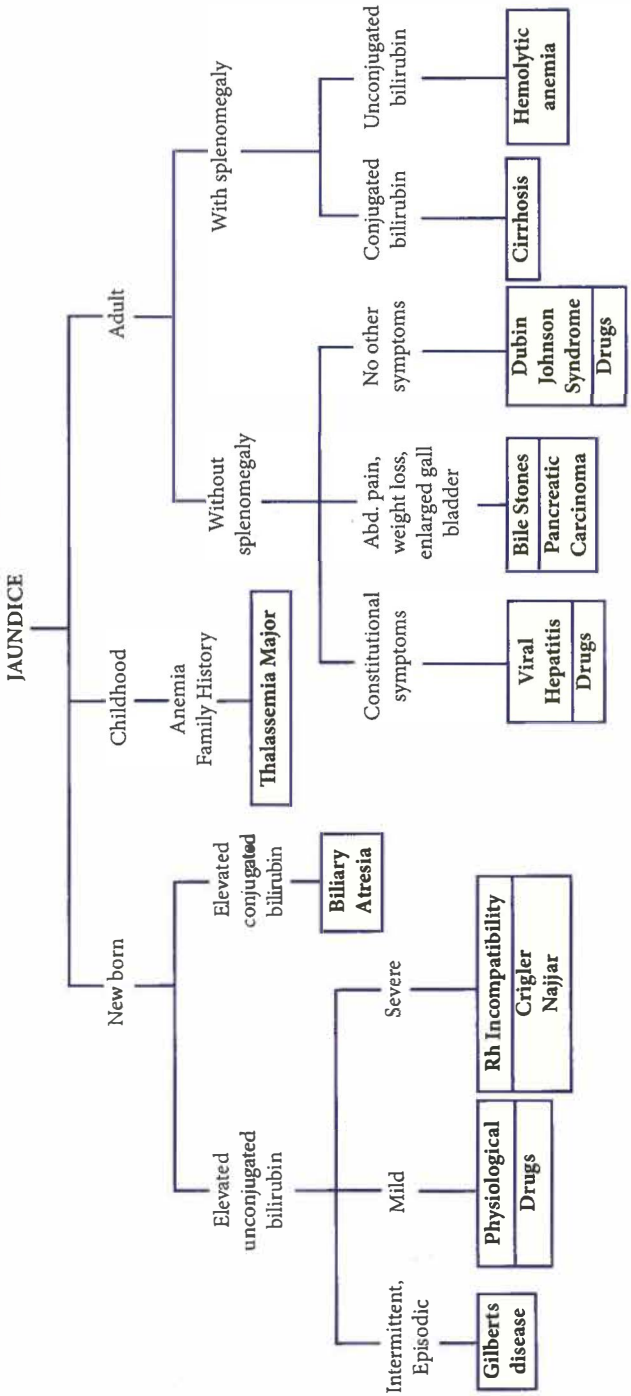


Fig. 2.4: Bilirubin Metabolism

Bilirubin Metabolism

1. **Breakdown phase:** Hemoglobin released by breakdown of aged cells is broken down into globin and heme in the spleen. The heme is further broken into iron and bilirubin. Bilirubin attaches to serum albumin and is transported to the liver where it is taken up. Bilirubin (unconjugated) bound to albumin cannot be excreted by kidneys.
2. **Conjugation phase:** In the liver, bilirubin is separated from albumin and conjugated to glucuronide by glucuronyl transferase. The conjugated bilirubin is water-soluble and can be excreted by kidneys.
3. **Alimentary phase:** The conjugated bilirubin is excreted through the bile canaliculi and reaches the intestines where it is converted to stercobilinogen and urobilinogen by the intestinal bacteria. About 70% of this is absorbed in the colon and brought back to the liver and re-excreted (enterohepatic circulation). Unabsorbed sterco-bilinogen gives brown color to the feces.
4. **Excretion phase:** Circulating urobilinogen is carried to the kidneys for excretion in the urine as urobilinogen.



2. Hemoglobinopathies: Sicklecell anemia, homozygous beta thalassemia, sickle thalassemia, HbE thalassemia
3. Enzyme deficiency (E6PD, pyruvate kinase).
4. Paroxysmal nocturnal hemoglobinuria (PNH)

B. ***Extra-Corpuscular Defects:***

1. *Infections*: Malaria, *Clostridium welchii*
2. *Drugs:* L. Methyl dopa, quinine, phenacetin, sulfonamides
3. *Physical agents:* Burns, Irradiation
4. *Poisons:* Snake Venom, Favism
5. *Immunological:* Mismatched blood transfusion, paroxysmal cold hemoglobinuria, lymphoma, CLL, SLE.
6. *Miscellaneous:* Uremia, cirrhosis of liver

II. Congenital Hyperbilirubinemia

A. *Unconjugated:*

1. Disturbance of bilirubin transport: Gilbert's syndrome.
2. Disturbance of bilirubin conjugation: Crigler Najjar syndrome.

B. *Conjugated:* Disturbance in excretion of bilirubin: Dubin Johnson syndrome and Rotor's syndrome.

III. Hepatocellular (Medical Jaundice-Hepatic)

A. ***Infections***

1. Viral hepatitis
2. Weil's disease (Leptospirosis)
3. Septicemia
4. Malaria, Typhoid

B. ***Toxic***

1. Anesthetic agents: Halothane, chloroform
2. Anticoagulants: Phenindione
3. Anti-tuberculous drugs: Rifampicin, P.A.S., I.N.H., Thiacetazone
4. Metals: Arsenic, mercury, gold, bismuth
5. Chemicals: D.D.T.
6. X-ray irradiations

C. ***Cirrhosis***

1. Portal
2. Biliary
3. Hemochromatosis

IV. Obstructive (Surgical Jaundice- Post-hepatic):

A. ***Extra-Hepatic:***

1. *Inflammatory:* Stone, stricture, parasites, acute cholecystitis
2. *Neoplastic:* Carcinoma of the head of the pancreas; neoplasm of bile ducts, gall bladder and ampulla of Vater
3. *Congenital:* Biliary atresia

B. ***Intra-Hepatic:***

1. Cholestatic phase of infective hepatitis
2. Drugs: Steroids, chlorpromazine, PAS, sulfonamides, chlorpropamide tolbutamide, methyl testosterone, erythromycin.
3. Pregnancy with cholestasis.

8 › Pallor

Pallor is paleness of skin and mucous membrane either as a result of diminished circulating red blood cells or diminished blood supply.

Causes

I. Anemia

A. Hemorrhagic

B. Hemolytic

C. Dyshemopoietic

1. Deficiency of iron, folic acid or Vitamin B 12
2. Aplastic anemia
3. Systemic and infiltrative diseases
4. Chronic infection
5. Pregnancy
6. Malignancies

II. Vasoconstriction

A. Shock : Hypovolemic / cardiogenic

B. Exposure to cold

C. Fright

D. Syncope and postural hypotension

E. Arterial Occlusion

III. Cutaneous

A. Thick skin and nails

B. Edema (edema causing diseases)

C. Myxedema

Sites where anemia is detected

1. Lower palpebral conjunctiva
2. Tongue
3. Soft palate
4. Palm and nails
5. Other mucosal areas like vaginal or rectal mucosa



Fig. 2.6 : Pallor evident in lower palpebral conjunctiva

9 Lymphadenopathy

Lymphadenopathy is inflammatory or non-inflammatory enlargement of lymph nodes.

Examination

The ***lymph nodes*** of the neck should be examined by standing behind the patient with the patient's neck slightly flexed. The nodes must be examined from above downward - submental, submandibular, tonsillar, cervical, posterior auricular & occipital groups.

In the left **supra-clavicular fossa**, a lymph node may be palpable (***Virchow's node***) which occurs due to metastasis from stomach or testicular malignancy.

The **axillary glands** should be examined by inserting the fingers in the axilla with the patient's arm slightly abducted. The arm is then abducted and the apical, anterior, posterior, medial and lateral groups of lymph nodes are examined.

The **supratrochlear lymph nodes** are palpated on the medial aspect of the arm between the groove of biceps and brachialis muscle, an inch above the arm fold.

The **inguinal nodes** are examined in the supine position with the thigh extended. Both the medial and lateral groups of lymph nodes are examined.

Scalene nodes are present behind the sternomastoid muscle and may be palpable. In suspected malignancy, biopsy it taken from that area, even if the nodes are not palpable.

Inspection: Most of the superficial lymph nodes are visible when enlarged. The site of lymphadenopathy often gives the clue to its cause. Tuberculosis often affects the upper deep cervical nodes, secondary syphilis affects supratrochlear nodes, carcinoma of stomach affects the left supraclavicular nodes whereas filariasis affects the inguinal nodes.

The skin overlying the lymph nodes may show redness indicating underlying inflammation. Ulceration or sinus may be present in tuberculosis.

Palpation: Raised temperature and tenderness is noted. If present, suggests acute inflammation. The surface is smooth normally but matted in tuberculosis and irregular in malignancy and inflammation.

The consistency of the nodes is noted. Normally it is firm. It is rubbery in Hodgkin's disease, firm and shotty in syphilis, matted in tuberculosis and hard in malignancy. The mobility of the nodes is noted. Normally they are mobile and free from skin. In certain inflammatory conditions and malignancy they may be fixed and non-mobile.



Fig. 2.7 : Bilateral cervical lymphadenopathy due to TB - before and after anti - TB treatment.

Causes

I. **Inflammatory**
   A. Acute Lymphadenitis
   B. Chronic Lymphadenitis:
      1. Septic
      2. Tuberculosis
      3. Syphilis
      4. Filariasis
      5. Lymphogranuloma inguinale
      6. HIV with PGL or AIDS

II. **Neoplastic**
   A. Primary: Lymphosarcoma
   B. Secondary: Carcinoma, sarcoma, malignant melanoma

III. **Hematological:**
   A. Hodgkin's disease
   B. Non-Hodgkin's lymphoma
   C. Chronic lymphatic leukemia

IV. **Immunological:** Serum sickness, drug reaction, SLE and rheumatoid arthritis

Causes of Generalised Lymphaenopathy

1. Tuberculosis
2. Infectious Mononucleosis
3. Secondary Syphillis
4. H.I.V.
5. Hodgkins Lymphoma
6. Lymphatic Leukemia
7. Sarcoidosis, Brucellosis, Toxoplasmosis

Differential Diagnosis

Acute Lymphadenitis

1. Enlarged, tender and fixed lymph nodes.
2. Overlying skin may become red, hot and brawny.
3. Primary infective focus may be found.

Chronic Septic Lymphadenitis

1. Enlarged, slightly tender lymph nodes which may or may not be matted.
2. If abscess has occurred, fluctuation in the centre and pitting on pressure at the periphery will be evident. It is often difficult to differentiate from tuberculous lymphadenitis.

Tuberculous Lymphadenitis

1. Commonly affects the deep cervical, mesenteric and axillary glands.
2. The lymph nodes may be discrete (when it resembles chronic septic lymphadenitis) or may be matted due to periadenitis. If caseation has occurred, cold abscess results which may burst forming tuberculous ulcer or sinus which takes a long time to heal.
3. Fever with chills weight loss, anorexia and respiratory complaints may be present.

Syphilitic Lymphadenitis

1. Painless, firm, discrete and shotty glands which do not suppurate.
2. In secondary syphilis, generalized lymph-adenopathy occurs involving especially epitrochlear and occipital glands.
3. Other evidence of syphilis with positive tests for syphilis like WR, VDRL, TPI, and FTA ABS.

Filarial Lymphadenitis

1. Pain, tenderness and swelling of the inguinal lymph nodes, spermatic cord and scrotum.
2. Lymphangiectasia (dilation of lymph vessels) of the inguinal region and spermatic cord.
3. Eosinophilia and microfilaria can be demonstrated in the blood.
4. Lymph node biopsy may reveal adult worm.

Lymphogranuloma Inguinale

1. Suppurative lymphadenitis with ulceration, sinus formation and extensive scarring of the inguinal lymph nodes.
2. Frei's test is confirmatory.

Lymphosarcoma

1. Commonly affects the cervical glands which are enlarged, firm and fixed.
2. The overlying skin is stretched and shiny with dilated blue veins under it.

3. Highly malignant tumor grows rapidly and invades the surrounding tissues.

Secondary Carcinoma

1. The nodes are enlarged, irregular and fixed to all structures including the skin.
2. It has stony hard consistency.
3. Primary growth may be detected.
4. Patient may be cachectic and wasted.

Hodgkin's Disease

1. Affects **young adolescent males**.
2. **Cervical glands** are affected early but later all lymph nodes are involved.
3. **Lymph nodes** are elastic and rubbery, discrete and movable with little tendency towards matting, softening or suppuration.
4. **Pressure symptoms**: Edema, venous engorgement and cyanosis of head and neck may occur due to pressure on the superior vena cava and the bronchus by the mediastinal glands. Root pains and paraplegia may develop due to pressure on the spinal cord.
5. **Hepatosplenomegaly and anemia** occur.
6. **Pel Ebstein's type of fever** (recurrent bouts of remittent fever) may occur.
7. **Weight loss** more than 10% of body weight and night sweats.
8. Peripheral smear will show **lymphocytosis and eosinophilia.**
9. Lymph node biopsy will show **Reed Sternberg's cell.**

Non-Hodgkin's Lymphoma

Similar to Hodgkin's lymphoma in clinical presentation except:

1. Enlargement of nodes in Waldeyer's ring and supratrochlear glands
2. Symptoms are less common
3. Can be a manifestation of HIV infection
4. Diagnosis confirmed by histological examination of the bone marrow.

Infectious Mononucleosis

1. Acute onset of fever, chills, sore throat, headache, malaise and tiredness occurs
2. The lymph nodes are enlarged, discrete and slightly tender affecting especially the cervical and submandibular nodes.
3. Non-tender splenomegaly may occur.
4. Petechial rash may occur at the junction of soft and hard palate on the fourth day and may persist for 3-4 days.
5. Peripheral smear shows leucocytosis (absolute lymphocyte count more than 1500/cmm) with atypical lymphocytosis.
6. Paul-Bunnel test may be positive in 1:32 dilution or more usually in the first 10 days.

HIV Associated Lymphadenopathy

1. Commonly called PGL or persistent generalised lymphadenopathy.
2. Usually seen in stage of intermediate immune depletion following HIV infection (Refer Pg. 113).

10 Edema

Edema is the collection of fluid in the interstitial spaces or serous cavities. It becomes evident only when 5-6 liters of fluid has accumulated in the water depots. Pitting on pressure occurs when the circumference of the limb is increased by 10%.

Mechanism

One or more of the following factors may be responsible.

1. Increased capillary permeability when it is damaged e.g. acute inflammation.
2. Increased capillary pressure e.g. cardiac failure.
3. Decreased osmotic pressure of the blood e.g. hypoproteinemia.
4. Damaged lymphatic drainage e.g. filariasis.

Site

Venous edema commonly occurs in the lower limbs

which are most dependent. However, if the patient is recumbent, edema may be present only over the sacral region which is, then, most dependent. Lymphatic edema may occur in either limbs or over scrotum depending upon the site of involvement.

Causes

Bilateral:

A. Cardiac: CCF, LVF, pericarditis
B. Renal: Acute nephritis, nephrotic syndrome
C. Hepatic: Cirrhosis of liver, portal hypertension
D. Venous: Inferior vena cava obstruction
E. Endocrine: Myxedema
F. Allergic: Angioneurotic edema
G. Nutritional: Anemia, hypoproteinemia, beriberi.
H. Toxic: Epidemic dropsy



Fig. 2.8: Bilateral Pitting Edema

Unilateral:

A. Lymphatic:
   1. Filariasis
   2. Pressure by new growth, metastasis
   3. Radiation
B. Traumatic: Bruises, sprains, fractures
C. Infections: Cellulitis, boils, carbuncle
D. Metabolic: Gout
E. Venous: Venous thrombosis, varicose veins.
F. Hereditary: Milroy's disease



Fig. 2.9: Unilateral Edema - Filariasis (Elephantiasis)

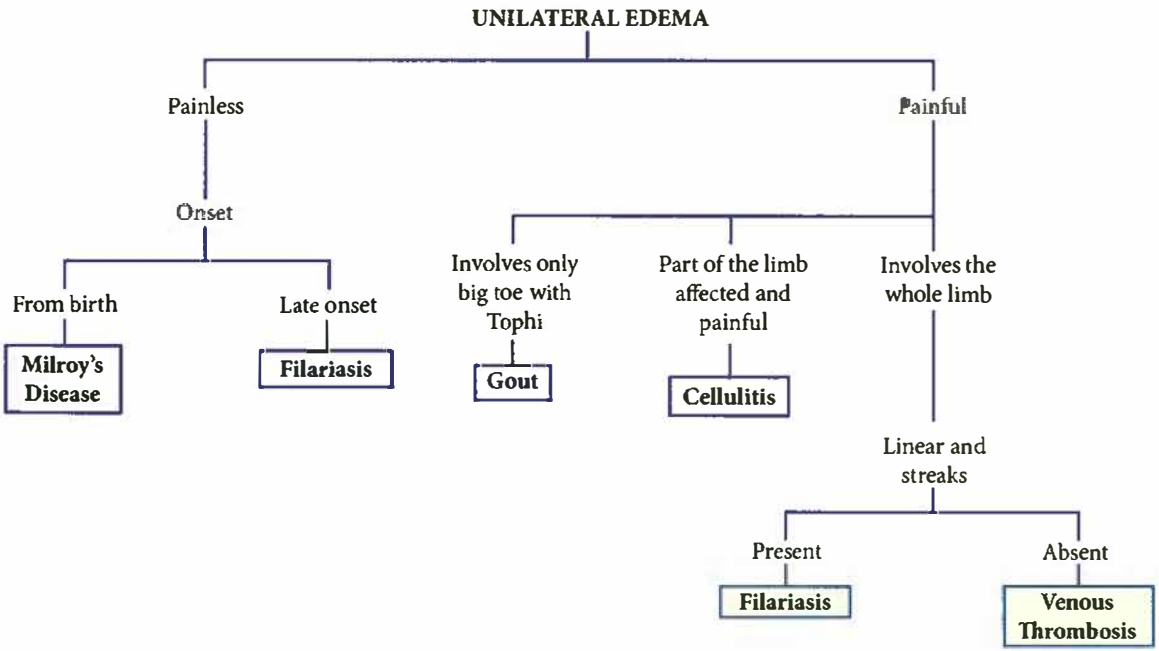


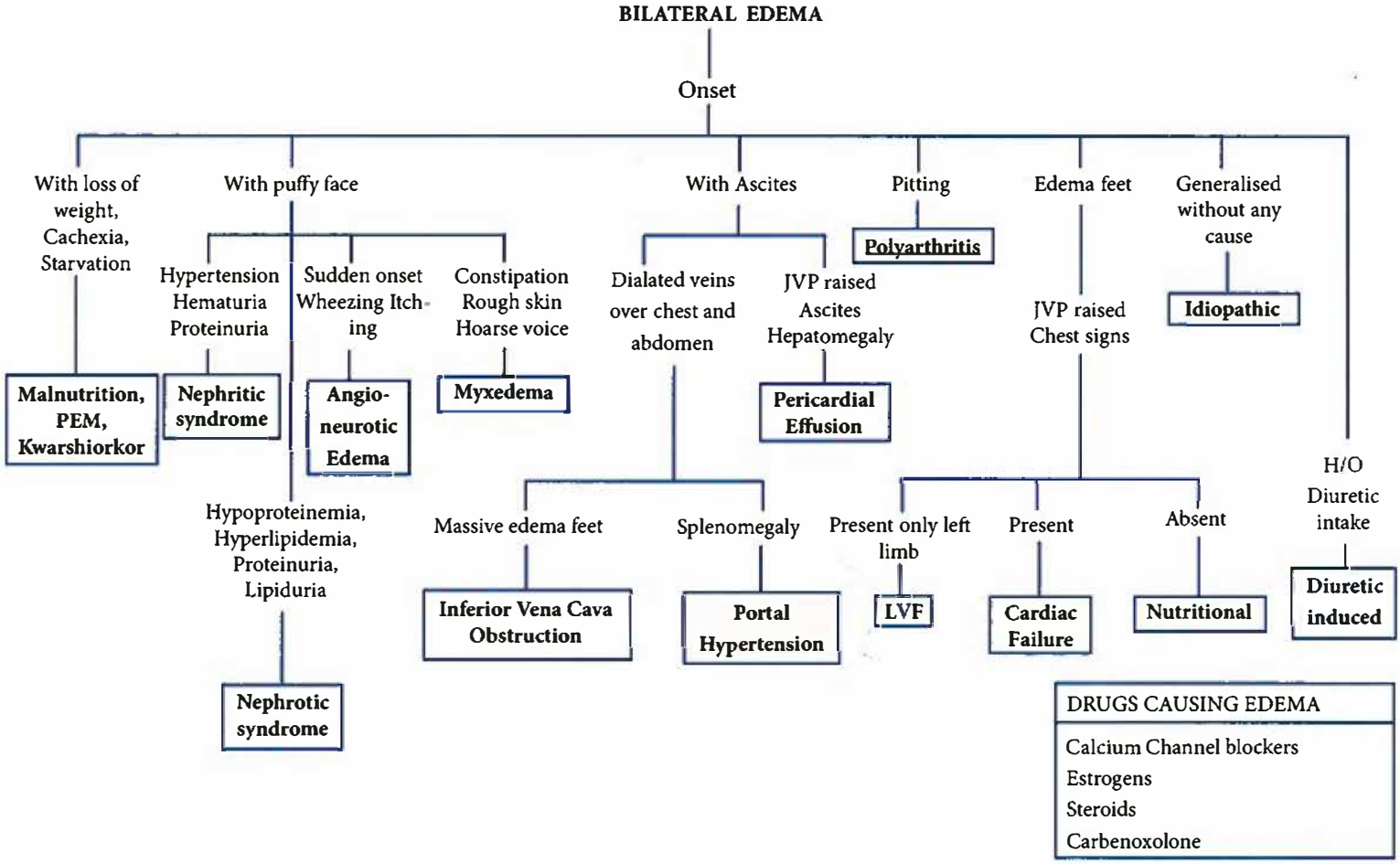
Fig 2.10: Varicose veins

Differential Diagnosis

1. **Cardiac**
   A. **Congestive Cardiac Failure:** The edema is found on the most dependent parts of the body as gravity plays an important part. Hence, in an ambulatory patient edema is in the feet, ankles and legs whereas in the recumbent patient it is mainly over the sacrum, lumbar region and genitalia. It is most marked in the evening.
   B. **Left ventricular failure:** Accumulation of fluid in the lung occurs much earlier than edema of the feet, resulting in dyspnea, cough and basal rales.
   C. **Pericardial effusion:** Since there is obstruction to the flow of blood into the right atrium, edema of feet may occur, but no edema of lungs occurs because the heart is able to pump the little blood it receives into the lungs and general circulation. It is associated with raised JVP, hepatomegaly and ascites.

2. **Kidney**
   A. **Acute nephritis:** Edema is generalized and not restricted to the dependent parts of the body. It is more noticeable in the early morning. The fluid accumulates initially in the loose connective tissues, hence it is most marked around the eyelids and face. The cause of edema is damage to the endothelial lining of the capillaries, disturbance of fluid and sodium excretion and later also due to hypoproteinemia.
   B. **Nephrotic sydrome:** Swelling is generalized and massive due to hypoproteinemia following massive albuminuria.
3. **Hepatic** (Portal hypertension): Here ascites occurs before edema of feet. This occurs due to hypoproteinemia and compression of the hepatic branches of the portal vein. Ascites leads to pressure on the venous circulation in the lower limbs leading to edema of the legs.
4. **Venous** (Inferior vena cava obstruction): This is characterized by bilateral nondependent painless pitting edema. Collateral dilated veins are usually present in the flanks with flow of blood from below upwards.
5. **Endocrine** (Myxedema): Here edema is non-pitting, associated with puffy face, weight gain, weakness, alopecia, hoarse voice, rough dry skin, constipation, anemia and menstrual disturbances.
6. **Allergic** (Angioneurotic edema): This often resembles myxedema with swelling over the face and limbs. There is usually intense itching and bronchospasm.
7. **Nutritional:** This is characterized by dependent edema with puffiness of face, pallor and cachexia.
8. **Filariasis:** In filariasis, edema occurs due to destruction of the lymphatic filter action of the lymph glands with consequent blocking and dilation of the lymph vessels. Subsequently there is transudation of lymph, rich in proteins, into the tissues. Later connective tissues proliferate leading to elephantiasis. This is characterized by unilateral non-pitting edema with rough skin. There may be history of fever with rigors especially at night and initially pitting edema. Blood smear may show microfilaria.
9. **Gout:** This commonly affects the big toe with marked pain, edema and deformity of the part involved. Tophi may be present. There may be history of renal colic or renal stones.
10. **Venous Thrombosis:** This is characterized by unilateral painful pitting edema.




BILATERAL EDEMA
Onset
With loss of weight, Cachexia, Starvation
Malnutrition, PEM, Kwarshiorkor
With puffy face
Hypertension Hematuria Proteinuria
Nephritic syndrome
Sudden onset Wheezing Itching
Angio-neurotic Edema
Constipation Rough skin Hoarse voice
Myxedema
Hypoproteinemia, Hyperlipidemia, Proteinuria, Lipiduria
Nephrotic syndrome
With Ascites
Dialated veins over chest and abdomen
Massive edema feet
Inferior Vena Cava Obstruction
Splenomegaly
Portal Hypertension
JVP raised Ascites Hepatomegaly
Pericardial Effusion
Pitting
Polyarthritis
Edema feet
JVP raised Chest signs
Present only left limb
LVF
Present
Cardiac Failure
Absent
Nutritional
Generalised without any cause
Idiopathic
H/O Diuretic intake
Diuretic induced
DRUGS CAUSING EDEMA
Calcium Channel blockers
Estrogens
Steroids
Carbenoxolone

11 〉 Skin and its Appendages

Examination of skin often gives important clues to local or systemic diseases. The following features should be noted:

I. **Color:** It may be pale, flushed, cyanosed, yellow, etc.

II. **Pigmentation:** Pigmentation may occur in several diseases. Some common medical conditions associated with pigmentation are:

1. **Endocrine:** Addison's disease, Cushing's disease, thyrotoxicosis.
2. **Deficiency:** Pellagra, Kwashiorkor, megaloblastic anemia.
3. **Infections:** Kala azar, chronic malaria, secondary syphilis, tuberculosis, leprosy, HIV, etc.
4. **Metabolic:** Hemochromatosis.
5. **Skin disease:** Neurofibromatosis, lichen planus, acanthosis nigricans, etc.
6. **Miscellaneous:** Malignancy, pernicious anemia, exposure to sunrays or radiations.

III. **Hypopigmentation:** Hypopigmented patches may occur in leprosy, leukoderma, albinism, fungal infections of skin, etc.

IV. **Eruptions:** Various types of eruptions may occur as follows:

1. **Macules:** (Not raised above the skin). This may occur in typhoid, syphilis and purpura. If they are not generalized, they are called roseolar.
2. **Papules:** (Raised tiny nodule < 5 mm): This may occur in measles, chickenpox, smallpox and following drugs like sulfonamides.
3. **Pustules:** These are papules containing pus.
4. **Nodules:** (Large papules as solitary projection from the skin : 5 mm - 5 cm). This may occur in erythema nodosum, leprosy, tuberculosis, secondary syphilis.
5. **Vesicles:** (small blisters < 5 mm). This may occur in herpes, chickenpox and smallpox.
6. **Bullae:** Fluid-filled lesion > 5 mm.
7. **Wheal:** (Elevated patches on the skin with centre paler than the periphery) Allergy.

V. **Neurocutaneous Stigmata (Phakomatoses)**

1. **Cafe-Au-Lait spots:**

Dark brown patches resembling coffee in milk. They are considered significant if they are more than 5 in number or single one >15 mm. They are seen in:

a. Neurofibromatosis (regular outline without deep indentations)
b. Albright's syndrome (irregular outline with deep indentations)
c. Tuberous sclerosis

Schwartz criteria for significant cafe-au-lait spots

a. > 5 in number, more than 2 cm

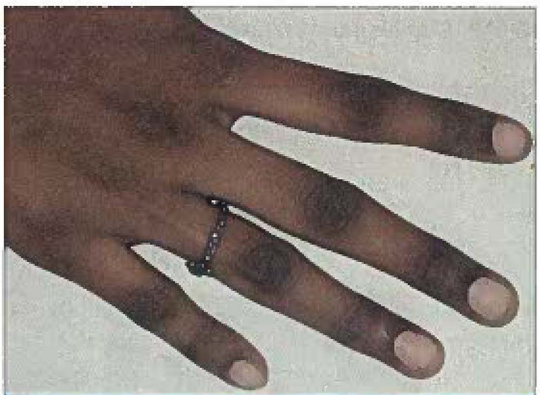


Fig. 2.11 : Hyperpigmented knuckles due to megaloblastic anemia



Fig. 2.12 : Leukodermoid Vitiligo

b. Two > 5 cm
c. One in axilla
d. Axillary freckle

2. **Tuberous sclerosis:** (EPILOIA)

Epilepsy
Low IQ
Adenoma Sebaceum

3. **Sturge Weber Syndrome:**

Hemangioma on face and cerebrum

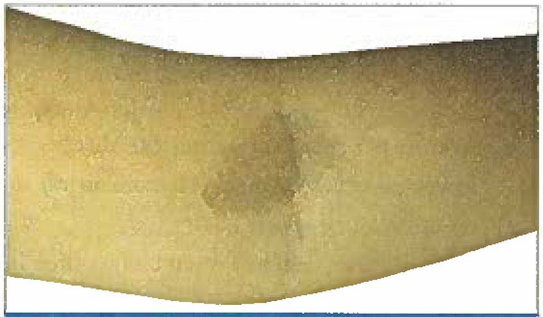


Fig. 2.13: Cafe-au-lait spots

VI. Hemorrhage: Hemorrhage under the skin may be classified as follows:

1. **Purpura:** Hemorrhage into the skin
   a. *Palpable:* Vasculitis syndromes due to inflammation of the vessel wall.
   b. *Non-Palpable:*
      i. Petechiae <3 mm
      ii. Ecchymosis > 3 mm
2. **Hematoma:** Hemorrhage large enough to produce elevation of skin.

Causes of hemorrhage under the skin:

1. *Deficiency:* Vitamin deficiency, scurvy.
2. *Infection:* Meningococcal meningitis, SBE, HIV.
3. *Hematological:* Thrombocytopenia, acute leukemia, chronic lymphatic leukemia, chronic myeloid leukemia (in terminal phase) platelet dysfunction and aplastic anemia.

VII. Types of Skin

1. **Dry skin:** This is seen in myxedema and dehydration.
2. **Moist skin:** This occurs when there is profuse perspiration as in shock, following myocardial infarction, crisis of pneumonia and thyrotoxicosis.
3. **Thick skin:** This occurs in Myxedema, acromegaly and scleroderma.
4. **Thin skin:** This occurs in old people and following wasting diseases.
5. **Pinched skin:** suggests dehydration.

VIII. Hair: Changes in hair that occurs in some of the diseases are as follows:

1. **Falling of hair:** Following infectious fevers e.g. typhoid.
2. **Patchy hair loss:** Alopecia areata, syphilis.
3. **Loss of outer third of the eyebrows:** Leprosy, Myxedema.
4. **Absence of axillary, pubic and facial hair:** Hypopituitarism, hypogonadism.
5. **Excessive hair growth in women:** Cushing's syndrome, adrenocortical syndrome.

IX. Nails: The nails should be examined for the following:

1. **Pallor**
2. **Koilonychia:** Spoon-shaped deformity of the nail which is present in iron deficiency anemia.
3. **Onychia:** Deformity of the nail e.g. following fungal or tuberculous infection.
4. **Discoloration:** This occurs in Raynaud's disease and silver and mercury poisoning.
5. **Clubbing and cyanosis** (Refer Pgs. 15, 16)

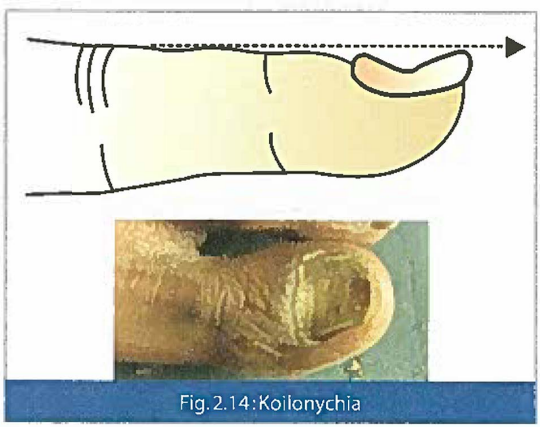


Fig. 2.14: Koilonychia

6. **Hemorrhages:** Splinter hemorrhages may be present under the nail beds in SBE and bleeding disorders.
7. **Trophic changes:** Ribbing, brittleness and often falling of nails may occur in syringomyelia, leprosy and tabes dorsalis.

12 Vertebral Column

The vertebral column in a normal upright position has two antero-posterior curves - one with a concavity forwards in the upper dorsal region and the other with a slight convexity forwards in the dorsolumbar region. Normally, there is no lateral curvature. The vertebral column should be examined for any abnormality, angular deformity, swelling or tenderness.

Normally the vertebral column has both anterior as well as lateral mobility. This can be tested by asking the patient to bend forwards, backwards and sideways. Limitation of movements and pain, if any, should be looked for.

I. Scoliosis

Scoliosis is an abnormal lateral curvature of the spine.

Causes:

1. *Congenital*
2. *Postural*: Carrying heavy weight in one arm.
3. *Compensatory:* Reduced length of one lower limb.
4. *Reflex:* To relieve pain as in sciatica or renal colic
5. *Neurological:* Poliomyelitis, syringomyelia, muscular dystrophy, hereditary ataxia.
6. *Rickets*
7. *Functional*

II. Kyphosis

Kyphosis is an abnormal anteroposterior curvature of the spine with forward concavity and dorsal prominence.

Causes:

1. *Congenital:* Wedge shaped vertebra.
2. *Postural:* Carrying weights on the back
3. *Disease of bone and joints:* Tuberculosis (Pott's spine), rheumatoid arthritis, rickets, osteoarthritis, osteitis deformans, fracture of the vertebral body, new growth of the spine.
4. *Neurological:* Muscular dystrophy, hereditary spastic paraplegia, Friedreich's ataxia, syringomyelia, poliomyelitis, cerebral palsy, neurofibroma, etc.

III. Lordosis

Lordosis is an abnormal anteroposterior curvature of the spine with forward convexity.

Causes:

1. *Physiological:* Pregnancy
2. *Secondary* to hip disease and congenital dislocation of the hip
3. *Muscular dystrophy*
4. *Large abdominal tumors*

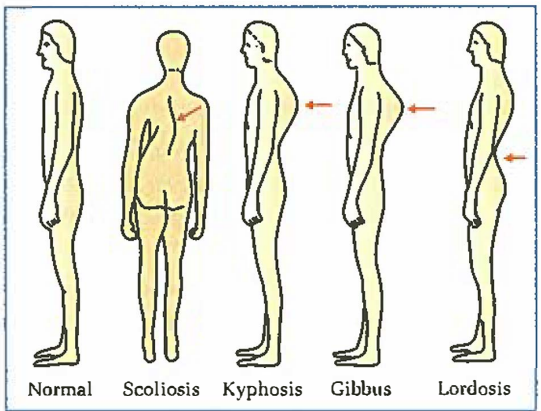


Fig. 2.15: Vertebral Column

IV. Pes Cavus

Pes cavus is the increased anteroposterior curvature of the arch of the foot.

Causes:

1. *Idiopathic*
2. *Spinocerebellar atrophy:* Friedreich's ataxia, peroneal muscular atrophy
3. *Spinal cord disease:* Poliomyelitis, spina bifida
4. *Cerebral palsy*

13 › Thickened Nerves

Causes:

1. **Leprosy**
2. **Neurofibromatosis**
3. **Diabetes**
4. **Amyloidosis**
5. Charcot Marie Tooth syndrome
6. Sarcoidosis
7. Refsum's disease
8. Rusy Levy syndrome
9. Dejerine Sotta's syndrome
10. Idiopathic hypertrophic neuropathy
11. CIDP (Chronic Inflammatory Demyelinating Polyneuropathy).

14 › Joints

I. History

1. Onset
2. Pain and swelling in the joint
3. History of trauma, tuberculosis, typhoid, exposure to venereal disease, pneumonia, bacillary dysentery, bleeding tendencies, renal colic.
4. Family history of hemophilia, tuberculosis gout, etc.

II. Examination of Joints

A. *Inspection:*

1. Joints affected
2. Position of the joint and fixed deformity
3. Swelling
4. Signs of inflammation over the joint
5. Muscular wasting just above the joint

B. *Palpation:*

1. Local temperature
2. Tenderness
3. Swelling-fluctuant or non-fluctuant
4. Bony components and its relation to the joint

C. *Movements (active and passive):*

1. Pain on movement
2. Restriction of movement
3. Excessive mobility
4. Protective muscular spasms
5. Grafting on movement

D. *Measurements:*

1. Length of the limb
2. Circumference of the limb
3. Relations of various bony points

III. General And Systemic Examination

1. Evidence of gonorrhea, syphilis and tuberculosis
2. CNS: A.R. pupils, Rhomberg's sign and absent deep reflexes (syphilis); dissociate anesthesia, flaccid weakness in the upper limb and spastic paraplegia (syringomyelia).

Causes of Arthritis

Acute Arthritis

1. Traumatic
2. Infection: Gonorrhea, septic, typhoid, bacillary dysentery, rheumatic, Reiter's syndrome. etc.
3. Gout
4. Scurvy
5. Hemophilia
6. Acute attacks in chronic arthritis

Chronic Arthritis

1. *Infection:* Tuberculosis, syphilis, rheumatic
2. *Collagen disease:* Rheumatoid, SLE., Polyarteritis nodosa
3. *Degenerative:* Ankylosing spondylitis
4. *Neuropathic:* Tabes dorsalis, syringomyelia
5. *Miscellaneous:* Hemophilia, gout.

Differential Diagnosis

Septic Arthritis

1. Acute onset with symptoms of septicemia

2. A single large joint or multiple small joints are involved
3. Joints are painful, especially on movement
4. Spontaneous dislocation and fibrous or bony ankylosis may occur.

Tuberculous Arthritis

1. There is insidious onset. It commonly affects the upper limbs in adults and lower limbs in children.
2. Tuberculous focus may be present in the body
3. Night starts due to involvement of the articular cartilage may occur
4. Muscular deformity and wasting may be present
5. Rise of local temperature with a spongy feel of the thickened synovial membrane may be present
6. Restriction of movements is common
7. Cold abscess and sinus may occur
8. X-ray: Generalized decalcification, obliteration of joint space with erosion of the articular ends. Pathological dislocation and recalcification may be present.

Gonococcal Arthritis

1. It occurs 3 weeks after the primary infection
2. Onset is sudden, with fever
3. It may be monoarticular (knee or elbow) or polyarticular and may be manifested by acute arthralgia or acute arthritis (redness, heat and edema)
4. Gonococci may be demonstrated in urethral discharge.

Reiter's Syndrome

This is characterized by multiple acute arthritis, non-gonococcal urethritis and often conjunctivitis.

Typhoid Arthritis

It occurs in the fourth week of typhoid fever when the patient first gets on his feet. There may be spontaneous dislocation of the hip joint.

Syphilitic Arthritis

1. Characteristically there is painless, symmetrical arthritis with free movements
2. Arthralgia and hydrarthrosis are seen in secondary syphilis
3. Gummatous arthritis occurs in the tertiary stage

Rheumatic Arthritis

1. It is common between 5-25 years.
2. There may be antecedent Streptococcus hemolyticus infection
3. The onset may be rapid with relapses and remissions
4. Multiple joints are affected with fleeting arthritis
5. Affected joints may be painful, tender and swollen
6. Other evidences of rheumatic fever: Carditis, chorea, rheumatic nodules and erythema marginatum may be present
7. Elevated ESR, positive ASO titer and C reactive protein may be present

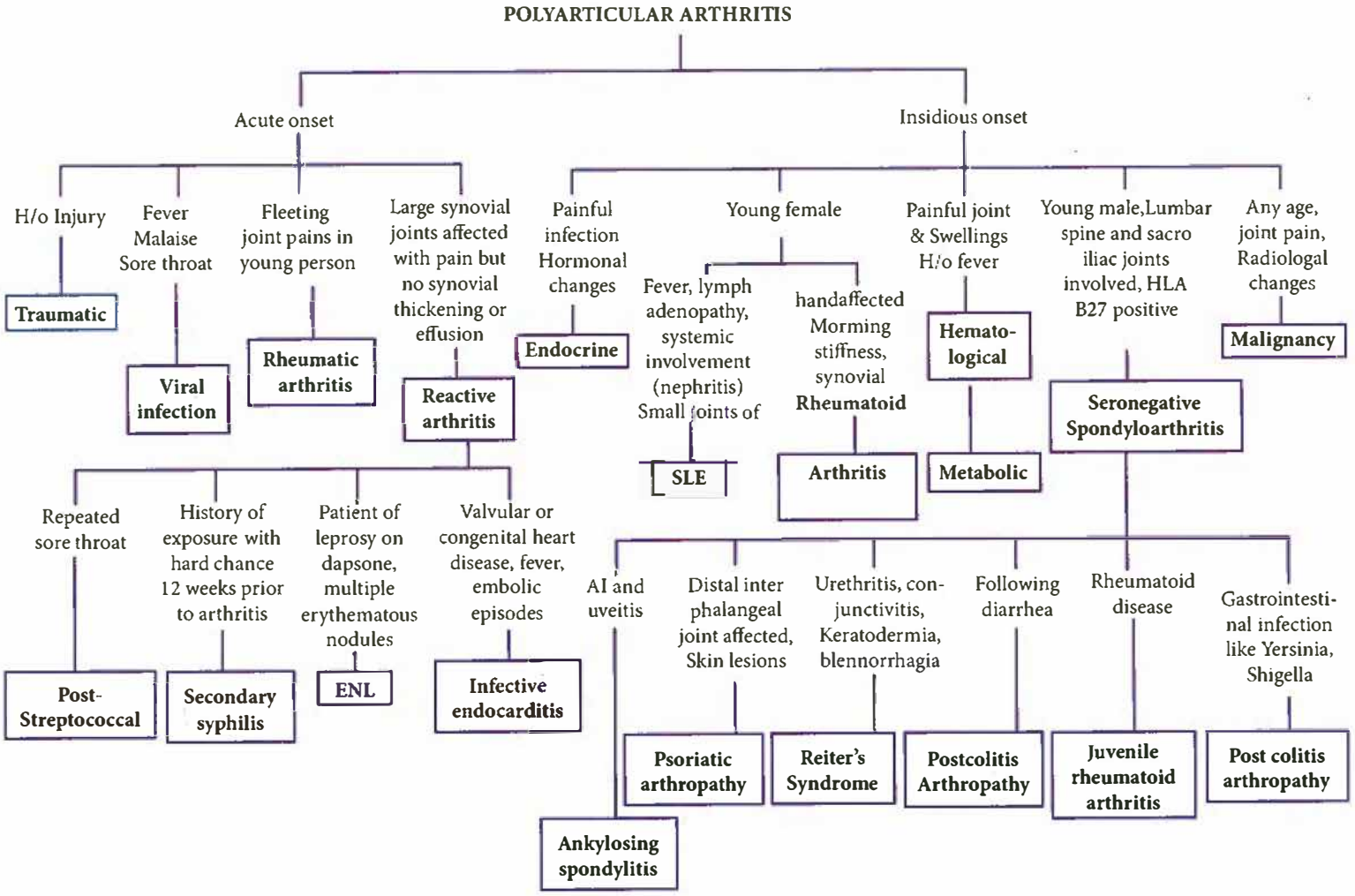
Rheumatoid Arthritis

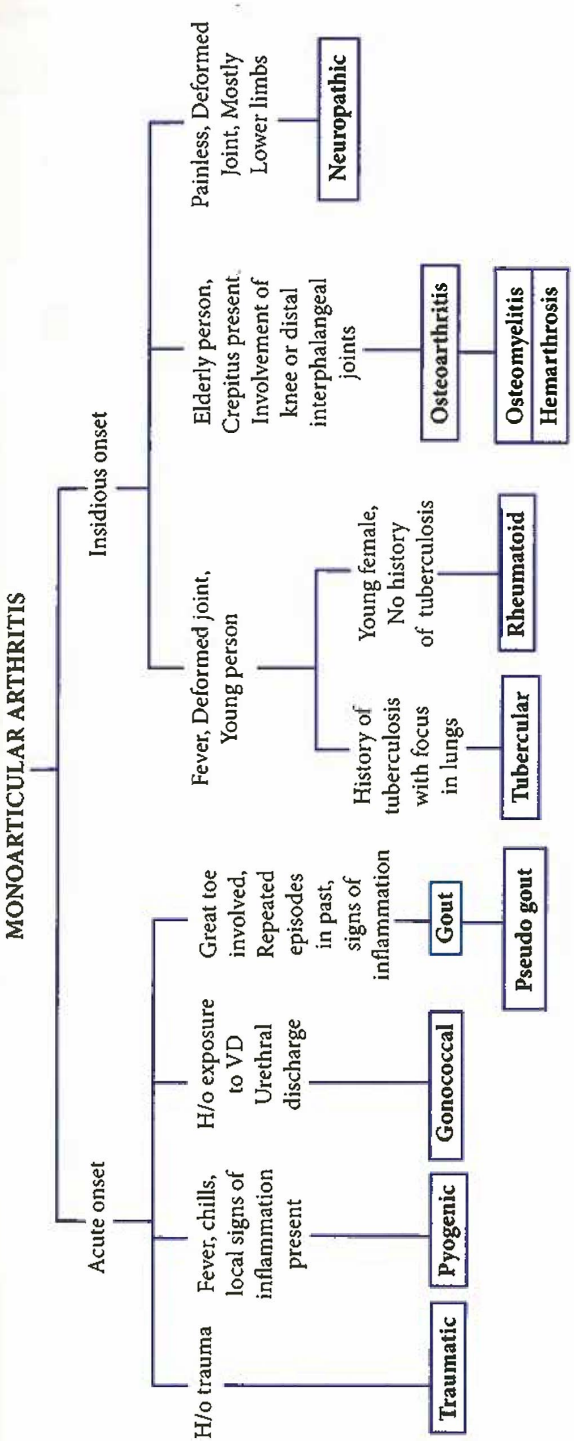
1. It commonly affects women between 24-40 years age
2. Characteristically it is bilaterally symmetrical, affecting the small joints of the hand or foot and may spread to large joints
3. Periodic painful swelling of the joints with stiffness and deformity (e.g. ulnar deviation of the hand, flexion deformity etc.) may occur
4. Muscle spasm and muscle wasting may be present
5. Restriction of movement is common
6. X-ray: Decalcification and diminished joint space may be seen

Still's disease is juvenile rheumatoid arthritis with splenomegaly and lymphadenopathy.

Osteoarthritis

1. It is common in men over 40 years
2. Asymmetrical affection of one or more joints is present
3. Morning stiffness especially after rest and at the onset of movements may be present. It is relieved by movements since the increased synovial secretion caused by movements lubricates the dry joint and relieves the pain.


POLYARTICULAR ARTHRITIS
Acute onset
Insidious onset
H/o Injury
Traumatic
Fever
Malaise
Sore throat
Viral infection
Fleeting joint pains in young person
Rheumatic arthritis
Large synovial joints affected with pain but no synovial thickening or effusion
Reactive arthritis
Repeated sore throat
Post-Streptococcal
History of exposure with hard chance 12 weeks prior to arthritis
Secondary syphilis
Patient of leprosy on dapsone, multiple erythematous nodules
ENL
Valvular or congenital heart disease, fever, embolic episodes
Infective endocarditis
Painful infection Hormonal changes
Endocrine
Young female
Fever, lymph adenopathy, systemic involvement (nephritis) Small joints of
SLE
handaffected Morming stiffness, synovial
Rheumatoid
Arthritis
Painful joint & Swellings H/o fever
Hemato-logical
Metabolic
Young male,Lumbar spine and sacro iliac joints involved, HLA B27 positive
Seronegative Spondyloarthritis
Any age, joint pain, Radiologal changes
Malignancy
AI and uveitis
Ankylosing spondylitis
Distal inter phalangeal joint affected, Skin lesions
Psoriatic arthropathy
Urethritis, con-junctivitis, Keratodermia, blennorrhagia
Reiter's Syndrome
Following diarrhea
Postcolitis Arthropathy
Rheumatoid disease
Juvenile rheumatoid arthritis
Gastrointestinal infection like Yersinia, Shigella
Post colitis arthropathy



4. Pain restricts movements. Grafting may be felt on passive movements
5. Heberden's nodes may be present.
6. X-ray: Diminished joint space with osteophytes may be seen

Gout

1. It occurs usually in obese men between 25-40 years
2. There is asymmetrical affection of the big toe. Later other joints may be affected. Relapses and remissions are common.
3. There is sudden onset of acute agonizing pain usually at night
4. Initially the tissues around the joint are red, swollen and edematous. Later, ligaments and bone ends are infiltrated by the chalky deposits which form tophi. If the skin over the tophi gives way, chalky discharge results.
5. Movements are painful. Muscles wasting may occur later
6. Serum uric acid is elevated

Hemophilic Joints

1. It is common in young boys with positive family history. It is a sex-linked recessive disorder
2. There is sudden painful bilateral hemorrhagic effusion into the knee joints
3. Clotting time is increased, activated partial thromboplastin time (APTT) is prolonged and antihemophilic globulin (AHG) levels or Christmas factor levels in blood are low
4. Ultimately chronic disabling arthropathy results

Neuropathic Joints

1. Osteoarthritis in the denervated joints (Tabes dorsalis, syringomyelia, peripheral neuropathy)
2. There is little pain but marked destruction of the bone.

Scurvy

1. It is common in malnourished children
2. There is painful swelling of the knee joint
3. Hemorrhages and petechial hemorrhages in

skin and at hair roots may occur which requires examination with magnifying glass.

Ankylosing Spondylitis

1. It is common in boys between 15-25 years
2. There is insidious, progressive involvement of spinal joints especially sacroiliac joint
3. Movements of the joint are restricted due to pain and stiffness. Later, there is kyphosis and progressive ankylosis
4. Muscles spasms and atrophy may be present.

15 › Temperature

The body temperature refers to the temperature of the viscera and tissues of the body. It is kept within the normal level by maintaining a balance between the heat gain and heat loss, which is regulated by the hypothalamus.

The body temperature is best recorded with a mercury thermometer, which should be kept in position for about a minute. Usually temperature is recorded in the axilla. However, if there is a lot of perspiration, oral temperature should be taken. In cholera, rectal temperature is recorded which may be high, whereas the skin temperature may be subnormal.

The normal body temperature varies from 36°C -37.5°C. There is normally a diurnal variation of 1°C, the lowest temperature being between 2-4 am and highest in the afternoon.

Fever or pyrexia is an increase of more than 1°C or any rise above the maximal normal temperature. The following terms are used when recording the body temperature:

		Temp in °C	Temp in °F
1.	Hypothermia	35°	95°
2.	Subnormal	35.0 - 36.7°	95 - 97°
3.	Normal	36.7 - 37.2°	98 - 99°
4.	Mild fever	37.2 - 37.8°	99 - 100°
5.	Moderate fever	37.8 - 39.4°	100 - 103°
6.	High fever	39.4 - 40.5°	103 - 105°
7.	Hyperpyrexia	> 40.5°	> 105°

Types of Fever

1. **Continuous fever:** The temperature remains above normal throughout the day and does not fluctuate more than 1°C in 24 hours e.g. lobar pneumonia, typhoid, urinary tract infection, infective endocarditis, brucellosis, typhus, etc.

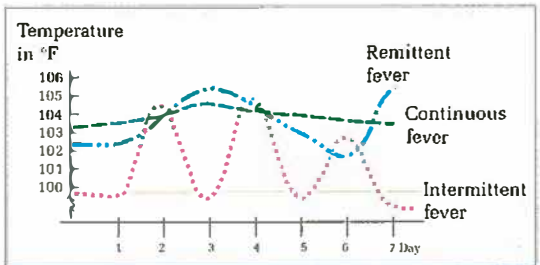


Fig. 2.16: Types of fevers

2. **Remittent fever:** The temperature remains above normal throughout the day and fluctuates more than 1°C in 24 hours e.g. typhoid, infective endocarditis, etc. This type of fever is most common in practice.
3. **Intermittent fever:** The temperature is present only for some hours in a day and remits to normal for the remaining hours. When the spike occurs daily, it is quotidian, when every alternate day, it is tertian and when every third day, it is quartan. Intermittent fever is seen in malaria, kala-azar, pyemia, septicemia etc.
4. **Hectic or septic:** The temperature variation between peak and nadir is very large and exceeds 5°C e.g. septicemia.
5. **Pel Ebstein type:** There is a regular alternation of recurrent bouts of fever and afebrile periods. The temperature may take 3 days to rise, remains high for 3 days and remits in 3 days, followed by apyrexia for 9 days seen in Hodgkin's lymphoma.
6. **Low grade fever:** Temperature is present daily especially in the evening for several days but does not exceed 37.8°C at any time. Usually it does not indicate disease, but it is commonly present with tuberculosis.

Causes of Fever

1. **Infections:** Bacterial, viral, rickettsial, fungal parasitic, etc.
2. **Neoplasms:** Fever may be present with any neoplasm but commonly with hypernephroma, lymphoproliferative malignancies, carcinoma of pancreas, lung and bone and hepatoma.

3. **Vascular:** Acute myocardial infarction, pulmonary embolism, pontine hemorrhage, etc.
4. **Traumatic:** Crush injury.
5. **Immunological:**
   a. Collagen disease, SLE, rheumatoid arthritis.
   b. Drug fever
   c. Serum sickness
6. **Endocrine:** Thyrotoxicosis, Addison's disease.
7. **Metabolic:** Gout, porphyria, acidosis, dehydration
8. **Hematological:** Acute hemolytic crisis
9. **Physical agents:** Heat stroke, radiation sickness.
10. **Miscellaneous:** Factitious fever, habitual hyperpyrexia, cyclic neutropenia

Special Types of Fever

1 **Fever with rigors:** This occurs in:
   a. Malaria
   b. Kala azar
   c. Filariasis
   d. Urinary tract infection, pyelonephritis
   e. Cholangitis
   f. Septicemia
   g. Infective endocarditis
   h. Abscesses, any site
   i. Lubar pneumonia
2. **Fever with herpes labialis:** Elevated body temperature may activate the herpes simplex virus and cause small vesicles around the angle of the mouth (herpes labialis). It occurs with:
   a. Pneumonia
   b. Malaria
   c. Meningitis
   d. Severe streptococcal infection
3. **Fever with rash:** This is seen in:
   a. Chicken pox
   b. Small pox
   c. Measles
   d. Rubella
   e. Typhus
   g. Allergy
4. **Fever with membrane in the throat:** Occurs in:
   a. Diphtheria
   b. Infectious mononucleosis
   c. Agranulocytosis
   d. Moniliasis
   e. Vincent's angina.
5. **Fever with delirium:** This is common in:
   a. Encephalitis
   b. Typhoid state
   c. Meningitis
   e. Pneumonia (especially in alcoholics and elderly people with dementia)
   f. Hepatic encephalopathy
6. **PUO (Pyrexia of Unknown Origin)**
   a. Temperature >101°F (38.3°C) on several occasions.
   b. Duration >3 weeks
   c. Duration >1 week in hospital with failure to reach diagnosis.

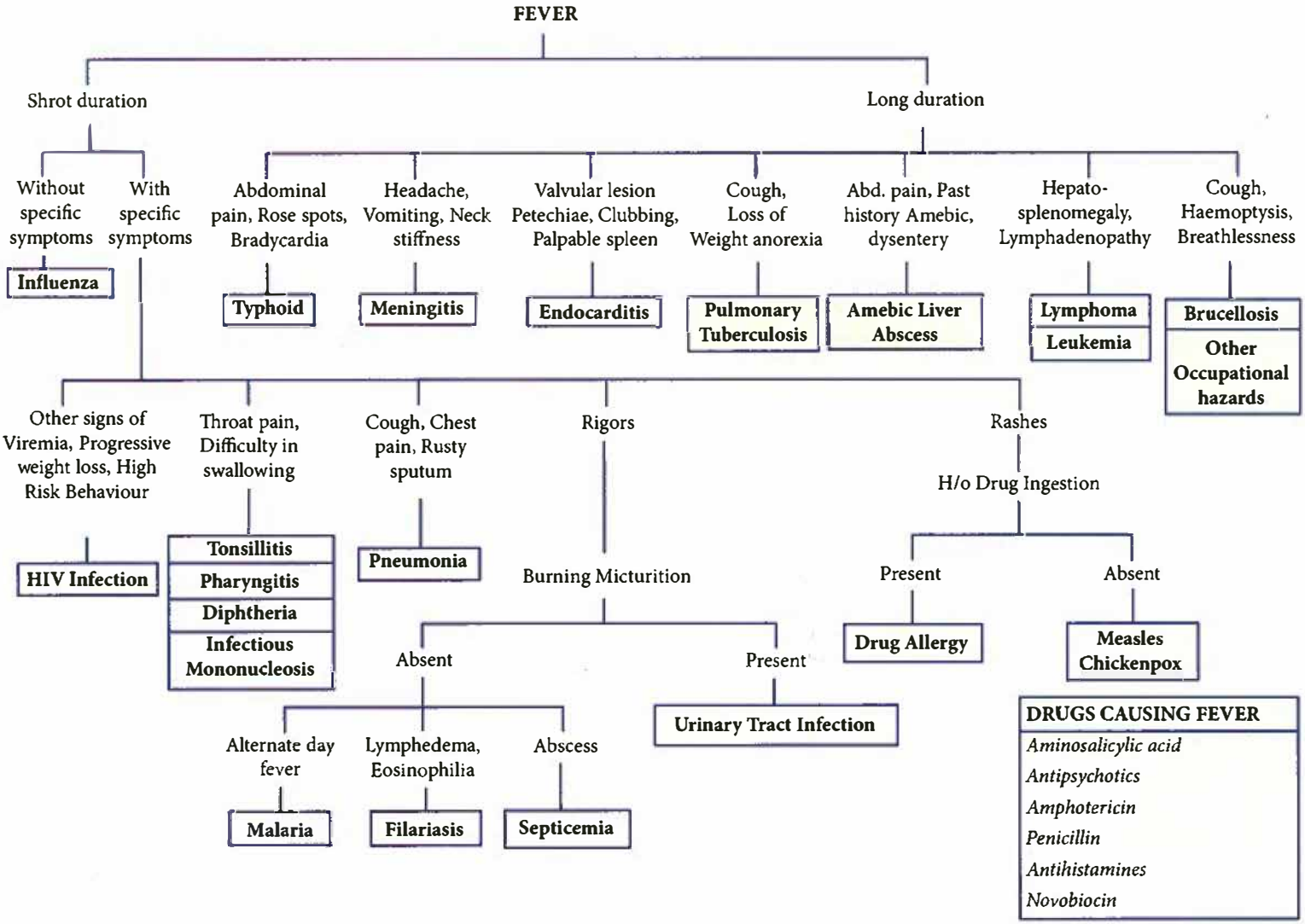
   Classification
   a. Classical PUO (lymphoma, collagen vascular disease, abcess, TB, viral infection, endocarditis)
   b. Nosocomial PUO: hospitalized, no fever on admission (thrombophlebitis, catheter infections, deep vein thrombosis, drug fever, transfusion reaction)
   c. Neutropenic PUO : Absolute neurophil count <500 (fungal infection, perianal infection)
   d. PUO in HIV infection (TB, Pneumocystis jiroveci, toxoplasma, cryptococcus, CMV, Non Hodgkins Lymphoma).

Hyperpyrexia

Hyperpyrexia is said to occur when body temperature is more than 105°F.

Causes

1. Tetanus
2. Malaria
3. Septicemia
4. Heat Stroke


FEVER
Shrot duration
Long duration
Without specific symptoms
With specific symptoms
Abdominal pain, Rose spots, Bradycardia
Headache, Vomiting, Neck stiffness
Valvular lesion Petechiae, Clubbing, Palpable spleen
Cough, Loss of Weight anorexia
Abd. pain, Past history Amebic, dysentery
Hepato-splenomegaly, Lymphadenopathy
Cough, Haemoptysis, Breathlessness
Influenza
Typhoid
Meningitis
Endocarditis
Pulmonary Tuberculosis
Amebic Liver Abscess
Lymphoma
Leukemia
Brucellosis
Other Occupational hazards
Other signs of Viremia, Progressive weight loss, High Risk Behaviour
Throat pain, Difficulty in swallowing
Cough, Chest pain, Rusty sputum
Rigors
Rashes
H/o Drug Ingestion
HIV Infection
Tonsillitis
Pharyngitis
Diphtheria
Infectious Mononucleosis
Pneumonia
Burning Micturition
Present
Absent
Drug Allergy
Measles
Chickenpox
Absent
Present
Urinary Tract Infection
Alternate day fever
Lymphedema, Eosinophilia
Abscess
Malaria
Filariasis
Septicemia
DRUGS CAUSING FEVER
Aminosalicylic acid
Antipsychotics
Amphotericin
Penicillin
Antihistamines
Novobiocin

5. Encephalitis
6. Pontine hemorrhage
7. Neuroleptic malignant syndrome

Benefits of Fever

In some human diseases, fever is beneficial, e.g. widespread cancer, neurosyphilis, chronic arthritis, etc. Fever was often induced in these diseases by injection of milk protein or BCG vaccine.

It has been suggested that fever is associated with release of endogenous pyrogens, which activate the T cells and thus enhance the host defense mechanism.

Harmful Effects

1. Hypercatabolism-nitrogen wastage and weight loss.
2. Fluid and electrolyte imbalance - due to sweating.
3. Convulsions and brain damage
4. Circulatory overload, arrhythmias, etc.

Hypothermia

Hypothermia is decreased body temperature.

Causes

1. *Endocrine:* Hypothyroidism or myxedema, hypopituitarism (Simmonds cachexia), hypoglycemia
2. *Toxic:* Alcoholic intoxication, barbiturate poisoning, ketoacidosis
3. Exposure to cold
4. Autonomic dysfunction or dysautonomias

16 Pulse

Definition : Pulse is a wave which is felt by the finger, produced by cardiac systole travelling in the peripheral direction in the arterial tree at a rate faster than the column of blood.

A normal pulse wave is transmitted peripherally taking 30 msec to reach the carotids, 60 msec to reach the brachial artery, 80 msec to reach the radial artery and 75 msec to reach the femoral artery.

The normal pulse has a small anacrotic wave on the upstroke, which is not felt. This is followed by a big tidal or percussion wave which is felt by the palpating finger. On the following downstroke there is a notch (dicrotic notch) followed by a wave (dicrotic wave) both of which are not normally palpable.



Fig. 2.17 : Palpation of Radial Artery

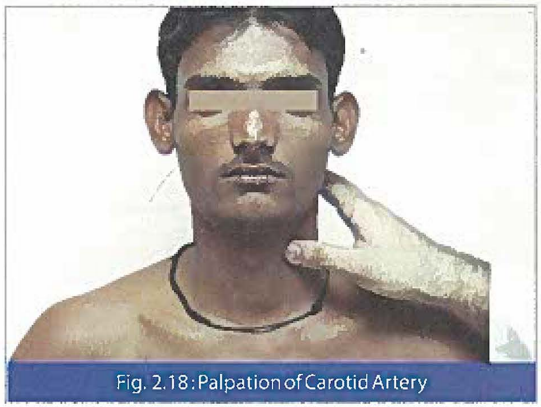


Fig. 2.18 : Palpation of Carotid Artery



Fig. 2.19 : Palpation of Dorsalis Pedis Artery

Pulse is assessed by:

1. Rate (No. of beats/min)



Fig. 2.20 : Palpation of Brachial Artery



Fig. 2.21 : Palpation of Popliteal Artery

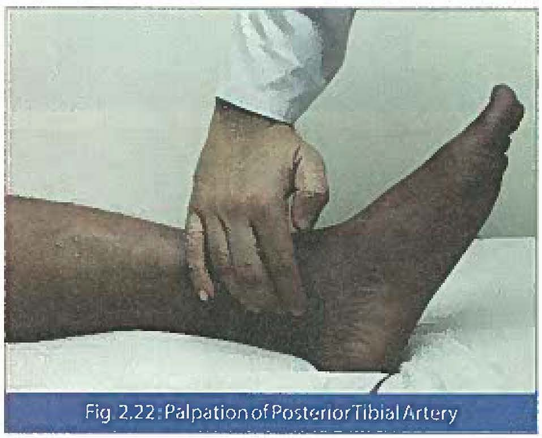


Fig. 2.22 : Palpation of Posterior Tibial Artery

a. Tachycardia (Refer Pg. 422)
b. Bradycardia (Refer Pg. 422)

2. Rhythm
   a. Regular
   b. Regularly irregular (e.g. second degree heart block 3:2, 4:3, Wenkeback; Ventricular Bigemini or Trigemini).
   c. Irregularly irregular (e.g. atrial fibrillation, ventricular or atrial ectopics)
3. Force, volume, tension
4. Equality
5. Peripheral pulses (e.g. femoral, posterior tibial, dorsalis pedis)
6. Radio-radial delay (pre-ductal coarctation of aorta), radio-femoral delay (post ductal coarctation of aorta) (Refer Pg. 255)
7. Apex pulse deficit (atrial fibrillation)

The normal pulse appears at regular intervals and has a rate between 60-100 per min. There may be a mild variation in the rate between the two phases of respiration which is called sinus arrhythmia.

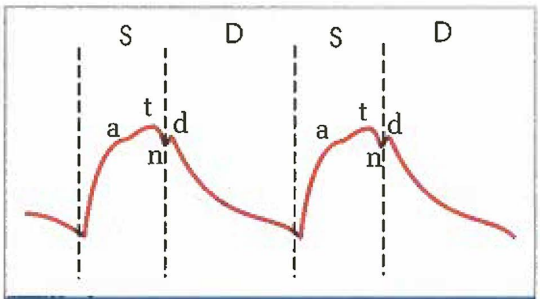


Fig. 2.23 : Normal pulse wave. a: Anacrotic wave; t: tidal wave; d: dicrotic wave; n: dicrotic notch; S: Systole; D: Diastole

I. **Anacrotic Pulse:** is a slow rising, twice beating pulse where both the waves are felt during systole. The waves that are felt are the anacrotic wave and the tidal wave. It is best felt in the carotids in aortic stenosis.

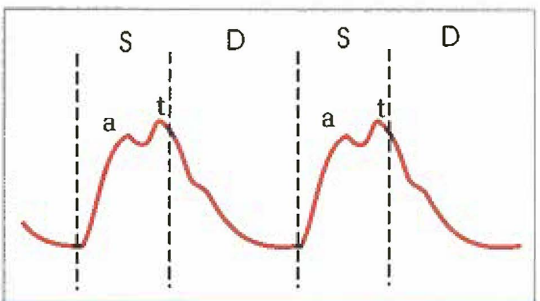


Fig. 2.24 : Twice beating Anacrotic pulse (slow rising)

II. **Pulsus Bisferiens** is a rapid rising, twice beating pulse where both the waves are felt during systole. Here the percussion wave is felt first followed by a small wave. It is seen in:

A. *Idiopathic hypertrophic subaortic stenosis:* Here initially there is no obstruction to the outflow

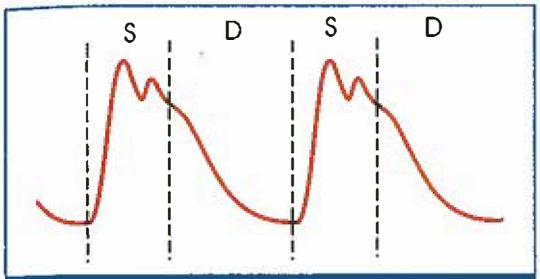


Fig. 2.25 : Pulsus Bisferiens (rapid-rising)

and about 80% of the stroke volume is ejected in the early part of systole. The obstruction occurs in mid systole when aortic valve approximates the hypertrophied septum. Hence, there is a dip, as suddenly the flow ceases, followed by a secondary rise as the L.V. overcomes the obstruction.

B. *Severe A.I. with mild A.S.*: The volume flow is initially increased due to severe A.I. Mild A.S. causes an extra high velocity jet to be shot out resulting in the second wave.

III. Dicrotic Pulse is a twice-beating pulse where the first percussion wave is felt during systole and the second dicrotic wave is felt during diastole. It is seen when the peripheral resistance and diastolic pressures are low as in:

A. Fevers like typhoid fever

B. Congestive cardiac failure

C. Cardiac tamponade

D. Following open heart surgery

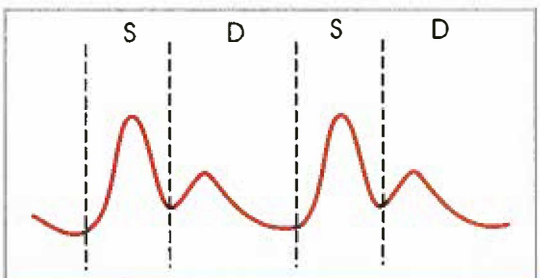


Fig. 2.26 : Dicrotic pulse

IV. Pulsus Parvus Et Tardus is a slow-rising pulse with a late systolic peak (Pulsus Tardus) and which is also low in volume and amplitude (Pulsus Parvus). It is characteristically seen in severe Aortic Stenosis. It is best felt in the carotids.

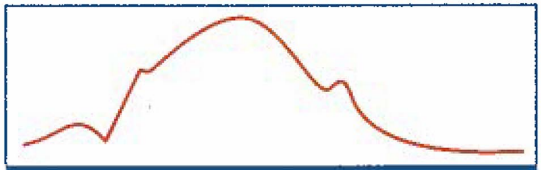


Fig. 2.27 : Pulsus parvus et tardus

V. Pulsus Alternans is characterized by a strong and weak beat occurring alternately, probably due to alternate rather than regular contraction of the muscle fibers of the left ventricle.

Causes

A. Left ventricular failure

B. Toxic myocarditis

C. Paroxysmal tachycardias

D. For several beats following a premature beat

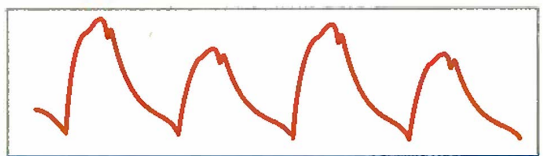


Fig. 2.28 : Pulsus alternans

VI. Pulsus Paradoxus: Normally systolic blood pressure falls by 3-10 mm. during inspiration. This is because though there is increased venous return to the right side of the heart there is relative pooling of the blood in the pulmonary vasculature as a result of lung expansion and more negative intrathoracic pressure during inspiration. This decreases the venous return to the left atrium and ventricle and subsequently causes a fall in left ventricular output decreasing the arterial pressure. When the systolic blood pressure falls more than 10 mm. Hg. during inspiration the pulse is erroneously called pulsus paradoxus although it merely is an exaggeration and not a reversal of the normal.

The paradox of this phenomenon is that in extreme cases the peripheral pulse can disappear on inspiration while, paradoxically, heart sounds remain audible during the "missed beats".

A **reverse pulsus paradoxus** may occur in patients receiving continuous airway pressure on a mechanical ventilator.

Causes

A. Superior vena cava obstruction.

B. Lung conditions.

1. Asthma
2. Emphysema
3. Airway obstruction

C. Cardiac

1. Pericardial effusion
2. Constrictive pericarditis
3. Severe congestive cardiac failure

NB: If the thoracic cage is immobile as in ankylosing spondylitis, pulsus paradoxus does not occur.

VII. **Pulsus Bigeminus (Coupling)** is coupling of the pulse waves in pairs, followed by a pause.

Causes

A. Alternate premature beats.

B. A.V. block, every third sinus impulse being blocked.

C. Sinoatrial block with ventricular escape.

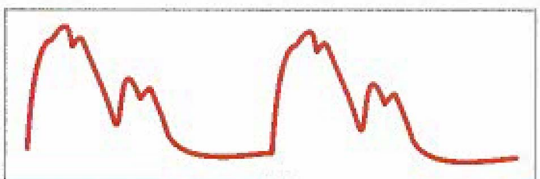


Fig. 2.29: Pulsus bigeminus

VIII. **Thready Pulse:** The pulse rate is rapid and the pulse wave is small and disappears quickly. This is seen in shock especially cardiogenic.

IX. **Waterhammer Pulse** is a large bounding pulse associated with increased stroke volume of the left ventricle and decrease in the peripheral resistance, leading to a wide pulse pressure. The pulse strikes the palpating finger with a rapid, forceful jerk and quickly disappears. It is best felt in the radial artery with the patient's arm elevated. It is caused by the artery suddenly emptying because some of the blood flows back from the aorta into the ventricle.

Causes

A. *Physiological*

1. Fever
2. Chronic alcoholism
3. Pregnancy

B. *High output states or syndromes*

1. Anemia
2. Beriberi
3. Cor pulmonale
4. Cirrhosis of liver
5. Paget's disease
6. Arteriovenous fistula
7. Thyrotoxicosis

C. *Cardiac lesions*

1. Aortic regurgitation
2. Rupture of sinus of Valsalva into the heart chambers
3. Patent ductus arteriosus
4. Aortopulmonary window
5. Bradycardia
6. Systolic hypertension



Fig. 2.30: Waterhammer Pulse



Fig. 2.31 : Measuring Apex Pulse Defecit by Simultaneously Palpating Radial Artery and Auscultating the Apex

Usually palpation of Carotid Pulse gives better information about the character of pulse than peripheral arteries like the Radial artery. However Pulses Alternans, Bisferiens and water hammer pulse are better felt at the peripheral arteries.

Apex Pulse Deficit

It is the difference between the heart rate and pulse rate, counted simultaneously, by two people, for 1 minute. When only one person is examining, the radial artery is palpated simultaneously while ausculating the apex. The heart beats which are not transmitted to the radial pulse are counted as the Apex Pulse Deficit.

i. Apex Pulse Deficit > 6 - Atrial Fibrillation

ii. Apex Pulse Deficit < 6 - Ventricular. Premature Beats.

17 › Jugular Venous Pulse (JVP)

Normal: 3-5 cm

Procedure: The patient is given a backrest to keep him

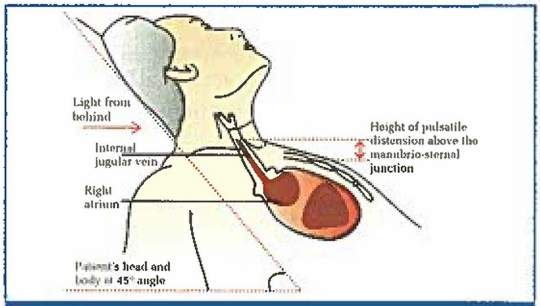


Fig. 2.32 : Measurement of Jugular Venous Pressure

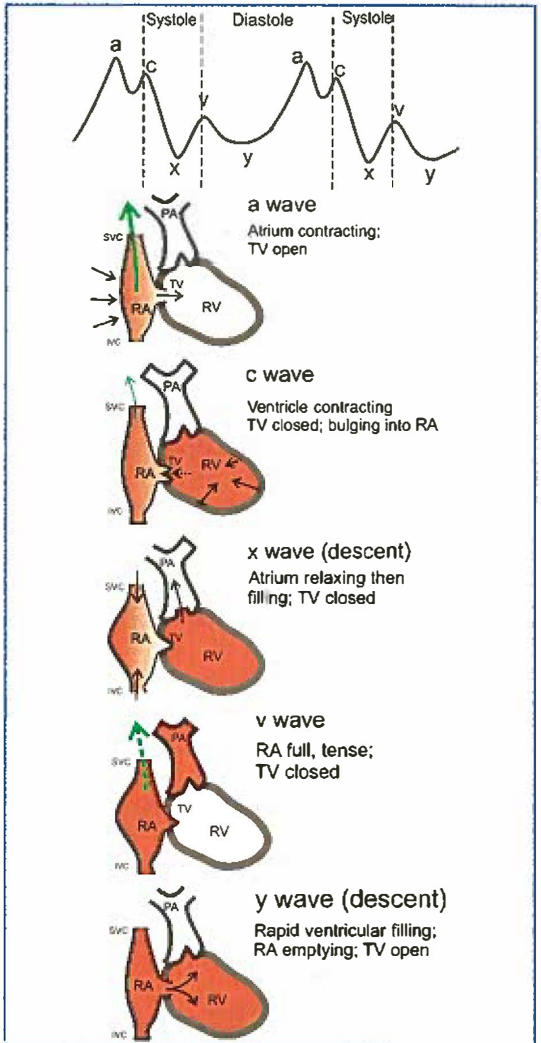


Fig. 2.33 : Normal Jugular Venous pulse. a: Atrial contraction; c: tricuspid valve closure; x: Atrial relaxation; v: Atrial filling; y: Rapid ventricular filling; RA: Right atrium; RV: Right ventricle; TV: Tricuspid valve; PA: Pulmonary artery; SVC: Superior vena cava; IVC: Inferior vena cava

at 45°. In this position, normally, the internal jugular vein is just seen above the clavicles. The upper level of the vein is noted and a ruler is kept at that level, parallel to the ground. Another rule is put perpendicular to the first ruler up to the angle of Louis. The distance from the angle of Louis to the first ruler gives the jugular pressure. In the supine position the jugular pressure may falsely appear elevated whilst in the upright position it is falsely lowered.

Significance: The jugular veins are in direct continuity with the superior vena cava and the right atrium. Hence it reflects pressure changes in the right atrium.

NORMAL JVP: The normal JVP consists of three positive pulse waves (a, c and v) and two negative pulse waves (x and y).

THE 'A' WAVE is produced by retrograde transmission of the pressure pulse produced by right atrial contraction. In normal subjects the 'a' wave is often the largest positive wave visible, coinciding with the fourth heart sound.

Abnormalities of 'a' waves:

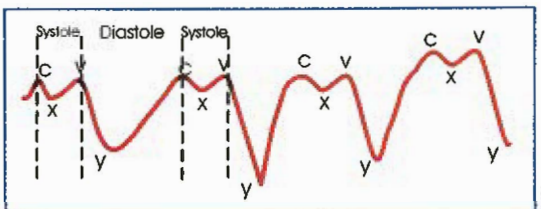


Fig. 2.34 : JVP in atrial fibrillation. Absent 'a' wave

A. *'a' wave is absent* in atrial fibrillation

B. *'a' wave is diminished* in

1. Tachycardia
2. Prolonged PR interval

C. *Large or giant 'a' waves* are present in

1. Tricuspid stenosis
2. Tricuspid atresia
3. Right atrial myxoma
4. Pulmonary stenosis
5. Pulmonary hypertension

D. *Cannon 'a' waves* occur in --

1. Complete heart block when the right atrium and right ventricle contract simultaneously with a closed tricuspid valve.

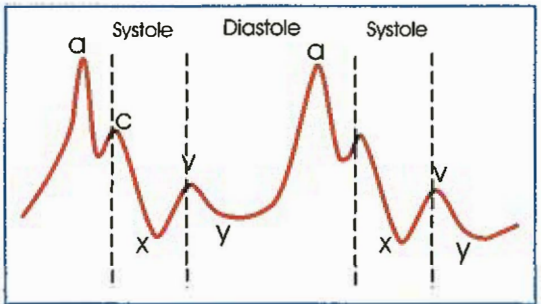


Fig. 2.35 : JVP in tricuspid stenosis : giant 'a' wave

2. Ventricular tachycardia.
3. Ectopic beats.

THE 'C' WAVE is produced by two events:

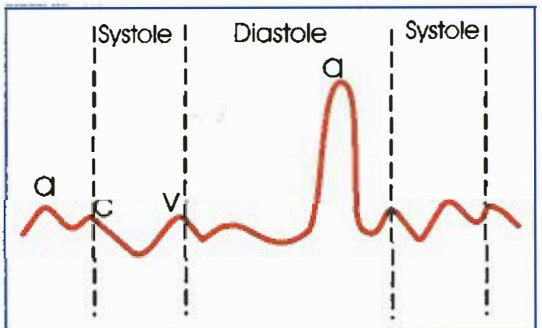


Fig. 2.36 : JVP in complete heart block - cannon wave

A Impact of the carotid artery adjacent to the jugular vein.

B. Retrograde transmission of a positive wave in the right atrium produced by the right ventricular systole and the bulging of the tricuspid valve into the right atrium.

It normally begins at the end of the first heart sound and reaches its peak shortly after the first heart sound. The 'c' wave is not often seen clinically.

THE 'X' WAVE: 'x' descent is produced by:

A. The downward displacement of the tricuspid valve during ventricular systole and resultant fall in right atrial pressure.

B. Continued atrial relaxation.

Abnormalities of 'x' wave

A. The 'x' descent is obliterated or may be replaced by a positive wave ('s' wave) in tricuspid regurgitation. This 's' wave may fuse with the 'c' and 'v' waves to produce a giant 'V' wave (Fig. 2.24).

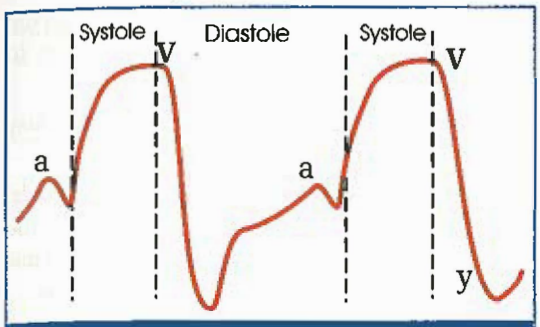


Fig. 2.37: JVP in tricuspid regurgitation - severe obliteration of 'X' descent and prominent 'V' wave

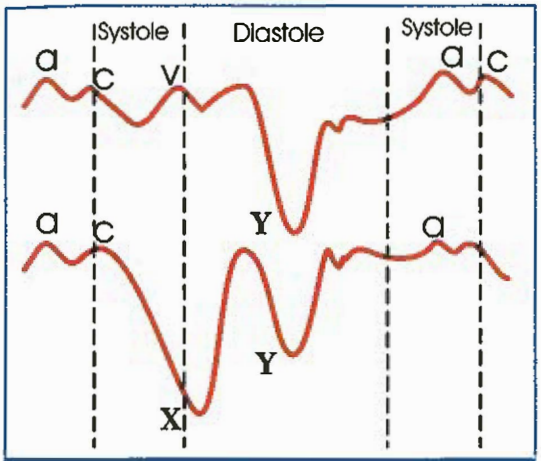


Fig. 2.38: JVP in constrictive pericarditis - usually a prominent 'Y' descent (top). Sometimes 'X" descent may be more prominent than 'Y' descent (bottom)

B. The 'x' wave may sometimes be prominent in constrictive pericarditis (Fig. 2.25). Cardiac tamponade restrictive chodeography

THE 'V' WAVE occurs because of right atrial filling with the tricuspid valve closed during ventricular systole.

Abnormalities of 'v' wave: Giant 'v' waves, as discussed earlier, appear in tricuspid regurgitation.

THE 'Y' WAVE : The 'y' descent is produced by opening of the tricuspid valve and subsequent rapid inflow of blood from the right atrium to the right ventricle leading to a sudden fall of pressure in the right atrium which is reflected in the jugular veins. It corresponds with the third heart sound.

The ascending limb of the 'y' wave is due to continuous diastolic inflow of blood into the great veins, right atrium and ventricle, which are all in free communication during diastole.

Abnormalities of 'y' descent:

A. Rapid for HRCP 'y' descent occurs in
   1. Constrictive pericarditis (Friedreich's sign).
   2. Severe heart failure.
   3. Tricuspid regurgitation (Early & Deep).

B. A short 'y' descent occurs in tricuspid stenosis on rt. atrial myxoma.

Elevated venous pressure occurs in

1. Right ventricular failure
2. Cardiac tamponade
3. Tricuspid stenosis
4. Superior vena cava obstruction
5. Hyperkinetic circulatory state
6. Increased blood volume
7. Pulmonary diseases like asthma, emphysema

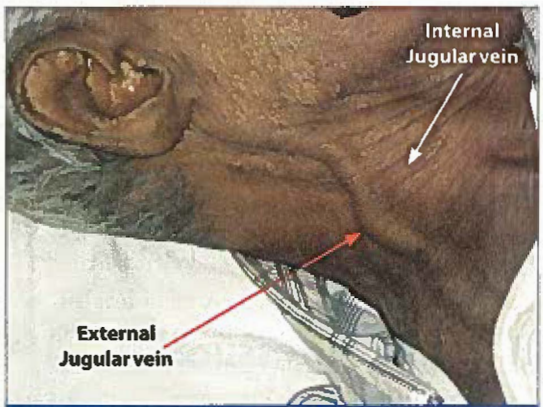


Fig. 2.39: Dilated Neck Vein

Differences between JVP and Carotid Pulse

		JVP	Carotid Pulse
1.	Appearance	Better seen than felt	Better felt than seen
2.	Number of waves	Multiple	Single
3.	Pressure below the angle of mandible	Obliterates the wave	No change
4.	Changes with respiration and change of position	Present	Absent

Kussmaul's sign: Normally inspiration lowers the JV pressure giving an inspiratory collapse, because intrathoracic pressure falls and there is increased blood flow into the thorax. In contrast, when the intrapericardial pressure is raised as in ***constrictive pericarditis*** there is a paradoxical increase in JV pressure on inspiration. This is Kussmaul's sign.

Hepatojugular Reflux

Normally, when pressure is applied over the abdomen (right hypochondrium) for 30 seconds, initially there is a rise in JV pressure (due to increased venous return), followed by a fall (due to the capacity of normal myocardium to accommodate the extra venous return). However, in early cardiac failure, even before jugular pressure is elevated, there is a sustained elevated pressure in the jugular veins (for more than a minute) on pressure over the abdomen because the failing heart cannot compensate for the extra venous return. This is positive hepatojugular reflux.

There is **no rise in jugular venous pressure on applying pressure over abdomen in:**

1. Budd Chiari syndrome
2. IVC Obstruction

Decreased venous pressure in seen in:

1. Shock
2. Dehydration

18 › Blood Pressure

Systolic BP is controlled by the stroke volume of the heart and the stiffness of the arterial vessels. Diastolic BP is controlled by the peripheral resistance.

BP varies from moment to moment with respiration, emotion, exercise, meals, alcohol, tobacco, bladder distension, temperature and pain. It is also influenced by circadian rhythm, age and race. BP may be modified by obesity or arrhythmia.

Shortly after Scopine Riva-Rocci had invented the sphygmomanometer, the Russian surgeon Korotkoff suggested that by placing a stethoscope over the brachial artery at the antecubital fossa distal to the Riva-Rocci cuff, sounds could be heard. The origin of these sounds is still not clear. Vibratory and flow phenomenon are probably responsible. The phases are:

- *Phase I:* The first appearance of faint clear tapping sounds *(Thuds)* which gradually increase in intensity.
- *Phase II:* The softening of the sounds which may become *swishing or blowing.*
- *Phase III:* The return of *sharper softer* sounds, which become crisper, but never fully regain the intensity of phase I sounds. Neither phase II nor phase III has any known clinical significance.
- *Phase IV:* Distinct abrupt *muffling* of sounds, which become soft and blowing.
- *Phase V:* The point at which all sounds *disappear* completely.

Phase I is taken as systolic pressure and phase V as diastolic pressure.

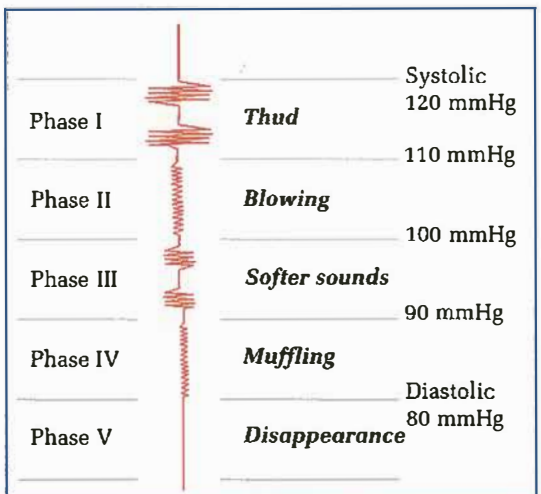


Fig. 2.40: Korotkoff sounds

Apparatus

1. **Mercury sphygmomanometer:** The pressure changes are reflected by a rise of mercury. It is an accurate method of taking blood pressure. However, the instrument is bulky and heavy.
2. **Aneroid meter:** The pressure changes are reflected by a change in the needle which is connected to the spring. Though the instrument is small and non-bulky, it has to be frequently reset to ensure accuracy.
3. **Electronic BP meter:** The pressure changes are measured electronically.

Technique

1. Clothing should be removed from the arm. If it cannot be removed, it is better to leave it as it is, rather than fold the clothing into tight constricting bands.
2. The cuff should be encircled around the arm. If the bladder does not encircle the arm completely, the centre of the bladder should be over the brachial artery. The rubber tubes from the bladder are usually placed inferiorly at the site of the brachial artery, but it is better to place it superiorly or posteriorly so that the antecubital fossa can be easily auscultated.

   The normal cuff is 25 cm in length and 12 cm in width.
3. The bell gives better sound reproduction but a diaphragm is easier to secure with the finger of one's hand and covers a large area.
4. *The bladder is inflated quickly to a pressure 20 mm Hg above the systolic pressure, recognized by disappearance of the radial pulse. The bladder is then deflated 2 mm Hg per second. The Korotkoff phase I (appearance) and phase V (disappearance) are recorded to nearest 2 mm. In children, phase IV may be preferable. If Korotkoff sounds are weak, the patient is asked to raise the arm and open and close the fist 5-10 times before inflating the bladder.* ***The pressure, patient position, the arm and the cuff size should be recorded.***
5. To measure BP in the legs a thigh cuff containing a large bladder (18 x 24 cms) for adults should be wrapped around the thigh of the prone patient and the Korotkoff sounds auscultated in the popliteal fossa in the usual way. Diastolic BP in the legs is equal to that in the arms provided the bladder is adequate in size. Systolic BP in lower limbs is 20 mm Hg more than upper limbs.
6. For children, pediatric size cuff should be used.

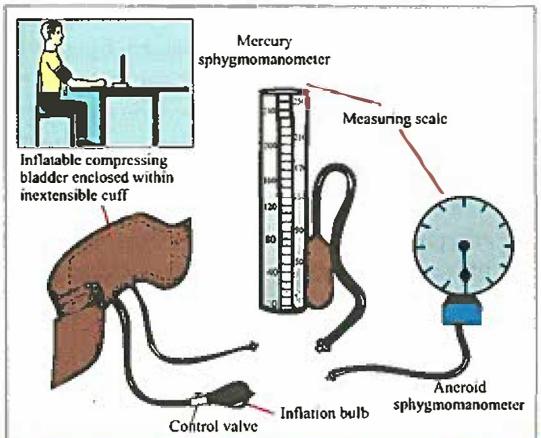


Fig. 2.41 : Blood Pressure Measurement

Guidelines for Measurement of BP

1. Explain the procedure to the patient to allay anxiety.
2. Avoid exertion, meals or smoking for 30 minutes before BP is measured. No exogenous adrenergic stimulants (e.g. phenylephrine in nasal decongestants) should be used. The patient must be allowed to rest for 5 minutes before BP is measured.
3. The room should be warm and quiet.
4. High BP may be erroneously recorded in an obese person because the inflatable rubber bladder may be too short for the obese arm (Recommended dimensions are 12 x 35 cms). When the bladder does not completely encircle the arm, the centre of the bladder must be placed directly over the brachial artery.
5. The arm must be supported to the heart level. In the supine position the arm is usually at the heart level. In sitting and standing positions the arm must be horizontal with fourth intercostal space at the sternum. In normal people there is no significant difference in BP between supine, sitting and standing positions provided the arm is supported at the heart level. Some anti-hypertensive agents cause postural hypotension and when this is expected, BP must be measured in both lying and standing positions.
6. If the arm is unsupported, the patient will perform isometric exercise, which may elevate the diastolic BP by 10%. This is especially so in hypertensive patients on beta-adrenergic blocking agents. To avoid this the arm must be supported.
7. The BP may be higher in right arm by 2-10 mm Hg. Most pressures in practice are measured on the right arm. However if the BP is higher by 10

mm Hg in one arm further measurements should be made in the arm with the higher BP.

8. The cuff should be snugly fitted to the arm. A cuff which is too tight may give a false lower blood pressure and a loose cuff may give a false higher BP.
9. Repeated inflation of the cuff may cause venous congestion of the limb and elevate both systolic and diastolic BP. To avoid this the cuff should be inflated as rapidly as possible and deflated completely between successive readings. At least 15 seconds should be allowed between successive measurements.
10. Auscultatory Gap: Is the interval of blood pressure when the Korotkoff sounds disappear and then re-appear at a lower pressure during auscultatory method of measury B.P. This leads to errors of underestimation of systolic BP or overestimation of diastolic B.P. This can be avoided by doing the palpatory method first, followed by auscultatory method.

Unequal BP in two arms

1. In normal individuals, BP may vary upto 10 mm Hg in the two arms.
2. Supravalvular aortic stenosis (right sided higher BP)
3. Preductal coarctation of aorta (right sided higher BP)
4. Unilateral occlusive disease of the arteries - Atherosclerosis, embolism, aortoarteritis, thoracic outlet syndrome, etc. (BP will be low on the affected side)

Conditions Diagnosed by Measuring BP

1. Hypertension
2. Hypotension
3. Pulsus paradoxus
4. Pulsus alternans
5. Coarctation of aorta (Hypertension in upper limb, hypotension in lower limb)
6. Aortic incompetence (Hill's sign)
7. Autonomic dysfunction - postural hypotension.

19 › Hypertension

Hypertension (HT) is the silent killer of mankind. Most sufferers (85%) are asymptomatic and hence early diagnosis is a problem. The dividing line between normal and abnormal BP is arbitrary because BP is dependant upon many factors like age, race, sex, etc.

Definitions and Classification

The definition of hypertension is not universal because normal BP varies. The Sixth Joint National Committee Criteria (JNC VII) classifies hypertension for adults aged 18 years and older into the following stages:

Table 2.7 : JNC VII Criteria for Classification of Blood Pressure

Category	*Systolic mmHg*		*Diastolic mmHg*
Normal	<120	AND	<80
Pre-Hypertension	120-139	OR	80-89
Hypertension			
Stage 1	140-159	OR	90-99
Stage 2	≥160	OR	≥100

1. **Target BP** is < 140 mmHg systolic and < 90 mmHg.

   For diabetics OR chronic renal failure BP should be:

   < 130 mmHg systolic; < 80 mmHg diastolic

   For diabetics WITH chronic renal failure BP should be:

   < 125 mmHg systolic; < 75 mmHg diastolic
2. **Hypertensive emergencies** (malignant hypertension) are characterized by severe elevations in BP (> 180/120 mmHg) with evidence of impending or progressive target organ dysfunction. They require immediate BP reduction. (e.g. pappiledema, retinal exudates, retinal hemorrhages, nephropathy, hypertensive encephalopathy, intracerebral hemorrhage, acute MI, acute left ventricular failure with pulmonary edema, unstable angina pectoris, dissecting aortic aneurysm, eclampsia).
3. **Hypertensive urgencies** (accelerated hypertension) are associated with severe elevations in BP without progressive target organ dysfunction (e.g. upper levels of stage II

hypertension associated with severe headache, shortness of breath, epistaxis). Retinal damage may be present but without pappiledema.

4. **Isolated systolic hypertension** is systolic BP≥140 mmHg and diastolic BP <90 mmHg. It is seen predominantly in elderly due to arteriosclerosis. It may fluctuate from time to time, high in morning, lower at night.
5. **Pulse pressure** = SBP - DBP (Normal 30-60 mmHg).
6. **Mean BP** = 2/3 DBP + 1/3 SBP.

Labile hypertension: The patient is hypertensive at one time and normotensive at another time.

White Coat Hypertension: The patient's BP is high when measured by a professional but is normal when measured in casual circumstances (at home). It is diagnosed by 24-hour ambulatory BP monitoring.

Causes

1. **Essential Hypertension**
2. **Renal**
   a. Acute nephritis
   b. Interstitial nephritis and pyelonephritis
   c. Polycystic kidneys
   d. Renal artery stenosis
   e. Diabetic nephropathy
3. **Endocrine:** Pheochromocytoma, Cushing's syndrome, thyrotoxicosis, myxedema
4. **Neurological:** Raised intracranial tension, lead encephalopathy, etc.
5. **Pregnancy induced HT**
6. **Cardiovascular HT:** Co-arctation of aorta, aortic regurgitation, arteriosclerosis
7. **Drugs:** Glucocorticoids, OCPs, sibutramine, cocaine, etc.
8. **Miscellaneous:** Polycythemia, polyarteritis nodosa, obstructive sleep apnea, hypercalcemia

Effects of Hypertension

The common organs damaged by long-standing hypertension are heart, kidneys, blood vessels, retina and central nervous system.

1. **CVS:** Increased myocardial work leads to concentric hypertrophy of left ventricle, angina pectoris and accelerated coronary artery disease. There is systolic as well as diastolic dysfunction.
2. **Kidneys:** Progressive arteriosclerosis involves both the efferent and afferent renal arterioles and capillaries of glomerular tuft. This leads to compromise in renal function, shrinkage of kidney, proteinuria.
3. **CNS:** Hypertension may cause micro-aneurysms (Charcot-Bouchard aneurysms) which may rupture and cause cerebral hemorrhage. Accelerated atherosclerosis may cause cerebral thrombosis, embolism and infarction. Cerebral arteriolar spasm may cause hypertensive encephalopathy.

   Sites of hypertensive bleed are: cerebellum, thalamus, basal ganglia (putamen), pons.
4. **Fundus**

   Keith Wagner Classification

   Grade I: Mild generalized arteriolar attenuation.

   Grade II: Deflection of veins at AV crossing (AV nicking) + marked generalized arteriolar attenuation.

   Grade III: Grade II + copper wire + cotton woolspots + flame-shaped hemorrhages + hard exudate.

   Grade IV: Grade III + silver wire + papilledema.

Symptoms

The clinical features may be due to the elevated BP itself, target organ involvement or due to underlying disease, as in secondary hypertension.

Symptoms due to hypertension

1. Headache: This occurs usually in the morning hours. It is throbbing and usually frontal.
2. Dizziness: The patient feels unsteady
3. Epistaxis: This occurs due to increased pressure causing rupture of the capillaries of the nose. The bleeding would reduce the circulating volume, and lower the BP (Natures way of lowering the BP and prevention of hemorrhage in the vital organs).

Symptoms due to Affection of Target Organs

1. CVS:
   a. Dyspnea on exertion (incipient LVF)
   b. Anginal chest pain (IHD)
   c. Palpitations
2. Kidneys: Hematuria, nocturia, polyuria
3. CNS:
   a. Transient ischemic attacks (TIA or stroke) with focal neurological deficit
   b. Hypertensive encephalopathy (headache, vomiting, convulsions, unconsciousness, focal neurological deficit)
   c. Dizziness, tinnitus and syncope
4. Retina: Blurred vision or sudden blindness

Symptoms due to Underlying Diseases

1. Edema and puffy face - Acute nephritis
2. Weight gain, hirsutism and stria - Cushing's syndrome
3. Weight loss, tremors, palpitations and sweating - Hyperthyroidism/pheochromocytoma
4. Weakness - Primary hyperaldosteronism
5. Joint pains, bronchospasm & peripheral vascular disease symptoms - Polyarteritis nodosa

Signs

General Examination

1. Moon face, buffalo hump and truncal obesity - Cushing's syndrome



Fig. 2.42: Moon face in Cushing's syndrome

2. Puffy face, rough skin, obesity - Myxedema
3. Tremors, tachycardia, exophthalmos, thyroid dermopathy and goitre- Hyperthyroidism
4. Prognathism, clubbed hand, coarse features - Acromegaly
5. Pigmentation - Neurofibromatosis
6. Radio femoral delay and collateral vessels over the chest wall - Coarctation of aorta
7. Weaker left radial - Preductal coarctation
8. Waterhammer pulse - Aortic incompetence



Fig. 2.43: Exophthalmos in hyperthyroidism



Fig. 2.44: Hyperthyroid dermopathy ("orange-peel appearance") in lower limbs with few vitiligo patches

Cardiovascular System

1. Cardiomegaly
2. Third and fourth heart sound gallop
3. Loud second heart sound
4. Early diastolic murmur - due to AI

Respiratory System

1. Basal crepitations - LVF
2. Rhonchi - LVF, Polyarteritis nodosa

Abdomen

1. Hepatomegaly - Cardiac failure
2. Palpable kidney lump - Polycystic kidney, hypernephroma
3. Bruit over renal artery - Renal artery stenosis
4. Bruit over abdominal aorta - Abdominal aortic aneurysm

Investigations

To assess target organ damage

1. X-ray chest for heart size
2. ECG for LV hypertrophy and evidence of IHD
3. Echocardiogram for LV systolic and diastolic functions
4. Urinalysis - proteinuria>200 mg/day and hematuria suggest renal involvement. Further investigations include serum creatinine, renal sonography, isotopic renogram, renal biopsy.

To Detect the Cause of Hypertension

1. X-ray chest
   a. Rib notching suggests coarctation of aorta
   b. Mediastinal widening suggests aortic dissection
2. Imaging of abdomen (Sonography, CT scan, MRI) to detect:
   a. Polycystic kidney
   b. Tumour of kidney
   c. Renal calculi
   d. Adrenal tumour
   e. Pheochromocytoma
3. Urinary catechols or breakdown products (Metanephrine or VMA) - Pheochromocytoma
4. Echocardiogram - coarctation of aorta
5. IVP - for renovascular hypertension, kidney tumours and stones
6. Aortography - for aneurysm and coarctation of aorta

Treatment of Hypertension

I. **Non-pharmacological Treatment/ Lifestyle Modifications**

These have been practice over the years, even when no drugs were available and their value established. They help to control hypertension in some, but are useful as adjuvants to drug treatment in almost all patients. They include the following:

1. ***Salt restriction:*** Modest sodium restriction to up to 110 mmoles/day (2.4 g sodium or 6 g sodium chloride) is effective in controlling hypertension in mild to moderate hypertension because sodium and water retention is involved in large proportion of hypertensives.
2. ***Weight reduction:***In overweight persons, reduction of 1 kg may reduce 1.6/1.3 mmHg BP. It also modifies other CVS risk factors like diabetes and dyslipidemia. BP is lowered by:
   a. Reduced circulating volume which reduces venous return and cardiac output
   b. Reduced sympathetic activity and plasma nor-epinephrine
   c. Reduction in hyperinsulinemia
3. ***Stop smoking:*** Smoking acutely raises BP. In addition, it is an independent and most important reversible coronary risk factor. Since tolerance develops to nicotine-induced hemodynamic effects, chronic smoking may not be associated with high BP.
4. ***Diet:***
   A. Lactovegetarian diet and high intake of polyunsaturated fish oils have high potassium levels and lower BP by:
      i. Increased sodium excretion
      ii. Decreased sympathetic activity
      iii. Decreased renin-angiotensin secretion and direct dilatation of renal arteries
   B. Adequate calcium, magnesium intake should be maintained in the diet.
   C. Saturated fat and cholesterol intake should be reduced for overall cardiovascular health.

5. ***Limit of alcohol intake*** to <1 ounce/day of ethanol (24 ounces beer, 8 ounces wine or 2 ounces 100-proof whiskey)
6. ***Relaxation:*** Various forms of relaxation like yoga, biofeedback and psychotherapy lower BP, especially in those with sympathetic
7. ***Regular exercise***

II. **Pharmacological Treatment**

1. ***Diuretics:*** Oral diuretics were the most widely used anti-hypertensive agents. They are effective alone in 50% of mild hypertensives. Thiazides are very effective. They are well tolerated and need to be given only once a day. They enhance the potency of other anti-hypertensives. They act by reducing extracellular fluid volume and cardiac output and they help to counteract the hypertensive effect of high salt intake. They can aggravate diabetes by suppressing release of insulin due to hypokalemia. Hyperlipidemia, hyperuricemia, hypokalemia, hyponatremia, hypomagnesemia may occur. Now they are usually used in combination therapy.
2. ***Beta blockers:*** Reduce cardiac output and lower BP but raise the peripheral resistance on acute administration (which increases BP). However, on chronic administration, BP falls to pretreatment levels. In mild to moderate hyper-tension, it lowers the BP to less than 90 mmHg in more than 50% patients. Drug withdrawal, if needed, should be done slowly, or rebound hypertension may occur. They can be combined with diuretics, calcium blockers, ace inhibitors and vasodilators. They may precipitate bronchospasm, cardiac failure, peripheral vascular disease, impotence and depression.
3. ***Calcium Channel Blockers:*** Lower BP by:
   a. Natriuresis and diuresis due to increased GFR and decreased aldosterone
   b. Anti-angiotensin-II effect
   c. Direct negative inotropic effect which lowers cardiac output
   d. Peripheral vasodilatation

   Nifedipine was the commonest used calcium blocker. Now Amlodipine is replacing it. Felodipine, nicardipine, nitrendipine and clinidipine are other useful calcium blockers. These drugs are especially useful in elderly hypertensives. Flushing, headache, palpitations, edema and hypotension may occur.
4. ***ACE Inhibitors:*** Renin released from the kidney acts on circulating angiotensinogen to produce angiotensin I, which is converted to angiotensin II by converting enzyme. Angiotensin II is a potent vasoconstrictor and it stimulates aldosterone, which retains sodium and causes hyper-tension. ACE inhibitors act by inhibiting the converting enzyme preventing the formation of angiotensin II and lowering of BP. They also act by reducing the degradation of bradykinin - a potent vasodilator, which lowers the BP.

   ACE Inhibitors cause regression of ventricular hypertrophy, attenuation of reperfusion injury-induced ventricular arrhythmias, preload and afterload reduction and coronary vaso-dilatation. These drugs have no adverse effects of lipids, uric acid or glucose metabolism. They lower the BP by 15-25%. Diastolic pressure is lowered more than systolic pressure. Concomitant sodium restriction and diuretics further lowers BP by 15-25%.

   ACE Inhibitors are useful in renovascular hypertension. High angiotensin II is however required to maintain adequate filtration pressure behind the stenotic lesion. ACE Inhibitors decrease the perfusion pressure and lead to azotemia. Thus, they are contraindicated in bilateral renal artery stenosis. These drugs are useful in hypertensive diabetics because of neutral effect of carbohydrate metabolism. In addition they decrease microalbuminuria. Captopril also improves insulin sensitivity. It has a short duration of action and is used for cardiac failure. Enalapril, lisinopril, perindopril, ramipril, etc. are longer acting ACE inhibitors and useful in hypertension. Tissue specific ACE inhibitors like Quinapril, Ramipril, Perindopril, Fosinopril are available.

5. ***Angiotensin II Blockers*** are useful in patients with ACE Inhibitor-induced cough and in elderly hypertensives. Losartan, Irbesartan, Valsartan, Candersartan are available.
6. ***Alpha Blockers:*** Adrenergic stimulation of alpha-1 receptors in the vascular smooth muscles causes vasoconstriction and hypertension. Alpha blockers attenuate vasoconstriction, and thereby decrease vascular resistance and blood pressure. Prazosin was the first alpha blocker with short duration of action. Terazosin and doxazosin are longer acting, once a day alpha blockers. The efficacy can be enhanced by the concomitant use of diuretics. The most dramatic adverse effect is the first dose postural hypotension/syncope.

   Alpha blockers also have other beneficial effects like lowering of lipids, regression of left ventricular hypertrophy, enhancing insulin sensitivity (hence ideal for diabetic hypertensives) and relief of obstructive symptoms in benign prostatic hypertrophy.
7. ***Vasodilators:*** These drugs act on the arteriolar smooth muscles, causing vasodilatation and lowering of BP. However, reflex tachycardia and increase in cardiac output limits its usefulness in severe coronary artery disease. These effects can be reduced by combining hydralazine with beta blockers. Minoxidil is the other vasodilator whose usefulness is limited due to hirsutism in females. Diazoxide and nitroprusside are parenteral vasodilators useful in hypertensive emergencies.

20 〉 Hypotension

Definition: Hypotension is diminished blood pressure. This could be acute or chronic.

Acute Recumbent Hypotension

Causes

1. *Cardiovascular:* Acute myocardial infarction, pulmonary embolism, dissecting aneurysm, ventricular tachycardia, cardiac rupture
2. *Intravascular volume contraction:* Hemorrhage, vomiting, diarrhea, burns, intestinal obstruction, peritonitis, etc.
3. *Anaphylaxis*
4. *Gram negative septicemia*

Clinical Features

1. Due to shock: Tachycardia, vomiting, fainting
2. Due to causative disease
3. In vasovagal attacks, hypotension with bradycardia
4. In postural hypotension, fall of BP occurs on suddenly on assuming an erect posture from supine posture

Treatment

1. *Of the cause*
2. *Posture:* The patient should be in lying position with legs raised.
3. *For vasovagal attacks:* Atropine 0.6 mg IV
4. *For anaphylaxis:* Hydrocortisone hemi-succinate 100 mg IV, repeated as required
5. *For postural hypotension:* This is best treated by advising the patients to assume the erect posture slowly and to wear elastic stockings and abdominal binder.
6. *Vasoconstrictors:* Dopamine, nor-epinephrine and ephedrine have been tried.
7. *Salt:* Adequate amount of salt (NaCl) in diet helps to expand the plasma volume.
8. *Fludrocortisone Acetate: (0.1 - 0.2 mg)* causes fluid retention and avoids postural fall of BP.

Chronic Hypotension

A number of healthy subjects have a systolic BP of 80-100 mm Hg, which is compatible with long life expectancy. Only some patients complain of weakness, lethargy, easy fatigability, dizziness and fainting on assuming erect posture or standing inactive for long periods. This occurs due to interference with neural pathways between the vasomotor center and efferent sympathetic nerve endings in the blood vessels and heart, so that the normal rise in cardiac output and vasoconstriction on assuming erect posture are abolished.

Causes

1. *Cardiac:*
   a. Low output cardiac failure
   b. LV dysfunction
   c. Cardiac tamponade
   d. Constrictive pericarditis
   e. Tight mitral stenosis
   f. Left atrial myxoma
2. *Supine hypotension of pregnancy*
3. *Endocrine*
   a. Addison's disease
   b. Myxedema
   c. Hypopituitarism
   d. Serotonin secreting tumors
4. *Neurogenic*
   a. Diabetic neuropathy
   b. Extensive lumbosacral sympathectomy
   c. Peripheral neuropathy
   d. Tabes dorsalis
   e. Syringomyelia, Multiple sclerosis
5. *Chronic idiopathic orthostatic hypotension*

Chronic Idiopathic Orthostatic Hypotension

This occurs due to primary autonomic insufficiency due to degeneration of central or peripheral autonomic nervous system. It is common in the elderly who may develop syncope, hypotension, convulsions but no tachycardia on standing. They may have associated anhydrosis, loss of hair, diminished lachrymal and salivary secretion, bladder atony and impotency.

Treatment

1. *Mechanical:* Elastic bandages over legs, head up position in bed etc.
2. *Volume expansion with high fluid and salt intake*
3. *Fludrocortisone supplement* (0.01 mg/day)
4. *Drugs:*
   a. Sympathomimetics: Ephedrine, amphetamine, L-dopa
   b. Prostaglandin synthesis inhibitors like indomethacin
   c. Alpha 2 receptor agonists
   d. Partial Beta agonist (pindolol)
   e. Erythropoietin
   f. Somatostatin analogue (octreotide) prevents splanchnic pooling after eating)
   g. Midodrine for neurogenic causes
5. *Atrial pacing*

Shy-Drager Syndrome

This is chronic orthostatic hypotension with degeneration of CNS, mainly involving extra-pyramidal tracts, basal ganglia and dorsal nucleus of Vagus. These patients have intact peripheral autonomic nervous system but are unable to activate it. (In primary autonomic insufficiency there is depletion of nor-epinephrine in the peripheral autonomic ganglia). In both these, catecholamine blood levels do not rise on standing, although it may be normal at recumbency in chronic orthostatic hypotension but reduced in primary autonomic insufficiency.

Abdomen

3

1 › Proforma

History

I. Anorexia, nausea, vomiting, dysphagia, flatulence, eructation, retrosternal burning, water brash

II. Diarrhea, constipation, clay stools, worms in stools, mucus and blood in stools

III. Abdominal pain, lump, and distension

IV. Hematemesis, melena, bleeding per rectum

V. Jaundice, gynecomastia, loss of libido, loss of hair (for liver cell failure), reversal of normal sleep cycle.

VI. Fever, weight loss

VII. Alcohol, smoking

VIII. Past history of tuberculosis, malaria, kala-azar, leukemia, hemolytic crisis (sudden pallor and dyspnea) sexual contact, drugs.

General Examination

I. Vital signs - TPR, BP

II. Built and nutrition, BMI (body mass index)

III. Pallor, Clubbing, Nails (chalky-white nails koilonycnia) cyanosis, icterus.

IV. Edema feet, lymphadenopathy, JVP

V. Signs of liver cell failure: Scanty hair, palmar erythema, spider nevi, parotid swelling, gynecomastia, testicular atrophy, Dupuytren's contractures, flaps (asterixis), paper money skin.

VI. Stigma of tuberculosis: Scars and sinuses in neck, lymphadenopathy, phlyctenular conjunctivitis, thickened spermatic cord, chest signs, etc.

VII. Skin extoriations, ecchymosis or petechiae, cutaneous markers of GI malignancy.

VIII. Eye : Kayser - Fleischer ring on slit lamp Examination of cornea.

IX. Miscellaneous: Bony tenderness, genitals.

Alimentary System Examination

I. **Oral cavity**

- A. Teeth
- B. Tonsils
- C. Tongue
- D. Oropharynx

II. **Abdomen:**

A. Inspection:

1. Skin
2. Shape of abdomen
3. Umbilicus
4. Abdominal movements
5. Pulsations
6. Dilated veins
7. Peristalsis
8. Scars and sinuses
9. Hernial orifices

B. Palpation:

1. Tenderness, guarding and rigidity on superficial palpation.
2. Liver, spleen, kidney, gall bladder, colon, or any other lump (Its size, surface, borders, tenderness and bruit)
3. Fluid thrill

C. Percussion:

1. Horseshoe and shifting dullness.
2. Dullness over any lump, if palpable.
3. Renal angle tenderness (i.e. angle between one 12th rib & outer border

of erector spinae) seen in perinephric abscess.

D. Auscultation:
   1. Peristalsis
   2. Rub
   3. Arterial Bruit or venous hum
   4. Puddles sign

E. Miscellaneous:
   1. Abdominal girth
   2. PR examination
   3. Proctoscopy

2 › Examination

A. Inspection

The abdomen can be divided in to 9 regions by drawing 2 horizontal and 2 vertical imaginery lines. The 2 vertical lines are drawn by joining mid clavicular point to the mid inguinal point. The upper horizontal line is drawn at the lower most bony point of the rib cage, usually the 9th or 10th costal cartilage (Sub costal plane - corresponds to the body of L3 vertebra). The lower horizontal line is drawn at the upper border of the tubercles of the iliac crests (Trans tubercular plane - corresponds to the upper border of L5 vertebra). The 9 quadrants are shown in Figure.

I. **Shape of Abdomen :** The shape of the abdomen in most normal persons with normal musculature is scaphoid or boat-shaped i.e. the abdominal wall sinks slightly within the bony margins of the abdominal surface.

   In every muscular person, the lateral margins of the rectus muscle is visible in the center. Usually the medial edges of both the recti are contiguous. However they may be separated as a congenital defect, after pregnancy or with obesity and ascites. This is called divarication of recti. Distension of the abdomen occurs due to fat (obesity), fluid (ascites), feces, flatus, fetus, full urinary bladder and (fatal) new-growth. They can be differentiated as follows:

1. **Fat :** Pendulous abdomen with symmetrical, globular, enlarged and accentuated cutaneous folds
2. **Fluid :** Fluid thrill, shifting and horseshoe dullness
3. **Flatus:** Generalized tympany more at the periphery
4. **Feces:** Generalized distension occurs, more in the flanks. Fecal masses may be felt.
5. **Fetus:** Central dullness, tympany in the flanks, history of amenorrhea and fetal parts may be palpable
6. **Full bladder:** Tender, rounded, cystic mass may be palpable above symphysis pubis, which may disappear after micturition
7. **Fatal new growth:**
   a. Abdominal dullness overlying the growth
   b. In ovarian growth, the distance between the umbilicus and symphysis pubis is greater than that between the xiphisternum and umbilicus

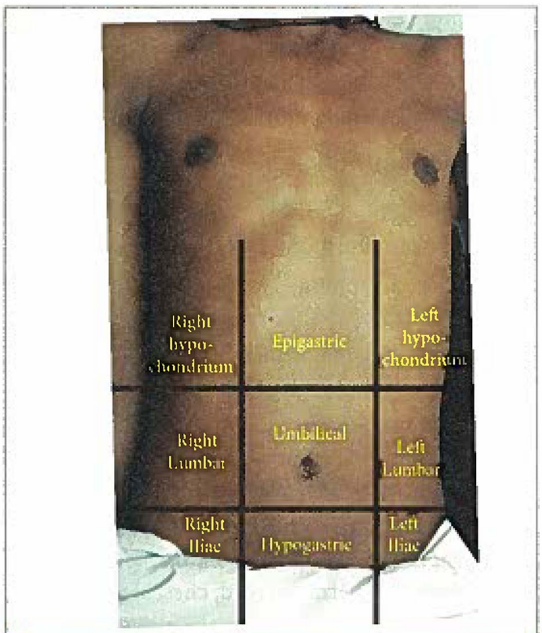


Fig. 3.1 : Inspection of Abdomen - 9 Quadrants

Generalized distension occurs in ascites, obesity and patients with excessive flatus. Localized distension occurs with individual visceromegaly and with neoplasms, e.g. hepatomegaly produces abdominal distension in the right hypochondriac region whereas full bladder produces marked distension of hypogastrium.

Scaphoid or sunken abdomen is seen with starvation and malignancy, especially of stomach and esophagus.

II. **Umbilicus:** Normal umbilicus is usually inverted and situated centrally in the mid-abdomen. The distance between the xiphisternum and the umbilicus is equal to the distance between the umbilicus and symphysis pubis.

In ascites, the distance between xiphisternum and umbilicus is greater than that between umbilicus and symphysis pubis, whereas in ovarian tumor the distance between xiphisternum and umbilicus is less than that between umbilicus and symphysis pubis.

In ascites, the umbilicus is transversely stretched (smiling) or flattened or everted whereas in obesity, the umbilical cleft is deeper than normal.

Everted umbilicus may occur with herniation of bowel or fat into the widened umbilical ring. Sometimes, umbilicus may exude fluid e.g. ascitic fluid in massive ascites or feculent material in enteric fistulae, or clear fluid in patent urachus (crying umbilicus). A faint blue discolouration around the umbilicus (Cullen's sign) or in one or both flanks (Grey Turner's sign) may occur in acute hemorrhagic pancreatitis or ruptured ectopic pregnancy. Cherry red swelling of the umbilicus suggests inflamed Meckel's diverticulum.



Fig. 3.2: Ascites with umbilical hernia

III. **Abdominal Movements:** Normally the abdominal wall bulges during inspiration and falls during expiration. In diaphragmatic paralysis the abdomen bulges during expiration. In peritonitis, the abdominal movements are absent.

IV. **Pulsations:** Normally pulsations are not visible over the abdomen. They may be visible in the following conditions:

1. **Aortic pulsations** are visible in the nervous, anemic individual.
2. **Aortic aneurysm** produces expansile pulsations in any position.
3. **Transmitted pulsations** from a tumor overlying the aorta disappear in knee-elbow position because the tumor falls away from the aorta in that position. This is not so if the tumor is adherent to the aorta.
4. **Right ventricular pulsations** are seen only in the epigastrium and correspond with apex beat
5. **Congested liver,** in addition, produces pulsations posteriorly.

V. **Dilated Veins:** Suggest venous obstruction.

When dilated veins are present, the direction of the blood flow can be found by emptying (milking) a section of the vein and pressing each end of the emptied part with a finger. One finger is released and the

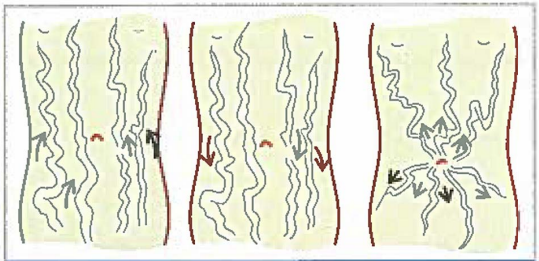


Fig. 3.3 : Dilated veins over the abdomen. Left: Inferior vena cava obstruction (flow from below upwards). Middle: Superior vena cava obstruction (flow from above downwards). Right: Portal vein obstruction (caput medusae)



Fig. 3.4 : Dilated veins

filling of the vein is noted. Similarly, the other finger is released and filling of the vein is noted. Blood enters more rapidly and fills the vein from the direction of the blood flow.

In ***inferior vena cava obstruction*** there will be dilated veins on the sides with flow of blood from below upwards. This occurs because the blood bypasses the inferior vena cava and travels from the lower limbs to the thorax via the veins of the abdominal wall. These veins are anastomotic channels between the superficial epigastric vein and circumflex iliac veins below and the lateral thoracic vein above conveying the diverted blood from the long saphenous vein to the axillary vein.

In ***portal vein obstruction,*** the engorged veins are centrally placed and may form a cluster around the umbilicus (caput medusa). The blood in these veins flows in all directions away from the umbilicus. They represent opening of anastomosis between portal and systemic veins.

VI. **Peristalsis :** Peristalsis is best elicited by patiently observing the abdomen of the patient. If it is not visible, an attempt to visualize it should be made either by making the patient swallow fluids or by applying a sharp tap with the finger over the abdominal wall.

Peristaltic wave of the stomach is seen in pyloric stenosis in the epigastrium and left hypochondriac region, moving from left to right. Peristaltic wave of the large intestine (transverse colon) is seen in the same region but moving from right to left. Peristaltic wave of small intestine is seen in a ladder pattern down the centre of the abdomen.

VII. **Hernial Sites:** The hernial sites in the groin should be seen for any swelling. If there is no swelling, the patient should be asked to stand up, turn his head to one side and cough. If there is an impulse on coughing it suggests hernia.

To differentiate between femoral and inguinal hernia, the index finger of the examiner is placed on the pubic tubercle (traced up along the tendon of adductor longus) and the patient asked to cough. If the impulse is medial and above the index finger it is inguinal hernia. If the impulse tends to bulge straight out through the posterior wall of the inguinal canal, it is direct, whereas if it travels down obliquely along the inguinal canal, it is indirect.

VIII. **Skin Over the Abdomen:** Smooth and glossy skin indicates abdominal distension whereas wrinkled skin suggests old distension which has been relieved.

Abdominal striae (stretch marks) represent the rupture of subepidermal connective tissue as a result of recent or past abdominal distension. It is seen commonly following pregnancy, in obesity, in massive ascites and following corticosteroid

therapy. When they first form, the striae are reddish or pink. If the state of distension stabilizes or the cause regresses, the colour fades to white.

B. Palpation

For palpation of the abdomen, the patient must lie on his back, shoulders raised slightly and legs flexed to relax the abdomen. He should keep his mouth open and breathe quietly and deeply. The abdomen is palpated with the flat of the hand initially, but the fingers are used to locate the margins of any viscera or tumor.

I. **Tenderness:** Tenderness is pain on pressure. It is commonly found in inflammatory lesions of the viscera and the surrounding peritoneum.

The site of tenderness often suggests the diagnosis

1. *In the epigastrium* - Peptic ulcer
2. *In the right hypochondrium* - Hepatitis, cholecystitis
3. *In the right iliac fossa* - Appendicitis (Mc Burney's Point)
4. *Purely visceral pain* such as gastric or intestinal colic is not associated with any tenderness.

Rebound tenderness can be elicited by exerting a firm pressure with the hand and releasing it. In deep seated, subacute conditions, the patient complains of severe pain (e.g. appendicitis).

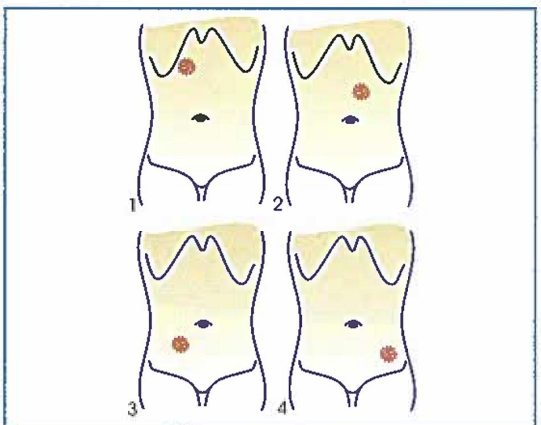


Fig. 3.5 : Site of tenderness in (1) Hepatitis and cholecystitis, (2) Peptic ulcer, (3) Appendicitis and (4) Colitis

II. **Guarding :** Abdominal guarding is due to muscular contraction, which often occurs as a part of the defense mechanism over a tender region. If the patient is put in a comfortable position and his mind set at rest by explaining that no undue pain will be caused by the examination, the abdominal muscles gradually relax.

III. **Rigidity:** Abdominal rigidity is due to muscular contraction, which occurs as a part of the defense mechanism over an inflamed organ. It cannot be voluntarily relaxed. It occurs in the following:

1. Perforation of a hollow organ
2. Peritonitis
3. Acute pancreatitis or cholecystitis
4. Intestinal strangulation
5. Thrombosis of superior mesenteric artery
6. Ruptured ectopic gestation
7. Twisted ovarian cyst or torsion of fibroid

Pancreatobiliary secretions are more irritating to the peritoneum than bacteria are, and so board-like rigidity suggests a chemical peritonitis most commonly from perforated gastric or duodenal ulcer. Bacterial peritonitis rarely produces board-like rigidity until late. It usually causes increased resistance to compression.

IV. **Viscera**

A. **Liver:** The patient must be lying in the supine position with hip and knee flexed, to relax abdominal muscles. The examiner moves his right hand from the right iliac fossa gradually upwards until a sense of increased resistance is noted. The size of the liver must be recorded as fingerbreadths or centimeters below right costal margin. The liver edge is accurately located by the fingertips. It is normally

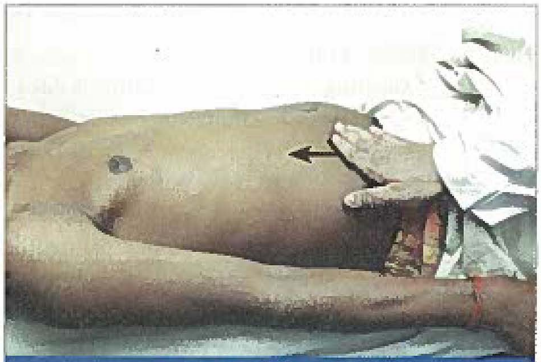


Fig. 3.6: Palpation of Liver



Fig. 3.7: Palpation of Pulsatile Liver in Tricuspid Regurgitation

sharp, firm and regular. The surface of the liver is palpated next. Normally it is smooth. An irregular nodular surface indicates cirrhosis. Liver may be enlarged and pulsatile in tricuspid regurgitation.

B. **Spleen** can be palpated by following methods:

1. **Classical:** The patient is put in the supine position and palpated from the right iliac fossa to the left hypochondriac region. The edge of the spleen may be felt on deep inspiration.
2. **Bimanual:** The patient is put in the right lateral position, one hand of the examiner is put over the lower chest and the spleen is palpated with the other hand. A soft spleen, which may be missed by the classical method, may be palpated by this method.



Fig. 3.8: Palpation of Spleen - Classical Method

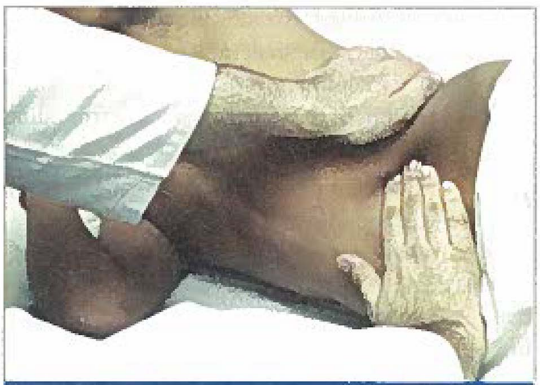


Fig. 3.9: Palpation of Spleen - Bimanual Method

3. **Hooking:** The patient is put in right lateral position and the examiner stands on the left side and feels the spleen by hooking his fingers over the left costal margin.

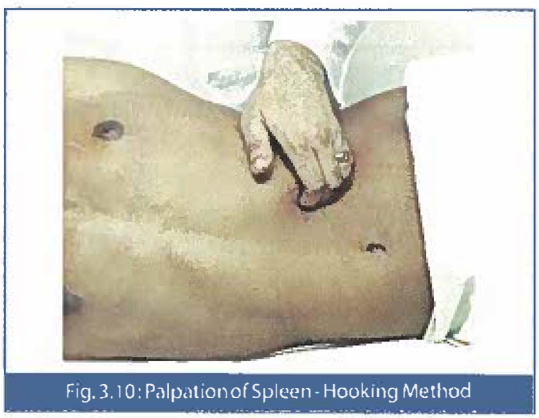


Fig. 3.10: Palpation of Spleen - Hooking Method

4. **Dipping:** This method is used when there is severe ascites which may mask an enlarged

spleen. The patient is put in the supine position and the examiner palpates as in the classical method except that he dips his fing-ers into the abdomen with each palpation, so that the fluid is displaced temporarily to the side. This facilitates palpation of the spleen.

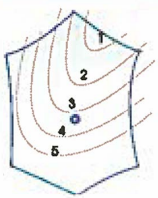


Fig. 3.11 : Palpation of Spleen - Dipping Method

Splenomegaly (Enlarged Spleen)

Table 3.1 : Hackett's Classification of Splenomegaly

Grade	*Stage*	*Examination*
	0	Not palpable
Mild	1	Just palpable by bimanual method
Moderate	2	Mid-way between costal margin and umbilicus
Moderate	3	Upto umbilicus
Severe	4	Between umbilicus and pubic symphysis
Severe	5	Upto pubic symphysis



Mild splenomegaly: Just palpable

Moderate: Easily palpable,but not reaching umbilicus

Massive: Extending up to umbilicus or beyond

Causes of splenomegaly: (Refer Pg.67)

C. **Gall bladder:** The gall bladder is palpated in a similar manner as liver. Normally it is not palpable. When distended, it is palpated as a firm, smooth, rounded or globular swelling with distinct borders just lateral to the rectus abdominis muscle. Its upper border merges with the lower border of liver or disappears beneath the costal cartilage and hence is not usually felt.

Causes of enlarged gall bladder:

1. Carcinoma of the head of the pancreas and malignant obstruction of the common bile duct. This is associated with jaundice (courvoisier's law).
2. Mucocele of the gall bladder due to impaction of a stone at the neck of the gall bladder. Here there is no jaundice
3. Carcinoma of the gall bladder

D. **Kidneys:** The left kidney is palpated by keeping the left hand posteriorly in the loin and the right hand anteriorly in the left lumbar region. Then the patient takes a breath, the left hand is pressed forwards and the right hand backwards, upwards and inwards. The right kidney is likewise palpated on the right side. Normally the kidneys are not palpable unless placed low in position or enlarged. Its lower pole is felt as a rounded firm swelling between both the hands (bimanual palpation) and can be pushed from one hand to the other (ballotable).

E. **Abdomen:** Doughy feel of abdomen in TB peritonitis.

C. Percussion

Uniform enlargement of the abdomen may be because of gas or fluid in the abdomen. In the former there is tympanic note on percussion while in the latter there is dullness.

1. **Shifting dullness:** This is seen with moderate ascites. The abdomen is percussed starting from the midline. The upper border of fluid in each flank is determined. The pleximeter finger is kept in position on one flank and the patient is turned to the other side. After waiting for about 15 seconds, percussion at the same point produces a tympanic note as the intestines float up. The abdomen is then percussed towards the other flank. There is an increased width of dullness on the other side due to shift of fluid.

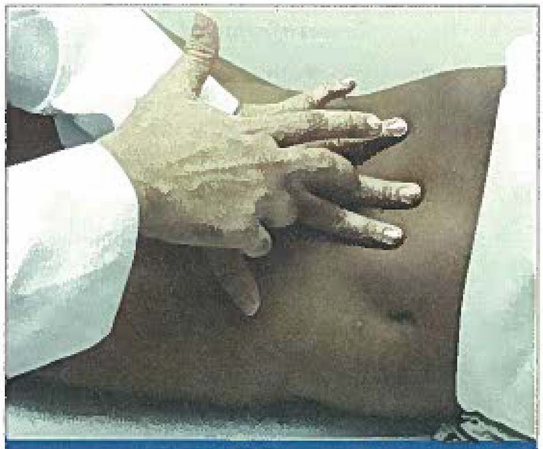


Fig. 3.12: Shifting Dullness

2. **Horseshoe shaped dullness:** This is seen with moderate ascites. The abdomen is percussed in various directions from the umbilicus outwards. Area of dullness appears horse-shaped with a concave upper border. This is because fluid accumulates in the dependent parts and the intestines float up.

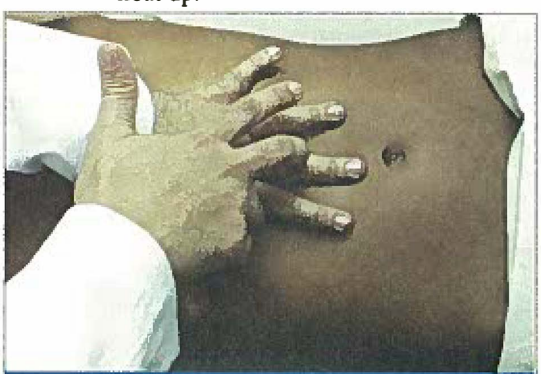


Fig. 3.13: Horseshoe Dullness

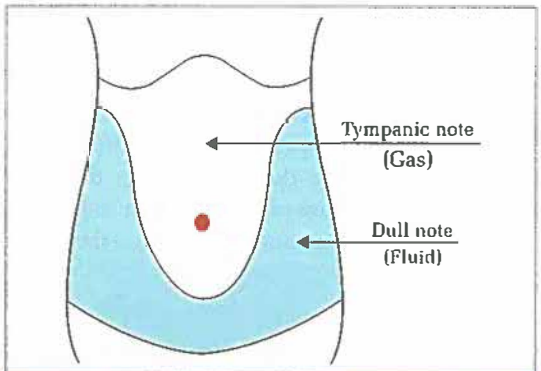


Fig. 3.14: Horseshoe shaped dullness on percussion

3. **Fluid thrill**: This is seen in tense ascites. One hand is kept over one flank and a sharp flick is delivered with the other hand over the opposite flank. The patient is asked to keep ulnar edge of one hand in the midline. A tap is felt by the palpating hand in case of tense ascites.



Fig. 3.15: Fluid Thrill

4. **Puddles Sign**: It is to be elicited in minimal ascites (150 ml). The patient is asked to go "on all fours" so the fluid collects in the mid-abdomen which is dependant. One flank is lightly flicked with one hand and the most dependant part is auscultated. The chestpiece of the stethoscope is then moved to the opposite flank. A change in the intensity of the note heard indicates fluid.

In addition to determining fluid, percussion helps to delineate the outline of an enlarged

viscera or abdominal tumor. It helps to differentiate enlarged spleen (dull note) from an enlarged left kidney (resonant note because of the intervening colon).

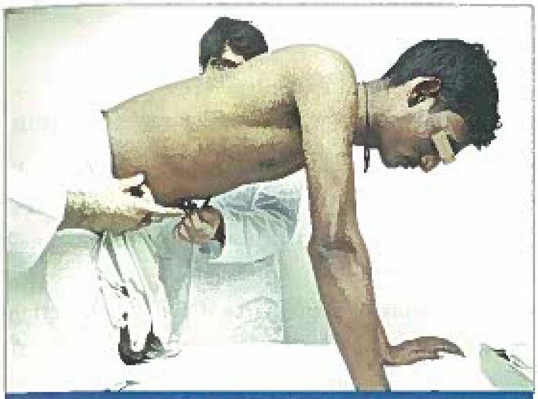


Fig. 3.16 : Puddles Sign

5. **Tidal Percussion** : The upper border of the liver can be accurately determined by percussion.

Liver Span : Percussion is started anteriorly in the right midclavicular line from second intercostal space downwards and repeated in the anterior, mid and posterior axillary lines and the scapular line posteriorly. The normal liver dullness is in the fifth space in the midclavicular, seventh space in the anterior axillary and ninth space in the scapular lines. The normal liver span in an adult as judged by liver dullness measures 10-12 cm in men and 8-11 cm in women. The upper border of the liver may be percussed in the fourth or third space in the midclavicular line in patients with amebic abscess of liver or any abscess on the superior surface of liver. The liver dullness is lower in the sixth or seventh right intercostal space in emphysema, right-sided pneumothorax, when there is air in the peritoneal cavity, acute yellow atrophy of the liver and in terminal cirrhosis.

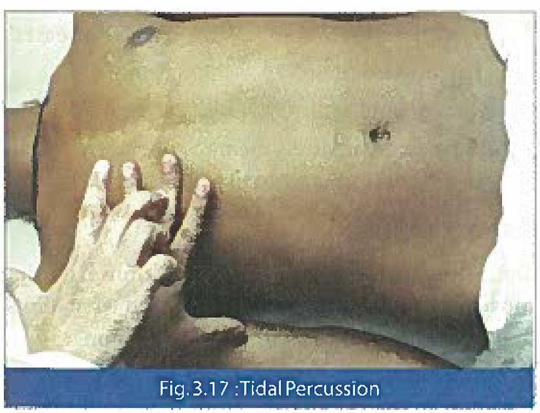


Fig. 3.17 : Tidal Percussion

D. Auscultation

Auscultation of the abdomen is done for the following:

1. **Peristalsis** : These are intestinal sounds generated by contractions of the muscular walls of the gut and the resultant vibration of the gut wall produced by movement of a gas-fluid mixture through the gut. These bowel sounds (peristalsis) persist in the fasting state due to the presence of intestinal secretions and swallowed air. Loud bowel sounds (hyperperistalsis) accompanied by abdominal distension and crampy abdominal pain suggests partial bowel obstruction. Absence of bowel sounds for at least 5 minutes strongly suggests bowel atony or ileus. Borborygmi refers to audible peristalsis which can be heard even without a sthethoscope.
2. **Arterial Bruit** : These are variable harsh sounds in tempo with the pulse due to turbulence in arterial flow. This may occur by unusually acute angulations at arterial branch points, arteriosclerotic plaques, extreme tortuosity of an artery, compression of an artery or massive blood flow through very vascular tumors like hemangioma or hepatoma. Bruits over the liver suggests very vascular tumor like hepatoma or angioma. Similarly, over the spleen it suggests vascular tumor. Bruit over the aorta, if soft, has no significance. However a loud bruit suggests aortic aneurysm, atherosclerosis or extreme tortuosity of the aorta, Bruit over the kidneys in the flanks suggests renal artery stenosis.

3. **Venous Hum :** Venous hum is continuous, softer and lower pitched than bruit. It signifies portal systemic shunting of venous flow when portal flow is obstructed. It is usually heard over the liver area and umbilicus.

Fetor Hepaticus

Definition : This is the fecal smell of the breath similar to that of a freshly opened corpse of a mouse.

Mechanism: Normal demethylating process is inhibited by liver damage. Hence, methionine is converted to methyl mercaptan, which gives the typical smell.

Causes

1. Acute liver cell disease/failure: Poor prognostic sign and often precedes coma.
2. Extensive portal collateral circulation

Spider Nevi

Synonyms: Arterial spider, Spider telangiectasis, Spider angioma

Definition: An arterial spider is a central arteriole, from which numerous small vessels radiate resembling a spider's legs.

Sites: Arterial spiders are found in the territory of the superior vena cava. They are commonly seen on the face, neck, forearm and shoulder.

Appearance: They range in size from 3 to 15 mm in diameter. They are pulsatile and blanch on pressure. When the skin is stretched or compressed they fill from the centre to the periphery.

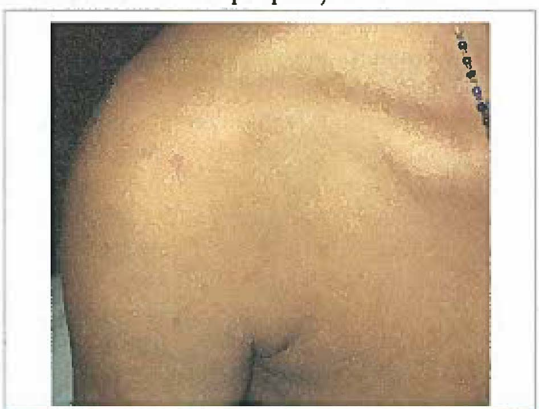


Fig. 3.18 : Spider nevi

Small vessels in the skin associated with arterial spiders have been compared to the silk thread in American paper money. Therefore, the skin is called **paper money skin**.

Causes

1. In alcoholics
2. Cirrhosis
3. Viral hepatitis
4. Normal persons especially children
5. Pregnancy
6. Rheumatoid arthritis
7. Thyrotoxicosis

Mechanism : The selective distribution of spider nevi is not understood.

1. Exposure of upper parts of the body to certain elements may damage the skin so that it is susceptible to develop spider nevi when an appropriate internal stimulus exists.
2. Estrogen excess may be responsible. It forms arterioles of the endometrium in uterus during pregnancy, which resembles spider nevi.

Significance : Appearance of fresh spiders suggests progression of liver damage. ***Spider nevi disappear if*** liver function improves or blood pressure falls due to shock or hemorrhage.

Palmar Erythema

Definition : Palmar erythema is bright red warm palms. The thenar and hypothenar eminences and soles of feet are especially erythematous. The erythema blanches on pressure.

Causes

1. In alcoholics
2. Cirrhosis
3. Viral hepatitis
4. Thyrotoxicosis
5. Rheumatoid arthritis
6. Leukemia
7. Pregnancy
8. Febrile diseases
9. Familial

Significance : Palmar erythema is not so frequently seen in cirrhosis, as are vascular spiders.

Asterixis (Flaps)

Definition : Asterixis are rapid flexion-extension movements at metacarpophalangeal and wrist joints. Therefore they are seen as a flapping tremor.

Significance : In liver disease, it indicates that the patient is in hepatocellular failure.

Demonstration : The patient is asked to stretch out his hands in front of him, parallel to the ground, with fingers extended and abducted.

Causes

1. Hepatocellular failure
2. Uremia
3. Respiratory acidosis - CO_2 narcosis
4. Drugs - anticonvulsants, (phenytoin, carbamazepine and phenobarbitone).
5. Brain stem lesions

3 〉 Hepatomegaly

Definition : Hepatomegaly means enlarged liver. An enlarged liver may not always be palpable if it is slightly enlarged and a palpable liver is not always enlarged.

Causes

I. Infective:
- A. *Along the biliary tree: Cholangitis.*
- B. *Along the portal vein:*
  1. Amebiasis
  2. Schistosomiasis
  3. Bacterial infections
- C. *Along the hepatic artery:*
  1. Bacterial: Typhoid, brucellosis, tuberculosis
  2. Viral: Infective hepatitis, infectious mononucleosis
  3. Spirochetal: Syphilis, Weil's disease
  4. Protozoal: Malaria, kala azar
  5. Fungal: Actinomycosis, histoplasmosis
- 6. Parasitic: Echinococcus

II. Congestive:
- A. Cardiac failure
- B. Cardiomyopathy
- C. Constrictive pericarditis
- D. Budd Chiari syndrome

III. Cirrhosis (in early stages)

IV. Biliary obstruction:
- A. Gall stones
- B. Strictures

V. Degenerative and Infiltrative disease:
- A. Fatty
- B. Amyloid
- C. Gaucher's disease
- D. Niemann Picks disease
- E. Hodgkin's disease
- F. Leukemias
- G. Multiple myeloma

VI. Tumors:
- A. Primary - Hepatocellular, cholangiocellular sarcomas
- B. Secondary

VII. Toxic: Alcohol, arsenic, phosphorous, chlorpromazine

Painful Hepatomegaly

1. Cardiac failure
2. Viral hepatitis
3. Hepatic amebiasis
4. Pyemic abscess of liver
5. Hepatoma
6. Actinomycosis of liver
7. Weil's disease (Leptospirosis)

Pulsatile Liver: Tricuspid insufficiency

Bruit over the Liver

1. Hepatoma
2. AV malformation

Differential Diagnosis

I. Viral Hepatitis **(Refer Pg. 71)**
- A. Prodromal symptoms of gastrointestinal upset e.g. anorexia, abdominal discomfort
- B. Fever, malaise
- C. Dark colored urine
- D. Jaundice on 3rd or 4th day
- E. Enlarged tender liver with mild intercostal tenderness
- F. Palpable spleen in 25% cases

II. Amebic Liver Abscess
- A. Moderate to huge, tender liver
- B. Fever with rigors

C. Rt. upper abdominal tenderness
D. Blood and mucus in stools in the past
E. Shift of liver dullness upwards
F. Investigations-moderate leucocytosis, diminished movements of diaphragm on screening, aspiration of anchovy sauce material from liver with demonstration of trophozoites in it.

III. Pyemic Liver Abscess

A. *Signs of septicemia*
   1. High fever with rigors and profuse sweating
   2. Anemia, tachycardia, leucocytosis, positive blood culture

B. *Local signs*
   1. Pain, tenderness, edema and redness over lower right intercostal spaces
   2. Marked tender hepatomegaly
   3. Shift of liver dullness upwards

IV. Malaria : (Refer Pg. 90)

A. Fever with chills and rigors, coming down with sweating. Paroxysms of fever every 72 hours with *Pl. malariae* and 48 hours with the other types
B. Splenomegaly, mild to massive, always present when liver is enlarged
C. Anemia
D. Peripheral blood smear and bone marrow show presence of parasites

V. Kala Azar : (Refer Pg. 95)

A. Long continued fever
B. Hepatosplenomegaly
C. Anemia, weight loss
D. Dark pigmentation
E. Demonstration of Donovan bodies in reticulo-endothelial cells e.g. in bone marrow, liver and spleen
F. Serological tests - Napier's Aldehyde test, Antimony, Brahmachari's and W.K.K. complement fixation test, immuno-fluoscent. Antibody test, Indirect Hemogglutination test and ELISA may be positive

VI. Hydatid Cyst

A. The liver is non-tender (unlike liver abscess). If cyst is on the surface, rounded, localized, smooth swelling (unlike carcinoma and syphilis) is present
B. When the cyst is tense there may be a hydatid thrill
C. No jaundice or splenomegaly is present
D. There is history of contact with dogs
E. Urticaria may be present if hydatid fluid is absorbed
F. *Investigations:* Eosinophilia, positive complement fixation test, calcification of cyst wall demonstrated by radiology and positive Casoni's test

VII. Congestive Hepatomegaly

A. Slight to markedly enlarged, firm, smooth, tender liver, pulsatile if there is tricuspid incompetence
B. Other evidence of cardiac failure: Edema of feet, raised JVP and ascites
C. In severe cases, dyspepsia and jaundice
D. Evidence of cardiac lesion

VIII. Cirrhosis of Liver: (Refer Pg. 82)

A. ***Signs of liver cell failure:*** Palmar erythema, spider nevi, gynecomastia, testicular atrophy, flapping tremors, ascites, jaundice, Dupuytren's contracture, parotid gland swelling, alopecia, loss of libido.
B. ***Evidence of portal hypertension:*** Splenomegaly, ascites (out of proportion to edema of feet), hematemesis, dilated veins over chest well, bleeding per rectum

IX. Hemochromatosis

A. A triad of cirrhosis, diabetes mellitus and pigmentation of skin may be present.
B. Ascites is rare
C. Cardiac complications may occur
D. Increased stores on iron in serum and reticuloendothelial cells

X. Malignancy

A. Markedly enlarged liver with upward

increase of liver dullness, a hard often irregular edge, with uneven knobby hard nodules, sometimes umbilicated. Sudden enlargement of the nodule is due to hemorrhage

B. Pain in the hepatic region and over the right shoulder. Dragging and fullness in the right hypochondrium

C. Jaundice - deep yellow to deep olive green

D. Cachexia, loss of weight, and dry shriveled skin may be present

E. Ascites and edema of legs may occur

F. There may be evidence of primary or pre-existing cirrhosis

XI. Biliary Obstruction

(Commonly due to gall stones):

A. Deeper jaundice than in cirrhosis

B. History of colicky pain

C. Clay-coloured stools with dark urine

D. Fever with rigors due to cholangitis

XII. Alcoholic Liver Affection:

A. Smooth, tender, enlarged and firm liver is present.

B. Right upper abdominal pain, anorexia, nausea and vomiting may occur.

C. There may be profound weakness, jaundice, spider nevi and palmar erythema.

XIII. Leukemias (Refer Pg. 102)

XIV. Hodgkin's Disease (Refer Pg. 107)

XV. Amyloidosis

A. Evidence of chronic wasting disease

B. Liver large, smooth, rubbery and non-tender

C. Jaundice, ascites and generalized edema

D. Splenomegaly

E. Albuminuria (kidney affection) and diarrhea (gastrointestinal affection)

F. Congo Red test is positive. Liver biopsy, kidney biopsy and rectal biopsy for amyloid infiltration may also be positive.

4 〉 Splenomegaly

Definition : Splenomegaly is an enlargement of the spleen (Refer Pg. 55). The spleen has to be two and a half times its normal size to become palpable; therefore an enlarged spleen is not always palpable. In ptosis of spleen, it is palpable, though not enlarged.

Evidence of Enlargement of Spleen

1. Predominant left sided abdominal distension, if massive splenomegaly
2. Splenic mass moves downwards on inspiration
3. A notch is felt on the anterior border
4. Left abdominal pain if massive splenomegaly

Causes

I. Infective:

A. *Bacterial:* Septicemia, SBE, typhoid, syphilis.

B. *Viral:* Infective hepatitis, infectious mononucleosis

C. *Protozoal:* Malaria, kala azar, trypanosomiasis

D. *Fungal:* Histoplasmosis

II. Congestive:

A. *Suprahepatic:*

1. Congestive cardiac failure
2. Constructive pericarditis
3. Budd Chiari syndrome

B. *Hepatic:*

1. Cirrhosis
2. Schistosomiasis
3. Sarcoidosis
4. Congenital hepatic fibrosis

C. *Intrahepatic:* Portal vein thrombosis - Extra hepatic portal HT.

III. Blood Diseases:

A. Polycythemia rubra vera

B. Hemolytic anemia - Thalassemia

C. Leukemias

D. Lymphoma

E. Myelofibrosis

Table 3.2: Distinguishing Features between Splenomegaly and other Left Sided Abdominal Masses

	Spleen	Kidney
1. Enlargement	Forward and inward	In the loin
2. Notch	Present	Absent
3. On inspiration	Moves well	Moves less
4. Hand insinuation between lump and lower costal margin	Not possible	Possible
5. Loin fullness	Absent	Present
6. Percussion note	Dull	Resonant

	Spleen	Malignant growth of stomach / pancreas
1. Edge, notch	Present	Absent
2. Crossing to right side	If splenic enlargement is severe, it crosses the midline at or below the umbilicus	In pancreatic enlargement the tumor crosses the midline above the umbilicus

	Spleen	Carcinoma Splenic flexure of colon
1. *Direction of* enlargement	*More forwards* and inwards	*Transverse*
2. Edge, notch	Present	Absent
3. Percussion	Dull	Resonant (rarely dull)
4. Intestinal symptoms	Abdominal	Blood and fullness mucus in stools, alternating diarrhea and constipation
5. Lymphadenopathy	Absent	Left supraclavicular glands may be palpable
6. Barium studies	Normal	Show pathological lesion

IV. Infiltrative and degenerative disorders:

A. Gaucher's disease

B. Niemann Picks disease

C. Amyloidosis

V. Neoplastic: Hemangiomas, sarcomas, cysts, metastasis

VI. Miscellaneous:

A. Connective tissue disorders.

B. Rupture of spleen and hematoma.

Types of Splenomegaly

I. Massive Splenomegaly:

A. Kala azar , chronic malaria

B. Chronic myeloid leukemia

C. Extrahepatic portal hypertension

D. Myelofibrosis

II. Moderate Splenomegaly:

A. All the above as in I

B. Hodgkin's disease, leukemias, lymphomas, polycythemia rubra vera

C. Hemolytic anemias

D. Biliary cirrhosis

E. Hemochromatosis

F. Tumors and cysts

G. Tuberculosis

III. Mild (slight) Splenomegaly:

A. All the above as in I & II

B. Acute infections: Typhoid, septicemia, IE

IV. Acute Splenomegaly:

A. Acute infectious fevers: Typhoid, malaria, IE

B. Injury: Hematoma, ruptured spleen

C. Vascular causes: Splenic infarct, thrombosis of splenic vein

D. Connective tissue disorders: SLE, rheumatoid arthritis, Felty's and Still's disease

E. Tumors and cysts

V. Hepatosplenomegaly:

A. *Infective*: Malaria, kala azar, infective hepatitis, IE

B. *Hematological conditions:* Leukemia, lymphomas, Hodgkin's disease, chronic hemolytic anemias

C. *Congestive:* CCF, pericarditis, Budd Chiari syndrome and portal hypertension

D. *Storage disorders:* Glycogen storage, Amyloidosis

VI. Hepatosplenomegaly with Lymphadenopathy

A. Acute Leukemia

B. Hodgkin's and Non-Hodgkin's Lymphomas

C. Infectious mononucleosis
D. Disseminated Tuberculosis
E. HIV infection or AIDS
F. Sarcoidosis

VII. Splenomegaly with Pallor and Icterus:

A. Hemolytic anemia
B. Cirrhosis of liver with portal hypertension

VII. Splenomegaly with Petechiae and Ecchymosis:

A. Acute Leukemia, blast crisis in CML and CLL stage IV
B. SBE
C. SLE

Differential Diagnosis

The following are discussed under hepatomegaly:

1. Viral hepatitis
2. Pyemic liver abscess
3. Malaria, kala azar
4. Hydatid cyst
5. Congestive hepatomegaly
6. Cirrhosis
7. Leukemias, Hodgkin's disease
8. Amyloidosis

I. Infective Endocarditis (IE)

A. Feature of septicemia
B. Embolic episodes
C. Cardiac lesions

II. Infectious Mononucleosis

A. Onset with fever, sorethroat, rash, pruritus
B. Hepatosplenomegal with lymphadenopathy
C. Mild transient jaundice may occur
D. Paul Bunnell test may be positive (1:56)
E. Typical peripheral smear: Lymphocytosis and Downey cells

III. Enteric Fever (Typhoid): (Refer Pg. 98)

A. Continuous fever with stepladder rise
B. In second week rose spots may appear
C. In third week relative bradycardia with dicrotic pulse, soft splenomegaly and gastrointestinal disturbances occur
D. Rising Widal test titre, and positive blood culture help to confirm the diagnosis

IV. Portal Vein Occlusion

There is sudden onset of severe abdominal pain, hematemesis, tender splenomegaly and ascites

V. Polycythemia Vera

A. Brick red colour of skin, cyanosis of lips and ears
B. Hepatosplenomegaly
C. Nervous symptoms
D. Hemorrhages

VI. Hemolytic Anemias

A. Anemia, jaundice, splenomegaly
B. Pigmented gallstones
C. Ulcer over the malleoli

VII. Felty's Syndrome

Felty's syndrome is characterized by chronic splenomegaly with chronic rheumatoid arthritis and neutropenia. There may be associated hepatomegaly, lymphadenopathy, weight loss, pigmentation of skin and ulceration of legs.

VIII. Systemic Lupus Erythematosus

A. General symptoms: Fever and weight loss
B. Skin lesions: Erythema, purpura, urticaria, malar rash and subcutaneous nodules
C. Polyarthritis
D. Hepatosplenomegaly
E. Other system involvement
F. L.E. cell demonstration.
G. ANA and double strand DNA test positive

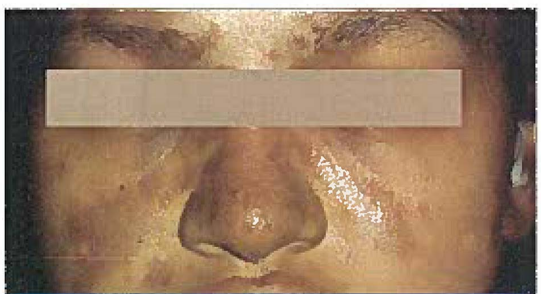


Fig. 3.19: Malar rash (butterfly rash) of SLE

5 › Ascites

Definition : Ascites is the accumulation of free fluid in the peritoneal cavity

Diagnosis

I. Generalized distension of abdomen with more fullness in the flanks

II. Shifting dullness can diagnose 500 ml fluid

III. Horse-shoe-shaped can diagnose 1 litre fluid

IV. Fluid thrill seen in tense ascites

V. Other signs:
   - A. Transverselystretchedumbilicus('laughing' umbilicus)
   - B. Divarication of recti
   - C. Tense and shiny skin
   - D. Widened subcostal angle
   - E. Lower ribs pushed outwards and upwards

VI. Diagnosis of small quantity of fluid (**Puddle sign**): The patient is put in knee chest position so that the fluid gravitates down to the anterior abdominal wall. The stethoscope is placed over this and the anterior abdominal wall is flicked for a puddle sound. This can diagnose even 150 ml fluid.

Causes

I. Transudates
- A. Cardiac failure
- B. Hypoproteinemia
- C. Anemia
- D. Beriberi
- E. Nephrotic syndrome
- F. Portal hypertension
- G. Epidemic dropsy
- H. Polyserositis
- I. Meigs syndrome

II. Exudates
- A. Peritoneal disease
  1. Infections: Tuberculosis, bacterial, fungal and parasitic infections
  2. Neoplasms
- B. Collagen disorders
- C. Eosinophilic gastroenteritis
- D. Gynecological: Endometriosis, struma ovarii

III. Miscellaneous
- A. Pancreatic
- B. Bile
- C. Chylous
- D. Myxedema

Table 3.3 : Transudate and Exudate

		Transudate	*Exudate*
1.	Process	Passive	Active
2.	Serous structures	Others	Only local
3.	Appearance	Clear	Clear/turbid
4.	Specific Gravity	< 1.015	> 1.015
5.	Proteins	< 3 gm/dl	> 3 gm/dl
6.	Cells	Few mesothelial cells	Polymorphs or Lymphocytes
7.	Clot formation	Nil	Present
8.	Gradient*	≥ 1.1 g/dL	< 1.1 g/dL

Serum albumin minus ascitic fluid albumin (SAAG)

Routine exudate / transudate system is no longer used in ascites

It is advisable to calculae SAAG to classify ascite as follows:

1. **High SAAG ascites (SAAG ≥ 1.1 g/dl)** - It indicates portal Hypertensive Ascites with sensitivity & specificity of 97%. Causes : i) cirrhosis of liver; ii) cardiac cirrhosis; iii) Budd Chiari syndrome; iv) veno occlusive disease; v) portal vein thrombosis and vi) Fulminant liver failure
2. **Low SAAG ascites (SAAG < 1.1 g/dl).** Causes : i) Tuberculosis; ii) Nephrotic syndrome; iii) pancreatitis; iv) biliary ascites; v) peritoneal carcinomatosis

Mechanism of Ascites Production

1. Increased hydrostatic pressure intravascularly
2. Decreased osmotic pressure intravascularly due to hypoproteinemia
3. Increased osmotic pressure extravascularly
4. Increased lymphatic pressure

Causes of Hemorrhagic Fluid

1. Trauma of thoracic duct
2. Parasite infections e.g. filariasis
3. Tuberculosis
4. Thrombosis of subclavian vein
5. Malignancy involving thoracic duct

Causes of Purulent Fluid

1. Abdominal infections.
2. Penetrating wound of abdomen
3. Pyemia and septicemia
4. Rupture or perforation of an organ
5. Ruptured amebic liver abscess
6. Pelvic inflammatory disease

Causes of Ascites Disproportionate to Edema of Feet

1. Cirrhosis of liver
2. Constrictive pericarditis
3. Restrictive cardiomyopathy
4. Hepatic venous occlusion
5. Tuberculous peritonitis
6. Intra-abdominal tumor

Differential Diagnosis

I. Cirrhosis of Liver

- A. Signs of liver cell failure
- B. Signs of portal hypertension
- C. Ascitic tap: Transudate

II. Tuberculous Peritonitis

- A. Fever with evening rise in temperature
- B. Night sweats
- C. Tender doughy abdomen
- D. Ascitic tap: Exudate
- E. Liver and spleen usually not palpable

III. Malignant Peritonitis

- A. Diffuse abdominal pain
- B. Weight loss
- C. Hemorrhagic ascitic fluid with positive malignant cells

IV. Portal Vein Thrombosis

Sudden rapid development of ascites, melena, splenomegaly and hematemesis.

V. Constrictive Pericarditis

- A. Pulsus paradoxus
- B. Raised JVP on inspiration (Kussmaul's sign)
- C. Apex beat not palpable
- D. Hepatomegaly with ascites
- E. Pericardial knock
- F. Calcification of pericardium on X-ray. On screening poor pulsations

VI. Budd-Chiari Syndrome (Hepatic vein thrombosis)

- A. Large, tender liver
- B. Absent hepatojugular reflux
- C. Biopsy: Centrilobular congestion and necrosis

VII. Bacterial Peritonitis

Signs of septicemia with ascites and a focus of infection (e.g. indwelling catheter).

VIII. Pancreatic Ascites

Intermittent abdominal pain with massive refractory ascites and increased serum amylase.

IX. Congestive Cardiac Failure

- A. Starts with edema of feet, more in the evening
- B. Raised JVP
- C. Tender hepatomegaly
- D. Heart size may be enlarged

X. Nephrosis

- A. Starts with puffiness of face, more in the morning
- B. Pallor
- C. Massive proteinuria
- D. Hypercholesterolemia

XI. Anemia, Hypoproteinemia

- A. Gross anemia
- B. Edema out of proportion to ascites
- C. Serum proteins Albumin-globulin ratio (A:G) reversed

XII. Beriberi

- A. Cardiac enlargement and tachycardia
- B. Tender calf muscles with blunting of sensations and absent deep reflexes

XIII. Epidemic Dropsy

- A. Family history of edema
- B. Preceding or accompanying other gastro intestinal symptoms

C. Cardiac symptoms may be present

D. Diffuse blotchy erythema of skin and other cutaneous nodules

E. Glaucoma

F. Detection of argemone oil in cooking medium

Management of Ascites

I. Treatment of cause

II. Diet: Low sodium diet

III. Diuretics: Spironolactone or furosemide or combination

IV. Abdominal paracentesis if cardiorespiratory embarrassment with or without albumin

V. TIPS (Transjugular intrahepatic portosystemic shunt)

VI. Porta venous shunts for refractory ascites

6 › Abdominal Lump

Physical Examination

I. General

Appearance: Anemic, jaundiced or emaciated. Lymph nodes, especially supraclavicular.

II. Local

A. *Inspection:*

1. Skin overlaying
2. Position, size, shape and surface
3. Movement on respiration
4. Hernial sites
5. Scrotum

B. *Palpation:*

1. Local temperature
2. Tenderness
3. Muscular rigidity
4. Confirming inspection findings regarding the lump
5. Margins: It must be determined whether it is possible to get all round the lump or not, well defined or ill-defined, notch present or absent
6. Consistency: Soft, firm or hard. Hard swellings are usually malignant, soft swelling may be cystic.
7. Mobility: This should be determined by hand in all directions, i.e. from side to side and above downward.
8. Parietal or intra-abdominal: This can be found out by making the abdominal muscles taut by raising the shoulders or the legs. If the lump becomes less prominent it is intra-abdominal. If it becomes more prominent it is parietal. If mobile over the contracted muscles it is superficial to the muscles and if it is fixed it is adherent to the muscle
9. Hernial sites for expansile impulse on coughing
10. Pulsations (if present): Expansile (aortic) or transmitted (lump over aorta). If lump is not adherent to aorta, pulsations disappear when the patient is in knee-chest position.

C. *Percussion:*

1. For dullness of the tumor
2. Dullness over liver and spleen or resonance over kidneys
3. Fluid thrill and shifting dullness present in ascites, absent in ovarian tumor

D. *Auscultation:* For rub (perisplenitis and perihepatitis)

Differential Diagnosis

Abdominal Quadiants : The differential diagnosis of abdominal lump can be made based on location of the lump in one of the abdominal quadrant.

- The abdomen is divided into nine regions by four imaginary planes (two horizontal and two vertical).
- Two horizontal planes are transpylonic and transtubercular planes.
- Transpyloric plane - It passes through the tips of the 9th costal cartilage anteriorly and through

the body of LI Vertebra near its lower body posteriorly.

- Transtubercular plane - It passes through the tubercles of the iliac crest and the body of L5 vertebra.
- Two vertical lines are the right & left lateral planes corresponding to the midclavicular line or either side.

Right Hypochondriac Region

I. **Swellings in the Abdominal Wall : Cold Abscess**

1. Fluctuant swelling with no signs of inflammation
2. Swelling becomes prominent when the abdominal muscles contract
3. Irregularity in the affected rib or deformity of the spine.

II. **Intra-Abdominal Swellings**

A. Hepatic

1. It moves with respiration but is not mobile sideways
2. The swelling is continuous with the liver dullness without a band of colonic resonance

B. Gall Bladder

1. Oval smooth swelling, the size of an egg
2. Moves with respiration, can be moved sideways but cannot be pushed down into the loin (like kidney swelling)

Chronic Cholecystitis and Cholelithiasis

1. Pain over the right rectus muscle radiating to the inferior angle of scapula, aggravated after fatty meals. Often the patient makes an attempt to get relief by frequent belching or vomiting but relief is seldom complete.
2. Gall bladder may be palpable.
3. Murphy's sign is positive: i.e. Tenderness under the right costal margin at the lateral border of the rectus muscle when the patient takes a deep breath. This occurs due to the descent of the inflamed gallbladder, which touches the examiner's fingers.

   If a stone is present in the common bile duct there is a triad of intermittent colic, intermittent jaundice and fever with chills and rigors.
4. **Courvoisier's law** : In a patient with obstructive jaundice, a palpable gall bladder is seldom due to gall stones. This is because the gall bladder is usually shriveled & non distendable in long standing gall stone disease.

   Therefore, in a pt. with obstructive jaundice, a palpable gall bladder indicates malignancy of gall bladder or pancreas.

   Exceptions to courvoisiers law i.e. Obstructive jaundice with a palpable gall bladder due to gall stone occurs in

   i. Double impaction of the stone (in the bile duct & in the cystic duct)

   ii. Gall stones in the cystic duct (Mirizzi's syndrome)

   iii. Mucocele of gall bladder

C. Sub-Phrenic Abscess

1. Pain in the right hypochondrial region referred to the shoulders
2. Diffuse tender swelling in the right hypochondrial region
3. Signs of septicemia: High fever with rigors, sweating and marked tachycardia
4. Screening: Raised and fixed diaphragm with gas under it
5. Features of the causative condition e.g. perforated peptic ulcer, liver abscess

D. Stomach and Duodenum

1. Carcinoma of Pylorus:
   a. There is an irregular firm lump, which moves on respiration
   b. Patient is usually elderly and has anorexia and weight loss

c. Barium meal would show filling defect

2. Sub-acute Perforation of a Peptic Ulcer
   a. Localized, tender, inflammatory mass may be present with a central abscess
   b. History of peptic ulcer
   c. Barium meal would reveal the ulcer

E. Hepatic Flexure of Colon

1. Tuberculosis (Hypertrophic variant)

   This usually causes a lump in the right iliac fossa, which may be drawn towards the right hypochondriac region by fibrosis.

2. Carcinoma of Colon
   a. This commonly occurs in men above the age 40 years.
   b. There is alternate diarrhea and constipation.
   c. The lump is irregular, firm and moves poorly on respiration.
   d. Occult blood may be present in stools.
   e. Filling defect may be seen on barium enema.

3. Intussusception
   a. There is sudden intermittent abdominal pain with vomiting.
   b. Absolute constipation may be replaced later by passage of blood and mucus (red current jelly) per anum without fecal odour.
   c. There may be curved, sausage shaped lump in the line of the colon with its concavity towards the umbilicus. The lump may harden under examining fingers synchronously with an attack of screaming.
   d. Barium enema would show typical pincer shaped ending of the radio-opaque material.

F. Kidney Lump

General features

- Reniform or kidney shaped mass which moves with respiration
- It is better felt in the loin than anteriorly
- It is usually ballotable
- There is a band of colonic resonance over the swelling

1. Hydronephrosis
   a. Cystic fluctuant swelling with typical characteristics of a renal lump
   b. Pain in the loin if it is very large
   c. Hematuria
   d. IVP: Clubbing of the minor calyces and dilatation of the pelvis

2. Pyonephrosis
   a. All the features of hydronephrosis
   b. Renal angle tenderness (i.e. angle between teh 12th sib & outer border of erector spinae).
   c. Septicemia: Fever with rigors and sweating, dry furred tongue, leucocytosis and positive blood culture
   d. Urine examination: Pus cells and white cell casts present
   e. Cystoscopy: Red and swollen ureteric orifice on the affected side

3. Polycystic Kidneys
   a. Bilateral renal swelling in a man with or without dragging pain in the loin
   b. Hematuria
   c. Uremia
   d. Urine: Low specific gravity with albumin and a few casts
   e. IVP: Attenuated and elongated (spider leg) calyces with terminal clubbing or cupping.

4. **Renal Stones**
   a. Fixed, dull aching pain in the renal angle radiating from loin to groin aggravated by movements and relieved by rest
   b. Tenderness in the renal angle
   c. Renal lump palpable only if associated hydronephrosis
   d. Albuminuria, pyuria and hematuria may be present
5. **Wilm's Tumor**
   a. Commonly seen in boys below 5 years of age.
   b. Painless, huge enlargement of kidneys without hematuria (hematuria occurs later when the tumor bursts into the renal pelvis)
   c. IVP: Filling defect in the renal pelvis or spider leg deformity of the calyces. Plain X-ray abdomen often reveals the tumor
6. **Hypernephroma**
   a. Common in adult males
   b. Painless lump in the abdomen
   c. Painless hematuria
   d. Development of recent varicocele
   e. Evidence of metastasis: Spontaneous fracture, hemoptysis
   f. IVP: Spider leg deformity of the calyces, frequently distorted by the tumor. Complete absence of excretion or scattered patches of dye in kidney areas.
7. **Perinephric Abscess**
   a. Evidence of septicemia
   b. Tenderness and rigidity in the renal angles.
   c. Scoliosis of the lumbar spine with concavity towards the affected side.

Epigastrium

I. **Epigastric Hernia**
   A. Swelling in the midline in the parietal wall between xiphisternum and umbilicus
   B. Dragging pain, discomfort or pain after food resembling peptic ulcer

II. **Stomach and Duodenum**
   A. Congenital Hypertrophic PyloricStenosis
      1. Common in infants about 3 weeks old
      2. Projectile vomiting and wasting
      3. Visible peristalsis of the stomach
      4. Pylorus may be felt as a well defined cylindrical lump
   B. Carcinoma of Stomach: Refer Pg. 73

III. **Liver: Refer Pg. 73**

IV. **Subphrenic Abscess: Refer Pg. 73**

V. **Kidneys: Refer Pg. 74**

VI. **Transverse Colon: Refer Pg. 74**

VII. **Pancreas:**

Pseudopancreatic Cyst

It is a collection of fluid in the lesser sac of the peritoneal cavity, resulting from trauma or inflammation.

Features:

1. Smooth rounded fluctuant swelling
2. Barium meal and abdominal sonography will show the swelling to be posterior to the stomach

VIII. **Aorta** *(Aneurysm of the upper part of the abdominal aorta):* Swelling in the epigastrium exhibits expansile pulsation. (It can be differentiated from the transmitted pulsations by the knee elbow position).

Left Hypochondriac Region

I. **Parietal Swellings:** Refer below.

II. **Spleen:** Refer Pg. 67

Right and Left Lumbar Regions

I. **Parietal Swellings**
   A. Umbilical Hernia
      1. Common in fat multiparous women above the age of 40 years
      2. Swelling situated just above the umbilicus where the two recti divaricate and thus allow the hernia to come out. Expansile impulse on

coughing and reducibility of swelling .is present

Desmoid Tumor of the Rectus Sheath

It is a fibroma that arises from a deeper part of the rectus abdominis muscle either spontaneously or after an abdominal operation. The features are:

1. It is common is females
2. Firm rounded swelling which recurs after operation (Recurrent growths become more malignant than the original one)

II. Small Intestine and Mesentery

Tuberculosis with Tabes Mesenterica

1. Irregular firm lump in sickly children and young adults
2. Subacute intestinal obstruction
3. Tuberculous lesions in the lungs and lymph nodes

III. Retroperitoneal Sarcoma

1. Young patient
2. Huge, firm, nodular mass attached to the posterior abdominal wall
3. Edema of feet if there is pressure on inferior vena cava

IV. Stomach and Duodenum: Refer Pg. 73

V. Colon: Refer Pg. 74

Right Iliac Fossa

I. Parietal Swellings: Refer Pg. 75

II. Appendicular Lump

1. Irregular, firm, tender lump initially fixed, slightly movable later and tympanic
2. Leucocytosis
3. Signs of inflammation over the skin if the abscess approaches the surface

III. Ileocecal Region

A. Hyperplastic Ileocecal Tuberculosis

1. Irregular, firm, tender, intermittent lump of long duration
2. Caecum is pulled upwards
3. Tuberculous manifestations in lymph nodes and lungs
4. Barium meal: Filling defect with spasm of the terminal ileum and elevated position of the cecum

B. Carcinoma of the Cecum : Refer carcinoma of colon, Refer Pg. 74

C. Amebic Typhlitis

1. Irregular, firm, tender lump
2. History of amebic dysentery
3. Stools will show E. histolytica

D. Impaction by Round Worms

Irregular lump

IV. Iliopsoas Sheath

A. Iliac Abscess

This results from infection of a hematoma in the traumatized iliacus muscle. It resembles appendicular lump except:

1. The symptoms are all along over the iliac fossa and not shifted to this area
2. A clear space is found between the abscess and the iliac crest in case of an appendicular lump but not in an iliac abscess

B. Cold Abscess from Pott's Disease

1. Since it gravitates down deep to the inguinal ligament into the thigh, fluctuation on either side of the inguinal ligament is present.
2. Gibbus of the spine clinically and confirmed radiologically.

V. Gall-Bladder

A huge distended gall bladder with enlarged liver may descends as low as the right iliac fossa.

VI. Unascended Kidneys

1. Swelling characteristically reniform
2. IVP: Pelvocalyceal system in connection with the swelling

VII. Undescended Testes

When palpable, it is always pathological:

1. Hard, irregular, fixed lump if malignant
2. Absence of tests in scrotum

VIII. Uterus and the Appendages

Swellings in connection with the uterus and

the appendages usually are associated with menstrual disturbances. Vaginal examination will confirm the origin of the swelling in the right iliac fossa.

Hypogastrium

I. **Parietal Swellings:** Refer Pg. 75

II. **Urinary Bladder**
   1. Globular swelling in the hypogastrium which may extend from symphysis pubis to the umbilicus
   2. The lump is tender and dull on percussion
   3. Pressure induces a desire for micturition

III. **Uterus and its Appendages**

Spherical midline swelling above symphysis pubis harder than urinary bladder (it should be a rule to exclude swelling of the bladder by passing a catheter before concluding that it is uterine swelling).

IV. **Fallopian Tube and Ovary**
   A. Chronic Salpingitis
      1. Attack of pelvic peritonitis: Pain, fever and bladder disturbances
      2. Mass in the midline or on one or other side of the midline
      3. Vaginal examination confirms the diagnosis
   B. Ovarian Cyst or Tumor
      1. Mass arising from one side of the pelvis but later on may become central
      2. Menstruation normal or scanty
      3. Vaginal examination confirms attachment to the uterine appendages
      4. Swelling has dullness over the front of the abdomen with resonance in the flanks (In ascites resonance in the center and dullness in the flanks)
   C. Ruptured Tubal Gestation
      1. History of missed periods
      2. A lump few days after the leakage

V. **Pelvic Abscess** *(it may follow acute appendicitis, salpingo-oophoritis and puerperal sepsis)*
   1. Constitution symptoms
   2. Copious discharge of mucus per rectum and frequency of micturition.
   3. Rectal examination reveals bulging of the anterior wall of the rectum.

Left Iliac Fossa

I. **Parietal Swellings:** (As above).

II. **Sigmoid Colon**
   A. Carcinoma
      1. Increasing constipation
      2. Loaded colon proximal to stenosis, pits on pressure
      3. Barium enema: Constant filling defect
   B. Diverticulitis
      1. Evidence of diverticulosis: Flatulent distension of lower abdomen, usually in patients over 40 years age
      2. Evidence of inflammation: Pain and tenderness in the left iliac fossa
      3. Barium enema: Saw tooth appearance of multiple diverticula with narrowing of the colon

III. **Iliopsoas Sheath:** (As above)

IV. **Undescended Testes:** (As above)

V. **Unascended Kidneys:** (As above)

7 Acute Viral Hepatitis

Etiology: Acute viral hepatitis can be caused by any one of the following:

1. **Hepatitis A Virus:** This is an RNA virus

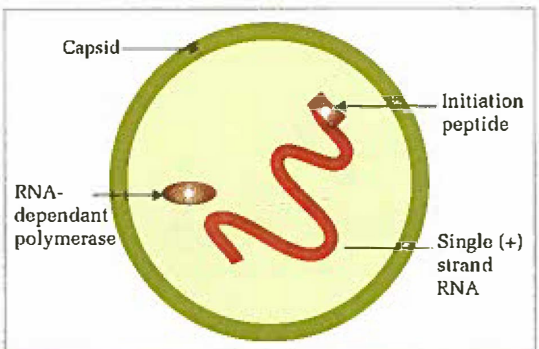


Fig. 3.20: Hepatitis A Virus

transmitted by feco-oral route. Incubation period is 2-6 weeks. Usually it does not lead to chronic disease or carrier state. Acute infection is anicteric in 50% of patients. Usually seen in children below 15 years age.

2. **Hepatitis B Virus:** This is a DNA virus transmitted parenterally. The incubation period is 2-25 weeks. About 10% of patients develop chronic disease or a carrier state.

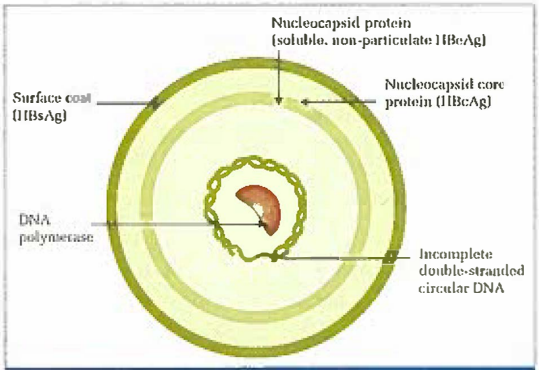


Fig. 3.21 : Hepatitis B Virus

3. **Hepatitis C Virus (formerly called non-A non-B hepatitis)** is a single stranded RNA virus transmitted parenterally. The incubation period varies from 2-25 weeks. About 20-30% develop chronic hepatitis, 50% of which is chronic active hepatitis which would ultimately lead to cirrhosis of liver.

4. **Hepatitis D Virus or Delta agent:** This is a small incomplete RNA virus which is infectious only in presence of Hepatitis B surface antigen. It is thus a "**superinfection**" to hepatitis B infection or a "**co-infection**" which occurs simultaneously with a rise in liver function tests. It usually has a chronic severe clinical course.

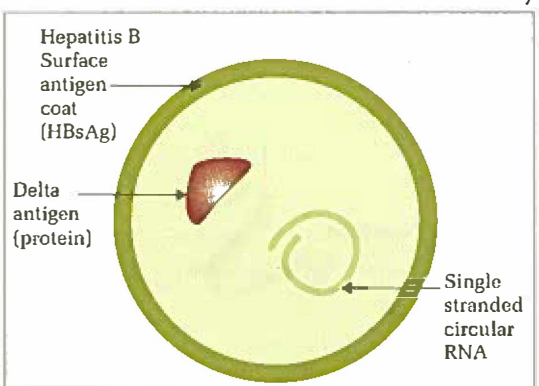


Fig. 3.22 : Hepatitis D Virus (Delta agent)

5. **Hepatitis E Virus (formerly called enterically transmitted non-A non-B hepatitis)** is an RNA virus. It resembles Hepatitis A, is transmitted by feco-oral route and is found to occur in endemic areas like India, Asia, Africa and Central America. It is seen to occur in individuals who are immune to HAV infection. Usually seen in adults and used to be wrongly labelled as 'A' in the past.

6. **Hepatitis F, G and H viruses** have been recently described.

7. **Other viruses:** Epstein Barr virus, cytomegalo virus, herpes simplex virus, rubella virus and virus of yellow fever may all cause hepatitis.

Clinical Features

1. Influenza-like syndrome is common in hepatitis A with malaise, anorexia and fatigue
2. Arthritis and urticaria is common with hepatitis B and is probably due to circulating immune complexes
3. Jaundice with dark urine and light stool occur in 50% of patients
4. Tender hepatomegaly is common and splenomegaly occurs in 20% of cases

Complications of Acute Viral Hepatitis

1. Fulminant hepatic failure
2. Relapsing hepatitis
3. Cholestatic hepatitis
4. Post-hepatitis syndrome
5. Chronic hepatitis
6. Cirrhosis of liver
7. Hepatocellular carcinoma
8. Aplastic anemia
9. Henoch Schonlein purpura
10. Renal failure
11. Connective tissue disease
12. Papular acrodermatitis

Diagnosis

I. ***To diagnose Viral Hepatitis***
   1. Typical clinical features

2. Elevated SGOT, SGPT, LDH, bilirubin and alkaline phosphatase

II. ***To diagnose the type of hepatitis (Tables and Figs. 3.8, 3.9 & 3.10)***

1. In Hepatitis A, anti-HAV IgM antibody is elevated early followed by anti-HAV IgG in 2-3 months.
2. In Hepatitis B, HBsAg is positive. In acute recent infection anti-HBeAb denotes marked infectivity. HBsAg +ve for >6 months indicates carrier state (See Table).
3. In Hepatitis C, anti-HCV may be positive, especially in chronic carriers. The most sensitive indication is the presence of HCV RNA.
4. In Hepatitis D, HDAg or rising anti-HDV antibody titre may be present.
5. In Hepatitis E, anti-HEV antibodies or HEV RNA may be present.

Treatment

1. *Rest:* Prolonged bed rest is not usually needed but patients feel better with restricted activities.
2. *Nutrition:* A high calorie diet should be given. It is usually given in the morning because many patients experience nausea in the evening. If there is persistent vomiting, intravenous fluids must be given. Usually excessive fatty foods are not tolerated well and are hence avoided.
3. *Drugs:* There are no specific drugs useful for viral hepatitis. All hepatotoxic drugs as well as alcohol must be withdrawn.
4. *For post hepatitis syndrome:* The patient requires reassurance.

Table 3.5 : Diagnostic Approach in Acute Hepatitis

Diagnosis	Anti-HAV IgM	HBsAg	Anti-HBc IgM
1. Acute Hepatitis A	+	–	–
2. Acute Hepatitis B	–	±*	+
3. Chronic Hepatitis B	–	+	–
4. Acute Hepatitis A & B	+	±*	+
5. Acute Hepatitis A on Chronic Hepatitis B	+	+	–
6. Acute Hepatitis C, D or E**	–	–	–

*HBsAg may be sometimes below detectable levels by the conventional tests, hence can be negative

**anti-HCV, HDAg, anti-HEV can be tested if all three serological tests above are negative.

Table 3.4 : Differentiating Features of Various Hepatitis

		Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
1.	*Type of virus*	RNA	DNA	RNA	Incomplete RNA	RNA
2.	*Incubation period*	15-45 days	30-150 days	15-150 days	30-150 days	15-60 days
3.	*Age of onset*	Usually pediatric age group < 15 yr	All ages	Adults	All ages	Young adult
4.	*Transmission*	Feco-oral	Percutaneous Sexual Perinatal	Percutaneous Blood borne	Percutaneous Sexual Perinatal	Feco-oral
5.	*Severity*	Mild	Often severe	Moderate	Often severe	Mild
6.	*Jaundice*	Common	Common	Uncommon	Common	Common
7.	*Progression to Chronicity:*	None	5-10%	Approx. 50%	<10% coinfection 70% superinfection	None
8.	*Carrier state*	None	0.1-30%	1%	Variable	None
9.	*Prophylaxis*	IG or vaccine	HBIG or vaccine	No vaccine available	Hepatitis B vaccine	No vaccine available
10.	*Prognosis*	Good	Worse with age and debility	Moderate	Worse in chronic cases, good in acute cases	Good except in pregnancy

Table 3.6 : Interpretation of Serological Tests of Hepatitis B

		HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe
1.	Acute HBV infection	–	–	IgM	–	–
2.	Acute HBV infection with high infectivity	+	–	IgM	+	–
3.	Chronic HBV infection with high infectivity	+	–	IgG	+	–
4.	Chronic HBV infection with low infectivity	+	–	IgG	–	+
5.	Recovery from HBV infection	–	+	IgG	–	±
6.	Remote past HBV infection and low level HBsAg carrier	–	–	IgG	–	±
7.	Immunisation with HBsAg (after vaccination) or False positive or Remote past infection	–	+	–	–	–
8.	HBsAg of one sub-type and hetero-type anti-HBs (common) seroconversion from HBsAg to anti-HBs (rare)	+	+	+	±	±

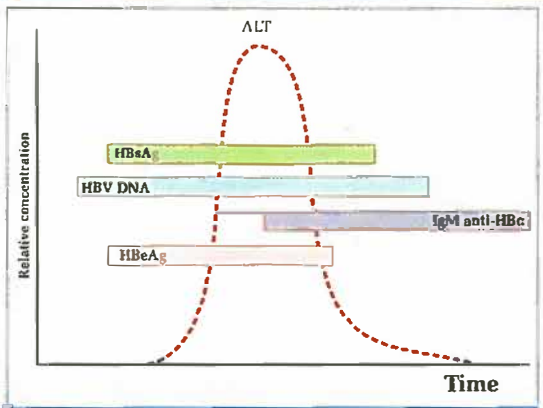


Fig. 3.23 : Acute Hepatitis B virus infection

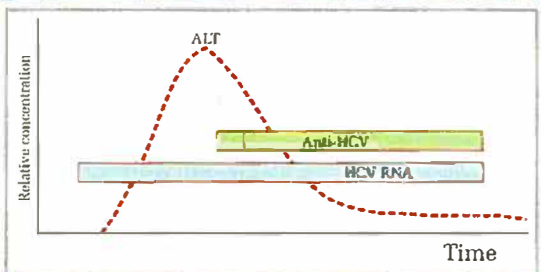


Fig. 3.24 : Acute Hepatitis C Virus Infection

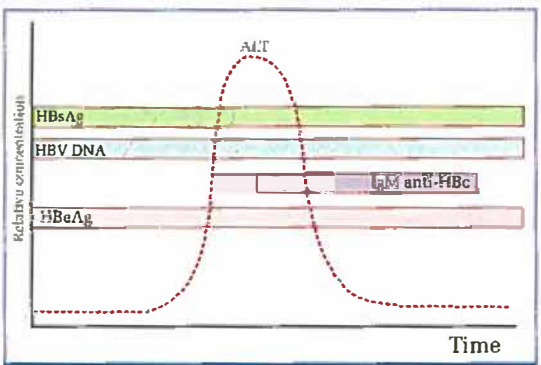


Fig. 3.25 : Reactivation of Chronic Hepatitis B virus infection

Prevention

1. The patient should avoid salivary transmission to others by avoiding kissing, spitting, sharing food, cigarettes or utensils and sexual contact. Infected stools and urine in Hepatitis A and E infections must be disposed off carefully
2. **Immunization**
   a. **Hepatitis A:** All Immune globulin (IG) preparations contain anti-HAV. It should be given within 2 weeks of contact in the dose of 0.02 ml/kg. For travelers a dose 0.06 ml/kg should be given every 6 months. Hepatitis A vaccine is now available.
   b. **Hepatitis B:** A vaccine for active immunization has been prepared from HBsAg carrier serum as well as by genetic engineering from recombinant yeast.

   For pre-exposure prophylaxis, Hepatitis B vaccine must be given at 0, 1 and 6-month interval. The dose is 20 mcg I.M. for immuno-compromised adults and 10 mcg I.M. for infants and children under 10 years.

   For post-exposure cases, a combination of HBIG (for rapid achievement of high circulating titre of anti-HBs) and hepatitis B vaccine (for long lasting immunity) is given.

For perinatal exposure of infants of HBsAg positive mothers, HBIG 0.5 ml should be given in thigh at birth followed by Hepatitis B vaccine 10 mcg started with a week of birth and repeated at 1 and 6 months.

For percutaneous exposure a single dose of 0.06 ml/kg of HBIG is given followed by three doses of hepatitis B vaccine.

Usually patients retain protective levels for 5 years after complete vaccination.

c. **Hepatitis D:** There is no immunoprophylaxis to prevent delta superinfection. Susceptible persons are vaccinated with Hepatitis B vaccine.

d. **Hepatitis C and E:** IG prophylaxis in this hepatitis is not known to be beneficial and is not recommended.

Variants of Acute Viral Hepatitis

1. *Fulminant hepatitis:* There is rapid onset of liver failure due to rapid liver cell necrosis which occurs due to modification of host response to viral infection, allowing rapid viral replication

   Hepatitis B and C and superinfection with delta agent accounts for majority of the cases. Mortality in 3 weeks is 30% and 90-100% above age 60 die. Clinically there is progressive jaundice, hepatic encephalopathy and hepatorenal syndrome prothrombin time is elevated.

2. *Cholestatic hepatitis:* There are features of obstructive jaundice with alkaline phosphatase elevated more than SGPT, during the course of viral hepatitis. It is to be differentiated from biliary obstruction. The prognosis is excellent, recovery occurs over few months.

3. *Relapsing hepatitis:* This occurs several weeks or months after apparent recovery. Sometimes it may be a second bout of hepatitis with a different virus.

4. *Viral hepatitis with autoimmune features:* It occurs in 5% of patients with Hepatitis B due to circulating immune complexes.

   Anorexia, malaise, fatigue, urticaria, angioedema migrating arthralgia and non-deforming arthritis of knee, ankle and wrist may occur along with vasculitis and glomerulonephritis. Prognosis is excellent as these rarely persist beyond 2 weeks.

5. *Hepatitis with aplastic anemia:* This is rarely seen with acute viral hepatitis. The mortality rate is high and no treatment has been effective.

Chronic Viral Hepatitis

Overview

- Chronic hepatitis is a condition characterised by persistent liver inflammation for more than 6 months after initial exposure or diagnosis of liver disease.
- Cause of chronic hepatitis are : a) chronic viral hepatitis (hep. B, Hep. C); b) Auto immune hepatitis; c) Drug induced; d) Cryptogenic (unknown cause).
- Complications of chronic hepatitis include cirrhosis, portal HT, liver failure & HCC (hepatocellular carcinoma).

Chronic Hepatitis B (CHB)

- The risk of chronicity depends on the age & immune function when a person is infected. Infection at birth is associated with a 90% chance of chronic infection while injection in young adulthood in immunocompetent person is associated with a risk of chronicity of only approximately 1-5%.
- Symptoms of chronic hepatitis range from none, to non specific complaints (fatigue, Right upper quadrant pain), to complication of cirrhosis.
- Extrahepatic manifestation, occur in up to 20% of patients with CHB & include arthralgias, PAN, glomerulonephritis mixed essential cryoglobulinemia, polymyalgia rheumatica and papular acro dermatitis (Gianotti Crosti Syndrome in children).

Diagnosis

Serologic & Virologic tests

1. Diagnosis of HBV infection based largely on detection of HBsAg

Table 3.7 : 4 phases of chronic HBV insertion

	HBeAg	Anti HBc	ALT	Liver biopsy	Treatment
1. Immune tolerant	+	-	N	N or minimal inflammation	No
2. Immune active (HBeAg + ve)	+	-	↑	Active inflammation	Yes
3. Reactivation (HBeAg-ve)	-	+	↑	Active inflammation	Yes
4. Inactive carrier	-	+	N	N or minimal inflammation	No

N = Normal

2. When HBsAg is detected, further laboratory testing to assess disease status & need for treatment is indicated.
   i. ALT levels
   ii. HBV DNA Quantitative (viral load)
   iii. HBeAg & Anti HBe : To define the type of CHB & end point of therapy.
   iv. Tests for liver disease activity - platelet count, total bilirubin, albumin & PT / INR
   V. Liver biopsy → To determine histologic grade & stage of disease.

Treatment

1. Goals of treatment
   i. Prevention of long term complications (cirrhosis, HCC) & mortality
   ii. Primary goal : sustained suppression of HBV DNA.
   iii. Secondary goal: a) Decreased or normalised serum ALT; b) improved liver histology, c) HBeAg loss or seroconversion; d) HBsAg loss.

Indications for HBV treatment

Treatment indicated

1. Decompensated cirrhotic patients.
2. Any HBV DNA detectable in cirrhotic patients.
3. Fulminant liver failure
4. HBsAg +ve patients on immunosuppression
5. CHB with elevated ALT levels & HBV DNA >2000 IU/ml.

Treatment not indicated

1. Immune tolerance phase
2. Inactive carrier
3. Acute hepatitis B

Drugs

Current 1st line therapies

1. Pegylated interferon α- (exception : pregnancy, decompensated cirrhosis)
2. Nucleoside analogs → Entecavir, Tenofovir

Specific drugs

1. Pegylated interferon α : Consider in young, non cirrhotic pts. with low viral load and high ALT.
   Treatment : 180 μg/wk s/c for 48 wks.
2. Nucleoside analogues : High antiviral potency; negligible adverse effects, oral administration, safe and effective for all ages, suitable for cirrhotic and HIV coinfected pts.
   i. Lamivudine : 100 mg/day; high rate of resistance. (specific point mutation YMDD motify of the HBV polymerase).
   ii. Adefovir dipivoxil : 10 mg / day; potentially nephrotoxic.
   iii. Entecavir : 0.5 - 1 mg/day; low rate of resistance.
   iv. Tenfovir : 300 mg / day; low rate of resistance. Adverse events : ↓ sed bone density, Fanconi synd. (rare).
   v. Others : a. Emtricitabine; b. Clevudine.

Duration of Therapy

1. HBeAg +ve : Treat until HBeAg seroconversion and stop after consolidation, period 6-12 months after HBeAg seroconversion.
2. HBeAg - ve : Treat indefinitely because relapse is common after stopping of therapy.

8 › Cirrhosis of Liver

Definition

Cirrhosis of liver is chronic diffuse liver disease of

varied etiology and characterized by hepatic cell necrosis, resulting in collapse, proliferation of connective tissue (fibrosis), nodular regeneration and altered intrahepatic circulation.

Classification

1. **Viral Hepatitis:** Hepatitis B, C and D may lead to cirrhosis of liver.
2. **Alcohol:** An intake of about 80 gm of alcohol daily, for 15 years, may lead to cirrhosis.
3. **Prolonged cholestasis**
4. **Cardiac failure** of long duration induces fibrosis around the central vein.
5. **Drugs:** INH-Isoniazid, methotrexate and methyldopa may cause cirrhosis.
6. **Congenital disorders:**
   a. *Hemachromatosis:* Excessive iron absorption and deposition in the liver leads to cirrhosis. Other features are diabetes, bronze colored skin and myocarditis.
   b. *Wilson's disease:* Excessive deposition of copper leads to cirrhosis. Other features are lenticular degeneration (involuntary movements, rigidity), greenish yellow ring at the limbus of cornea (Kayser Fleischer ring) and deficiency of ceruloplasmin.
   c. *Galactosemia:* There is deficiency of the enzyme galactose-1-phosphate-uridyl transferase. Galactose from milk is not converted to glucose. Infants on milk diet may have malnutrition, diarrhea, jaundice, cataract and hepatosplenomegaly with cirrhosis of liver.
   d. *Alpha-1-antitrypsin deficiency:* The normal levels of this enzyme are 150-350 mg/L. Levels less than 80 mg/L may cause cirrhosis (mechanism unclear), pancreatitis and recurrent lung infections with emphysema.
7. **Miscellaneous:**
   a. *Nutrition:* A diet low in proteins especially in methionine and choline may cause fatty liver and cirrhosis. A diet rich in unsaturated fats (as in vegetable oils) may increase the susceptibility of liver to cirrhosis. Similarly, a diet very rich in calories and carbohydrates may cause relative protein deficiency and contribute to liver necrosis by infections and toxins.
   b. *Infections:* Malaria, kala-azar and dysentery cause malnutrition and contribute to cirrhosis. Schistosomiasis produces hepatic fibrosis, which may progress to cirrhosis.
   c. *Toxins:* Aflatoxin-contaminated foodstuffs may produce cirrhosis. It is produced when groundnuts, pulses or other nuts stored in moist conditions get contaminated with a fungus - Aspergillus flavus.
   d. *Autoimmunity:* Autoimmune antibodies as produced in SLE may lead to cirrhosis.
   e. *Cryptogenic:* The cause of cirrhosis is not identified.

Pathology

The liver is firm, has a gritty feel on cutting and the cut surface shows fibrous bands surrounding nodules of various sizes.

Microscopic examination would show necrosis, collapse, fibrosis, regeneration and altered circulation.

Regenerating nodules, by compressing the blood supply of the liver cause ischemic damage of the liver even after the disappearance of the primary cause of liver injury.

Clinical Features

Cirrhosis of liver may progress for years before any clinical suspicion is aroused because even 10% of healthy liver tissue is adequate for metabolic functions and liver tissue has a remarkable capacity to regenerate. The presenting features of cirrhosis are ascites, edema, hematemesis or hepatic coma. The clinical features can be classified as those due to liver cell failure and those due to portal hypertension.

I. **Due to Liver cell failure:**
   1. Palmar erythema, spider nevi
   2. Gynecomastia, testicular atrophy and loss of libido
   3. Jaundice - usually mild, may be severe terminally
   4. Ascites, edema and scrotal swelling
   5. Flapping tremors

Table 3.8 : Differences between Biliary and Portal Cirrhosis

		Biliary Cirrhosis	*Portal Cirrhosis*
1.	Sex	Female	Male
2.	Pain and Pruritus	Marked	Uncommon
3.	Jaundice	Marked	Mild
4.	Splenomegaly	Slight	Marked
5.	Ascites	Uncommon	More common
6.	Hepatomegaly	Marked	Slight
7.	Clubbing	Present	Rare
8.	Xanthomas	May be seen	Absent
9.	Cholesterol	Marked increase	Normal or diminished
10.	Alkaline phosphatase	Marked increase	Slight increase or normal

6. Alopecia
7. Parotid swelling, Dupuytren's contracture
8. Wasting
9. Chalky whitenails

II. **Due to Portal Hypertension:**

1. Splenomegaly and hypersplenism
2. Dilated veins over the chest wall
3. Hematemesis, melena and bleeding per rectum
4. Ascites

III. **Liver** is usually not palpable because it is shrunken. However in a thin individual or with alcoholic cirrhosis, it may be palpable with a sharp edge and an irregular nodular surface.

Complications

1. Due to portal hypertension: Hematemesis, thrombosis of portal vein.
2. Due to liver cell dysfunction: Hepatic encephalopathy.
3. Due to regenerating nodule: Hepatic encephalopathy.
4. Due to ascites: Hernia
5. Due to associated infections: Tuberculosis, pneumonia and secondary bacterial peritonitis.
6. Hepatorenal syndrome

Treatment

1. *Bed rest* till improvement.
2. *Diet:* 2000 calories with about 100 gm proteins. Fats and carbohydrates as much as the patient tolerates. Salt is restricted if edema or ascites is present. Supplemental Vitamin B complex should be given.
3. *Diuretics: Spironolactone* is an aldosterone antagonist that antagonizes the effects of excess aldosterone present in cirrhotics due to inadequate elimination of aldosterone by liver. 100 mg/day may be given. Maximum dose 400 mg. *Frusemide* can also be added up to 80mg.
4. *Removal of cause:* Withdrawal of alcohol, D-penicillamine for Wilson's disease, etc.
5. *Corticosteroids and immunosuppressants* may be helpful in active post-hepatitis cirrhosis.
6. *Antifibrotic agents* like colchicine and propylthiouracil are still experimental.
7. *Interferon's* utility is limited once cirrhosis sets in. It is useful only if there is actively replicating virus B or C and patient is awaiting transplant
8. *Transjugular Intrahepatic Porto-systemic shunts (TIPS)*
9. *Artificial Liver Support*
10. *Hepatocyte transplant and orthoptic liver transplant.*

9 Portal Hypertension

Definition : Portal Hypertension is defined by a pathologic increasse in portal pressure above the upper limit of 5 mm Hg.

Portal HT becomes clinically significant when the portal pressure increases above the threshold value of 10 mm Hg (eg. formation of varices) or 12 mm Hg (e.g variceal bleeding, ascites). Portal pressure values between 6 and 10 mm Hg represent subclinical portal hypertension.

Portal HT is the most common & lethal complication of chronic liver disease. It is responsible for the development of gastroesophageal varices and portal hypertensive gastropathy, variceal hemorrhage, ascites,

renal dysfunction, portosystemic encephalopathy, hypersplenism & hepatopulmonary syndrome.

The portal vein - systemic collateral circulation develops & expands in response to elevation of the portal pressure. The main sites of collatteral formation are :

1. Gastro-esophageal junction,
2. Rectum,
3. Retroperitoneum and
4. Anterior abdominal wall via the umbilical vein (caput medusae).

Causes

I. **Pre-hepatic:**
   1. Portal vein thrombosis
   2. Splenic venin thrombosis
   3. Massive splenomegaly (Banti's syndrome)
   4. A-V Fistula

II. **Hepatic:**
   1. Presinsuoidal - Schistosomiasis, Congenital hepatic firbosis, non cirrhotic, portal fibrosis (NCPF)
   2. Sinusoidal - Cirrhosis, alcoholic hepatitis, Wilson's, hemochromatosis
   3. Post Sinusoidal - Hepatic sinusoidal obstruction (venoocclusive syndrome) primary biliary cirrhosis.

III. **Post-hepatic:**
   1. Budd Chiari syndrome
   2. IVC webs
   3. Cardiac causes - constrictive pericarditis, restrictive cardiomyopathy, severe CCF.

Clinical Features

1. Splenomegaly
2. Hematemesis and melena
3. Ascites
4. Encephalopathy

Treatment

I. **Treatment of cause:** If the underlying cause can be identified, it should be treated.

II. **Treatment of Variceal bleeding:**

   A. **Local Measures**

   1. *Sclerotherapy:* Sclerosing agents like sodium tetradecyi sulphate and 3% phenol in water are injected through upper GI endoscopy, around the varices. They obliterate the blood vessels and prevent future bleeds. It stops variceal bleed in 80% of patients and can be repeated if bleeding recurs. However, if there is active bleeding, sclerotherapy is hazardous and first the bleeding should be controlled by balloon tamponade.
   2. *Banding:* This is a technique to stop variceal bleeding in which the varices are sucked into an endoscope

Table 3.9 : Differential Diagnosis

		Cirrhosis of Liver	*Non-cirrhotic portal fibrosis (NCPF)*	*Extra-hepatic portal venous obstruction (EHPVO)*
1.	Site of obstruction	Intrahepatic, sinusoidal and post sinusoidal	Intrahepatic sinusoidal	Extrahepatic
2.	G.I. bleeding	Recurrent and frequent	Infrequent	Infrequent
3.	Hepatic encephalopathy	Common	Rare (May follow shunt surgery)	Rare
4.	Ascites	Common	Rare	Rare
5.	Splenomegaly	less than 5cm	10-20 cm.	10-20 cm.
6.	Hepatomegaly	Firm, irregular	Firm, smooth	Absent
7.	Portal vein pressure	High	High	Normal
8.	Hepatic wedge pressure	High	High/Normal	Normal
9.	Liver biopsy	Nodularity, loss of liver architecture and fibrosis	Phlebosclerosis, phlebo-thrombosis with preserved liver architecture	Normal

accessory, allowing them to be occluded with a tight rubber band. The occluded vari subsequently sloughs with variceal obliteration. However it is less easy to apply in acute bleeding.

3. *Balloon tamponade:* This is done with Sengstaken-Blakemore tube which possesses two balloons and exerts pressure in the lower esophagus and fundus of the stomach. The tube is passed through the mouth and its presence in the stomach is checked by auscultating over the upper abdomen while injecting air into the stomach. Gentle traction is used to maintain pressure on the varices. Initially only the gastric balloon is inflated, which would control the bleeding. If the esophageal balloon is also inflated, it is important to deflate it for 10 mins every three hours to prevent esophageal mucosal damage. This usually stops the variceal bleed, but only allows for time for more definite therapy.
4. *Shunt surgery:* Portocaval shunts also give excellent results with low morbidity and mortality and is a one time procedure unlike sclerotherapy which may have to be repeated. However, the incidence of hepatic encephalopathy is high and death could result from liver failure. Hence it is only used when other measures fail and offered only to patients with good liver functions.

B. Drugs: Splanchnic flow can be reduced by vasopressin, somatostatin (octreotide) and terlipressin.

1. *Vasopressin:* It is given as an IV infusion, 0.4 units per min. until bleeding stops or for 24 hours and then 0.2 units per min. for a further 24 hours. It can cause angina, myocardial infarction and arrhythmias. Nitroglycerine transdermally or IV should be used to combat this. ECG monitoring is necessary.
2. *Somatostatin and Octreotide*, a synthetic form of somatostatin is given in the dose of 50 mcg IV followed by an infusion of 50 mcg hourly. It is an expensive drug, but the drug of choice.
3. *Terlipressin:* It is not an active drug, but vasopressin is released from it in sufficient amounts to reduce portal pressure without producing systemic side effects. It is given in the dose of 2 mg IV every 6 hours until bleeding stops and then 1 mg IV for further 24 hours.

C. Prophylaxis

In patients with variceal bleed, recurrent bleeding is very common. This could be prevented by regular sclerotherapy, banding or drugs like beta-blockers or nitrates. Propranolol 80-160 mg/day reduces portal venous pressure and can be used to prevent recurrent variceal bleed. Beta-blockers are now routinely used in prophylaxis. However, they carry a theoretical risk of increasing the hepatic blood flow and thus hepatic encephalopathy. Nitrates are second line agents used in patients who are intolerance to beta blockers.

D. TIPS (Transjugular Intrahepatic Portal Shunt) used for patients awaiting liver transplant.

E. Liver Transplant

III. Treatment of Enlarged Spleen:

Massive splenomegaly, hypersplenism and splenic infarction may require splenectomy and shunt surgery.

IV. Treatment of Ascites:

Salt restricted diet with diuretics spironolactone and of furosemide.

Massive ascites requires therapeutic tapping.

Autoimmune liver disease

- Autoimmune hepatitis is a chronic hepatitis

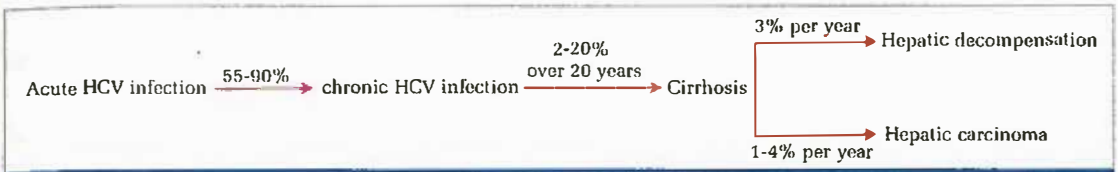


Fig. 3.26: HCV Infection

characterized by immune & autoimmune features.

- Characterised by presence of circulating hyper gammoglobulinemia and auto antibodies with interface hepatitis on liver biopsy.
- Treatment in with anti-inflammatory / immunosuppressive therapy e.g. steroids and Azathioprine.
- Liver transplantation in patients who do not respond to medical therapy.

Chronic Heaptitis C

- HCV infection is a leading cause of morbidity and mortality with a global prevalence of 3%.
- Natural history

Diagnosis

1. Detectable **anti - HCV** indicate exposure but does not confirm active infection, because anti-HCV persistent indefintely after spontaneous or therapeutic resolution .
2. **HCV RNA viral load** should be performed in all patients with positive anti-HCV assay & in patients in whom antivrial treament is being considered.
3. **HCV genotype** - 6 major genotypes (1 to 6)

Treatment

1. Standard therapy consists of combination of pegylated interferon (PEG IFN) and Ribavarin
2. Sustained virolgical response (SVR) i.e. HCV RNA negative 24 weeks after end of treatment is achieved in 45-80% of patients depending on the genotype.

Future

Protease inhibitors such as Boceprevir and Telaprevir and Polymerase inhibitors such as safosuvir combined with Ribavarin with or without PEG IFN will further enhance treatment response and minimise the emergence of viral resistance.

Wilson's Disease

- Wilson disease is a genetic disorders (autosomal recessive) in which copper accumulates in the liver & brain is excess of normal metabolic needs.
- **Diagnosis**: i) Low levels of serum cerruloplasmin i.e. less than 20 mg / dl (Normal : 20-50 mg / dl); ii) Hepatic copper concentration above 250 µg / g. dry copper wt.; iii) clinical findings include presence of kayser fleischer rings, stigmata of chronic liver disease & neurologic findings.

Treatment is life long

i. Chelating agents eg. D-penicillamine, Trientene
ii. Zinc salts
iii. Liver transplantation for acute liver failure or decompensate liver disease.

10 Alcoholic Liver Disease (ALD)

Alcohol induced liver injury results from chronic alcoholic ingestion which may be classified as :

1. Alcoholic fatty liver (AF)
2. Alcoholic hepatitis (AH)
3. Alcoholic cirrhosis of liver (AC)

Alcohol dehydrogenase (ADH) Acetaldehyde Dehydrogenese (ALDH) Co2 Alcohol Acetaldehyde + H2o

Oriental flush syndrome : Results from impaired metabolism of acetaldehyde caused by inheritance of the ALDH22 allele seen mainly in persosn from East Asia (eg. Japan) causing toxic systemic effects such as nausea, headache, flushing & tachycardia of acetaldehyde accumulation. Therefore, tense patients get symptom of excessive flushing after consuming alcohol.

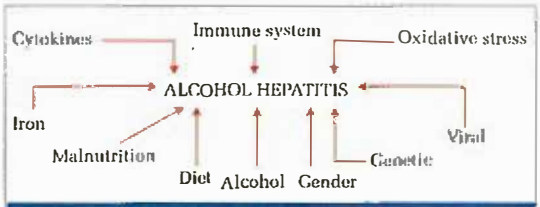


Fig. 3.27 : Risk factors / cofactors required for the development of advanced ALD

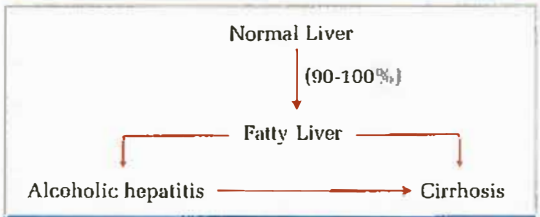


Fig. 3.28 : Percentage of heavy drinkers who develop different stages of ALD

Risk factors of ALD

1. Quantity : Risk of developing cirrhosis with ingestion of >60-80 g / day of alcohol in men & >20 g/day in women for 10 years or longer.
2. Gender : Increased susceptibility to ALD at amounts > 20 g/day (2 units) [1 unit = 10 gm].
3. Hepatitis C : Concurrent HCV infection associated with younger age for severity, more advanced histology and decreased survival.
4. Genetics : Gene polymorphisms include alcohol dehydrogenase (ADH) and the cytochrome P450 system (CYP4502E1).
5. Malnutrition : Nutritional status important risk factor for the development of ALD & diet.

Pathogenesis

The mechanism whereby alcohol produces different liver lesions is poorly understood. Fatty change may be due to increased production and decreased use of fatty acids in the liver cells following the conversion of alcohol to acetaldehyde by alcohol dehydrogenase. For the development of alcoholic hepatitis, fibrosis and cirrhosis, production of toxic metabolites called adducts during the conversion of acetaldehyde to acetate may be responsible. In addition, immune reaction to liver cells altered by alcohol may also be involved. Determinants of liver injury are :

Alcoholic Fatty Liver (AF)

AF occurs in most heavy drinker but is reversible on cessation of alcohol consumption.

Pathology: The liver is enlarged, greasy, yellow and firm. Hepatocytes are distended with fatty vacuoles which push the nucleus to the periphery. This occurs because fatty acid oxidation is impaired and they are taken up by the cells and esterified to form triglycerides.

Clinical features: The clinical features are minimum or absent. There may be tender hepatomegaly only.

Investigations: Usually all laboratory tests are normal. Sometimes there may be elevation of SGOT and alkaline phosphatase.

Prognosis: AF has good prognosis. Complete resolution occurs after cessation of alcohol intake.

Treatment: Alcohol intake must be stopped. Nutritious diet with high doses of vitamin B complex must be given.

Alcoholic Hepatitis (AH)

AH is an inflammatory lesion characterized by infiltration of the liver with leucocytes, liver cell necrosis and alcoholic hyaline deposition.

Pathology: Liver cells are ballooned, degenerated and necrosed with infiltration with polymorphs and lymphocytes. Hepatocytes contain Mallory bodies or alcoholic hyaline which are clumps of perinuclear, deeplyeosinophilic material that represents intermediate filaments. Mallory bodies are not diagnostic but do usually suggest alcoholic hepatitis. They are also seen with morbid obesity, jejuno-ileal shunt, uncontrolled diabetes mellitus, Wilson's disease, Indian childhood cirrhosis, etc.

Clinical Features: This varies from asymptomatic patient to mild illness to fatal liver cell failure.

Typically it resembles *Viral hepatitis*

1. Anorexia, nausea, vomiting, abdominal pain, malaise, weight loss and jaundice
2. Fever as high as 39 - 40°C may be seen in 50% of cases
3. Tender hepatomegaly is usually present. Splenomegaly occurs in 33% cases
4. Signs of liver cell failure like spider angioma, jaundice, ascites, edema, GI bleeding and encephalopathy may be present
5. Cholestatic jaundice may occur in some

Most of the patient recover after several weeks to months after abstinence, however, histological abnormalities may persist for 6 months.

Investigations

1. Anemia may occur from GI bleeding, nutritional deficiency (folate and B12 deficiency), hypersplenism, direct bone marrow suppressant effect of alcohol and hemolysis due to acanthocytosis.
2. Leucocytosis is usually present. However, leucopenia and thrombocytopenia could occur due to hypersplenism.
3. Alkaline phosphatase may be elevated.
4. SGOT is high but rarely more than 300 units. Unlike in viral hepatitis where SGPT is higher compared to SGOT, in alcoholic hepatitis SGOT is much higher than SGPT. This is because of greater inhibition of SGPT synthesis by ethanol which may be partially reversed by pyridoxal phosphate.
5. Serum prothrombin is prolonged due to reduced synthesis of Vitamin K dependent clotting factors.
6. Serum albumin is usually reduced due to impairment in hepatic protein synthesis. Globulins are high due to non-specific stimulation of reticuloendothelial system. Hyperbilirubinemia may be present, due to decompensation.
7. Hypomagnesemia and hypophosphatemia may occur due to dietary deficiency. Hypokalemia may occur due to hyperaldosteronism (aldosterone is normally destroyed in liver).
8. Gamma Glutamyl Transpeptidase (GGPT) is raised due to alcoholic abuse irrespective of liver disease due to microsomal enzyme induction.

Prognosis

In milder cases, clinical recovery can occur completely. However, repeated bouts of alcoholic hepatitis may lead to irreversible progressive liver injury, abstinence from alcohol can reduce long term morbidity and mortality.

Marked hyperbilirubinemia, elevated creatinine, elevated prothrombin time (more than 1-5 times normal), ascites and encephalopathy are associated with poor short term prognosis.

Prognosis

3 models shown to predict short term prognostic in Alcoholic hepatitis.

1. *Discriminant function (DF) (Maddrey's score)*: [4.6 x (patients prothrombin time - control value in seconds)] + S. bilibrubin (mg/dl). DF value ≥ 32 has a poor prognosis with 1 month mortality rates of 35-45%.
2. *Model for End Stage Liver Disease (MELD)* : It includes S. bilirubin level, INR & S. Creatinine levels. A score of ≥ 21 is highly predictive of 90 day mortality.
3. *Glassgow Alcoholic Hepatitis Scale (GAHS)* : It includes S. bilirubin, INR, BUN, Age & WBC count. A score of ≥ 9 at days 1 & 7 is suggestive of severe alcoholic hepatitis & a poor prognosis.

Alcoholic Cirrhosis of Liver (AC)

AC is diffuse fine scaring with loss of liver cells and small regenerating nodules (micronodular)

Pathology: With continued alcohol intake, liver cells are destroyed and fibroblasts appear at the site of injury and stimulate collagen formation. Septae of connective tissue appear in the periportal and pericentral zones which eventually connects portal triad and central vein. The remaining liver cells which are surrounded by connective tissue, regenerate and form nodules. Usually, cell loss exceeds regeneration. The liver shrinks and becomes hard and nodular

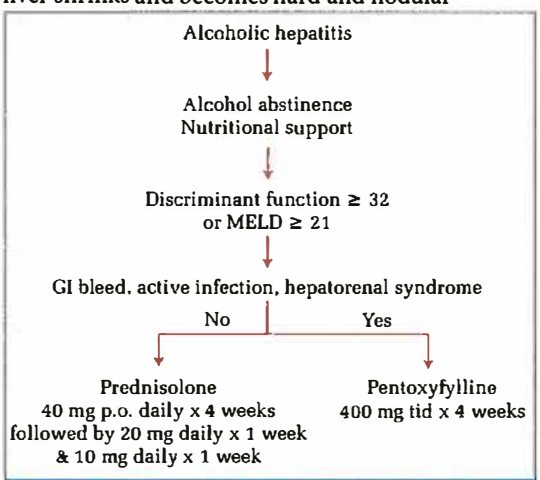


Fig. 3.29 : Treatment Algorithm for Alcoholic Hepatitis

Clinical Features: It is usually silent in 10% of cases. The clinical manifestations are like cirrhosis of liver.

Dupuytren's contracture due to fibrosis of palmar fascia with resulting flexion contracture of the digits and *parotid swelling* are associated with alcoholism rather than cirrhosis.

Laboratory Tests: Similar to alcoholic hepatitis. Elevated *blood ammonia* may also occur due to impaired liver function and shunting of portal venous blood around the cirrhotic liver.

Prognosis: Similar to alcoholic hepatitis

Treatment: Similar to cirrhosis of liver

11 › Malaria

Malaria is a common tropical disease caused by a protozoa, plasmodium, through the bite of female anopheles mosquito.

Types

There are mainly four types of plasmodium infection causing malaria as follows:

1. Plasmodium falciparum (Malignant tertian malaria)
2. Plasmodium vivax (Benign tertian malaria)
3. Plasmodium malariae (Quartan malaria)
4. Plasmodium ovale

Life Cycle (Fig. 3.30)

When an infected mosquito bites an individual, its saliva, rich in parasites (sporozoites) is injected. The sporozoites enter he circulation and then the liver (pre-erythrocytic phase). It multiplies in the liver cells forming merozoites. After 5-9 days, the merozoites enter the red blood cells (erythrocytic phase) forming trophozoites which subsequently mature to become schizonts. The schizonts are discharged into the blood stream when the red cells degenerate. This results in an attack of malarial fever. The red cells are destroyed by the spleen which enlarges and some of the schizonts continue to develop in the liver (exo-erythrocytic phase) causing a relapse. This phase is absent in falciparum malaria.

Some of the merozoites for unknown reasons do not form schizonts but develop into male and female gametes. During the mosquito bite, these gametocytes are ingested. They fertilize in the mosquito's stomach and develop into sporozoites which localize in the salivary glands of the mosquito. These sporozoites enter the human blood stream on a subsequent mosquito bite and thus complete the cycle.

Clinical Features

1. **Onset:** The onset may be insidious with abdominal pain, nausea, dry cough and malaise. Rarely it may be acute and with fever and chills.
2. **Fever with rigors:** In the early stage, fever may be persistent for several days but soon it develops into a synchronous periodicity. A classical attack of fever has a chill, rise in temperature to 40-41°C, headache and myalgia. This is followed by several hours of profuse sweating and fall in temperature. In vivax and oval malaria these paroxysms occur every 48 hours (benign tertian) whereas in malaria, it occurs every 72 hours (quartan). In falciparum malaria, the temperature is usually persistently elevated or may progress to 48 hour cycle (malignant tertian malaria). These cycles may be repeated in case of benign tertian malaria due to exo-erythrocytic phase.
3. **Organomegaly:** Liver is moderately enlarged and tender. Spleen is often palpable in acute attack. It is soft to firm and occasionally tender.
4. **Miscellaneous:** Herpes simplex lesions may be present around the mouth. Rarely jaundice may occur.

Investigations

1. **Complete Blood Count and Demonstration of parasites:** There is normochromic normocytic anemia. Both thick and thin smears should be examined for detection and identification of the malarial parasites. *Blood smears must be repeated at intervals of 6-12 hours on multiple occasions.* Malarial parasites can also be demonstrated on bone marrow examination and by splenic puncture.

   Criteria for severe falciparum malaria:

   a. More than 5% of RBCs infected
   b. Parasites index more than 1,00,000/ul

c. More than 250 parasites per field on thick smear

d. Leucocytosis

2. **Serology:** Henry's melanin flocculation test, complement fixation test, passive hemaglutination test, gel precipitation test and immunofluorescent technique to demonstrate antibodies to malarial parasite are useful.

3. **Other investigations:** Serum electrolytes, BUN, creatinine, blood sugar, ECG, chest X-ray, arterial blood gases, blood culture, lumbar puncture if necessary.

4. **Newer Methods:** Polymerase Chain Reaction (PCR) and serological tests based on histidine rich protein 2 (HRP-2) (e.g. Parasite F and ICT Ff) and pLDH (e.g. Optimal).

Complications

1. **Cerebral malaria:** This is an altered state of consciousness due to the presence of *Pl. falciparum*. Patient usually has fever and non-specific symptoms for a few days before the development of cerebral malaria. There may be mild neck rigidity and retinal hemorrhages but no white exudates or papilledema. Deep reflexes are brisk and plantars extensor with absent abdominal reflexes. Psychiatric manifestations, convulsions and coma may occur. Rarely brainstem may be involved, manifested by convergence spasm, ocular bobbing and nystagmus. Cerebellar ataxia, may occur. Rare manifestations are cranial nerve palsy, extrapyramidal syndromes, polyneuropathy, mononeuritis multiplex, Guillain Barre-syndrome and rhabdomyolysis.

2. **Algid malaria (shock):** There may be subnormal temperature, weakness, prostration, feeling of cold, vomiting, rapid respiration and oliguria. Death may occur but the patient is conscious till the end. It could be due to adrenal crisis, absorption of endotoxin from gut or cachectin-tumour necrosis factor from endotoxin activated macrophages.

3. **Hematological abnormalities:**

   a. Normochromic anemia may occur due to hemolysis, inappropriate bone marrow response and increased sequestration and destruction in the spleen.

   b. Leucocytes are usually normal. However, leucocytosis without infection may occur due to cachectin (tumour necrosis factor) and carries grave prognosis.

   c. Thrombocytopenia may be due to decreased platelet production, decreased platelet survival, increased splenic uptake and sequestration and consumption by DIC.

   d. Bleeding may occur due to DIC.

4. **Renal failure:** (defined as urine output <400ml/24 hours and failure to improve after rehydration). The patient may present with loin pain, vomiting, diarrhea, polyuria followed by oliguria with passage of dark or black urine, with or without fever, tender hepato-splenomegaly, anemia, jaundice, hypotension, renal failure and coma. Acute glomerulonephritis and nephrotic syndrome may also occur. Intravascular hemolysis, hypovolemia, hyperviscosity and intravascular coagulation may be responsible for renal failure.

   Blackwater fever is a condition where renal failure is associated with severe intravascular hemolysis and hemoglobinuria. If the patient survives acute phase, urination commences in 4 days and increased creatinine levels return to normal in 3-4 weeks.

5. **Pulmonary edema:** This occurs due to

Table 3.10 : Complications of Plasmodium Infections

Plasmodium falciparum
• Cerebral malaria including seizures and coma
• Hypoglycemia, lactic acidosis
• Severe anemia
• Pulmonary edema
• Tropical splenomegaly (chronic)
• Black water fever
Plasmodium vivax
• Late splenic rupture (2-3 months after initial infection)
Plasmodium malariae
• Immune complex glomerulonephritis (with parasite antigen, host IgG and complement)
• Nephrotic syndrome

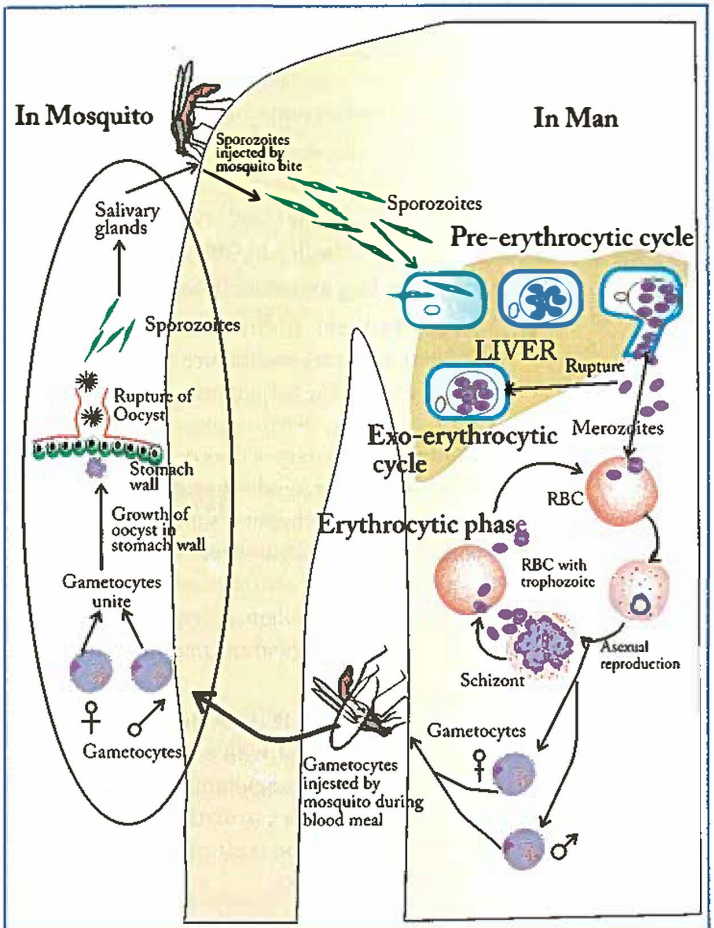


Fig. 3.30 : Life cycle of malaria

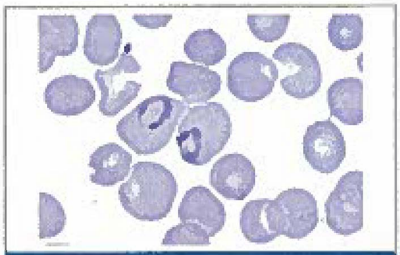


Fig. 3.31 : Plasmodium vivax : Ring form of trophozoites

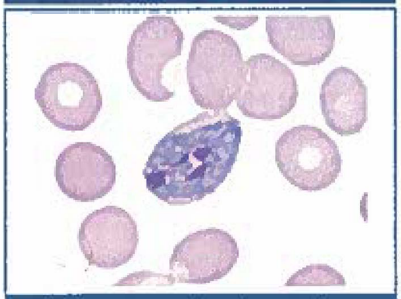


Fig. 3.32 : Plasmodium vivax : Schizont

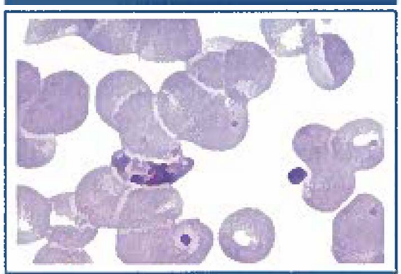


Fig. 3.33 : Plasmodium falciparum : banana shaped gametocyte

Table 3.11 : Characteristics of Plasmodium Species Infecting Humans

Characteristic	P. Falciparum	P. vivax	P. ovale	P. malariae
1. Duration of intrahepatic phase (days)	5-7	7-8	9	14-16
2. Duration of erythrocytic cycle (hours)	48	48	50	72
3. Red cell preference	Younger cells but can invade cells of all ages	Reticulocytes	Reticulocytes	Older cells
4. Morphology	Usually only ring forms; parasitemia level may exceed 2%, with multiple infections of a single erythrocyte; occ. banana shaped gametocyte	Irregularly shaped large rings and trophozoites; enlarged erythrocytes; Schufner's dots	Infected erythrocytes enlarged and oval; Schufner's dots	Band or rectangular forms of trophozoites common; no RBC enlargement; no Schuffner's dots
5. Pigment color	Black	Yellow-brown	Dark brown	Brown-black
6. Relapses	No	Yes	Yes	No

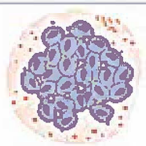
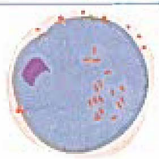
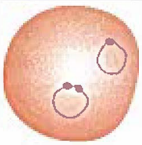
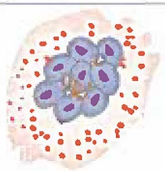
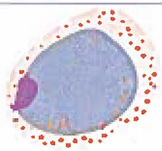
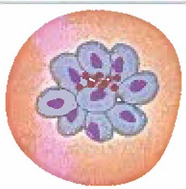
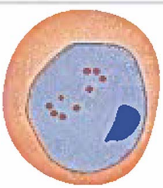
	RED CELL MORPHOLOGY AND GENERAL FEATURES	TROPHOZOITE (RING FORM)	SCHIZONT	GAMETOCYTE
P. vivax	Very enlarged red cells Pale, fine red stippling (Schuffner's dots) Low or moderate parasitemia All stages of life cycle present **Multiple parasites** per cell may be present	 Thick compact rings > 1/3 size of RBC with single large chromatic dot. Few Schuffners dots. Ameboid ring forms in mature trophozoites.	 12-24 medium-sized merozoites per cell; almost fill the cell Schuffner's dots present. 1-2 clumps of peripheral yellow-brown fine hemozoin pigment.	 Large and round or oval, almost fills the cell Red central or eccentric single nucleus Fine scattered pigment
P. Falciparum	Normal sized red cells, normochromic Maurer's clefts or dots may be present Heavy parasitemia Sometimes multiple parasites per cell often at margins **Often only ring forms** present	 Delicate rings < 1/3 size of RBC . Double chromatic dots per ring common. Small chromatin dot No Schuffner's dots.	**Schizont not usually seen in peripheral blood.** **(except occassionally in cerebral malaria)** If present, 8-24 very small merozoites, grouped irregularly and filling 2/3 of red cell.	 Crescent or banana-shaped, deforms the cell which may appear pale and empty. Diffuse chromatin, central single nucleus
P. ovale	Enlarged red cells, some oval shaped, some with fimbriated edges Pale, fine to coarse red stippling (Schuffner's dots) Low parasitemia Multiple parasites rare Fewer stages present	 Thick compact rings > 1/3 size of RBC . Single chromatic dot Numerous Schuffner's dots.	 8-12 large merozoites per cell. Daisy-head arrangement Schuffner's dots present. Central brown pigment.	 Oval shaped, fills 3/4 of the cell. Smaller than vivax. Coarse brown pigment, scattered mainly near periphery.
P. malariae	Normal or microcytic, normochromic red cells Lowest parasitemia Multiple parasites per cell rarely found No stippling All stages usually present	 Small, thick compact rings < 1/3 size of RBC. Single chromatic dot, double dots rare. Ameboid rings or band across cells in mature trophozoites.	 6 -12 large merozoites per cell. Daisy-head arrangement Central coarse dark brown pigment.	 Round, fills 1/2 to 2/3 of the cell. Prominent brown black pigment. Dark nucleus.

Fig. 3.34 : Features of Malarial Parasites in Peripheral Blood

increased capillary permeability due to effects of endotoxins and cytokines. Hyperparasitemia, renal failure and pregnancy are predisposing factors. It occurs suddenly after 1-2 days of starting treatment with increased respiratory rate, breathlessness, hemoptysis and collapse. It carries high mortality.

6. **Lactic acidosis:** Parasitized red cells interfere with micro circulatory flow leading to anaerobic glycolysis in tissues. This with hypotension and inadequate hepatic lactate clearance causes lactic acidosis, which is characterized by hyperventilation and circulatory failure resistant to volume expansion and inotropic agents. Prognosis is very poor.
7. **Gastrointestinal:** Nausea, vomiting and diarrhea with or without blood and pus may occur. Endotoxin that is absorbed from the gut results in cyto adherence of parasitized red cells in the blood vessels of villi leading to ischemic damage of the epithelium. There may be failure of normal hepatic clearance mechanism. Rarely pancreatitis occurs.
8. **Hypoglycemia:** This occurs due to quinine and quinidine, which stimulates pancreatic insulin secretion. There is also increase in glucose consumption by host and parasite, glycogen depletion and decreased gluconeogenesis. Pregnancy predisposes to hypoglycemia.
9. **Other infections:** Malaria has immunodepressant action resulting in high incidence of infectious diseases.
10. **Other complications:** Prostration, jaundice, orthostatic hypotension, aspiration pneumonia.

Differential Diagnosis of Severe Falciparum Malaria

1. Meningitis (bacterial, viral, protozoal, fungal)
2. Viral encephalitis (measles, Japanese B, rabies)
3. Enteric fever
4. Septicemia, puerperal sepsis
5. Severe or fulminant hepatitis
6. Leptospirosis
7. Relapsing fever
8. Trypanosomiasis
9. Hemorrhagic fever

Treatment

I. Supportive Measures

1. Fluid deficit assessment and correction
2. Fever control
3. Convulsion treatment

II. Specific Treatment

A. Treatment of Chloroquine-susceptible P. vivax, P. falciparum, P. ovale, P. malariae

Chloroquine: This is given in the dose of 600 mg (base) followed by 300 mg at 6, 24 and 48 hours. (In children 10 mg/kg of base as loading dose and 5 mg/kg subsequently). This is useful to treat acute attack of all types of malaria. It is curative for PI. falciparum malaria, but cannot prevent relapses due to exo-erythrocytic cycles of PI. vivax malaria. It can be given intravenously 600 mg diluted and given slowly followed by 900 mg over the next 24 hours.

Drug resistance: In vivo, the response to chloroquine treatment, given as 1.5 g base or 2.5 g salt over 3 days, is graded as below:

S:	Susceptible (Produces a cure)
RI:	Low-level resistance (clearance of parasitemia followed by recrudescence within 28 days)
RII:	Intermediate-level resistance (Decrease in parasitemia with parasite clearance from blood)
RIII:	High-level resistance (No detectable decrease or an increase in parasitemia)

B. Treatment of Chloroquine-Resistant P. falciparum

1. **Quinidine** is preferable to quinine for parenteral use. It is given IV, the loading dose being 10mg/kg dissolved in 300 ml normal saline infused over 1-2 hours. This is followed by constant infusion at 0.02 mg/kg/min till oral therapy with quinine can be given.
2. **Quinine hydrochloride:** 600 mg tds for 3-7 days is useful. This drug can be given intravenously if required for

cerebral malaria. The dose is 7 mg/kg over 30 min followed by 10 mg/kg over 4 hours and then 10 mg/kg over 8 hours or until the patient can complete 7 days of oral treatment. Doxycycline should also be simultaneously given in the dose of 100-200 mg/day.

3. **Mefloquine:** It has a rapid schizonticidal action in the single dose of 15 mg/kg orally maximum dose 1000-1250 mg. It may cause nausea, vertigo, light-headedness, confusion, psychosis and fits.
4. **Halofantrine:** This is effective in some parts of Africa against P. falciparum. It is given in the dose of 500 mg every 6 hours for 3 doses. In children the dose is 8 mg/kg.
5. **Qinghaosu:** This is discovered from herbs by Chinese and is effective for P. falciparum. Artemisinin derivatives are rapidly acting, safe and effective against multi-drug resistant infections. Artemether 3.2 mg/kg IM is given followed by 1.6 mg/kg IM every 12-24 hours until patient wakes up.

   Artesunate 2 mg/kg I.V. stat followed by 1 mg/kg 12 hourly.

   Orally - 100 mg B.D. Day 1 followed by 50 mg B.D. Days 2-5.
6. **Pyrimethamine and sulfadoxime:** A combination of pyrimethamine 25 mg and sulfadoxime 1500 mg helps to cure an acute attack of chloroquine resistant malaria.
7. **Exchange transfusion:** This is given for very high parasitemia (> 10%) and altered mental state.
8. **Ketoconazole, miconazole and liposomal amphotericin B** have been also found effective in refractory cases.

C. *Treatment of Chloroquine-resistant P. vivax:* Oral mefloquine or halofantrine

D. *Treatment of Persistent Hypnozoites in P.vivax or P. ovale Infections*

1. **Primaquine:** This should be given in the dose of 7.5 mg BD for 14 days usually after doing a G6PD test. This has no effect on acute attack.
2. **Bulaquine** is given 25 mg OD for 5 days.

III. **Treatment of Complications**

IV. **Prophylaxis**

1. Measures should be taken to prevent mosquito breeding e.g. proper sewage drainage, and preventing stagnation of water. Spreading oil over the water helps to kill the larva.
2. Protective measures should be taken by persons staying in endemic areas. This includes sleeping under mosquito net and wearing protective clothing.
3. Travelers to endemic areas must take prophylaxis as given in Table below.

Table 3.12 : Malaria Prophylaxis for Travelers

Areas with Chloroquine-susceptible P. falciparum
Chloroquine 300 mg of base once weekly for 1 week before exposure, during exposure and for 4 weeks after exposure.
Areas with Chloroquine-resistant P. falciparum
Mefloquine 250 mg of base once weekly for 1 week before exposure, during exposure and for 4 weeks after exposure or Chlorguanide (Proguanil) 300 mg daily for 1-2 days before exposure, during exposure and for 4 weeks after exposure
To Carry for self-treatment of febrile illness when medical treatment is not available immediately
Pyrimethamine-sulphadoxime single dose of 3 tablets containing 25 mg Pyrimethamine & 500 mg sulphadoxime

4. Malaria vaccines (DNA vaccine, recombinant protein vaccine and transmission blocking vaccine) are still experimental.

12 〉 Kala Azar

Kala azar is caused by Leishmania Donovani. It is endemic in India in Bihar, Bengal, Assam, Orissa, UP and Madras.

The parasite occurs in two forms - amastigote (leishmanial) stage in man or other vertebrates (dog, hamster, etc.) and promastigote (leptomonad) stage in sandfly. The amastigote form is a round or oval body, with thin cell membrane, round or oval nucleus with kinetoplast (DNA containing body and mitochondria) at right angles to the nucleus, a thin axoneme from kinetoplast to the margin of the body and a vacuole.

The promastigote form is found in sandfly and on culture medium. It consists of long slender spindle shaped bodies with a central nucleus, eosinophilic vacuole, and a flagellum.

Life Cycle (Fig. 3.35)

The sandfly bites the infected man and ingests along with blood parasites. The amastigote is transformed to promastigote in the stomach of the vector in 5-7 days. The promastigote multiples and is transformed during the next blood meal to another man.

The parasites are taken by the phagocytes and they

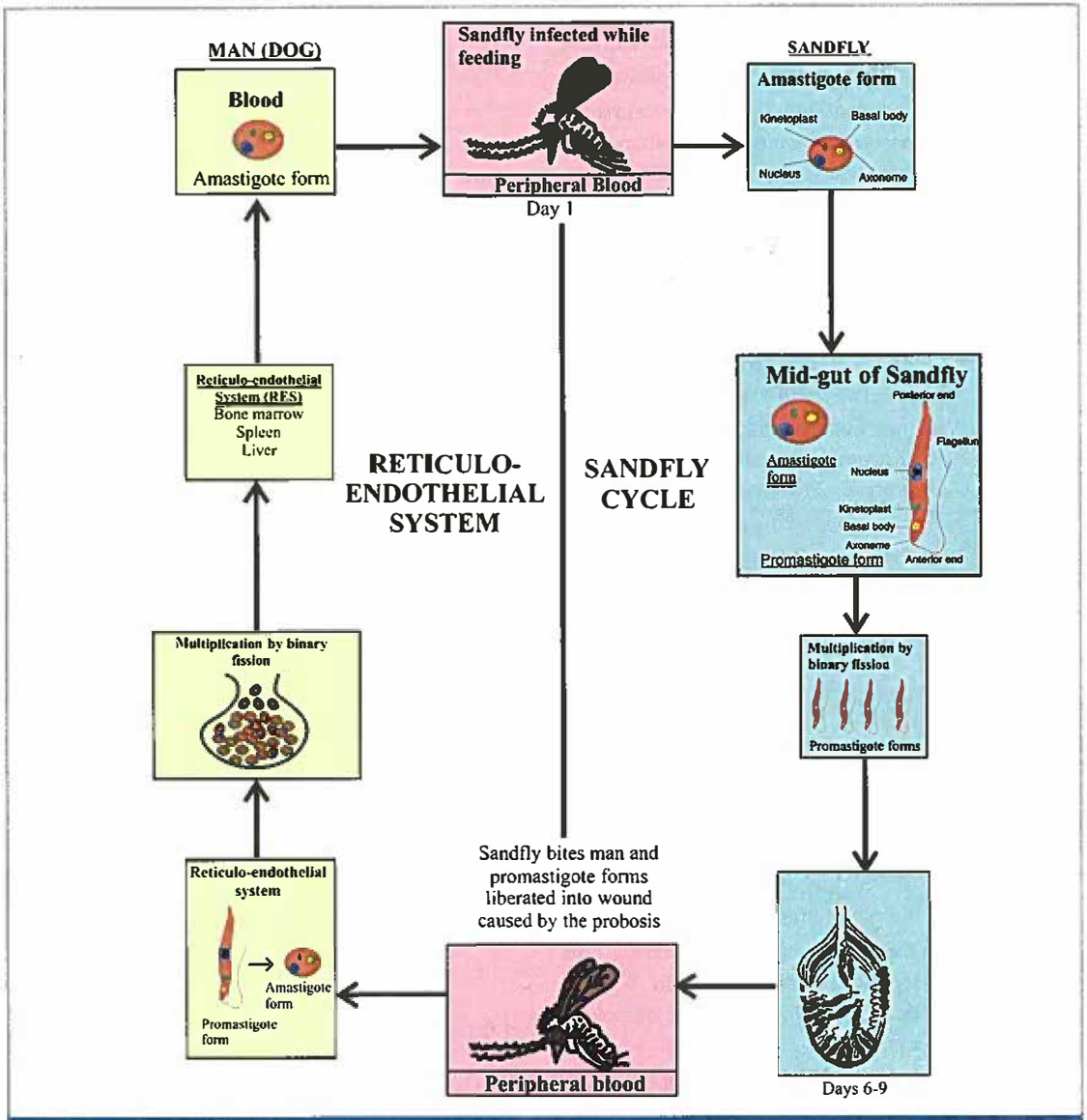


Fig. 3.35: Life cycle of kala azar

multiply within them by binary fission. The macrophages filled with the parasites rupture releasing the parasites in circulation which are taken by the cells of reticuloendothelial system. This leads to enlargement of spleen and liver . Gamma globulins particularly IgG is increased but the antibodies present are not protective.

Immunology

Amastigote excites a cellular reaction of histiocyte proliferation followed by invasion of lymphocytes and plasma cells by the parasites. The sensitized lymphocytes destroy Leishmania-filled macrophages. The increased IgG are responsible for formal gel reaction. Similarly specific antibodies (complement fixing, hemagglutinating and fluorescent) can be used for diagnostic purposes.

Clinical Features

Incubation period varies from few days to few years average 3-6 months.

1. *Pyrexia:* This may be continuous, remittent or later intermittent. The fever may be preceded by rigor or vomiting, but is not associated with headache, prostration or sweating. In 20% cases there may be two spikes of temperature within 24 hours (camel hump fever).
2. *Splenomegaly:* There is progressive enlargement of the spleen which may extend upto the right iliac fossa. Spleen increases in size with each episode of fever.
3. *Hepatomegaly and Lymphadenopathy:* Liver enlargement follows splenomegaly. Usually lymph nodes are not enlarged, but in African and Chinese form they may be enlarged.
4. *Skin:* The skin is dry, rough, harsh and hyperpigmented. Hair is brittle and sparse. Post-kala azar dermal leishmaniasis (PKDL) occurs one year or several years after recovery. They may develop in three forms - depigmented macular lesion like tinea versicolor, erythematous papules or erythematous nodules on ear and face (like nodules of leprosy) All the three types may be present in the same patient.
5. *Systemic features :* Unlike in other fevers there is no apathy, malaise or anorexia. However the patient may be emaciated and anemic with wasting, edema, hemorrhagic manifestations, diarrhea (GI involvement) and cough (due to lung involvement).

Complications

1. *Respiratory:* Pneumonia, pulmonary tuberculosis
2. *Gastrointestinal:* Amebic and bacillary dysentery
3. *Cancrum oris:* Ulcerative lesion near the angle of the mouth
4. Septic infection
5. Pancytopenia

Diagnosis

I. Direct Evidence:

Parasites may be demonstrated by microscopic examination of stained film or by culture examination.

a. *Microscopic examination:* Blood, bone marrow or splenic aspirate can be examined under the microscope. The amastigotes within the macrophages are referral to as LD bodies (Leishman-Donovan bodies).

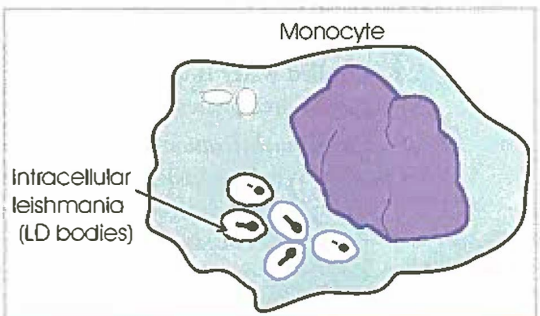


Fig. 3.36: Leishmania-Donovan (LD) bodies in monocytes in Kala-azar

b. *Culture:* About 1-2 ml. of blood, marrow or splenic aspirate is cultured in NMN (Navy, MacNeal and Nicolle) medium which consists of 2 parts of salt agar and one part of defibrinated rabbit's blood. The material for culture is inoculated into the water of condensation of the medium and incubated at 22-24°C for 1-4 weeks. At the end of each week, a drop of condensation fluid is examined for promastigote. This is

a slow method and may take one month to make a diagnosis

II. **Indirect Evidence:**

A. **Blood Count:** There is pancytopenia, but leucocytes are reduced more than erythrocytes. Eosinophils are usually absent.

B. **Serological Tests**

1. *Napiers aldehyde test:* One ml of serum is taken and to it a drop or two of 40% formalde-hyde is added. Jellification of milk white opacity within 2-20 minutes occurs if Kala-azar is of over 3 months duration due to increased gamma globulins. This test is also positive in myeloma, cirrhosis of liver, S Japonicum and African trypanosomiasis. However it is negative in cutaneous leishmaniasis.
2. *Chopra's Antimony test:* 4% urea stibamine solution is added to 1 in 10 dilution of serum in distilled water. Flocculationsoccur in positive cases.
3. *Brahmachari's test:* To 1 ml of serum, distilled water is added. In positive cases a precipitate forms.
4. *Complement fixation test:* This is done with Witebsky, Klingenstein and Kuhn (WKK) antigen and becomes positive in 3 weeks. However, it is not specific, being positive in tuberculosis, leprosy and trypanosomiasis.
5. *Other serological tests:* Indirect immuno-fluorescence and enzyme linked immuno-sorbent assay (ELISA) have also been found to be sensitive.

Treatment

1. *Sodium antimony gluconate:* One ml contains 100 mg of antimony. Daily 6 ml is given IM or IV for 10-15 days. In children 3 ml daily is given and in infants 2 ml daily is given. The course could be repeated after a gap of 15 days.
2. *Pentamidine isethionate:* It is given in the dose of 3-4 mg/kg. daily or on alternate days for 15 injections. Hypotension due to histamine release may occur. This is prevented by giving antihistaminics 20-30 minutes before each injection. It may also cause liver and kidney damage as well as precipitate diabetes mellitus.
3. *Amphotericin B:* In resistant cases of Kala azar it is given in the dose of 0.1-0.25 mg/kg in 5% dextrose slowly on alternate days 3-8 weeks.

Prevention

1. *Personal:* Using mosquito nets (22 meshes/inch) fumigation of sleeping quarters and avoiding sleeping on ground floor would help.
2. *Community:* Man is the reservoir of infection and treating all cases of Kala azar would help, Measures against eradication of sandflies would also be useful.

13 Typhoid

Definition

Typhoid is an infectious disease caused by salmonella typhi which is a gram negative, non-spore forming bacilli.

Epidemiology

Typhoid germs are contracted from food or drink contaminated with excreta from carriers or patients. The spread is facilitated by poor environmental hygiene. Immunity following the infection is not sufficient to prevent relapse.

Predisposing Factors

1. *Organism:* A large number of organisms have to be ingested by healthy person to suffer from typhoid. Smaller inocula may produce the disease if the organisms are very virulent or if the resistance of the host is poor.
2. *Stomach acidity:* The acid in stomach destroys salmonella that is ingested. Hence, patients having achlorhydria (no acid in stomach) or who take large amounts of antacids to neutralize the acid in stomach suffer more often from typhoid.

3. *Intestinal flora:* The normal intestinal flora produces short chain fatty acids which are lethal to salmonella. When these are reduced by antibiotics, the patient is more prone to typhoid.

Pathophysiology

Salmonella that cause enterocolitis after ingestion, invade the mucosal cells and multiply within them. They do not penetrate beyond lamina propria and multiply in the lymphoid tissues (Peyer's patches) of the small intestine. Inflammatory changes occur with accumulation of leucocytes. Enterotoxin liberated by the bacteria may form abscess, which may burst causing ovoid ulcers. This may cause hemorrhage and if the ulcer reaches the serosa, perforation occurs.

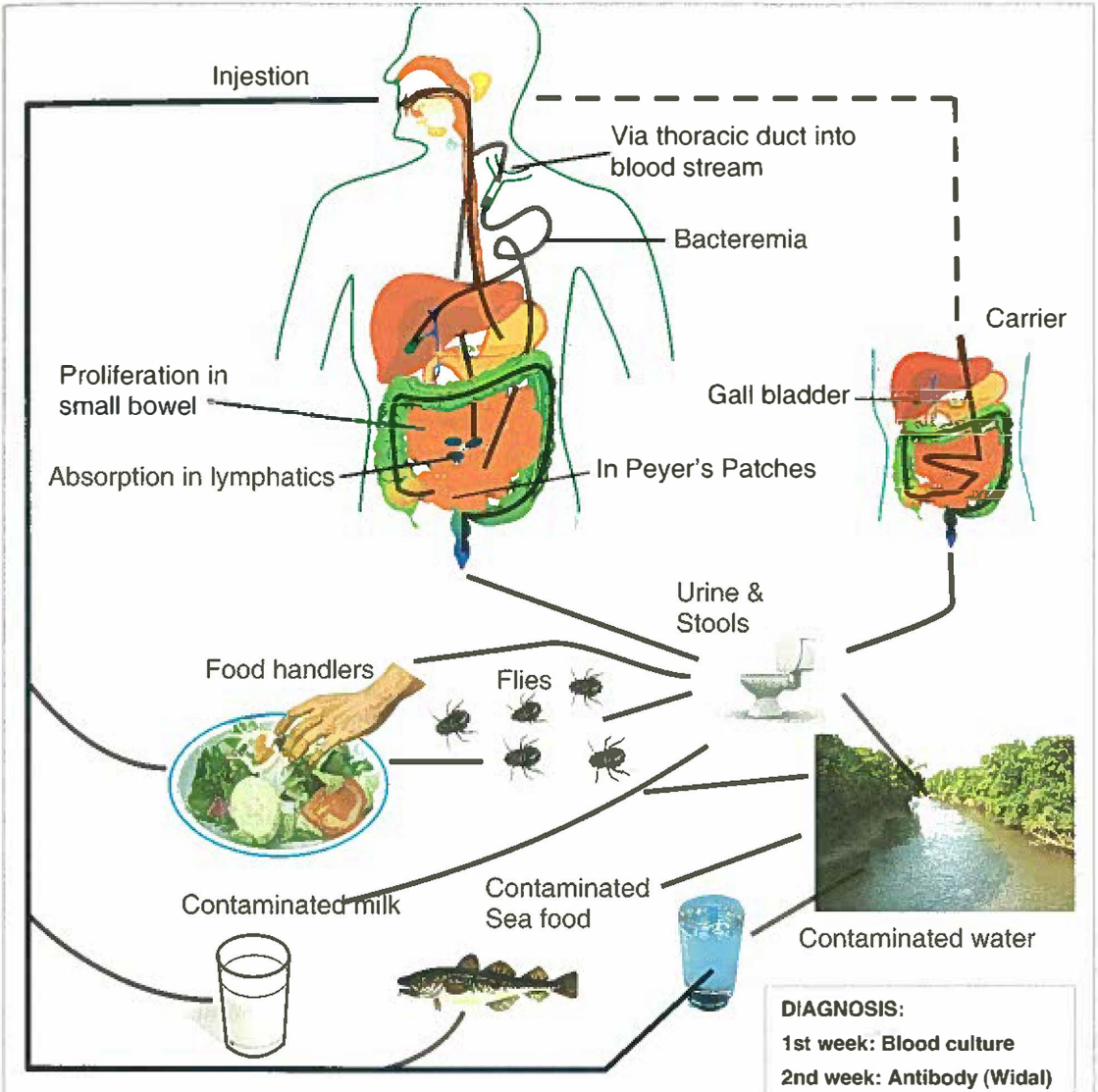


Fig. 3.37 : Life cycle of enteric fever

Clinical Features

I. **Enterocolitis:** In enterocolitis, the infection is usually localized in the small intestines and colon. The incubation period is usually 12 - 72 hours but may be up to 2 weeks.
   1. Nausea, vomiting and an early chill are common initially followed by colicky abdominal pain and diarrhea of watery, green, offensive stools.
   2. Blood mixed with stool and high fever may occur if there is involvement of colon.

   Symptoms may subside within a week or two.

II. **Enteric Fever:** This is clinical syndrome characterized by fever, headache, prostration, cough, splenomegaly and leucopenia, caused by S. typhi or paratyphi. The incubation period is 7-14 days. The onset is insidious with the following features:
   1. *Fever:* Usually, there is a continuous fever, which typically rises in the stepladder pattern in the first week, but it may be remittent type. Rigors and sweats are not common. It is usually accompanied by dull headache.
   2. *Abdomen:* Mild abdominal discomfort and distension occurs with nausea, vomiting and constipation, which are followed by diarrhea (pea soup stools). Hepatomegaly and splenomegaly occurs.
   3. *Rose-spots:* These are erythematous, maculopapular lesions 2 - 4 mm in diameter which blanch on pressure usually seen on the upper abdomen, back and chest. They occur in the first or second week.
   4. *Miscellaneous:* Cough due to 'typhoid bronchitis' and relative bradycardia may occur.

III. **Clinical course:** In the pre-antibiotic era, the patient gradually recovered or developed complications in the third or fourth week. Relapse occurs in 5-10% of untreated patients and 15-20% of patients on treatment.

Chronic Carrier State

Chronic carriers are those who excrete salmonella organism in their feces for at least one year. Usually they are typhoid patients or persons with biliary tract disease. The gall bladder serves as a reservoir of infection and this carrier state is asymptomatic. It may persist for lifetime without antibiotics or biliary tract surgery. Rarely, urinary carriers may be present.

Investigations

1. **Culture:** Salmonella organisms can be grown from blood culture or clot culture on MacConkey's agar in the first week in 90% of patient. In the second week, stool culture is more reliable. The organism can also be isolated in some cases from urine.
2. **Serology:** Widal test determines the agglutinins against somatic (O) and flagellar (H) antigens. This test is negative in the first week, becomes positive by second or third week and may remain positive for a prolonged period. Hence, a single positive test is of no diagnostic value, but a demonstration of a rising titer in a patient of fever is suggestive of typhoid fever.
3. **Leucopenia:** is usually present except in presence of complications or in children.

Complications

I. **Abdominal**
   1. **Hemorrhage** may occur at the end of the second week and is characterized by black stools, tachycardia, hypotension and diarrhea. There is no abdominal pain or rigidity or obliteration of liver dullness like in intestinal perforation. Transfusions may be needed if there is massive blood loss.
   2. **Perforation** may occur at the end of the second week or in the third week. It is characterized by acute pain in the lower abdomen, vomiting, abdominal distension, hypotension and tachycardia. The liver dullness may be obliterated and the abdomen becomes tender, rigid and silent (absent peristalsis).
   3. Tympanitis
   4. Cholecystitis
   5. Splenic infarction

6. Rarely-appendicitis, intussusception and pyogenic liver abscess

II. **Extra-abdominal**

1. Myocarditis, endocarditis
2. Osteomyelitis, arthritis, typhoid spine and Zenker's degeneration of rectus abdominis
3. Pulmonary infection and embolism
4. Thrombophlebitis
5. Electrolyte imbalance, shock and acute renal failure
6. Neurological: Meningoencephalitis, meningism, cranial nerve palsies, myelitis, ascending paralysis, Parkinsonism, athetosis, cerebellar ataxia, neuritis
7. Typhoid state: This is characterized by coma vigil, muttering delirium, carphologia (picking up clothes in bed) and subsultus tendinosis
8. Psychosis

Treatment

I. **ENTEROCOLITIS:** This is a self-limiting disease which requires only symptomatic treatment like fluid and electrolyte balance antiperistaltic agents etc. Antibiotics are used only if there is impaired host resistance.

II. **Enteric Fever:**

A. **General Measures:**

1. *Rest:* Patients with enteric fever must be given complete bedrest and preferably hospitalized because the incidence of complications is more in patients who have not taken adequate rest.
2. *Diet:* For the first dew days a semi-solid diet is advised and later a low-roughage, high-calorie diet like bananas is advised. This is to decrease the intestinal content in presence of friable intestines.
3. *Nursing care:* The general care of the patient includes good nursing and disinfection of excreta and bed linen in 2% Lysol. Fluid and electrolyte balance and vital signs must be regularly observed to detect any serious complications.
4. *Antipyretics:* Fever and body ache can be treated with paracetamol and tepid sponging.

B. **Antibiotics**

1. ***Conventional:*** Oral or IV *chloramphenicol* 500 mg 6 hourly in the first week followed by 500 mg 8 hourly for 2 more weeks. *Co-trimoxazole* 2 tablets TDS, *Amoxycillin* 1 gm 6 hourly or *Ampicillin* 500 mg 6 hourly are other useful drugs.
2. ***Quinolones:*** *Ciprofloxacin* 200 mg IV 8-12 hourly in a drip has been found to be very useful in chloramphenicol resistant typhoid fever, If the patient is not vomiting it can be given orally in the dose of 500 mg 8-12 hourly. *Ofloxacin* 200 mg daily for 7-10 days is also useful.
3. ***Cephalosporins:*** The drug of choice is *Ceftriaxone* 3-4 gm once daily for 7 days or 80 mg/kg once daily for 5 days. It is as effective as chloramphenicol in reducing fever in typhoid. *Other cephalosporins* are also effective (See Ch. 15)

C. **Steroids:** In the absence of intestinal complications, steroids can be used for severe toxicity, hyperpyrexia, septicemia and haemolysis along with antibiotics, It is given as prednisolone 30-60 mg daily in divided doses with antacids.

D. **Chronic carrier:** Ampicillin 1 gm 6 hourly for one week followed by 1 gm 8 hourly for 6-12 weeks is needed. Cholecystectomy may be advised for biliary carriers.

Prevention

I. Typhoid can be prevented by improving personal hygiene, sanitary disposal of excreta, pasteurization of milk, adequate water protection and identification, isolation and treatment of chronic carriers.

2. Vaccine:
   a. *Injectable Vaccine* : A vaccine (TAB) prepared from heat killed *S.typhi* organisms is available for immunization of high risk persons. It is given in the dose of 0.5 ml subcutaneously and repeated 4 weeks later in the dose of 1.0 ml. It gives protection for 2 years. Given >2 yrs. of age.
   b. Oral Vaccine (Ty21a) : Oral Vaccine - 1 tablet on alternate days for 4 doses. Contraindicated in pregnancy in children <6 yrs. of age. Repeated every 5 years.

14 Leukemia

Leukemia is a disease of unknown etiology, characterized by an uncontrollable and abnormal proliferation of leucocytes and their precursors, which infiltrate the body tissues.

Acute Leukemias

Acute leukemia is a hematological neoplasm characterized by proliferation of malignant hemopoietic blast cells. There should be more than 20% blasts cells in the bone marrow at clinical presentation. Untreated, acute leukemias are rapidly fatal, median survival being two months. Death occurs from infection or hemorrhage or both.

Acute leukemias are subdivided into acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL) on the basis of the blasts present, whether myeloblasts or lymphoblasts. The **morphology, clinical features, cytochemistry, immunophenotyping and molecular genetics** are used to subdivide AML and ALL into their subtypes (Tables 3.14, 3.15, 12.5, 12.6)

Acute Myeloid Leukemia (AML)

AML occurs at all ages. AML is subdivided into 8 subtypes (Table 11.2) based on morphology and cytochemistry according to FAB classification.

Acute lymphoid leukemia (ALL)

ALL occurs primarily in children and sometimes after the age of 40. FAB classification subdivides ALL into 3 subtypes (Table 11.3).

Table 3.13 : French American British (FAB) Classification

Acute Leukemias (>20% blasts in bone marrow)
Acute myeloid leukemia (AML): M0 to M7
Acute lymphoid leukemia (ALL): L1 to L3
Chronic Leukemias (<10% blasts on smear)
Chronic myeloid leukemias (CML)
Chronic lymphoid leukemias (CLL)

Clinical Features in AML and ALL

I. **Due to bone marrow failure**
   1. Due to anemia: Fatigue, pallor, dysnoea
   2. Bleeding manifestations: Easy bruising, petechiae, purpura, bleeding from various sites and in various tissues.
   3. Infections and/or fever: Infective lesions in mouth, throat, respiratory tract, skin.

II. **Due to Organ infiltration**
   1. Bony tenderness especially of the sternum
   2. Hepatosplenomegaly & lymphadenopathy (mediastinal, axillary, inguinal and cervical)
   3. CNS: Hemorrhage, meningeal infiltration and multiple cranial nerve palsies
   4. Skin or orbit: Chloromas
   5. Kidneys: Renal failure
   6. Heart: Cardiomyopathy and pericarditis
   7. Fundus: Roth spots, papilledema
   8. Testes: Swelling, particularly in ALL
   9. Gum hypertrophy in AML M4/M5

Peripheral Blood Picture in AML and ALL

1. Anemia: Normochromic, normocytic
2. Thrombocytopenia; DIC may be present in M3
3. Total WBC count may be increased, normal or low. Neutropenia is present.
4. Variable number of blast cells may be present. "Smear" cells may be present in some ALLs.

Bone Marrow in AML and ALL

1. Cellularity: Usually hypercellular
2. Leukemic blast cells > 30% should be present.
3. Erythroid cells and megakaryocytes reduced.

Table 3.14 : Classification of Acute Myeloid Leukemia (AML)

Subtypes (FAB)	Morphology (Bone Marrow)	Common Clinical Features	Diagnostic Tests/Cytochemistry
M0 Minimally Differentiated	Large agranular blasts Myeloid by immunophenotyping		Myeloperoxidase - (or <3% positive and + at electron microscopic level) PAS - (or <3% positive)
M1 Myeloblastic without maturation	Least differentiated blasts (>90%of NEC), **granular or agranular.** Auer rods +		Myeloperoxidase + (>3%) PAS + (diffuse)
M2 Myeloblastic with maturation	Differentiation to promyelocytess Blasts (>30- 89%of NEC) Monocytic cells <20% Auer rods + Abnormal neutrophils	8;21 Translocation Common in young patients	Myeloperoxidase + + PAS + (diffuse)
M3 Promyelocytic	Bundles of rod-like structures (Sultan bodies/"Faggots" in promyelocytes. Auer rods + Bilobed nuclei. Microgranular variant also present	Bleeding tendency due to DIC and thrombocytopenia. Young patients. 15; 17 Translocation	Myeloperoxidase + + + PAS + (diffuse)
M4 Myelomonocytic	Mixture of blasts (>30% of NEC) promyelocytic and monocytic differentiation (>20% monocytic lineage)	Gum hyperplasia	Myeloperoxidase + + PAS + (diffuse) Non-specific esterase + (monocytic cells only) Serum & urinary lysozyme increased
M5 **M5a: Monoblastic** **M5b: Monocytic**	> 80% monocytoid cells. M5a: Monoblasts only M5b: Monoblasts differentiated into promonocytes and monocytic cells	Gum hyperplasia. Hemorrhagic rash on skin. Lymphadenopathy, hepatosplenomegaly.	Non-specific esterase +++ Myeloperoxidase - PAS + (diffuse) Serum & urinary lysozyme increased
M6 Erythroleukemia	Over 50% cells are erythroid precursors with bizarre dyserythropoietic forms Myeloblasts (with Auer rods) 30% after excluding erythroid cells		Erythroblasts PAS + (block) Only myeloblasts are Myeloperoxidase +
M7 Megakaryoblastic	Fibrosis of bone marrow, megakaryoblasts >30%	Blood shows pancytopenia	PAS + (granular) Myeloperoxidase- Platelet peroxidase + (EM) Acid phosphatase ++ (diffuse)

NEC: Non-erythroid cells; PAS: Periodic Acid-Schiff

Treatment

I. Chemotherapy

Chemotherapy for ALL

A. **Induction**: Combination chemotherapy is used. Any one of the two regime may be used.

1. ***Vincristine*** 1.4 mg/m² IV every week for 1 month.

   L-Asparaginase 600 units/m² SC biweekly for 1 month.

   Prednisolone 40 mg/m² orally daily for 1 month

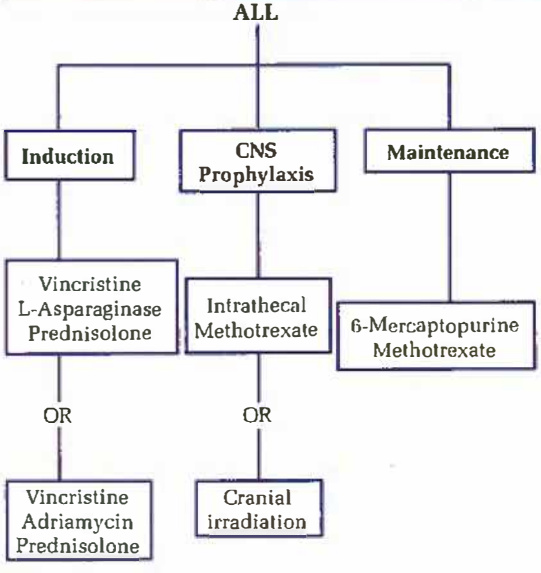
2. ***Vincristine*** 1.4 mg/m² IV weekly for 1 month.

   Doxorubicin (Adriamycin) 40 mg/m² IV weekly for 1 month.

Table 3.15 : Classification of Acute Lymphoblastic Leukemias (ALL)

FAB Classification	Morphology	Immunological Sub-Type	Diagnostic Tests	Prominent clinical features
L1 Small, monomorphic. More common in children	Small uniform blast cells with large regular nucleus surrounded by a thin rim of cytoplasm.	B-ALL or T-ALL (Null-ALL C-ALL rare)	c-ALL antigen + TdT + PAS + blocks in cytoplasm.	T-ALL type shows thymic enlargement
L2 Large,heterogenous. More common in adults	Heterogenous size of blasts with prominent nucleoli and relatively abundant cytoplasm.	Mostly T-ALL C-ALL or Null-ALL	Acid phosphatase + TdT + Anti-T +	T-cell type shows thymic enlargement.
L3 Burkitt cell-type Uncommon	Large blasts with multiple small vacuoles throughout a basophilic cytoplasm and over a homogenous nucleus	B-ALL	Surface immunoglobulin + TdT - Oil Red O +	Lymphdenopathy Spleen & liver enlargement.

TdT: Nuclear enzyme terminal deoxynucleotide transferase; PAS:Periodic acid-Schiff



Prednisolone 40 mg/m² orally daily for 1 month with either of the regimes.

The following is ensured:

a. Adequate hydration and good urine output.

b. Alkalinization of urine with soda-bicarb 2.0 gm four times a day.

c. Allopurinol 100 mg three times a day to prevent uric acid nephropathy.

After a course of the above medicines, bone-marrow aspiration is done to decide whether complete remission is achieved (Complete remission means normocellular bone-marrow with less than 5% blast cells). If it is not achieved, one more cycle of chemotherapy is given or alternative treatment is tried.

B. **CNS prophylaxis:** Intrathecal methotrexate 15 mg/m² every week for 4-8 weeks following complete remission, or cranial irradiation 1800-2400 rads. may be given to reduce the chance of neurological involvement.

C. **Intensification:** Methotrexate + Leucovorin

D. **Maintenance:** This includes administration of low dose chemotherapy over a period of 36 months. 6-Mercaptopurine 75 mg/m² daily is given orally, along with oral methotrexate 20 mg/m² once a week. During maintenance period, combination chemotherapy given for induction is also used intermittently. If the patient remains in continuous remission for 3 years maintenance treatment is stopped.

Result of treatment: 80% of patients go into complete remission and 40% are cured. The prognosis depends on age, initial total count, surface marker characteristics (T-cell/B-cell have bad prognosis), mediastinal mass.

Chemotherapy for AML

A. **Induction:**

DAT regime is given which consisting of:

Daunorubicin 45 mg/m² IV bolus on days 1, 2 and 3 or days 4,5 and 6.

Cytosine arabinoside 100 mg/m²/day by continuous IV infusion for 7 days.

Thioguanine 100 mg/m² orally twice a day for 7 days. Bone-marrow aspiration is done after 3 weeks and if evidence of leukemia persists, the above cycle is repeated.

B. **Consolidation therapy**: This includes 2-6 courses of combination therapy used for induction. Recently use of higher dose of cytosine arabinoside with daunorubicin or combination of non-cross resistant drugs has been found to be of some benefit.

C. **Maintenance therapy**:

Cytosine arabinoside 60 mg/m² once a week and *6-Thioguanine* 40 mg/m² twice a day orally for 4 days/week is given for 1-3 years. This increases the duration of disease-free survival.

D. **Bone-marrow transplant**: This has a high curative potential. It is done following complete remission. However, its limitations are high cost and non-availability of matched donors.

Results of treatment: Sixty percent achieve complete remission but only 20% get cured.

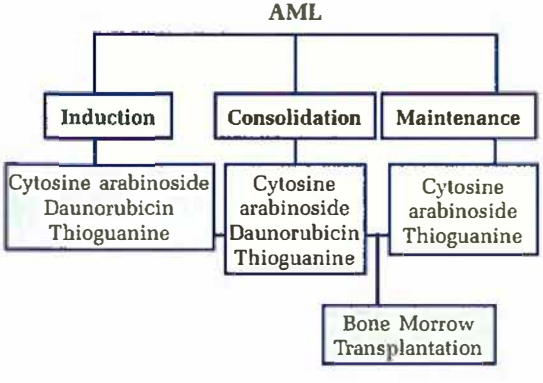
E. All-trans retinoic acid (ATRA) is used for the treatment of acute promyelocytic leukemia (APML)

II. Supportive Treatment

A. Blood/Platelet/ Granulocyte transfusions

B. Combination of higher antibiotics like aminoglycoside (gentamicin, amikacin, etc.) with cephalosporins (cefotaxime, cefazolin, ceftazidime, etc.

C. Treatment of oral, gastrointestinal and systemic fungal infections.



D. Allopurinol before starting antileukemic agents to prevent hyperuricemia.

E. Maintenance of good oral hygiene, adequate nutrition, electrolyte and acid base disorders.

III. Immunotherapy:

This is used because a patient in complete remission reacts to his blast cells as though they were foreign tissue. It may be attempted with BCG or allogenic irradiated leukemic cells.

Chronic Leukemia

Chronic leukemias have a more indolent behavior and better prognosis than acute leukemias. Chronic lymphoid leukemia (CLL) tends to occur in the elderly. Chronic myeloid leukemia (CML) is more common in middle age. Juvenile CML occurs in children below 3 years of age.

Clinical features in CML and CLL

I. **Due to anemia**: Pallor, fatigue, dysnea, etc.

II. **Due to Organ infiltration**:

1. Hepatosplenomegaly
2. Lymphadenopathy: Usually cervical, mediastinal and axillary. Lymphadenopathy is more common with CLL.
3. Cardiorespiratory: Pulmonary congestion, infiltration or collapse. Pleural effusion.
4. CNS: Meningeal infiltration, cranial nerve palsies and paraplegia
5. Skin: Pruritus and nodules, gout

III. **Due to thrombocytopenia**: Bleeding tendencies (epistaxis, hematemesis, etc.) in CLL. Platelets are normal or increased in CML.

IV. **Due to increased metabolism**: Fever, weight loss, malaise, perspiration and gout.

Peripheral Blood Picture in CML and CLL

1. Anemia: Normochromic, normocytic
2. Leucocytes increased

In CML:

Chronic phase shows 1,00,000-5,00,000/cc. with early granulocyte cells (metamyelocyte,

myelo-cyte, promyelocyte, band forms). Only occasional blast cells is seen (<10%). Neutrophil alkaline phosphatase is markedly reduced.

Blast crisis in CML is indicated by an increasing basophil count. It may be myeloid or lymphoid in origin. Myeloid blast crisis resembles AML, but Auer rods are not seen. Lymphoid blast crisis is rarer and shows lymphoblasts with characteristics such as TdT positivity.

In CLL:

50,000-2,00,000/cc. Majority(>90%) are mature small lymphocytes. "Smudge" or "smear" cells (degenerative forms) may be present. Absolute neutrophil count is normal. Neutropenia occurs in advanced CLL.

3. Platelets are normal or low.

Bone Marrow in CML and CLL

1. Cellularity: Hypercellular
2. Erythropoiesis is normoblastic, sometimes megaloblastic. Reduced erythroid precursors.
3. Leucopoiesis:

   In CML bone-marrow is hypercellular with myeloid: erythroid ratio increased. There may be myelocytes, promyelocytes, eosinophils and basophils. Blast cells or promyelocyte more than 30% suggests blast crisis in CML.

   In CLL both small and large lymphocytes are diffusely infiltrated (25-95%). Myeloid precursors are reduced.
4. Megakaryocytes are prominent in CML and reduced in CLL.
5. **Cytogenetics:** Philadelphia chromosome may be present in myeloid and erythroid precursor cells in 70-90% of CML cases.

Treatment

I. Chronic Myeloid Leukemia
   A. *Chemotherapy:*
      1. *Imatinib Mesylate* 400 - 800 mg daily is the drug of choice. Newer drugs if there is imatinib failure.
      2. *Busulfan* 4 mg/day orally, reduced to 2 mg/day when WBC count falls to 30,000/c.c.
      3. *Hydroxyurea* 1-2 gm orally till WBC count falls to 10,000/cm. It is used in patients with chronic myeloid leukemia not responding to busulfan.
   B. *Radiotherapy:* This may be useful as a symptomatic measure to reduce the size of massively enlarged spleen, when cytotoxic drugs have failed.
   C. *Splenectomy:* This may be required when enlarged spleen is causing symptoms.
   D. Bone Marrow Transplantation is the only curative treatment.

II. Chronic Lymphatic Leukemia
   A. *Chemotherapy:*
      1. *Chlorambucil* 6-10 mg/day for 14 days with a break of 14 days. When WBC count falls below 25,000/c.c. the dose is reduced to 2-4 mg/day. It is discontinued when the WBC count falls below 1,000-10,000/c.c.
      2. *Cyclophosphamide:* 2-3 mg/kg. I.V. for 6 days.
   B. *Radiotherapy:* This is useful for large granular masses if they cause symptoms.
   C. *Steroids:* Prednisolone 40 mg/day may improve hemoglobin or platelet count.
   D. *General supportive measures:*
      1. Blood transfusion
      2. Antibiotics
      3. Gamma globulins

Hairy Cell Leukemia (HCL)

Hairy cell leukemia is a rare type of chronic leukemia with pancytopenia and marked splenomegaly without lymphadenopathy. The typical "hairy" lymphoid cells of B-cell origin are seen in the peripheral blood and in bone marrow aspirates and splenic imprints. These cells also show a characteristic strong postive tartaric acid resistant acid phosphatase (TRAP) reaction.

15 › Malignant Lymphoma

Definition : Malignant Lymphoma refers to a large

variety of malignant lymphoproliferative disorders arising from lymphoid components of various organs. They are classified as Hodgkin's and Non-Hodgkin's lymphoma.

Hodgkin's Lymphoma

Definition

Hodgkin's disease is characterized by presence of Reed Sternberg cell and is caused by either viral infection or deranged immune mechanism.

Clinical Features

I. *Lymphadenopathy:* Cervical, mediastinal, axillary and inguinal. Unilateral initially, later bilateral. The glands are painless, discrete and firm.

II. *Hepatosplenomegaly:* Moderate to marked non-tender enlargement of liver and spleen.

III. *Constitutional:* Fever, night sweats, weight loss, anemia and cachexia may occur. Fever may be remittent, continuous, or Pel Ebstein's type (Fever for several days interrupted by periods of remission).

IV. *Due to infiltration* or *metastasis*

A. *Skin:* Pruritus, erythema and herpes zoster

B. *Bones:* Pain, tenderness and sclerosis (ivory vertebrae)

C. *CNS:* Pain, paresthesia and paraplegia

D. *GI:* Jaundice, ascites and intestinal obstruction

F. *Genitourinary:* Hematuria, retention of urine and backache

Stages (ANN Arbor Staging)

I. Involvement of a single lymph node region (I) or of a single extra lymphatic organ (Ie).

II. Involvement of two or more lymph node regions on the same side of the diaphragm (II) or involvement of extralymphatic organ and one or more lymph regions on the same side of the diaphragm (IIe).

III. Involvement of lymph node regions on both sides of the diaphragm (III). It may be accomp-anied by involvement of spleen (IIIs) or by involvement of extralymphatic organs (IIIe).

IV. Diffuse involvement of extralymphatic organs or tissues with or without associated lymph node involvement.

Each stage is sub-divided into two categories.

A. For those without symptoms.

B. For those with symptoms, e.g. fever, weight loss

Treatment

I. *Radiotherapy:* Most effective for stages I and II.

II. *Chemotherapy:* For patients with stages III and IV. MOPP or ABVD regime may be used.

A. **MOPP regime**

1. Mustine hydrochloride 6 mg/meter^2 I.V. on Day 1 and 8.
2. Oncovin (Vincristine) 1.4 mg/meter^2 I.V. on Day 1 and 8.
3. Procarbazine 100 mg/meter^2 orally from Day 1 to 14.
4. Prednisolone 40 mg/meter^2 orally from Day 1 to 14.

No drugs are given from Day 15-28. This is one course.

Six such courses may be given.

B. **ABVD regime**

1. Adriamycin 25 mg/m^2 IV bolus on day 1,8,14
2. Bleomycin 10 mg/m^2 IV boluson day 1,14
3. Vinblastine 6 mg/m^2 IV bolus on day 1,8,14
4. Dacarbazine 375 mg/m^2 IV bolus on day 1,14

The cycle should be repeated on 29th day.

III. *Splenectomy:* Laparotomy and splenectomy is advocated in many patients except with stage IV disease.

Advantages:

A. It can be determined whether spleen is involved.

B. It prevents recurrence in spleen, which is difficult to treat with radiotherapy due to the close proximity of left kidney and lung.

Non-Hodgkin's Lymphomas

Definition : Non-Hodgkin's lymphomas (NHL) are a heterogenous disease entity characterized by involvement of variety of anatomical sites other than lymph nodes e.g. skin, gastrointestinal tract, bone marrow etc.

Clinical Features

The clinical presentation has many similarities to Hodgkin's disease. However, the pattern of spread is variable and patients may present with disease in organs other than lymph nodes or with leukemic manifestations.

1. **Lymphadenopathy**: Asymmetrical painless enlargement of the peripheral lymph node may occur. Retroperitoneal and mesenteric lymph nodes are frequently affected.
2. **Hepatosplenomegaly**: Spleen is usually markedly enlarged. Liver is also enlarged.
3. **Anemia**: This occurs due to involvement of the bone marrow, hypersplenism, hemolysis or autoimmune disease.
4. **Gastrointestinal symptoms**: Abdominal pain, nausea, vomiting, diarrhea or intestinal obstruction may occur due to involvement of the gastrointestinal tract.
5. **Skin**: Skin deposits may occur and skin may be primarily involved in two unusual closely related T lymphocytic lymphomas -Mycosis fungoides and Sezary syndrome.

Treatment

The initial treatment will depend upon whether there is favorable or unfavorable cytologic pattern. Radiotherapy and chemotherapy are useful in majority of the patients. However, surgery is useful only in selected cases with primary extranodal lesions.

Table 3.16 : Classification of NHL (International Working Formulation)

Low Grade	Intermediate Grade	High Grade
1. Small lymphocytic	1. Follicular Large Cell	1. Large Cell Immunoblastic
2. Follicular Small Cleaved Cell	2. Diffuse Small Cleaved Cell	2. Lymphoblastic
3. Follicular Mixed Small Cleaved and Large Cell	3. Diffuse Mixed Small and Large Cell	3. Small Non-cleaved Cell (Burkitt's and Non-Burkitt's)
	4. Diffuse Large Cell	4. Miscellaneous (Mycosis fungoides, Histiocytic)

I. **Favorable NHL**

Therapeutic interventions are postponed until symptoms develop. Combination chemotherapy (Table) or total body irradiation is useful. The clinical course is characterized by continuous pattern of remission and relapse over a period of several years.

Table 3.17 : Combination Chemotherapy for NHL

Regime	Drug	Duration
I. CVP:	Cytoxan 600 mg/m² IV	Day 1 and 8
	Vincristine 1.4 mg/m² IV	Day 1 and 8
	Prednisolone 40 mg/m² oral	Days 1-15
II. CHOP:	Cytoxan 600 mg/m² IV	Day 1 and 8
	Adriamycin 50 mg/m² IV	Day 1
	Vincristine 1.4 mg/m² IV	Day 1 and 8
	Prednisolone 40 mg/m² oral	Days 1-15

II. **Unfavorable NHL**

Chemotherapy is the mainstay of treatment in diffuse lymphoma. The goal is to achieve complete remission, as lesser response is always associated with poor prognosis. Localized disease is potential curable by radiotherapy, however such localied disease is rare.

Burkitt's Lymphoma

1. This is B lymphoblastic lymphoma found in young African children
2. It may result from inability of the immune response to deal with Epstein Barr Virus.
3. It usually produces massive jaw lesions, extranodal abdominal involvement, ovarian tumors and lymphoid tissues of cervical and ileocecal region.
4. Histologically there is characteristic "starry sky" appearance of B lymphoblastic lymphomas with scattered histiocytic reticular cells.

Mycosis Fungoides

Mycosis fungoides, a chronic lymphoma of the skin, has three stages:

1. Premycotic stage: Lesions similar to eczema or psoriasis

2. Infiltrative or Plaque stage: This is with generalized exfoliative erythroderma and invasion of the blood by typical convoluted lymphoid cells (Sezary syndrome)
3. Nodular or tumour stage: Deeper invasion by the tumour and infiltration of lymph nodes and other organs.

16 Human Immunodeficiency Virus (HIV) Disease: Acquired Immune Deficiency Syndrome (AIDS)

HIV disease is an infectious disease cause by the human immunodeficiency virus.

AIDS occurs at a late stage of HIV infection, when the CD4+ T-lymphocyte count is <200/μL and there is documentation of an AIDS-defining condition (See Table).

Definition of HIV Infection

According to the HIV infection case definition(CDC 2008), a reportable case of HIV infection among adults and adolescents aged ≥13 years is categorized by increasing severity as Stage 1, Stage 2, Stage 3 (AIDS) or Stage unknown as shown in the table below:

Morphology of HIV

Etiology

AIDS is caused by an infection with HIV-1 or HIV-2 (Family Retroviridae, Subfamily Lentivirus). HIV-1 is the most common cause worldwide. HIV-1 has many different strains due to mutations. There are three groups M (major, subtypes A-J), O (outlier, rare) and N (very rare). In India, Group M subtype C predominates.

Transmission of HIV

1. *Sexual transmission*

   Intimate homosexual or heterosexual contact with an infected person can cause transmission of HIV. High risk of transmission is with:receptive anal

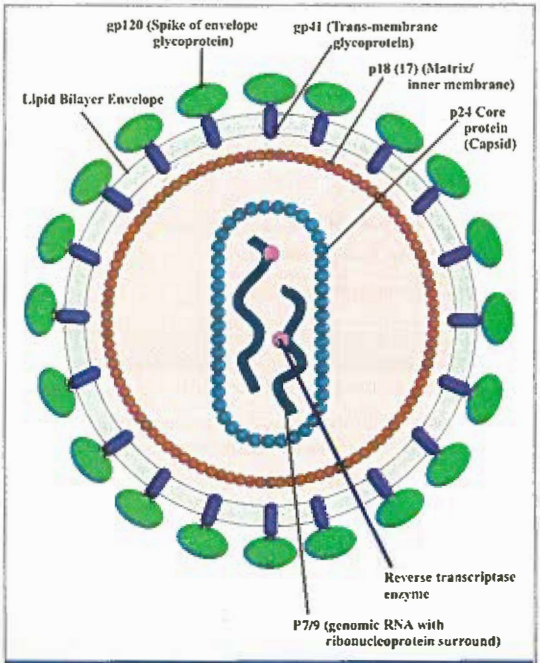


Fig. 3.38 : Schematic illustration of HIV components

Table 3.18 : Staging of HIV Infection

Stage	*Lab confirmation of HIV infection*	*CD4+ T-lymphocyte count per μL (T4)*	*CD4+ T-lymphocyte percentage (% CD4)*	*Clinical Evidence**
Stage 1	Confirmed Positive	***And*** T4:≥ 500	***Or*** % CD4: ≥ 29	None required (but no AIDS-defining condition)
Stage 2	Confirmed Positive	***And*** T4: 200 - 499	***Or*** % CD4: 14-28	None required (but no AIDS-defining condition)
Stage 3	Confirmed Positive	***And*** T4:< 200	***Or*** % CD4:<14	***Or*** Documentation of an AIDS-defining condition
Stage Unknown	Confirmed Positive	*No information*	*No information*	***And*** No information on presence of an AIDS-defining condition

Table 3.19 : AIDS Defining Conditions for Adults and Adolescents <13 yrs (as per CDC)

1. Candidiasis: esophagus, trachea, bronchi or lungs
2. Cervical cancer: invasive
3. Coccidioidomycosis, disseminated or extra pulmonary
4. Cryptococcosis - extra pulmonary
5. Cryptosporidiosis with diarrhea persisting for > 1 month
6. Cytomegalovirus disease (other than liver, spleen, lymph nodes)
7. Cytomegalovirus retinitis (with loss of vision)
8. Encephalopathy: HIV-related
9. Herpes simplex: Chronic ulcers lasting > 1 month or bronchitis, pneumonitis, or esophagitis
10. Histoplasmosis: Extra pulmonary or disseminated
11. Isosporiasis with diarrhea persisting > 1 month
12. Kaposi's sarcoma
13. Lymphoma: Burkitt's
14. Lymphoma: Lymphoblastic
15. Lymphoma: Primary, of brain
16. *Mycobacterium avium* complex or *M. kansasii*
17. *Mycobacterium tuberculosis*, any site (pulmonary, disseminated or extrapulmonary)
18. *Mycobacterial* infection: other species or unidentified species, extrapulmonary or disseminated
19. *Pneumocystis jirovecci (carinii)* pneumonia
20. Pneumonia: recurrent
21. Progressive multifocal leucoencephalopathy
22. *Salmonella* septicemia: Recurrent
23. Toxoplasmosis: brain
24. Wasting syndrome due to HIV

Table 3.20 : Definition of AIDS in adults

CONFIRMED HIV INFECTION WITH:
Clinical diagnosis (presumptive or definitive) of any AIDS-Defining condition (Table 3.19)
OR
CD4 count < 200/ μL or %CD4 <14 in asymptomatic adults or children aged >5 years

intercourse, vaginal intercourse (male to female higher than female to male), associated STDs or genital ulceration. Lower risk of transmission is with oral sex and circumcised males.

2. *Transmission by blood, blood products or other body fluids*

   High-risk: IV drug users who share contaminated needles, hemophiliacs, thalassemics and other transfusion recipients, organ transplant patients.

   Low-risk: Health care workers and laboratory personnel who work with HIV-infected specimens. The risk of transmission of HIV following skin puncture from a sharp object that is contaminated with blood from an HIV positive patient is 0.3% and after mucous membrane exposure 0.09%. (Similar risk for HBV transmission is 6-30% and HCV transmission is 1.8%).

   Very low risk: Transmission of HIV from an infected health care worker to patients through invasive procedures.

   No risk: Saliva, tears, sweat, urine cannot cause transmission of HIV. The virus cannot be passed through casual or family contact or by insects such as mosquitoes.

3. *Maternal-fetal/infant transmission*

   Mother to child risk of transmission is 20-30% before birth. The risk increases to 50-65% during birth and 10-20% via breast milk. A single dose of Nevirapine given to the mother at onset of labor and a single dose to the infant after birth reduces the risk of HIV transmission. Breast-feeding should be avoided. However, in developing countries like India, breast-feeding prevents infectious diseases and provides immunity to the child, and is therefore advocated after counseling the mother.

Pathophysiology and Immunopathogenesis

The main action of HIV is to cause the quantitative and qualitative deficiency of a subset of lymphocytes referred to as T4 (CD4+) *helper/inducer lymphocytes*. These lymphocytes express the CD4 cellular receptor for HIV on their cell surface along with the coreceptors (e.g. CCR5, CXCR4). The destruction of these lymphocytes leads in turn to suppression or compromise in the function of host cellular defense mechanisms, not only to HIV but also to opportunistic infectious agents.

Although the CD4+ T lymphocyte and CD4+ monocyte lineage are the principal cellular targets, HIV can

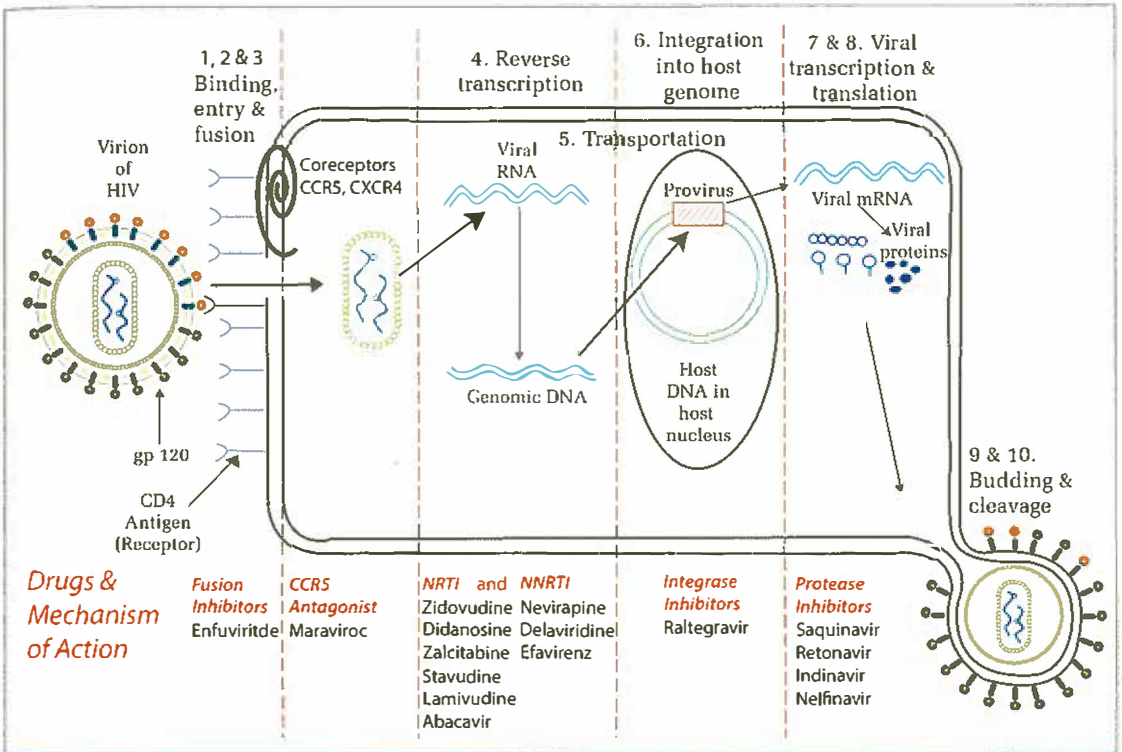


Fig. 3.39: Replication Cycle of HIV and Drugs targeting different stage of the cycle (Also Refer Ch. 15)

1. BINDING: HIV binds via the viral envelope protein *gp120* to the *CD4 receptor* on the target host cell.
2. CORECEPTORS (CCR5 and CXCR4) facilitate entry of virus into the host cell.
3. FUSION of the virus with the host cell membrane and internalization of pre-integration complex (viral RNA and enzymes surrounded by capsid protein).
4. REVERSE TRANSCRIPTASE ENZYME converts the viral RNA genome to double stranded DNA.
5. TRANSPORTATION of the DNA to the host nucleus.
6. INTEGRATION into the host genome by viral enzyme *integrase*. The HIV provirus remains latent at this stage until the infected cell is activated by a number of cellular and viral factors. This is the reason for the interval between the time of infection and disease expression.
7. TRANSCRIPTION of provirus DNA into viral messenger (mRNA) and genomic RNA.
8. TRANSLATION of mRNA into proteins.
9. BUDDING: The viral proteins, enzymes and genomic RNA are assembled at the cell membrane and budding of the progeny virus occurs at special regions of the host cell membrane.
10. RELEASE: The viral enzyme *protease* catalyses the release of mature virions from the host cell. The virions infect other host cells that express CD4 receptors.

potentially infect virtually any cell that expresses CD4 (e.g. T and B lymphocytes, macrophages, astrocytes, microglial cells, Langerhans' cells, fibroblasts, Chromaffin cells, dendritic cells, alveolar macrophages, thymus cells).

Immune Response to HIV Infection

Both humoral and cellular immune responses to HIV develop soon after primary infection.

Immune Abnormalities in HIV Disease

A broad range of immune abnormalities has been documented in HIV-infected patients. These include both quantitative and qualitative defects in lymphocyte, monocyte/macrophage, and natural killer (NK) cell function, as well as the development of autoimmune phenomena.

Laboratory Tests for Diagnosis of HIV Infection

Table 3.21 ; Laboratory Criteria for HIV Infection for Adults

Positive result from an HIV antibody screening test confirmed by a positive result from a supplemental HIV antibody test ***And/Or*** Positive result from any of the following HIV virologic (i.e., non-antibody) tests: HIV nucleic acid (DNA or RNA) detection test, HIV p24 antigen test or HIV isolation.

1. **Antibody Screening Tests:** The standard screening test for HIV infection is the detection of **anti-HIV antibodies** in the patient's serum using *enzyme-linked immunosorbent assay* (ELISA or EIA). HIV-1/HIV-2 combined **EIA** assays are now being used worldwide. This test is highly sensitive (>99.5%) but not optimally specific. False positive results can occur in cases of: antibodies to class II antigens, autoantibodies, hepatic disease, recent influenza vaccination, acute viral infections and children <18 months whose mothers are HIV-infected
2. **HIV Antibody Test** for **confirmation of positive ELISA tests is done by Western Blot** (immunoblotting) assay or immunofluorescence assay. It tests the presence of antibodies in the patients' serum against HIV antigens of specific molecular weights. Antibodies to HIV begin to appear within 2 weeks of infection, and the period of time between initial infection and the development of detectable antibodies is rarely longer than 3 months (window period).

   The CDC criteria for a positive interpretation of Western Blot test is the presence of antibodies to any two of three **proteins p24, gp41 and gp160/gp 120.**

   "Indeterminate" results are repeated after 4-6 weeks.
3. **Antigen Detection:** The detection of HIV by the **p24 antigen capture assay**, an ELISA-type assay, in serum or CSF is the key to early diagnosis. The p24 antigen is a soluble protein from the core of the virus. Plasma p24 antigen levels rise during the first few weeks following infection, prior to the appearance of anti-p24 antibodies. The antigen may be detected for upto six weeks and then disappears with antibody sero-conversion. The antigen is not detectable during the asymptomatic clinically silent phase for a variable period of upto 10 years or more. The reappearance of p24 antigen precedes onset of the symptomatic phase of AIDS.
4. **HIV DNA:Polymerase chain reaction (PCR) techniques** are used to detect very low levels of viral DNA integrated into the host genome.
5. **HIV RNA** levels in plasma or serum (plasma viral load or PVL) are determined by **RT-PCR**

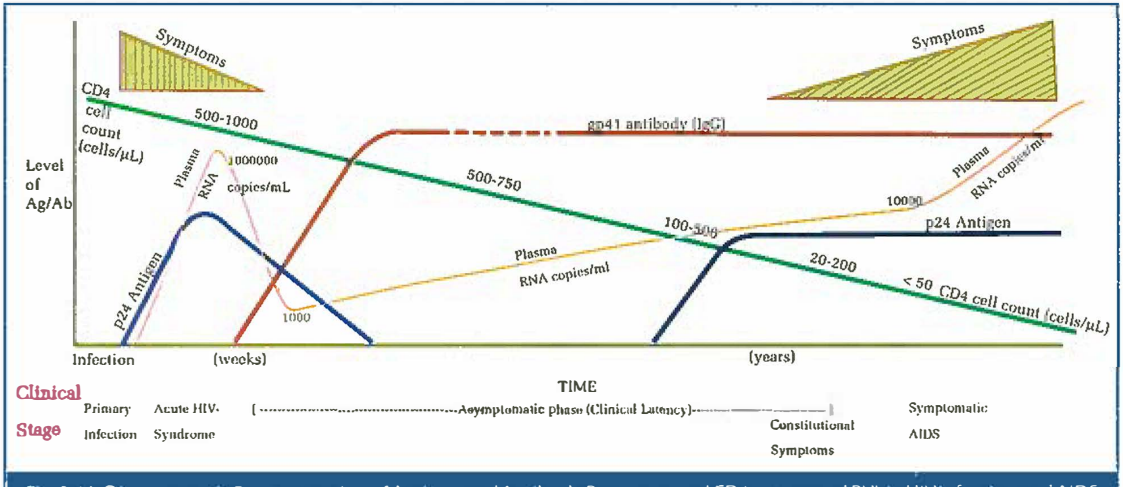


Fig. 3.40: Diagrammatic Representation of Antigen and Antibody Response and CD4 counts and PVL in HIV infection and AIDS

Table 3.22 : Initial Evaluation

History	Symptoms, past and present history (personal, high risk behavior, family history, gynecological, treatment etc.)
Physical Examination	Routine complete examination including dermatological, oral, genital, pelvic, systemic, fundus, etc.
Hematology& Urinalysis	Routine
Blood Chemistries	Routine including LFT, BUN, creatinine, etc.
Lipid profile and glucose (fasting)	To rule out existing CAD, diabetes prior to ART
HIV Antibody	Confirm HIV-1 infection & rule out HIV-2 infection
CD4+ T lymphocyte count	Baseline level by flow cytometry
HIV RNA levels (viral load)	Baseline plasma viral load (PVL)
HIV Resistance Testing	For patients with HIV RNA > 1000 copies/mL
Chest X-ray	To rule out TB & other infections
VDRL/TPHA	To rule out syphilis
Pap Smear& pregnancy test	To rule out cervical intraepithelial neoplasia & pregnancy prior to ART
Serology for hepatitis A, B, C	To rule out co-existing viral hepatitis
Mini-mental status examination	Baseline study

(reverse transcriptase PCR), bDNA (branched DNA) or nucleic acid sequence-based assays. These tests are useful for patients with a positive or indeterminate ELISA and an indeterminate Western blot or in patients in whom serologic testing may be unreliable (such as those with hypogammaglobulinemia).

6. **Viral Isolation:** HIV can be cultured from tissue, peripheral blood cells or plasma.

Monitoring of HIV Infection

Measurement of the CD4+ T lymphocyte count (flow cytometry) and level of plasma HIV RNA (plasma viral load or PVL) are important in the routine evaluation and monitoring of HIV-infected individuals. They are measured at diagnosis and usually every 3-6 months thereafter.

Clinical Manifestations of HIV Infection

Primary HIV Infection& Acute HIV Syndrome

It can be asymptomatic or associated with features of an acute viral syndrome of variable severity (50-70% of infected individuals) 3-6 weeks post-exposure. It is characterized by fever, lymphadenopathy, arthralgias, myalgias, maculopapular rash, urticaria, abdominal cramps, diarrhea, orogenital ulcers or aseptic meningitis. It lasts 1-2 weeks and resolves spontaneously as the immune response to HIV develops. Most patients will then enter a phase of clinical latency, although occasional patients will experience progressive immunologic and clinical deterioration. It can be identified by recent appearance of HIV antibody or by presence of viral products with negative or weekly reactive HIV antibody.

Asymptomatic Infection

The length of time between infection and development of disease varies greatly, but the median is estimated to be 10 years. HIV disease with active viral replication usually progresses during this asymptomatic period and CD4+ T-cell counts fall. The rate of disease progression is directly correlated with plasma HIV RNA levels. Patients with high levels of HIV RNA progress to symptomatic disease faster than do those with low levels of HIV RNA.

Symptomatic Disease

A variety of constitutional symptoms, PGL, neurological disease, secondary infectious diseases, secondary neoplasms or organ-specific disease can be seen in HIV-infected patients, either as primary manifestations of the HIV infection or as complications of treatment (Refer to Table 3.30)

Table 3.23 : Immunizations Recommended

Vaccine/ Immunization	*Recommendation*
Hemophilus influenza virus	All patients: Single dose as early as possible and annually
Streptococcus pneumoniae	All patients: Single dose as early as possible
Hepatitis B	All susceptible patients (anti HBc and anti-HBs negative:3 doses
Hepatitis A	All susceptible (anti-HAV negative) patients or at risk: 2 doses
DPT (Diphtheria, Pertussis, tetanus)	All patients. Booster every 10 years
IPV (Inactivated polio virus)	All patients not previously vaccinated: 3 doses of enhanced potency IPV vaccine or oral polio vaccine ifIPV not available
MMR* (Measles, mumps, rubella)	All patients not previously vaccinated and booster to those immunized but with no history of measles.
Typhoid, Cholera, Plague, Meningococcus, Japanese encephalitis, Hepatitis A	To patients traveling to endemic/ epidemic areas.
Yellow fever, BCG, Live oral typhoid. Live oral polio	Not recommended
Varicella Zoster immune globulin	Patients exposed to this virus

Table 3.24 : When to Start ART

Antiretroviral therapy should be initiated in:

1. Patients with a history of an AIDS-defining illness
2. Patients with a CD4 T-cell count <250 cells/μL or decreasing
3. Following patients (regardless of CD4 cell count):
   a. Pregnant women
   b. Patients with HIV-associated nephropathy (HIVAN), non-Hodgkin's lymphoma
   c. Patients co infected with HBV/HCV when treatment is indicated
   d. Patients with HIV RNA (PVL) >50,000 copies/ml or increasing
   e. Post Exposure Prophylaxis

Table 3.25 : ART Recommendations for Adult or Adolescents

Patient group	*Preferred first line*	*Preferred second line regimen*
Adult or adolescent	NNRTI + 2 NRTI	Boosted PI + 2 NRTI
Pregnancy with HIV	NVP + AZT + 3TC	Not applicable
HIV with TB	EFV + 2 NRTI	Boosted PI * + 2 NRTI
Hepatitis B with HIV	TDF + 3TC + NNRTI	Boosted PI + 2 NRTI
Hepatitis C with HIV	EFV + 2 NRTI	Boosted PI + 2 NRTI
HIV-2 or dual infection	3 NRTI	Boosted PI + 2 NRTI

NNRTI = Non-nucleoside reverse transcriptase Inhibitor; NRTI= nucleoside/nucleotide reverse transcriptase inhibitor; PI= Protease inhibitor; AZT= Azidothymidine, Zidovudine; EFV= Efavirenz; NVP = Nevirapine; LPV=Lopinavir /r= booster dose Ritonavir; RTV= Ritonavir; TDF= Tenofovir; 3TC= Lamivudine; RMP= Rifampicin; RFB= Rifabutin.
Boosted PI = PI boosted with Ritonavir

Table 3.26 : ART for Treatment-Naïve Patients (1-NNRTI + 2-NRTIs)

Preferred NNRTI	**Efavirenz**
Alternative NNRTI	Nevirapine
Preferred Dual NRTI	**Tenofovir + Emtricitabine**
Alternative Dual NRTI	Abacavir + Lamivudine
Alternative Dual NRTI	Zidovudine + Lamivudine

Immune Reconstitution Inflammatory Syndrome (IRIS)

When a patient starts anti-retroviral therapy (ART), his immune deficiencies improve. This sometimes results in uncontrolled inflammatory responses. Hence the patient may show worsening of clinical features or laboratory parameters in spite of improving CD4 counts and decreasing viral loads.

Manifestations of IRIS

1. Development of symptoms within 3 months of starting ART.
2. Symptoms
   a. Fever, wasting

Table 3.27 : Primary and Secondary Prophylaxis for prevention of OIs

Opportunistic Agent	Indications for starting	Drug & Dosage (First choice)
Mycobacteriumtuberculosis (TB)	Tuberculin test >5mm or high risk Or prior positive test without treatment	INH sensitive: INH 5 mg/kg/dayPO qds + pyridoxine 50 mg PO qdsx9 months
Pneumocystis carinii pneumonia (PCP)	CD4 < 200/mm³ or rapid clinical deterioration or prior PCP	TMP/SMX 1DS tablet PO qds Pentamidine aerosol 300 mg/month
Mycobacterium avium-intracellulare (MAC)	CD4 < 50/mm³ Or prior documented disease	Azithromycin 1200 mg PO weekly Or Clarithromycin
Toxoplasmagondii	Positive IgG antibody and CD4 <100/ mm³	TMP/SMX 1DS tablet PO qds
Herpes simplex	Frequent/severe recurrences	Acyclovir 200 mg PO tds or Famciclovir 250 mg PO bds
Candida albicans, Crytococcosis	CD4 < 200/mm³ Frequent/severe recurrences	Fluconazole 100-200 mg PO once/week

Table 3.28 : Evaluation and Management of the Drug Resistance

Evaluation	Assessment of symptoms of HIV disease Antiretroviral treatment history: Duration, drugs used, antiretroviral potency, adherence history, and drug intolerance/toxicity HIV RNA and CD4 T-cell count trends over time Results of prior drug resistance testing
Types:	
a. Virologic failure	HIV RNA level > 400 copies/mL in 24 weeks or > 50 copies/mL in 48 weeks or rising levels (after prior suppression of viremia)
b. Immunologic failure	Failure to achieve and maintain an adequateCD4 response despite virologic suppression
c. Clinical Failure	Manifestation of AIDS in a patient on ART (usually assoc. with virological & immunological failure)
Drug resistance testing	Genotypic or phenotypic testing carried out while the patient is taking the failing antiretroviral regimen (patient should not stop treatment regimen)
Goals of treatment	Re-establish maximal virologic suppression (HIV RNA <50 copies/mL) Change individual antiretroviral drugs to reduce or manage toxicity, if any Assess adherence frequently and simplify the regimen as much as possible
Antiretroviral treatment (ART)	Add at least 2 new (preferably 3) fully active agents to an optimized background antiretroviral regimen depending on results of resistance testing



Fig. 3.41 : Patient with lipodystrophy due to NRTI

b. Tuberculous cold abscesses, pericardial effusion, pleural effusion, ascites
c. Hepatospenomegaly or lymphadenopathy
d. Pneumonitis/pneumonia
e. Increase in cerebral space-occupying lesions, meningitis, encephalitis

Treatment of IRIS

1. Symptomatic treatment
2. NSAIDS
3. Severe IRIS: Prednisolone
4. Life-threatening IRIS: Stop ART

Management

General principles

1. Multidisciplinary approach to reduce HIV-related morbidity and mortality and improve quality of life.
2. Counseling, psychosocial support
3. Education of the patient about HIV, AIDS, transmission, risk of infections, neoplasms, etc.
4. Education of the general public, colleagues, employers and hospital staff.

Treatment of Constitutional Symptoms

1. ***Fever:*** Intermittent or long-term use of non-steroidal anti-inflammatory drugs.
2. ***Night sweats:*** Regular use of antipyretic agents since there is associated fever.
3. ***Chronic diarrhea:*** Symptomatic treatment (till no specific pathogen identified) with Loperamide, Diphenoxylate HCl/Atropine sulphate, Somatostatin.
4. ***Fatigue:*** Evaluate for thyroid or adrenal insufficiency, neuropathy, myopathy and depression and treat if detected.
5. ***Minor oral infections:*** Oral hairy leukoplakia needs no treatment unless severe (oral acyclovir). Periodontal disease is treated with chlorhexidine.
6. ***Headache:*** Symptomatic treatment with non-steroidal anti-inflammatory agents preferred to narcotics. Specific pathogen to be identified and treated.
7. ***Nutritional deficiencies*** (e.g. iron, Vitamin B12) to be corrected, if present.

Antiretroviral Therapy (ART)

The cornerstone of medical management of HIV infection is antiretroviral therapy (ART) since it suppresses HIV replication. The drugs that are currently licensed for the treatment of HIV infections are listed in Chapter 15.

Goals of Management of ART

1. Avoid transmission of HIV
2. Maintain CD4+ counts > 350cells/μL
3. Suppress PVL to undetectable levels (<50 copies/mL)
4. To prevent opportunistic infections
5. To manage side effects of ART
6. To reduce HIV-related morbidity and prolong survival, improve quality of life and to prevent vertical HIV transmission

ART Drugs (Also Refer to Ch. 15)

Management of Symptomatic AIDS and Advanced Disease

1. Continue treatment with *antiretroviral agents* as per Tables above. Ensure compliance.
2. Continue treatment of symptomatic complaints.
3. Patients with symptomatic disease pass from the stage of late moderate symptoms and immune function deterioration to one or more opportunistic life threatening manifestation and more severe immune dysfunction. There is an increasing risk of mortality as CD4+ counts fall to <50 cells/μL. These patients need more frequent clinical examination, diagnosis and immediate treatment.
4. Various systems are affected throughout the course of HIV infection and may be the direct result of HIV infection, manifestation of

Table 3.29 : Recommended PEP

Exposure	*Low Risk* Source HIV Negative*	*High risk** Source HIV Positive*
Less Severe (Solid needle, superficial injury)	2 drug PEP	3 drug PEP
More Severe (Large bore hollow needle, deep puncture, visible blood on device or needle used in patients' artery or vein)	3 drug PEP	3 drug PEP
Post Exposure Prophylaxis		
Low risk, HIV +ve low risk source & less severe exposure	AZT + 3TC (2 drug PEP)	TDF + 3TC
High risk, HIV +ve high-risk source & any type of exposure	AZT + 3TC + LPV /r (3 drug PEP)	AZT + 3TC + EFV

*Low risk: Asymptomatic or viral load < 1500 copies/ml

**High risk: Symptomatic HIV, AIDS, acute seroconversion and/or high viral load

opportunistic infections and neoplasms, or side effects of ART(Refer to Table 3.30).

Post Exposure Prophylaxis (PEP)

Antiretroviral drugsfor PEP should be started **within the first few hours** and no later than 72 hours after occupational and non-occupational exposureand continued for 28 days (See Table). HIV testingshould be done initially and following 3 and 6 months.

Prevention

Education, counseling, and behavior modification remain the cornerstone of HIV prevention efforts. While abstinence is an absolute way to prevent sexual transmission, other strategies include 'safe sex practices such as use of condoms together with the spermatocide nonoxynol-9. Avoidance of shared needle use by IDUs is critical. If possible, HIV-positive women should avoid breast-feeding (in India breast-feeding is beneficial and mixed feeding is absolutely contraindicated) as the virus can be transmitted to infants via this route. Prevention of exposure is the best strategy and stresses the use of universal precautions and proper handling of needles and other potentially contaminated objects.

Table 3.30 : Complications in HIV infection and AIDS - Features, Diagnosis and Treatment

System	Features	Diagnosis	Treatment
RESPIRATORY SYSTEM			
Upper Respiratory Tract Infection (URTI) *S.pneumoniae, H.influenzae*	Acute bronchitis, sinusitis, fever, nasal congestion, headache	CT/MRI	Antimicrobial agents
Pneumonia *S.pneumoniae, H.influenzae*	Pneumonia, sinusitis, bacteremia	X-ray	Antimicrobial agents
Pneumocystis pneumonia (PCP) *P.jiroveci (carinii)*	Fever, cough,dyspnea, night sweats, thrush, unexplained weight loss	X-ray; Demonstration of organism in sputum, BAL, transbronchial or open lung biopsy	Trimethoprim/ sulphamehtoxazole DS 2 tablets PO for 21 days followed by secondary prophylaxis
Tuberculosis: *M.tuberculosis*	Cough, hemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats	Positive sputum smear or X-ray showing TB	Anti-tuberculosis treatment: Standard 4-drug regimen for 6-9 months. For TB involving CNS: 12 months.
Atypical Mycobacterial infections *M.avium, M.intracellulare* ***(MAC)***	Weight loss, fever, night sweats; Dissemination to bone marrow, lung, liver, lymph nodes	Organisms in blood,sputum or involved tissue; X-ray	Clarithromycin 500 mg PO q12h + Ethambutol 15 mg/kg PO q24h; Can add rifabutin, ciprofloxacin or amikacin
Fungal infections of the lung *Cryptococcus, Coccidioides immitis, Aspergillus, Histoplasmosis*	Fever, cough, dyspnea, hemoptysis	Chest X-ray, sputum examination	Anti-fungal agents
Kaposi's Sarcoma (KS)	Purplish vascular nodules on skin, mucous membranes, viscera	Biopsy of suspected lesion; Chest X-ray	Optimal ART & observation;
	Single or limited lesions		Radiotherapy, intralesional vinblastine, cryotherapy
	Extensive disease		Interferon - α, liposomal daunorubicin
Lymphomas: Immunoblastic, Burkitt's, Primary CNS lymphomas	Fever, seizures, mass lesions in oral mucosa	MRI, CT scan	Combination chemotherapy,steroids, radiotherapy

System	Features	Diagnosis	Treatment
CARDIOVASCULAR SYSTEM			
HIV-associated cardiomyopathy	Edema, dyspnea, dilated cardiomyopathy with congestive heart failure	Chest X-ray, ECG. Echo	ART, treatment for heart failure, IV Immunoglobulin
Pericardial Effusion	Asymptomatic or chest pain, dyspnea, cardiac tamponade, pericardial friction rub	Echo, pericardial fluid culture and cytology	Treat underlying condition, start ART if idiopathic, NSAIDS, steroids. Pericardiocentesis if tamponade is present
Non-bacterial thrombotic endocarditis	Fever, weight loss, unexplained embolic phenomena	Heart murmur, Chest X-ray, Echo, blood culture	Antimicrobial therapy according to isolated organism
GASTROINTESTINAL SYSTEM			
Oropharynx: Thrush (*Candida*) Hairy leukoplakia (*EBV*) Aphthous ulcers	Dysphagia/odynophagia	Pseudomembrane, examination of scraping	*Candida:* Fluconazole 100 mg PO q24h *EBV: Topical* podophyllin or anti-herpes virus agents. *Aphthous ulcers:* Topical anesthetic, thalidomide
Esophagus: Esophagitis (CMV, HSV, Candida); Neoplasm (KS, lymphoma)	Odynophagia, retrosternal pain	Upper endoscopy	Systemic therapy as indicated
Stomach: Achlorhydria, Kaposi's sarcoma, Lymphoma	Achlorhydria: Gastric discomfort Obstructive jaundice	Gastric pH at endoscopy	Stop ART drug, if cause. Treat underlying condition.
Intestine: Infections due to: **Bacteria** (*S.typhimurium, Shigella, Campylobacter, S.typhi, S.flexneri*) **Fungi** (*Histoplasmosis, Coccidioidomycosis, Penicilliosis*) **Parasites** (*Cryptosporidia, Microsporidia, Isospora belli*) **Viruses** (CMV colitis)	Fever, anorexia, fatigue, malaise, diarrhea	Stool and blood examination & culture, Endoscopy with biopsy	Treat underlying infection as per diagnosis
Rectal: Infections (HSV), neoplams (KS)	Perirectal ulcers, erosions	Examination	Treat underlying condition as per diagnosis
AIDS Enteropathy	Chronic diarrhea, weight loss	Histology of small bowel	Treat underlying condition as per diagnosis
HEPATOBILIARY SYSTEM			
Hepatitis B	Asymptomatic or symptoms of hepatitis, elevated liver enzymes	HBAAb, HBSAg, HBCAb &in chronic cases HBEAg , HBEAb & HBV DNA levels, imaging	Enticavir + pegylated interferon. ART Combination Therapy Hepatitis A vaccine if non-immune.
Hepatitis C	Asymptomatic, elevated liver enzymes	HCV Antibody or HCV RNA positivem, imaging	Pegylated interferon + Ribavirin (C/I in pregnancy). Hepatitis A & B vaccine if non-immune.

System	Features	Diagnosis	Treatment
Granulomatous hepatitis, hepatic masses, biliary tract disease, Hepatitis G virus	Asymptomatic or symptoms of hepatitis, elevated liver enzymes	Liver enzymes elevated, liver biopsy, imaging	If ART-induced, stop offending drug.
ENDOCRINE SYSTEM			
Lipodystrophy	Truncal obesity, peripheral wasting or lipoatrophy	Increased plasma triglycerides, total cholesterol, apolipoprotein B, insulin, glucose	Gemfibrozil, atorvastatin
Avascular necrosis	Hip or shoulder pain	Osteonecrosis on MRI	Stop offending drug, if any
Lactic acidosis			Stop offending drug, if any
Hyponatremia (SIADH), hypothyroidism, hyperthyroidism	Symptoms of condition	Serum sodium, thyroid function tests	Stop offending drug, if any. Treat underlying condition as per diagnosis
RENAL AND GENITOURINARY SYSTEM			
HIV-associated nephropathy (HIVAN)	Asymptomatic to symptoms of renal failure	Proteinuria, ultrasound, biopsy	ART; ACE inhibitors and/or prednisone 60 mg/d for 1 month, then taper
Genitourinary tract infections (e.g. HSV, syphilis, candidiasis)	Skin lesions, dysuria, hematuria and/or pyuria, vaginal discharge, etc.	Clinical and Urine Examination	Treat underlying condition as per diagnosis
RHEUMATOLOGICAL DISEASES			
Immune Reconstitution Inflammatory syndromes (IRIS)	Refer Pg.114		
Arthritis - reactive (Psoriatic, septic)	Pain in joints. Urethritis, skin lesions & Conjunctivitis (gastroenteritis)	Arthrocentesis with culture, gram stain, urethral swab for Chlamydia and gonorrhea, HLA B27	NSAIDs, pain relievers Methotrexate causes increased OI, used only in severe cases
AIDS-associated arthropathy	Painful non-erosive arthropathy in multiple joints (knees, ankles)	MRI	NSAIDs and pain relievers
Polymyositis	Musculoskeletal pain for >3 months at multiple sites	Clinical examination & biopsy of muscle, EMG	Low dose naltrexone
HEMATOPOIETIC SYSTEM			
Anemia, neutropenia, thrombocytopenia (ITP, TTP)	Signs of Mild or severe anemia or neutropenia, bleeding in severe ITP	CBC, red cell indices, retic count, serum iron, B12, folate studies	*Anemia:* Blood transfusions; iron if IDA, erythropoietin; avoid drug, if drug-induced; *Neutropenia:* G-CSF if ANC <750/mm^3 *ITP:* ART
Lymphadenopathy	Inguinal Site	Biopsy of lymph node or bone marrow in patients with CD4+ <200/μL	ART
Persistent Generalized lymphadenopathy (PGL)	Enlarged lymph nodes >1 cm; In 2 or more extra-inguinal sites for >3 months with no obvious cause	Clinical examination	No treatment

System	Features	Diagnosis	Treatment
DERMATOLOGICAL DISEASES			
Seborrheic dermatitis	Waxy erythematosus plaques usually on face and scalp	Clinical appearance	ART, ketoconazole cream, topical steroid
Eosinophilic pustular folliculitis	Multiple erythematous, papular, severely pruritic eruptions on upper trunk, face	Skin biopsy	ART, corticosteroids, isotretinoin, phototherapy
Psoriasis& Ichthyosis	May be preexisting condition	Clinical examination	ART, standard therapy
Reactivation herpes zoster	Shingles – may be multi-dermatomal	Clinical examination, immunofluorescence to distinguish from HSV	Acyclovir, Famciclovir
Herpes simplex virus (HSV)	Skin & recurrent oral/ anogenital lesions	Viral culture of HSV	Acyclovir, Famciclovir
Molluscum contagiosum	White, umbilicated, diffuseskin eruptions in groin	Clinical appearance	ART
Condyloma acuminatum	Extensive vegetating lesions in perianal or oral area due to human papilloma virus	Clinical appearance; Histopathology	ART; Surgery, cryotherapy
NEUROLOGICAL DISEASES			
Opportunistic infections (Toxoplasmosis, Cryptococcosis, cytomegalovirus, TB)	*Toxoplasma:* Fever, headachace, focal neurological deficits, ocular disease *Crytococcus:* Meningitis. May also have pulmonary disease. *CMV:* Encephalitis, polyradiculitis,	*Cryptococcus*: CSF India ink examination. Detection of antigen in serum, CSF, tissues; MRI/CT; *T. gondii*IgG antibodies in serum	*Toxoplasma:* Sulfadiazine & pyrimethamine with leucovorin for 4-6 wks. And prophylaxis. *Crytpococcus:* IV amphotericin B 0.7 mg/kg daily with flucytosine 25 mg/kg qid for 2 wks followed by fluconazole 400 mg/day PO for 10 wks and 200 mg/day PO till CD4 + count > 200 cells/μL for 6 months *CMV:* Gancyclovir 5 mg/kg IV BDS + lifelong Valganciclovir 900 mg PO OD
Neoplasms (primary CNS lymphoma)	Focal neurological deficit or seizures, fever,	MRI/CT, SPECT, PET scan, EBV DNA Definitive diagnosis - stereotactic brain biopsy	ART Steroids and radiotherapy
Aseptic meningitis	Headache, photophobia, meningismus	CSF examination	Usually resolves spontaneously
HIV Encephalopathy (AIDS dementia complex)	Stage 0 to 4: mild to severe neurological symptoms (HIV-associated neurocognitive impairment (HCNI))	CSF examination; MRI/CT; HIV RNA in CSF; MMSE (mini-mental status examination)	ART with drugs which penetrate the CSF like AZT, ABC, d4T, NVP, IDV
Myelopathy or spinal cord disease	Vacuolar myelopathy or pure sensory ataxia; dementia	CSF examination	
Peripheral neuropathy (HIV/ Drug-induced)	Pain, aching, burning, or tingling at distal extremities	Clinical, EMG	Withdraw offending drug. Continue ART. Symptomatic treatment

System	Features	Diagnosis	Treatment
Progressive multifocal leukoencephalopathy (PML),	Multifocal neurologic deficits with or without changes in mental status	JC virus DNA levels in CSF; MRI	ART
OPHTHALMOLOGIC DISEASES			
CMV retinitis	Painless, progressive loss of vision	Ophthalmological exam; Differentiate from benign "cotton-wool spots"	Ganciclovir intraocular implant + valgancilovir for 21 days followed by maintenance dose
GENERALISED WASTING SYNDROME	Involuntary weight loss > 10% with fever, chronic diarrhea or fatigue lasting > 30 days.	Clinical examination	Steroids, given with caution due to OI Androgenic hormones, growth hormones, total parenteral nutrition
NEOPLASTIC DISEASES			
Kaposi's sarcoma, Non-Hodgkin's lymphoma, Primary CNSlymphoma, Cervical/anal cancer (see above)			

Respiratory System

4

1 › Proforma

History

I. *Cardinal symptoms:*
   A. Cough
   B. Expectoration
   C. Hemoptysis
   D. Breathlessness
   E. Wheeze
   F. Chest pain

II. *History of tuberculosis:*
   A. Evening rise of temperature, night sweats
   B. Anorexia and weight loss
   C. Hemoptysis
   D. Pleurisy, meningitis, lymphadenitis in past or in family, TB contact

III. *Habits:* Alcohol, smoking, tobacco or gutka chewing

IV. *Aspiration:* Foreign bodies, vomitus.

V. *For Industrial diseases:* Occupation, residence near factories or mills

VI. *Allergy:*
   A. Family history of asthma, hay fever, eczema
   B. Rhinitis and Sinusitis: Nasal discharge, pain and tenderness over sinuses, headache, recurrent cold

VII. *Past history:*
   A. Measles, influenza or whooping cough in childhood (If bronchiectasis)
   B. Diabetes
   C. Exposure to TB, STD, HIV

VIII. *Mediastinal compression:*
   A. Dysphagia
   B. Hoarse voice
   C. Dyspnea and dry cough
   D. Swelling over face

General Examination

I. *Built and nutrition*

II. *Nails and conjunctiva:* Pallor, clubbing, cyanosis, icterus

III. *Lymphadenopathy* (especially scalene node and cervical nodes), edema of feet, JVP

IV. *TPR, BP*

V. *Spine*

VI. *Stigma of tuberculosis:*
   A. Phlyctenular conjunctivitis
   B. Scars and sinuses in neck or bones
   C. Thickened spermatic cord
   D. Erythema nodosum
   E. Skin: Cutis vulgaris, scrofuloderma etc.

VII. *Neck:* Thyroid swelling. Tracheal tug

VIII. *Horner's syndrome:* Ptosis, miosis, anhydrosis, enophthalmos and absent ciliospinal reflex

IX. *Upper respiratory tract:*
   A. Sinus tenderness
   B. Throat and tonsils
   C. Posterior pharyngeal wall for posterior nasal drip
   D. Alae nasi

X. Gums and teeth

Respiratory System Examination

I. Inspection:

A. Shape of chest
   1. AP and transverse diameters: Barrel shaped chest, etc.
   2. Hollowing, bulging, flattening or retraction
   3. Sub-costal angle
   4. Shoulders
   5. Spine
   6. Spinoscapular distance on both sides

B. Respiratory Movements
   1. Respiratory rate
   2. Rhythm
   3. Character — Abdominal, thoracic, thoraco-abdominal or abdomino-thoracic
   4. Equality
   5. Accessory muscles of respiration
   6. Inter-costal retraction / fullness

C. Mediastinum
   1. Trailes sign
   2. Apex impulse

D. Miscellaneous
   1. Scars, sinuses
   2. Pulsations
   3. Dilated veins
   4. Shiny skin over lower chest (Empyema, hepatic amebiasis)

II. Palpation

A. Findings of inspection confirmed including Chest Movements

B. Mediastinum
   1. Trachea
   2. Apex beat

C. TACTILE VOCAL FREMITUS: TVF

D. Miscellaneous

Tenderness over lower inter-costal spaces. Other vibrations: Palpable rales, rhonchi, rub

III. Percussion:

A. Anteriorly

	Right Side	*Left Side*
1.	Kronig's isthmus	Kronig's isthmus.
2.	Clavicular percussion	Clavicular percussion
3.	Intercostal resonance	Intercostal resonance
4.	Liver dullness	Cardiac dullness
5.	Tidal percussion	Traube's area
6.	Shifting dullness	Shifting dullness
7.	Percussion myokymia	Percussion myokymia
8.	Skodaic resonance	Skodaic resonance

B. Posteriorly
   1. Supra-scapular
   2. Inter-scapular
   3. Infra-scapular

C. In Axilla
   1. Axillary
   2. Infra axillary

IV. Auscultation:

A. ***Breath Sounds***
   1. Normal or Diminished
   2. Type: Vesicular, bronchial or vesicular with prolonged expiration

B. Foreign Sounds: Rales, rhonchi or rub

C. Vocal Resonance

D. Miscellaneous
   1. Bronchophony
   2. Egophony
   3. Whispering pectoriloquy
   4. Succussion splash
   5. Coin test
   6. Post-tussive suction
   7. Post-tussive rales

Final Diagnosis

1. Anatomy (Where is the lesion?) e.g. Right upper lobe
2. Pathology (What is the lesion?) e.g. pneumonia
3. Etiology (What is the cause?) e.g. streptococci
4. Complications e.g. lung abscess
5. Risk factors e.g. smoking

2 Examination

A : Inspection and Palpation

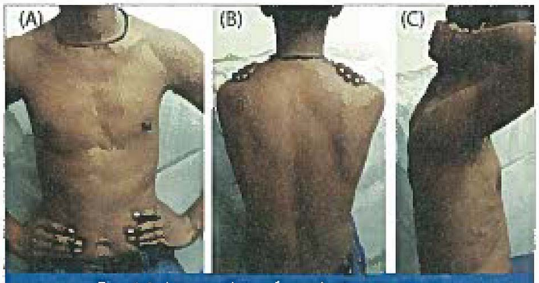


Fig. 4.1 : Inspection of respiratory system
(A) Anterior, (B) posterior and (C) Lateral

I. Shape of the Chest

Normally the chest is bilaterally symmetrical, with smooth contours, and slight recession below the clavicles. On cross-section, it is ellipsoidal in shape, its anteroposterior diameter is lesser than its transverse diameter with a ratio of 5:7. The subcostal angle is acute, about 70° and the interspaces are broader anteriorly than posteriorly.

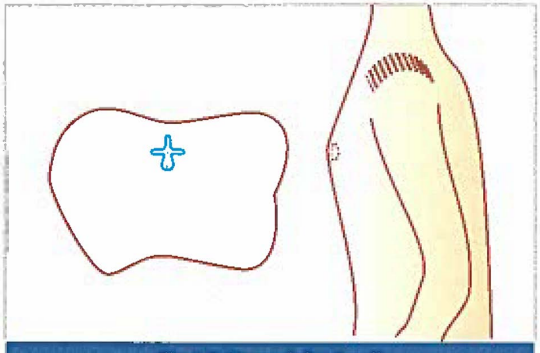


Fig. 4.2 : Normal chest wall

Abnormal Shapes of the Chest

1. ***Rickets (pigeon breast or keeled chest or pectus carinatum):*** There is depression on either side of the sternum often associated with bead like enlargement at the costochondral junction (*rickety rosary*) and a transverse groove passing outwards from the xiphisternum to the mid-axillary line (*Harrison's sulcus*). Sometimes, the sternum is unduly prominent and the cross-section is triangular.

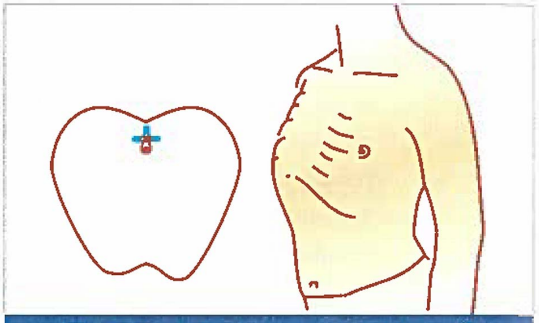


Fig. 4.3 : Pigeon breast appearance of chest wall

2. ***Funnel chest (Cobbler's chest or pectus excavatum):*** There is a depression in the lower part of the sternum which may be congenital, following rickets in childhood or an occupational deformity in cobblers. Due to the sternal depression, the normal cardiac shadow may appear enlarged on X-ray chest (***Pomfret's heart***).

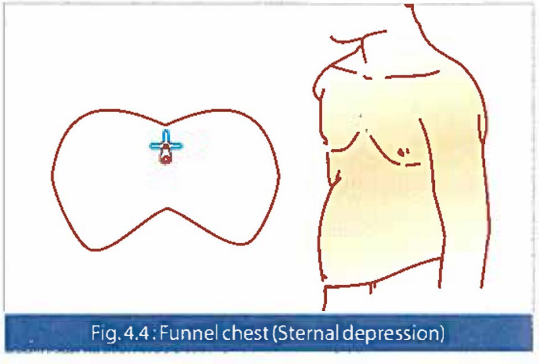


Fig. 4.4 : Funnel chest (Sternal depression)

3. ***Barrel shaped chest:*** The anteroposterior diameter is increased, the sub-costal angle is wide, the angle of Louis unduly prominent, the sternum is more arched, the spine is

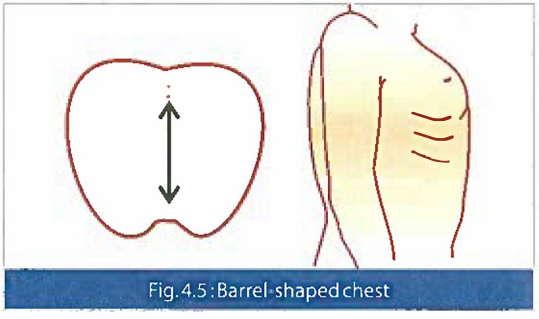


Fig. 4.5 : Barrel-shaped chest

unduly concave forwards and the ribs are less oblique. This is seen in **emphysema**, old age and infancy. The Ratio of AP diameter to transverse diameter is normally 5:7. In the barrel-shaped chest it is 1:1 or more.

4. ***Spinal deformities:*** Kyphosis or scoliosis (Ch. 1) due to any cause may lead to asymmetry and may decrease the size of the thoracic cage and restrict lung movements and volume.

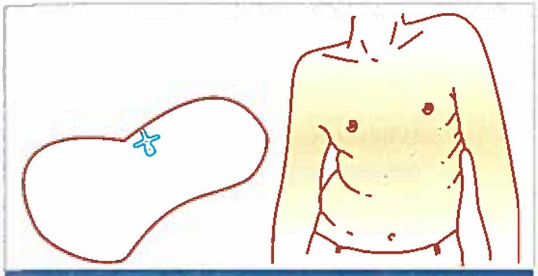


Fig. 4.6 : Chest wall appearance with Kyphoscoliosis.

5. ***Bulging:*** One side may bulge in pleural effusion, pneumothorax, tumors, aneurysm, empyema necessitans, cardiomegaly or scoliosis. Localized bulging is seen in aortic aneurysm, pericardial effusion, liver abscess, chest wall tumors etc.
6. ***Depression or flattening:*** One side of the chest or a part of it may be depressed or flattened in fibrosis, collapse, pleural adhesions, unilateral muscle wasting due to poliomyelitis or congenital absence of pectoralis muscles.
7. ***Flat chest (phthinoid chest):*** The anteroposterior diameter is reduced in chronic nasal obstruction due to adenoid lymphoid hypertrophy, bilateral TB or childhood rickets. In advanced TB, the scapula is winged and is called ***Alar chest***. AP : Transverse Diameter Ratio is 1:2 or less.

II. Respiratory Rate

The normal rate in adults is 16-20 respirations per minute (in children about 40 per min.) It bears a definite ratio with the pulse rate of about 1:4.

A. **Increased respiratory rate (tachypnea)**
   1. Exertion and excitement.
   2. Fevers e.g. pneumonias
   3. Anoxemia and acidosis
   4. Anemia and poisoning
   5. Pain whilst breathing e.g. pleurisy

B. **Decreased respiratory rate (bradypnea)**
   1. Narcotic poisoning e.g. opium
   2. Brain tumour

C. Dyspnea: Breathlessness

Table 4.1 : Dyspnea: American Thoracic Society (ATS) Scale

Grade	Degree	Description
0	None	Not troubled by shortness of breath on level or uphill
1	Mild	Troubled by shortness of breath on level or uphill
2	Moderate	Walks slower than persons of same age
3	Severe	Stops after walking 100 yds or after few minutes on level ground
4	Very Severe	Too breathless to leave the house or breathless on dressing or undressing

Table 4.2 : Dyspnea: Modified Medical Research Council (MMRC) Scale

Grade	Description
1	Breathlessness only with strenuous exercise
2	Breathless when hurrying on level or walking uphill
3	Walks slower than persons of same age
4	Stops after walking 100 yards or after few minutes on level ground
5	Too breathless to leave the house or breathless on dressing or undressing

III. Respiratory Rhythm

The normal respiration has *regular* rhythm with inspiration longer than expiration. *Irregular* respiration may be of the following types:

A. **Cheyne-Stokes Respiration:** This consists of rhythmical alteration of apnea and hyperpnea due to anoxemia. Anoxemia

abolishes spontaneous rhythmic activity of breathing. Consequent apnea results in accumulation of CO_2 in the body, thereby stimulating the respiratory centre and causing hyperventilation. This causes CO_2 washout and results in depression of respiratory centre and apnea and thus the cycle continues.

Causes:

1. Left ventricular failure
2. Increased intra-cranial pressure with damage to both cerebral hemisphere and diencephalon.
3. Narcotic poisoning: opium, barbiturates etc.
4. Uremia
5. Deep sleep



Fig. 4.7: Cheyne-Stokes Respiration

B. Kussmaul's respiration: This is characterized by deep and rapid respiration (air-hunger) and is seen in diabetic ketoacidosis, alcoholic or starvation ketoacidosis and in uremia.

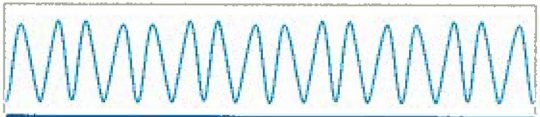


Fig. 4.8: Kussmaul's respiration

C. Biot's respiration (chaotic breathing): This is irregularly irregular respiration seen in meningitis or raised intracranial pressure.

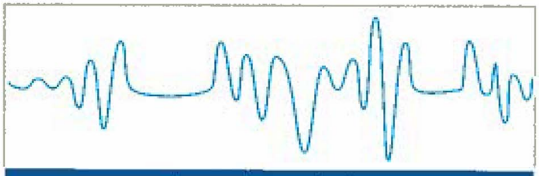


Fig. 4.9: Biot's respiration

D. Apneustic respiration : It is characterized by full inspiration followed by a pause, alternating with full expiration followed by a pause. Each pause is 2-3 seconds. It is seen in pontine lesions.

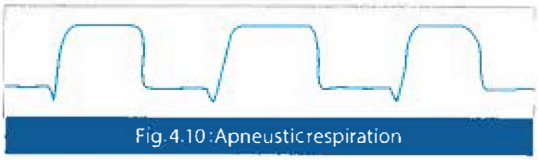


Fig. 4.10: Apneustic respiration

E. Stridor: This is characterized by prolonged inspiration through an obstructed upper airway, which produces a characteristic sound.

Causes:

1. Laryngeal or tracheal obstruction
2. Laryngeal diphtheria
3. Mediastinal growth

F. Wheezing: This is characterized by prolonged expiration through an obstructed lower airway, bronchi, bronchioles, etc. This can also occur in cardiac and renal asthma.

Table 4.3 : Differences between Stridor and Wheeze

Stridor	Wheeze
Inspiratory	Expiratory
Upper Airway	Lower Airway
Cause: Foreign body	Cause: Asthma

F. Stertor: Stertorous breathing occurs in coma or deep sleep or in dying patients (death rattle - rattling noise in throat).

IV. Type of Breathing

The normal breathing in males and some females is abdominothoracic i.e. both the abdomen and thorax are moving during the act of respiration but the abdominal movements are more prominent. The normal breathing in majority of females is thoracoabdominal i.e. the thoracic movements are more prominent than abdominal movements:

1. **Thoracic breathing:** The thoracic movements are predominant and abdominal movements are minimal. It occurs with diaphragmatic paralysis, peritonitis and severe ascites.
2. **Abdominal breathing:** The abdominal movements are predominant and thoracic movements are minimal. It occurs in pleurisy and collapse of the lung.

V. Movements of the Chest

Normally both the sides of the chest wall move uniformly and there is no bulging, or indrawing of the interspaces. Accessory muscles of respiration are usually not required for the act of breathing.

Normally, on taking a deep breadth, the chest circumference (measured at the level of the nipple) increases by 2 inches.

A. **Unilateral diminished movements**
   1. Obstruction to the main bronchus
   2. Consolidation
   3. Fibrosis of the lung and pleural adhesions
   4. Massive collapse
   5. Hydropneumothorax
   6. Pleural Effusion

B. **Bilateral diminished movements**
   1. Emphysema
   2. Bilateral fibrosis, collapse, consolidation or hydropneumothorax
   3. Bronchial asthma

The accessory muscles of respiration, alae nasi and sternomastoid are normally not required for respiration. However in any conditions that cause respiratory embarrassment, they are required to assist breathing and may therefore be prominent.

VI. Mediastinum

The mediastinum is normally central. The shift of the mediastinum can be detected by noting the position of trachea and apex beat. On inspection, sternocleidomastoid becomes more prominent on side to which trachea is shifted. This is **Trail Sign**.

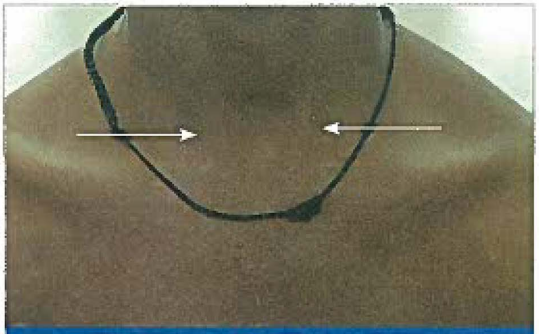


Fig. 4.12 : Inspection of Trachea - Trail Sign

The trachea is examined by inserting finger upward in the suprasternal notch and noting its relation to the two sternomastoid muscles. Normally the trachea may be shifted slightly to the right or is central.

The apex beat is examined with the palm of the hand and its position is noted. Normally the apex beat is in the fifth left intercostal space just inside the mid-clavicular line. It may be shifted inward or outward depending upon the shift of the mediastinum.

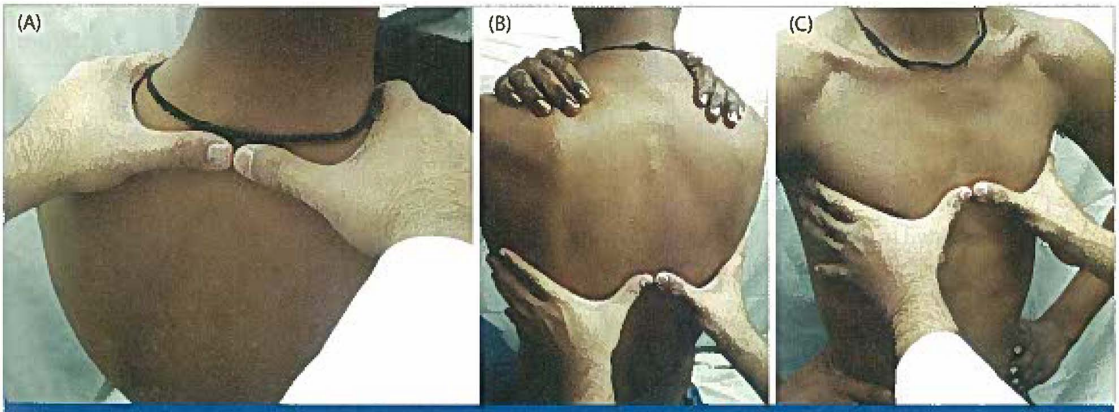


Fig. 4.11 : Palpation of respiratory movements (A) Apical, (B) Posterior and (C) Anterior

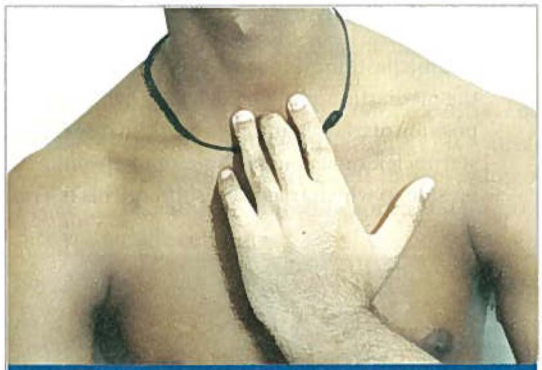


Fig. 4.13 : Palpation of Trachea

The position of mediastinum in various respiratory diseases is given in the table.

The apex beat alone may be shifted in scoliosis, funnel shaped depression of the sternum and with cardiac disease.

Table 4.4 : Position of Mediastinum in Respiratory Diseases

Central	*Shifted to same side (Pull)*	*Shifted to opposite side (Push)*
1. Bronchitis	1. Collapse	1. Pleural effusion
2. Bronchial asthma	2. Fibrosis	2. Pneumothorax
3. Bronchiectasis	3. Pleural thickening	3. Hydropneumothorax
4. Emphysema		
5. Pneumonia		
6. Lung abscess		
7. Interstitial fibrosis		

VII. Tactile Vocal Fremitus (TVF):

Definition

TVF is the tactile perception of vibrations communicated to the chest wall from the larynx via the bronchi and lungs during the act of phonation.

Mechanism

TVF occurs when sound vibrations from the larynx pass down the bronchi and cause the lungs and the chest wall to vibrate. However, the spoken tones must have the same fundamental frequency as the lungs and the chest wall. The fundamental frequency of female voice is often higher than that of the lungs, therefore TVF may be markedly diminished or absent in women. In children, although the fundamental frequency is high, TVF can be appreciated because it corresponds to the fundamental frequency of the small lungs.

Significance

I. ***TVF is increased in***
   1. Consolidation which may be due to pyogenic or tuberculous infections
   2. Following pulmonary infarction
   3. Surrounding a malignant lesion superficial cavity.

II. ***TVF is decreased in***

A. Pleural diseases:
   1. Pleural effusion
   2. Pneumothorax
   3. Hydropneumothorax

B. Bronchial diseases:
   1. Bronchial obstruction

C. Lung diseases:
   1. Emphysema
   2. Pulmonary fibrosis
   3. Pulmonary collapse



Fig. 4.14 : Tactile Vocal Fremitus

VIII. Other Vibrations

Normally when the patient breathes, the palpating hand does not feel any vibrations. However, vibrations may be felt in some diseases as follows:

1. **Pleural Friction Rub:** This occurs initially

in pleurisy due to rubbing of the two pleural surfaces. It is usually felt at the peak of inspiration or early expiration.

2. **Bronchial Fremitus:** This occurs in bronchitis, bronchial asthma and chronic obstructive lung disease.
3. **Palpable Rales:** This occurs in bronchiectasis, pulmonary fibrosis and pulmonary congestion.

IX. Tenderness

Tenderness over the chest wall may be present in local injury, myositis, amebic abscess of liver, pyogenic abscess of liver and empyema.

B : Percussion

The normal percussion note of the chest is due to the underlying lung tissue, containing normal amount of air in the air vesicles, air sacs and air passages. It has a distinctive and clear character with low pitch. The front of the chest yields a more resonant note than the back, because of the lesser bulk of musculature in front than at the back.

Impaired note: When the amount of air in the alveoli decreases, as in consolidation, infiltration, fibrosis and collapse of the lung, the lung fails to vibrate sufficiently to the percussion stroke. This causes loss of resonance resulting in an impaired note.

Dull-note: An impaired note of greater degree is a dull note. In addition to consolidation, infiltration, fibrosis and collapse of lung, it is found in pleural thickening.

Stony dull note: A percussion note completely devoid

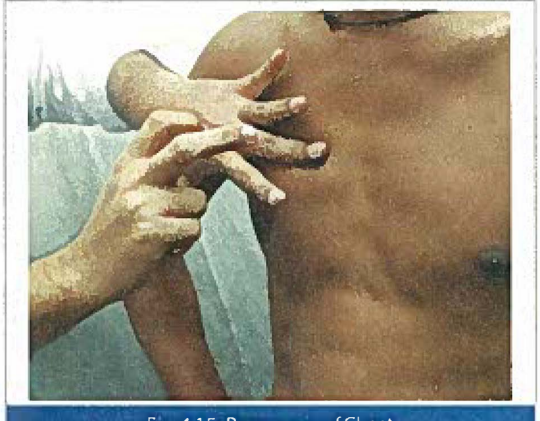


Fig. 4.15 : Percussoin of Chest

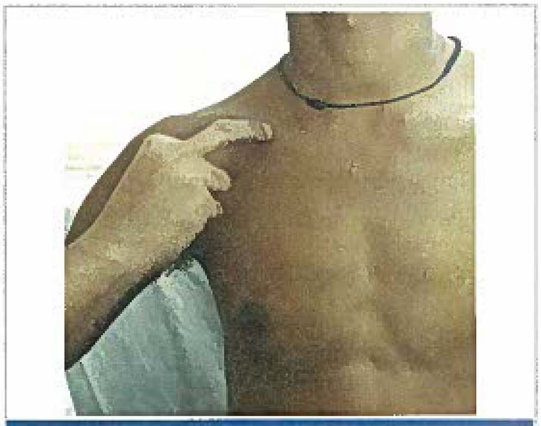


Fig. 4.16 : Clavicular Percussion

of resonance or displaying extreme dullness is a stony dull note. It is classically encountered over a pleural effusion, because fluid dampens the vibration of both the chest wall and the underlying relaxed lung. It may also occur in lung fibrosis with pleural thickening or with solid intrathoracic tumour.

Tympany: This is a drum like resonance, which is normally encountered over the stomach, intestines, larynx and trachea. When it occurs over the chest wall it may be due to:

1. Pneumothorax
2. Superficial empty cavity
3. Emphysema

Sub tympany (Skodaic resonance): A hyperreso-nant note with a boxy quality, which occurs due to the relaxed lung just above the level of pleural effusion.

Hyper-resonance: A note in between in pitch between normal resonance and tympany can be elicited over the normal lung tissue by keeping the chest wall in full inspiration, during percussion. It occurs in:

1. Pneumothorax
2. Emphysema
3. Large cavity with a thin wall
4. Congenital lung cyst
5. Emphysematous bullae
6. Eventration of diaphragm

Bell tympany: This is a high pitched tympanic or metallic sound, heard over the chest in case of massive pneumothorax. When a silver coin is placed on the affected side and percussed with a second silver coin,

the ear or stethoscope applied over the opposite side of the chest may detect a clear bell-like sound resembling the sound of "hammer on an anvil".

I. Kronig's Isthmus

Definition: Kronig's isthmus is a band of resonance 5-7 cms in width, connecting lung resonance over the anterior and posterior aspects of each side of the chest. It is bounded medially by dullness of the neck muscles and laterally by dullness of the shoulder muscles.

Abnormalities:

1. Absence on either side suggests pulmonary fibrosis due to tuberculosis.
2. Increased width of resonance suggests emphysema.

II. Liver Dullness and Span

Normal liver dullness is in the right intercostal space, in the fifth space in the mid-clavicular line, in the seventh space in the anterior axillary line and in the ninth space in the scapular line.

Liver dullness may be present in the fourth space in the mid-clavicular line in amebic or pyogenic abscess of the liver, diaphragmatic paralysis or collapse of the lower lobe of the lung.

It may be pushed down to the sixth space in the mid-clavicular line in emphysema, right-sided pneumothorax, air in the peritoneal cavity and terminal cirrhosis.

III. Cardiac Dullness

On the left side of the chest wall, the lung resonance is encroached by an area of cardiac dullness due to the presence of the heart. The cardiac dullness is normally in the third and fourth left parasternal line and the fifth left mid clavicular line.

This area of dullness may be decreased in emphysema, and left sided pneumothorax. It may be increased with cardiomegaly and push of the heart to the left side.

IV. Tidal Percussion

Percussion of the upper border of the liver dullness on the right side anteriorly, on inspiration and expiration serves to determine the range of lung expansion and movement of diaphram. It is restricted in :

1. Pulmonary diseases at lung base e.g. pulmonary fibrosis
2. Empyema
3. Hepatic amebiasis
4. Sub-diaphragmatic abscess.
5. Diaphram palsy

V. Traube's Area OR Space

It is bounded above by the lung resonance, below by the costal margins, on the right by the left border of liver and on the left by spleen.

It is normally occupied by the stomach, hence on percussion the note is tympanic due to stomach gas. If Traube's area is dull it suggests:

1. Pleural effusion on the left side.
2. Splenomegaly
3. Fundic tumor
4. Full stomach

VI. Shifting Dullness

In case of hydropneumothorax in sitting position there is a hyperresonant note above followed by dullness below. On changing the posture to supine, this area of dullness of the fluid changes as air and fluid will shift. This is shifting dullness and always signifies presence of both air and fluid.

VII. Coin-test

A coin is placed flat on the chest and struck with another coin. On auscultation of the back of the chest on the same side, a metallic or bell like sound is heard.

Cause: Pneumothorax

VII. Percussion Myokymia

In a chronically wasted individual as in pulmonary tuberculosis, a percussion stroke over the front of the chest, close to the sternum, may cause a transient twitching of the muscles, which

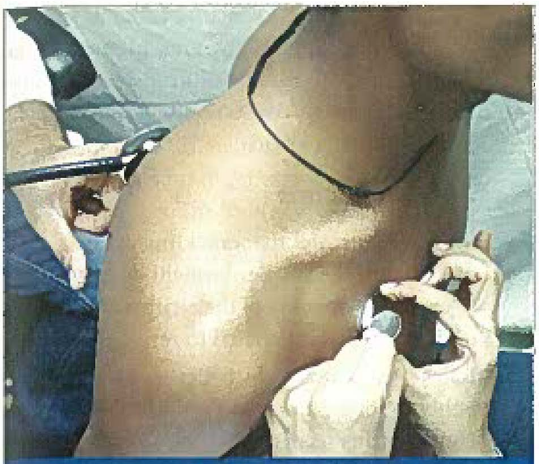


Fig. 4.17 : Coin Test

is more marked on the side of the pulmonary affection. This is called percussion myokymia.

Limitations of percussion

1. It is not possible to percuss deeper than 5 cm. Hence it is not possible to detect a lung lesion covered by a layer of air more than 5 cm thick or fluid 1 cm thick.
2. A lesion less than 2 cm in diameter does not cause any change in the percussion note.
3. Free fluid less than 200 ml in the pleural cavity may not be detected on percussion.

C : Auscultation

Auscultation of the chest must be done to note the type of breathing, presence of any foreign sounds and vocal resonance.

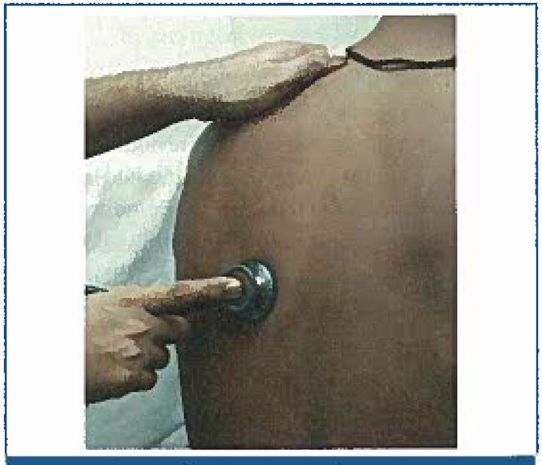


Fig. 4.18 : Auscultation

The stethoscope should be firmly placed over the chest to prevent sounds resulting from the movement of the chest. Hair on the chest wall may produce a crackling sound and may be mistaken as rales. A similar sound may occur in nervous patient due to shivering.

I. Breath Sounds

1. **Vesicular:** This is characterized by active inspiration due to the passage of air into the bronchi and alveoli followed without a pause by passive expiration due to the elastic recoil of the alveoli which occurs maximally in the early phases giving an apparent impression of short expiration. The character of the sound is rustling due to the passage through the alveoli which selectively transmits lower frequency sounds and dampens the high frequency sounds. It is normally heard over the chest.

   The normal breath sounds are vesicular and not bronchial because the lungs and chest wall act as an acoustic filter narrowing the range of audible frequencies to 100-400 Hz.
2. **Bronchial:** This is characterized by active inspiration due to the passage of air into the bronchi. The alveolar phase is absent (because of consolidation in alveoli) and hence expiration is also active, occupying the same duration of time as inspiration. Since the alveolar phase is absent there is no rustling quality to the sound but a hollow bronchial character because now both lower and higher frequency sounds are conducted.

   It is heard in patients with cavity,

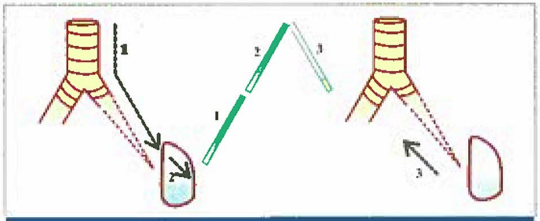


Fig. 4.19 : Vesicular breath sounds. 1. Tubular phase 2. Alveolar phase on inspiration. 3. On expiration.

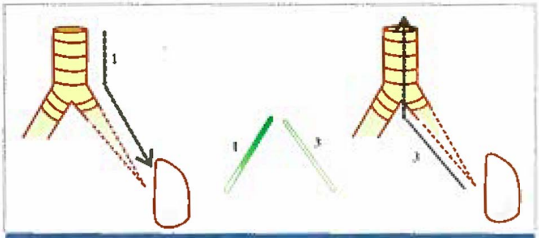


Fig 4.20: Bronchial breath sounds. 1. Tubular phase, (Alveolar phase absent) 3. On Expiration

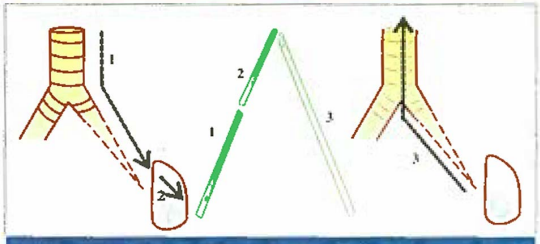


Fig 4.21: Vesicular breath sounds with prolonged expiration

consolidation, partial collapse, open pneumothorax and above the level of pleural effusion.

There are 3 types of bronchial breath sounds:

A. *Tubular:* This is a high-pitched bronchial sound heard in consolidation, above the level of pleural effusion and over cavity.

B. *Cavernous:* This is a low-pitched bronchial sound heard over an irregular cavity.

C. *Amphoric:* This is a low-pitched bronchial sound with high-pitched over-tones heard over smooth walled cavities and an open pneumothorax.

3. **Vesicular Breath Sounds with Prolonged Expiration** (Broncho-Vesicular):

Here there is active inspiration due to passage of air into bronchi and alveoli giving vesicular type of inspiratory sound. However during expiration there is increased resistance in the airway due to spasm causing expiration to be active and hence equal to or more than inspiration. Since the alveolar phase is present, there is no pause between inspiration and expiration.

It is heard in bronchial asthma, chronic bronchitis and emphysema. In emphysema, breath sounds are diminished because abnormally large amount of air dampens the breath sounds.

II. Foreign Sounds

Rales: Rales are the crackling sounds that originate in the smaller bronchi or alveoli, due to explosive opening of the airways in that part of the lung that is deflated to residual volume.

Rales were previously believed to be due to bubbling of air through liquid in the airways. However this seems unlikely because:

a. Rales may be present only in inspiration. Sounds caused by air bubbling through fluid should be heard during both phases of respiration.

b. Rales are constantly present in pulmonary fibrosis where there is no increase in secretions.

Causes

a. *Left heart failure:* Rales are present in the de-pendent parts of the lung, accentuated by exertion.

b. *Inflammatory exudates:* Bronchitis, Bronchopneumonia and pneumonia

c. Lung abscess, cavity and bronchiectasis

d. Pulmonary congestion, edema (eg ARDS) and fibrosis

e. COPD

Types

a. *Early inspiratory:* Due to opening of larger airways closed by the air-trapping mechanism during the previous expiration. They are scanty, low-pitched and not posture dependent, e.g. chronic bronchitis.

b. *Mid-inspiratory:* e.g. Bronchiectasis, cavity, lung abscess.

c. *Late-inspiratory:* Due to delayed opening of both the lungs in restrictive defects e.g. pulmonary edema and fibrosis. They are profuse, high pitched and **altered by posture**, e.g. bending forward or lying down reduces them.

d. *Expiratory rales:* These are characteristic of severe airway obstruction. They arise by the re-opening of temporarily closed by the trapping mechanism during expiration.

Rhonchi: Rhonchi or Wheeze is a continuous musical sound generated by air buzzing past the airway. The lung acts like the reed of a wind instrument, sounding when the passage of air vibrates the opposing airway walls which are just touching.

Causes

a. Bronchial asthma
b. Bronchitis
c. Chronic obstructive lung disease
d. Localized obstruction (Malignancy)
e. Tropical eosinophilia
f. Cardiac failure

Types

a. *Polyphonic:* This is the most common type of wheezing where an expiratory musical sound contains several notes of different pitch. They result from oscillation of several large bronchi simultaneously.
b. *Monophonic:* This is a single musical sound arising from a single airway brought to a point of closure as in chronic bronchitis or emphysema.
c. It is seldom loud enough to be heard by an unaided ear. An exception is stridor, a very loud monophonic musical sound produced by laryngeal or tracheal obstruction.

Stridor: Stridor is a loud inspiratory sound heard over the airways due to obstruction to the respiratory tract.

Laryngeal stridor is a high pitched sound heard over the larynx due to laryngeal obstruction with foreign body, diphtheria, anaphylaxis, laryngitis, etc. It is a medical emergency and the patient may require respiratory support.

Tracheal stridor is a low pitched sound heard over the trachea due to tracheal obstruction.

N.B.: **Obstruction of bronchi would cause wheeze or rhonchi.**

Pleural Friction Rub

Normally the parietal pleura slides smoothly over the visceral pleura due to the presence of a thin layer of lubricating secretion between the two layers. In pleural inflammation the roughened surfaces of pleura rub against each other giving rise to a characteristic friction rub.

Since the movement of the visceral over the parietal pleura is greatest at the lateral and posterior bases of the lung and decreases superiorly, the pleural rub is best heard at the bases in the axillary line.

Characteristics

1. Rubbing or creaking
2. Superficial sound close to the ear
3. Accentuated by increased pressure of the chest piece on the chest wall & deep inspiration.
4. Audible during both the phases of respiration, disappears on holding the breath.
5. Confined to a localized area
6. Not altered by coughing
7. Associated with local pain and tenderness.

Hamman's Mediastinal Crunch: It is a clicking, rhythmical sound synchronus with cardiac cycle. Heard with or without stethoscope e.g. Mediastinal Emphysema, esophageal rupture.

III. Vocal Resonance

The laryngeal vibrations can be normally audible through the stethoscope as vocal resonance. High- pitched sounds, which are not easily palpable, can be picked up as vocal resonance.

The vocal resonance of normal intensity conveys the impression of being produced near the stethoscope. It is examined by asking the patient to repeat the words "one, one, one" etc. and identical points on the chest wall should be alternately auscultated rapidly.

Vocal resonance may be diminished or absent in pleural effusion, pneumothorax, thickened pleura and emphysema.

Vocal resonance may be increased and altered as follows:

Table 4.4 : Respiration Findings in Various Pathological Processes

Pathological	*Chest Wall Process*	*Movement*	*Mediastinum*	*Percussion*	*Breath*	*Foreign Sounds*	*Vocal Resonance Sounds*
Consolidation	N	D	C	Dull	Tubular	Rales	WP+
Total collapse	Retraction	D	S	Dull	Abs.	Abs.	Abs.
Partial collapse	N or Retraction	D	S	Dull	Tubular	Rales Rhonchi	WP+
Fibrosis	Retraction	D	S	Impaired	Diminished	Rales	Diminished
Cavity	N or Retraction	D	C or S	Impaired Boxy	Amphoric, Cavernous	Rales	WP+
Pleural effusion	N	D	O	Stony dull	Abs below (Bronchial at level)	Abs	Abs. below (Egophony at the level)
Empyema	Buldging edematous	D	O	Stony dull	Abs. below (Bronchial at level.)	Abs.	Abs. below (Egophony at the level)
Pneumothorax	N	D	O	Hyper-resonant	Abs. or Am-photeric	Coint Test	Abs.
Hydropneumothorax	N	D	O	Shifting dull-ness	Abs.	Succussion splash	Abs.
Bronchial asthma	N	Accessory Muscles acting	C	N	Vesicular with prolonged expiration	Expiratory rhonchi	N
Bronchiectasis	N	D or N (Usu-ally at bases)	C	N	Vesicular	Coarse Leathery rales	N
Emphysema/COPD	Barrel shaped	D (Usually bilateral)	C	Hyper-resonant	Diminished vesicular with prolonged expiration	Rhonchi	Diminished

N = normal, S = Same Side, O = Opposite Side, C = Central, D = decreased, WP = whispering pectoriloquy, Abs = Absent, COPD = Chronic Obstructive Pulmonary Disease

1. **Bronchophony**

   This is increased vocal resonance where the sounds are loud and clear but the words are not distinguishable. This is seen in consolidation, large superficial cavity and just above level of pleural effusion.

2. **Egophony**

   When spoken voices are auscultated over the chest, a nasal quality is imparted to the sound which resembles the bleating of a goat.

   Causes: Above the level of pleural effusion and pneumothorax.

   Mechanism: The relaxed lung above the pleural effusion transmits the overtones but dampens the lower fundamental tones giving rise to egophony.

3. **Whispering Pectoriloquy**

   Whispered voice is transmitted to the chest wall with sufficient clarity to maintain its syllabic character, so that individual words are clearly distinguishable as if uttered directly into the examiner's ears.

Causes

a. Cavity communicating with bronchus.
b. Diffuse consolidation of lung adjacent to bronchus.

4. **Succussion Splash**

This is the splashing sound heard over the chest either with the stethoscope or with the unaided ear applied to the chest wall, when the patient is shaken suddenly by the examiner.

Causes

a. Hydropneumothorax
b. Large cavity containing fluid and air.
c. Herniation of stomach or colon into the thorax.

5. **Post-tussive Suction**

A sucking sound heard over the chest wall during the long inspiration that follows a bout of coughing. It indicate thin-walled compressible lung cavity, communicating with the bronchus.

6. **Post-tussive Rales**

Rales which are not audible during normal respiration but are heard after making the patient cough are post-tussive rales. They signify cavity filled with thick material which is dislodged during coughing allowing air to bubble through the remaining fluid, producing the rales.

3 Pleural Effusion

Definition: Pleural effusion is collection of excess quantity of fluid in the pleural space.

Pathophysiology: Pleural fluid is secreted by the parietal and visceral layers of pleura. Majority of the fluid is absorbed by the lymphatics and the remainder is absorbed by the lung or chest wall across the mesothelium. Excessive fluid collects (according to Frank Starlings law of hydrostatic pressure) due to excessive back pressure from the visceral surface (e.g. CCF), decrease in serum proteins (e.g. nephrotic syndrome), pulmonary inflammation or lymphatic obstruction (e.g. pneumonia, infiltrating tumor) or increase negative pressure in pleural space (e.g. Atelectasis).

Causes

I. Transudative Pleural Effusion
   1. Congestive Heart Failure
   2. Cirrhosis
   3. Nephrotic Syndrome
   4. Pulmonary Embolization
   5. Myxoedema
   6. Superior Vena Cava Obstruction

II. Exudative Pleural Effusion
   1. Infectious Diseases
      a. Bacterial Infections
      b. Tuberculosis
      c. Fungal Infections
      d. Viral Infections
      e. Parasitic Infections
   2. Neoplastic Diseases
      a. Metastatic disease
      b. Mesothelioma
   3. Pulmonary Embolization / Infarction
   4. Collagen Vascular Diseases
      a. Rheumatoid Arthritis
      b. Systemic Lupus Erythematosus
      c. Drug-Induced Lupus
      e. Sjogrens syndrome
      f. Wegners Granulomatosis
      g. Churg - Strauss Syndrome
      h. Sarcoidosis
   5. Gastointestinal disease
      a. Esophageal perforation
      b. Pancreatitis
      c. Intraabdominal abcess
      d. Amoebic Liver Abcess
      e. Diaphgramatic hernia
      f. After abdominal surgery
      g. Post-liver transplant
   6. Drugs and Toxins :
      a. Drug induced pleural diseases Nitrofurontoin, Methylsergide, Bromocriptine
      b. Toxins : Asbestos

7. Traumatic :
   a. Chest wall trauma
   b. Iatrogenic injury
   c. Post coronary artery bypass-surgery
   d. Hemothorax
   e. Radiation Injury
8. Chronic Uremia
9. Cardiac Disease
   a. Post myocardial infarction syndrome (Dressler's syndrome)
   b. Pericardial diseases
10. Others :
   a. Septicemia,
   b. Drug Allergies,
   c. Bleeding disorders,
   d. Chylothorax,
   e. Meig's syndrome (ovarian fibroma with ascites and right pleural effusion)

Types

I. Acute Pleural Effusion

Causes:

1. Trauma
2. Acute pancreatitis
3. Pulmonary infarction
4. Ruptured amebic liver abscess into the pleural cavity
5. Rupture of esophagus
6. Dissecting aneurysm of aorta leaking into the pleural space

II. Purulent Effusion (Empyema): Pus in pleural cavity

Causes:

1. Pyogenic infections: pneumonia, lung abscess, bronchiectasis
2. Septicemia
3. Penetrating wounds of chest, chest tube trauma, surgical procedures
4. Rupture of esophagus
5. Subphrenic abscess rupturing into thoracic cavity
6. Tuberculosis

III. Hemorrhagic Effusion (Hemothorax): Blood in pleural cavity i.e. Hematocrit of pleural fluid should be more than half of that of Peripheral blood. HCT of 1-20% is usually seen in carcinoma, trauma, pulmonary embolism.

Causes:

1. Trauma whilst tapping or central line placement
2. Iatrogenic
3. Tumour
4. Tuberculosis
5. Pulmonary infarction
6. Acute hemorrhagic pancreatitis
7. Bleeding or hemorrhagic disorders
8. Coxsackie B virus infection

IV. Tuberculous Pleural Effusion **(Refer Pg. 141)**

This is usually an exudate, rarely bilateral and hemorrhagic and may be AFB positive and culture positive.

V. Milky Effusion (Chylous, Opalescent)

A. Chylothorax: Pure chyle contains more than 400 mg of fat per 100 ml. Many large fat globules are present. Triglycerides > 110 mg/dl.

Causes:

1. Trauma to thoracic duct
2. Filariasis
3. Tuberculosis
4. Malignant growth of mediastinal glands
5. Thrombosis of left subclavian vein

B. Chyliform: Fat present is not derived from the thoracic duct but from degenerated cells. The fat globules are smaller.

Causes:

1. Tuberculosis
2. Carcinoma of lung and pleura

C. Pseudochylous: Milky appearance of the

fluid is not due to fat but due to lecithin, globulin and calcium phosphate.

Causes:

1. Tuberculosis
2. Nephrosis
3. Heart disease
4. Malignancy

D. **Cholesterol Effusion:** Peculiar glistening, opalescent appearance of fluid due to cholesterol crystals.

Causes:

Long-standing effusion, e.g. tuberculosis, carcinoma, nephroticsyndrome, myxedema and post myocardial infarction.

VI. Iatrogenic Pleural Effusion (including Drug-induced)

Causes:

1. Dialysis, especially peritoneal
2. Following thoracic surgery
3. Post-central line placement
4. Drugs e.g. Practolol, methysergide
5. Drug induced eosinophilia e.g. aspirin, PAS, sulphonamides, nitrofurantoin
6. Drug-induced lupus e.g. hydralazine, procainamide, alpha methyl dopa

VII. Recurrent Pleural Effusion

Causes:

1. Tumors
2. Tuberculosis
3. Collagenosis
4. Cardiac failure

VIII. Bilateral Pleural Effusion

Causes:

1. All conditions causing Transudative pleural effusion
2. Pleural metastasis
3. Lymphoma
4. Pulmonary infarction
5. Tuberculosis
6. Asbestosis
7. Septicemia
8. Rheumatoid disease, SLE, etc.

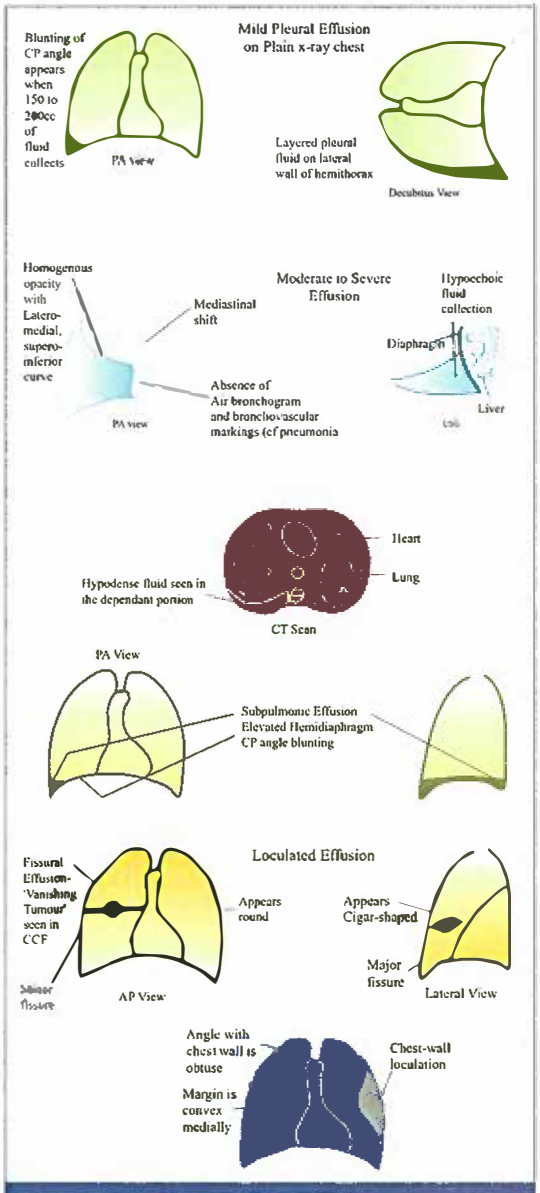


Fig. 4.22: Pleural Effusion

IX. Phantom (Vanishing) Tumor

This is a loculated fissural effusion in the lungs due to cardiac failure. It vanishes with anti-failure therapy like diuretics and does not need pleural tapping.

Diagnosis

I. Symptoms

A. *Pleuritic pain:* Pain in chest which increases

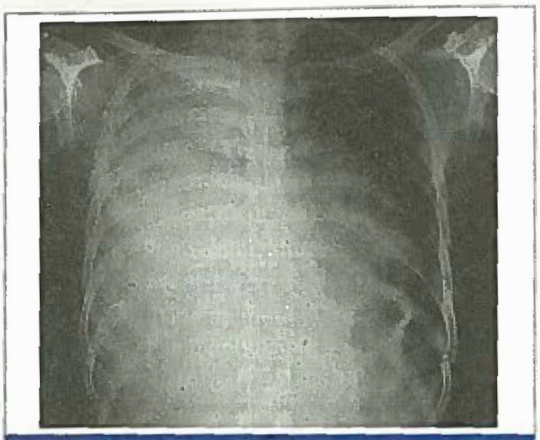


Fig. 4.23: X-ray of pleural effusion: Mesothelioma, showing increased density of hemithorax with central mediastinum and consolidation due to pneumonia

on inspiration, coughing, laughing and sneezing.

B. *Dyspnea:* If massive collection of fluid occurs rapidly.

C. Dry cough

D. *Systemic symptoms :* (may or may not be present) fever, anorexia, malaise, weight loss, indicative of underlying disease.

II. Signs: (500 cc of fluid is required to produce signs).

A. *Inspection:*

1. Bulging of intercostal spaces on the affected side with fullness of hypochondrium if large effusion.
2. Diminished mobility of the chest wall on the affected side.
3. Shift of the mediastinum to the opposite side. i.e. Trailes sign positive (sternomastoid muscle on the side of the mediastinal displacement may be prominent) as shift of trachea to one side causes relaxation of deep cervical fascia on that side and apex impulse is displaced to the side opposite to the effusion.

B. *Palpation*

1. Diminished mobility of the chest on the affected side.

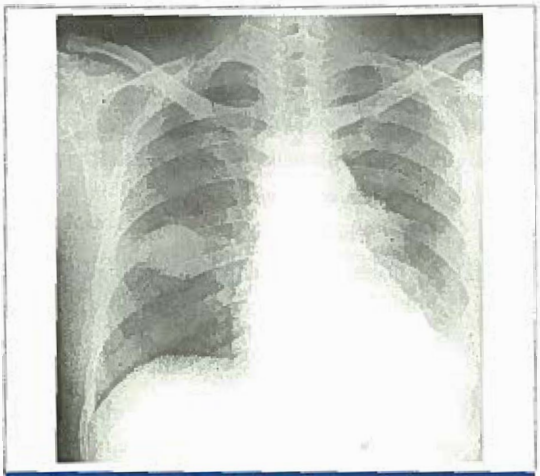


Fig. 4.24: Vanishing tumor

2. Shift of the mediastinum to the opposite side.
3. Diminished or absent TVF on the affected side below the level of the fluid and increased TVF at the level of the fluid.

C. *Percussion:*

1. Stony dullness with increased resistance and no shifting dullness below the level of fluid.
2. Skodaic resonance (boxy note) just above the effusion.
3. Obliteration of Traube's space if left sided effusion.
4. Grocco's triangle: Triangular area of dullness against the vertebral column at the base of the opposite lung, due to collapse of that lung.
5. Ellis' S shaped curve:
   a. It is a radiological illusion.
   b. In free pleural effusion the fluid collected in the pleural space assumes the highest position in axilla due to capillary action. Hence the stony dullness arising posteriorly near spine reaches the highest point in posterior axilla and then again comes down anteriorly.

D. *Auscultation:*
   1. Diminished or absent breath sounds below the level of the effusion.
   2. Bronchial breathing at the level of pleural effusion due to relaxed lung.
   3. Egophony at the level of the pleural effusion.
   4. Diminished or absent vocal fremitus below the level of the fluid.

III. **Investigations:**
   A. **CBC, ESR**
   B. **Sputum Examination: Gram and Ziehl-Neelsen's stain and culture.**
   C. **X-ray chest**
      1. Homogenous opacity
      2. Obliteration of costophrenic angle on the affected side (150 ml of fluid)
      3. Concave upper border (Ellis's curve)
      4. Shift of the mediastinum to the opposite side

   Radiologically, pleural effusion can be classified as free or loculated as given below:
      1. *Free classical:* Mild (blunting of costophrenic angle on lateral decubitus view) or moderate to severe (homogenous opacity with classical lateral-medial, superior-inferior curve with mediastinal shift to opposite side.
      2. *Free subpulmonic:* additional elevation of diaphragm
      3. *Loculated fissural:* Phantom/vanishing tumor (Refer Pg. 137)
      4. *Loculated along the chest wall*
   D. **Imaging:** Ultrasound, CT scan, HRCT scan (50 ml of fluid)
   E. **Thoracocentesis** to differentiate transudate from exudate
   F. **Pleural Biopsy**
   G. **Thoracoscopy**

Specific Features of Different Pleural Effusions (Pleural Fluid Analysis)

I. **Gross**
   A. Purulent / serous
   B. Hemorrhagic
   C. Milky
   D. Greenish: Pseudomonas, Streptococcus, Pneumococcus
   E. Gold paint: myxedema
   F. Anchovy sauce - ruptured amebic liver abscess

II. **Microscopic**
   A. Lymphocytic predominance — chronic conditions like tuberculosis, resolving pneumonia, fungal infections, carcinoma and myxedema
   B. Polymorphic predominance — Acute conditions like acute bacterial infections and rheumatic fever
   C. Eosinophilic predominance

Table 4.5 : Pleural Fluid with and without Systemic Eosinophilia

With Systemic Eosinophilia	*Without Systemic Eosinophilia*
1. *Tropical eosinophilia.*	1. *Pleuropulmonary amebiasis*
2. Pulmonary eosinophilia	2. Fungal infection
3. Vasculitis e.g. Polyarteritis nodosa	3. Foreign protein in pleural space
4. Hydatid disease	4. Blood in pleural space
5. Hodgkin's disease	5. Collagen disease, SLE
6. Drug induced	6. Pulmonary infarction
	7. Frequent aspiration
	8. Post-CABG

   D. WBC Count > 10,000 / mm^3 - Empyema, Pancreatitis, Pulmonary Embolism, Carcinoma, Collagen Vascular Diseases.

III. **Biochemical Investigations:**
   A. Proteins more than 3 gm% - exudate; less than 3 gm% - transudate.
   B. Sugar diminished in rheumatoid arthritis, infections, malignancy.
   C. LDH increased in tuberculous effusion.
   D. Amylase increased in pancreatitis rupture of esophagus and salivary gland abscess.

E. Adenosine deaminase activity is increased in tuberculous pleural effusion.

F. Hyaluronidase is increased in mesothelioma of pleura.

G. Light's criteria using serum and pleural fluid albumin and LDH are used to differentiate transudate from exudate.

Exudative Pleural Effusion meets atleast one criteria, Transudative meets none:

i. Pleural fluid protein / serum protein > 0.5.

ii. Pleural fluid LDH / serum LDH > 0.6.

iii. Pleural fluid LDH more than two thirds normal upper limit for serum.

These criteria misidentify 25% of transudates as exudates.

H. Serum-to-pleural fluid albumin gradient (serum albumin minus pleural fluid albumin) of <1.2 g/dL indicates the presence of exudate. Difference >3.1 gm/dl indicate it is Transudative.

Sequelae of Pleural Effusion

1. Permanent collapse of the lung (compression collapse)
2. Pleural thickening, adhesions and bronchiectasis
3. Empyema

Differential Diagnosis

I. Table 4.6 : Differences between Thickened Pleura and Pleural Effusion

	Thickened Pleura	*Pleural Effusion*
1. History	Long standing	Acute
2. Intercostal spaces	Depressed	Bulging
3. Mediastinum	No shift or shift to the same side	Shift to the opposite side
4. Percussion note	Dull	Stony dull with increased resistance
5. Breath sounds	Diminished	Absent
6. X-ray	No dense opacity, upper level not well-defined, cosophrenic angle not obliterated, calcification may be seen	Dense opacity, concave upper border, costophrenic angle obliterated

II. Table 4.7: Differences Between Empyema and Pleural Effusion

	Empyema	*Pleural Effusion*
1. Septicemia / Toxic look	Present	Absent
2. Intercostal spaces	Red, shiny, edematous, tender	Normal / Bulging
3. Clubbing	Present	Absent
4. Opacity on X-ray	Obliterates the rib shadows	Not so

III. Table 4.8 : Differences Between Pericardial and Pleural Effusion

	Pericardial effusion	*Pleural effusion*
1. Mediastinal shift	Absent	Present
2. Dullness posteriorly	Absent	Present
3. Traube's area	Not obliterated	Obliterated in left sided effusion
4. Heart sounds	Muffled	Diminished at the apex, but heard better elsewhere

IV. Table 4.9 : Differences between Liver Abscess and Right Pleural Effusion

	Liver Abscess	*Right Pleural Effusion*
1. Dullness highest point	In the mid-clavicularline	In the axilla
2. Tidal percussion	No movements of diaphragm	Movements may be present
3. Intercostal tenderness	Present	Present only in empyema

V. Effusion due to Heart Failure

1. Most common cause of pleural Effusion.
2. It is Transudative and usually bilateral.
3. Diagnostic thoracentesis is usually not required. Heart failure should be treated.
4. A pleural fluid NT - ProBNP > 1500 pg/ml is diagnostic of pleural effusion secondary to congestive heart failure.

VI. Synpneumonic or Parapneumonic Effusion :

This is said to occur when there is simultaneous pneumonia in the lung covered by pleural effusion.

1. It is associated with bacterial pneumonia, Lung abscess, or bronchiectasis which are the most common causes of exudative pleural effusion. It is also associated with malignancy and pulmonary infarction.
2. Patient usually present with Acute (Bacterial) or subacute (Anaerobic) onset of fever, chest pain, cough with expectoration; weight loss and mild anaemia if subacute.
3. The physical findings of pleural effusion which are altered are:
   a. Bronchial breath sounds are very well heard
   b. Rales may be present
   c. Vocal resonance is increased because the relaxed lung is filled with exudate in consolidation, which is a good conductor of sound.
4. Following features may indicate empyema:
   a. Patient not responding to current antibiotics.
   b. Grossly purulent fluid.
   c. Pleural fluid WBC > 50,000 / µl or PMN > 1000 / µl.
   d. Pleural fluid pH < 7.20. (other causes - oesophageal rupture, Rheumatoid pleural, TB pleuritis, Lupus Pleuritis)
   e. Pleural fluid glucose < 60 mg/dl.
   f. LDH > 1000 IU/L.
   g. Positive Microscopy or culture of pleural fluid.
   h. TNFα levels higher than 80 pg/ml also suggest Empyema.

VII. Effusion Secondary to Malignancy

1. Second most common type of Exudative Pleural Effusion. Lung carcinoma, Breast carcinoma and Lymphoma account for 75% of cases.
2. Dyspnea is out of propectin to the size of pleural effusion. Other systemic features to note are - weight loss, cachexia, clubbing, non-metastatic manifestations of the tumor.
3. Patient may present with signs of pleural effusion, collapse, consolidation, congestion or a local area of dullness.
4. Pleural fluid is exudative, glucose level is reduced.
5. For definitive diagnosis : Pleural fluid cytology (diagnostic), other modalities like Thorocoscopy, CT or USG guided biopsy of pleural thickening / nodules.

VIII. Mesothelioma

1. Primary tumours of mesothelial cells lining the pleural cavities; most related to Asbestos exposure.
2. Patients have chest pain and shortness of breath.
3. Most signs are similar to pleural effusion due to other causes, but mediastinal shift will be to the same side.
4. X-ray chest - Generalised pleural thickening with shrunken hemithorax.
5. Thoracoscopy or open pleural biopsy establishes the diagnosis.
6. *Treatment*
   a. Opiates for chest pain
   b. Oxygen for shortness of breath.

IX. Effusion secondary to pulmonary embolization

1. Patient usually presents with Dyspnea.
2. Pleural Effusion is exudative or transudative.
3. Treat underlying emboli i.e. Anticoagulation. If pleural effusion increases in size after anticoagulation, patient has either recurrent emboli or a complication like Hemothorax or Pleural infection.

X. Tuberculous Pleural Effusion

1. Usually associated with primary TB and occurs due to hypersenstivity reaction to tuberculous protein in pleural space.
2. Clinical features : Fever, weight loss, dyspnea, pleuritic chest pain, dry cough along with classical signs of pleural effusion.
3. Pleural fluid examination:
   a. Exudate with small lymphocytes predominant

b. ADA > 40 IU/L, IFN γ >140 pg/ml
c. Pleural fluid culture

4. Needle biopsy of pleura or thoracoscopy if required.
5. Treat underlying TB

XI. Effusion Secondary to Viral Infection

1. 20% of undiagnosed exudative effusions.
2. These effusions resolve spontaneously with no long term residual effusion.
3. Aggressive Management is not required, particularly if patient is improving.

XII. Hepatic Hydrothorax

1. Defined as Pleural Effusion, usually greater than 500 ml, in patients with cirrhosis and without primary cardiac, pulmonary or pleural disease. Pleural effusion occurs in 5-10% of patients with cirrhosis.
2. *Pathogenesis*

   Results from passage of peritoneal fluid through small openings in the diaphgram into the pleural space. The negative intra thoracic pressure favours the passage of fluid from intra-abdominal to the pleural space.
3. *Clinical manifestations*
   a. Patients present with shortness of breath, cough, hypoxemia, chest dicomfort.
   b. Ascites is not always present, although other features of cirrhosis may be present.
   c. Less common presentation
      i. Tension hydrothorax - severe dyspnea, hypotension.
      ii. Spontaneous Bacterial Empyema - defined as PMN cell count > 500 cells/mm^3 or positive culture with exclusion of a parapneumonic effusion.
4. *Pleural effusion* is transudative but thoracentesis is always done to rule out other causes of pleural effusion.
5. *Management*
   a. Sodium Restriction, diruetics (similar to ascites)
   b. Refractory hydrothorax management
      i. Thoracentesis - diuretics should be continued even after thoracentesis. Not more than 2 litres of pleural fluid should be removed, to prevent pulmonary edema and hypotension.
      ii. Transjugular intrahepatic portosystemic shunt (TIPS).
      iii. Pleurodesis - Mechanical / chemical.
      iv. Thoracoscopic repair - Diaphgramatic repair involving a pleural flap and surgical mesh reinforcement.
6. *Treatment of infection* - spontaneous bacterial empyema.
7. *Other treatment options* - Octreotide, terlipressin with albumin.

XIII. Chylothorax

1. *Causes :* Trauma (Most frequently during thoracic surgery), Tumor in mediastinum.
2. Patients have dyspnea and present with large pleural effusion.
3. Pleural fluid : Milky fluid, Triglyceride levels > 110 mg/dl.
4. Lymphangiogram and Mediastinal CT scan for Tumor / lymph nodes should be done if trauma is not the cause.
5. *Treatment*
   a. Insertion of ICD, octreotide.
   b. Pleuoperitoneal shunt if above modalities fail.
   c. Ligation of thoracic duct
6. Avoid prolonged ICD drainage of chycothoraces as it will lead to malnutrition and immunologic incompetence.

XIV. Hemothorax

1. Diagnosed when hematocrit of pleural fluid is more than one-half of that in peripheral blood.
2. *Causes* - Trauma, rupture of blood vessel or tumor

3. *Treated* with Tube Thoracostomy. It also allows quantification of bleeding.
4. Lacerated pleura treated by apposition of pleural surfaces.
5. If pleural hemorrhage exceeds 200 ml/h, thoracoscopy or thoracotomy should be done.

XV. Miscellaneous causes

1. Serum Amylases level elevated in *oesophageal rupture or pancreatitis*
2. *Intra abdominal abcess* - Patient is febrile, high PMN in pleural fluid; no pulmonary pathology.
3. *Ascites with pleural effusion* - Benign ovarian tumor (Meig's syndrome), Ovarian hyperstimulation syndrome.
4. *Post CABG* : (a) Effusion within first few weeks are typically left sided, bloody, large numbers of eosinophils, responding to one or two thoracentesis; (b) Effusions after first few weeks are typically left sided, clear, with small lymphocyte predominance and tend to recur.

Treatment

I For Pleural Effusion

1. *General:* Rest, adequate nutrition, vitamins
2. *Management of fluid:* **Thoracocentesis or pleural tapping** if large effusion, cardio-respiratory embarrassment or empyema

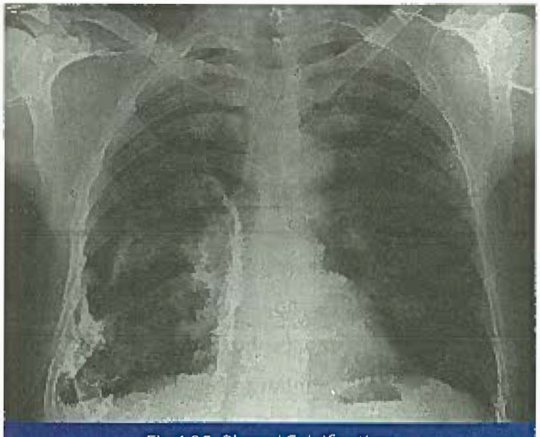


Fig 4.25 : Pleural Calcification

3. *Chest physiotherapy* to encourage expansion of lower chest
4. For recurrent pleural effusion e.g. malignancy.
   1. Pleurodesis - Pleural abrasion, Talc, Doxycycline.
   2. Placement of Small Indwelling Catheter

II. For Empyema

1. *Antibiotics:* The correct antibiotic could be best selected by culturing the pleural fluid followed by antibiotic sensitivity tests. The antibiotics have to be given for 3-6 weeks or even more till the patient becomes afebrile, WBC count returns to normal, drainage reduces to less than 100 ml/day and there is radiological clearance. The antibiotics used are a combination of Beta-lactam aminoglycoside and metronidazole.
2. *Intercostal drainage:* Continuous intercostal drainage with a tube may be required till the patient is afebrile, lung expansion is full and WBC count returns to normal.
3. *Intrapleural thrombolytic agents* like streptokinase diluted in 10 ml saline breaks down the loculation and improves drainage.
4. Thoracostomy with decortication.
5. Video Assisted Thoracic Surgery.
6. Open drainage and rib resection.

4 Collapse / Atelectasis of Lung

Definition

It is defined as airlessness with shrinkage of the lung which may be secondary to obstruction, compression, contraction or surfactant loss. Failure of the lung to expand at birth is called atelectasis neonatorum.

Classification

1. Acute or chronic - depending on rapidity of development of collapse.
2. Partial or total - depending on the degree of collapse.

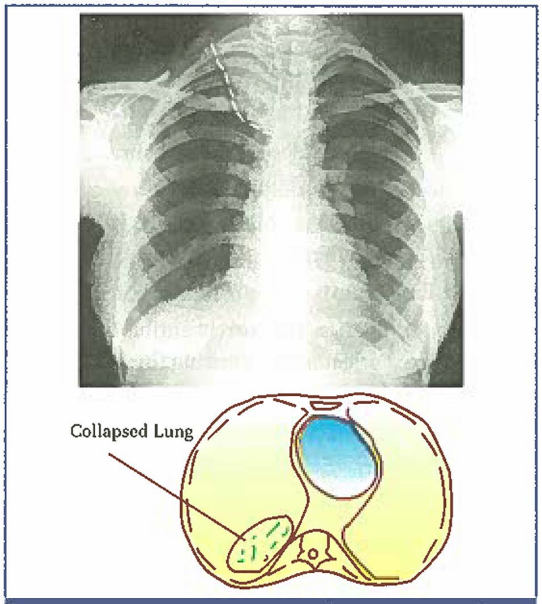


Fig. 4.26: X-ray showing collapse right upper lobe with consolidation and CT Chest showing collapsed lung

3. Mechanism of collapse - obstruction, compression, fibrosis or surfactant loss.

Causes

I. *Compression collapse*
   - A. Pneumothorax
   - B. Large neoplasm
   - C. Pleural effusion

II. *Absorption collapse* (due to obstruction)
   - A. *Within the lumen:*
     1. Foreign body
     2. Mucus plugs
     3. Blood
   - B. *Within the wall*

     Neoplasm e.g. adenoma, carcinoma
   - C. *Outside the wall*
     1. Aneurysm of aorta
     2. Enlarged lymph nodes
     3. Neoplasms

Diagnosis

I. Symptoms

The common symptoms are: Pain on the affected side, dry cough, breathlessness and fever. Presence of symptoms depends on:

A. Amount of the lung involved.

B. Rapidity with which it occurs.

C. Presence or absence of infection

II. Signs: Refer Table 4.4, Pg. 134

III. Investigations

1. *X-Ray chest*
   - a. Opacity of the involved segment or lobe producing silhouette sign
     - i. Middle lobe or lingular collapse producing blurring of Right or left heart border.
     - ii. Upper lobe collapse causing blurring of superior mediastinal border. Luftsichel sign - In case of complete upper lobe collapse hyperinflation of apical segment of lower lobe restores the silhouette of mediastinal boundaries.
     - iii. Lower lobe atelectasis does not obliterate cardiac borders (negative silhouette sign) and causes a retrocardiac shadow. Superior triangle sign - Lower lobe collapse resulting in para - tracheal opacity due to displacement of superior mediastinal structure.
     - iv. Double Lesion Sign : Results from collapse of two segments or lobes, which cannot be explained by one site of obstruction. It is useful to exclude a malignancy.
   - b. Signs of loss of lung volume
     - i. Shift of hilum.
     - ii. Shift of Trachea or Mediastinum.
     - iii. Elevation of hemi-diaphgram
     - iv. Crowding of bronchi / blood vessels.
   - c. Hyperinflation of rest of lung.
2. Computed Tomography Scan (CT Scan)
   - a. Findings similar to X-ray chest
   - b. In addition, helps to determine site of obstruction and etiology.

c. Useful in evaluating mediastinum, pleura, hilum, chest wall, rest of lung and concomitant pathologies.

3. Other Imaging Techniques : MRI, Virtual Bronchoscopy.
4. Pulmonary Function Test : Shows a restrictive pattern of abnormality.
5. Arterial Blood Gas Analysis : Shows Hypoxemia particularly if acute.

Complications

1. Infection
2. Spontaneous pneumothorax from ruptured bullae of compensatory emphysema

Treatment

Aims at treating underlying cause.

1. Pleural Aspiration / ICD in pleural effusion / pneumothorax, hydropneumothorax.
2. Removal of foreign body, impacted mucus.
3. Treatment of endobronchial tumor - surgery, radiation, chemotherapy, laser, airway stenting.
4. In case of mucus plugging. Mucolytis, nebulization, physiotherapy, measures like postural drainage, chest wall percussion and vibration, forced expiration technique.
5. Oxygen, Analgesics, Antibiotics for secondary infection.

5 Pulmonar Fibrosis / Interstitial Lung Diseases

Definition

Represent a large number of conditions that involve the parenchyma of the lungs - the alveoli, the alveolar epithelium, the capillary endothelium, spaces between these structures, as well as perivascular and lymphatic tissues.

They have similar clinical, roentgenographic, physiologic or pathologic manifestations.

ILD usually have an acute / chronic phase.

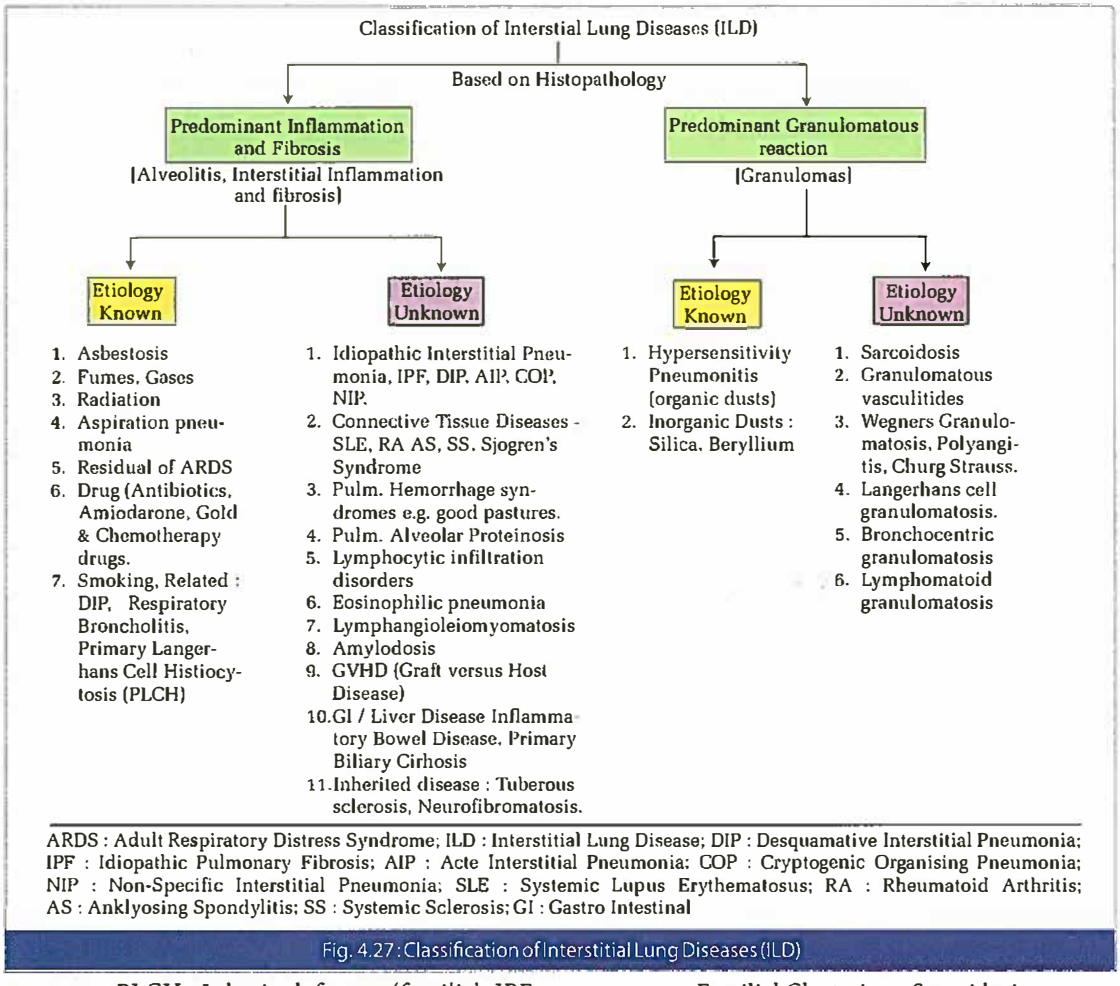
They can occassionally be recurrent with intervals of sub clinical disease.

Histopathologic patterns in ILD :

1. Desquamative Interstitial Pneumonia (DIP)
2. Respiratory Bronchiolitis
3. Diffuse Alveolar Damage (Acute or Organizing)
4. Bronchiolitis Obliterans with Organizing Pneumonia (BOOP)
5. Non-specific Interstitial Pneumonia (NIP).
6. Usuaul Interstial Pneumonia (UIP).
7. Lymphocytic Interstitial Pneumonia.

Diagnosis

1. *Duration of Illness:*
   i. Acute Presentation (days to weeks) : (a) Allergy (drugs, fungi, helminths), (b) Acute Interstitial Pneumonia (AIP), (c) Eosinophilic Pneumonia, (d) Hypersensitivity Pneumonitis (unusual)
   ii. Subacute Presentation (weeks to months) may occur in all ILD : (a) Sarcoidosis, (b) Drug Induced ILD, (c) Alveolar Hemorrhagic Syndrome, (d) Cryptogenic Organizing Pneumonia (COP), (e) Acute Immunologic Pneumonia - complicating SLE or Polymyositis.
   iii. Chronic Presentation (months to years) (Most ILD) : (a) Sarcoidosis, (b) Idiopathic Pulmonary Fibrosis, (c) Primary Langerhans Cell Histiocytosis (PLCH), Eosinophilic Granuloma or histiocytosis, (d) Pneumoconioses, (e) Connective Tissue Disorders.
   iv. Episodic Presentastion (Rare) : (a) Hypersensitivity pneumonitis, (b) COP, (c) Eosinophilic pneumonia, (d) Pulmonary Vasculitides, (e) Pulmonary hemorrhage, (f) Churg Strauss Syndrome.
2. *Age*
   a. Presentation - Between 20 and 40 Years - Sarcoidosis, CTD associated ILD, Lymphangio-leiomyomatosis (LAM),



ARDS : Adult Respiratory Distress Syndrome; ILD : Interstitial Lung Disease; DIP : Desquamative Interstitial Pneumonia; IPF : Idiopathic Pulmonary Fibrosis; AIP : Acte Interstitial Pneumonia; COP : Cryptogenic Organising Pneumonia; NIP : Non-Specific Interstitial Pneumonia; SLE : Systemic Lupus Erythematosus; RA : Rheumatoid Arthritis; AS : Anklyosing Spondylitis; SS : Systemic Sclerosis; GI : Gastro Intestinal

Fig. 4.27 : Classification of Interstitial Lung Diseases (ILD)

PLCH, Inherited forms (familial IPF, Gauches, disease.

b. Presentation older than 50 years - IPF.

3. *Gender*

a. LAM and Pulmonary involvement in Tuberous Sclerosis - Exclusively in Premenopausal women.

b. ILD in CTD - more common in men (exception ILD in RA)

c. Pneumoconiosis - More frequently in men.

4. *Family history*

a. Autosomal Dominant Pattern - ILD in Tuberous Sclerosis & Neurofibromatosis.

b. Autosomal Recessive Pattern - Niemann Pick, Gauchers, Hermansky Pudlak Syndrome.

c. Familial Clustering - Sarcoidosis

d. Familial Lung Fibrosis (older age, male sex, history of smoking are risk factors) - Mutations in surfactant (characterized by several patterns - NIP, DIP, UIP)

5. *Smoking History*:

a. 60% to 75% with IPF - have History of smoking.

b. Almost or always current smokers - PLCH, DIP, Good Pastures syndromes, Respiratory Broncholitis, Pulmonary Alveolar Proteinosis.

6. Occupation and Environmental History : Symptoms diminish or disappear after patient leaves the site of exposure; symptoms reappear on returning to exposure site.

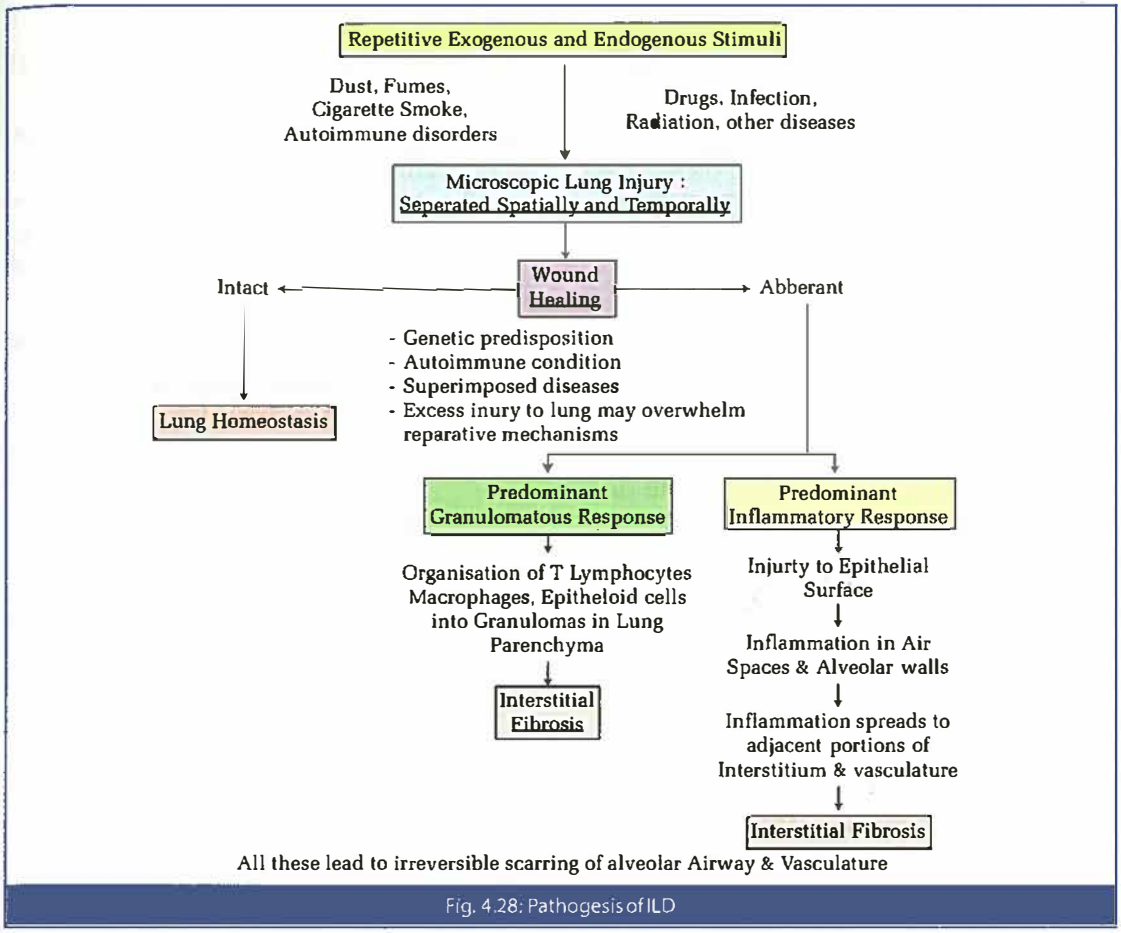


Fig. 4.28: Pathogesis of ILD

e.g. Hypersensitivity pneumonitis - symptoms temporally related to hobby (pigeon breeders) or workplace (Farmer's lung).

7. Other important past history
   a. History of Travel - for parasitic infection (causing pulmonary eosinophilia).
   b. History of risk factors for HIV infection from all patients : Several processes occur at time of initial presentation or during clinical course. e.g. HIV Infection, BOOP, AIP, Lymphocytic Interstitial Pneumonitis or Diffuse Alveolar Hemorrhage.

Idiopathic pulmonary fibrosis : (diffuse fibrosing alveolitis) (Hamman Rich syndrome)

It is the most common type of idiopathic interstitial pneumonia grouped under interstitial lung disease with predominant inflammatory type and unknown etiology. It has poor response to treatment and Bad Prognosis

Clinical Manifestations

1. It has a chronic presentation : Age Group > 50 yrs, Men more commonly affected; 60% to 75% are smokers.
2. Symptoms
   a. Exertional Dyspnea
   b. Non productive cough
   c. Fatigue
   d. Weight loss
3. Signs
   a. Tachypnea

b. Cyanosis : especially in advanced stages

c. Clubbing : especially in advanced stages

d. Bi-Basilar End Inspiratory Leathery Crackles.

4. Manifestation of Pulmonary Hypertension and Cor Pulmonale in Mid-Late stages of disease.

Investigation

1. *Routine* Tests - CBC, Sr. Creatinine, FBS
2. *LDH* - Non specific finding
3. *Other tests* - To rule out other diseases. e.g. ANA, RF - nonspecifically present in all ILF.
4. *ECG* - If PHT present - RVH, RAH, P-pulmonale.
5. *2-D Echo* - If PHT present - Rt. ventricular dilatation and/or hypertrophy.
6. *CXR* - Bi basilar reticular pattern; It correlates poorly with clinical or histopathologic stage of disease. Honey combing, if present, correlates with pathologic findings of small cystic spaces and progressive fibrosis and when present has poor prognosis. CXR may be normal.
7. *HRCT* - Patchy, predominantly basilar, subpleural reticular opacities, associated with traction bronchiectasis and honeycombing may also preclude the need for biopsy to diagnose IPF.
8. *Pulmonary Function Tests*

   A. Spirometery and Lung Volumes -

      i. Proven to have prognostic valve.

      ii. Restrictive defect - ↓TLC, ↓FRC, ↓RV, ↓FEV & ↓FVC (related to ↓TLC); FEV_1 / FVC normal or increased.

   B. Diffusion Capacity

      i. Diffusion capacity of lung for carbon monoxide (DLCO) is reduced - Due to effacement of alveolar capillary units and V/Q mismatch.

      ii. Severity of reduction does not evaluete with disease stage.

9. *Arterial Blood Gases (ABG)*

   i. Resting Hyponemia - may or may not be present.

   ii. Respiratory alkalolies.

   iii. CO_2 retention - late stages

   iv. Exercises or sleep induced hyponemia.

10. *Cardio - pulmonary exercise testing*

    i. Exercise testing with ABG monitoring to look for Arterial O_2 desaturation

    ii. Serial Assessment of resting and exercise gas exchange - excellent method for following disease activity and response to treatment.

    iii. 6-Minute walk test

    Global evaluation of sub - maximal exercise capacity.

    Walk distance and level of O_2 desaturation correlate with patient baseline lung function and mirrors patients clinical course.

11. *Histopathology*

Essential to confirm UIP pattern for diagnosis.

Surgical Bx required (Transbronchial Bn→Biopsy not helpful).

Histologic features

i. Affects peripheral, sub pleural parenchyma more severely.

ii. Histologic hallmark / chief diagnostic criteria.

Heterogenous appearance at low magnification with alternating areas of normal lung, interstitial inflammation, foci of proliferating fibroblasts, dense collagen fibrosis, honey comb changes.

iii. Patchy interstial Inflammation with lymphoplasmocytic infiltrate in alveolar septa; Hyperplasia of Type 2 pneumocytes

iv. Fibrotic zones : Composed of dense collagen, Extent of fibroblastic proliferation - predictive of disease progression.

v. Honeycomb changes

Cystic fibrotic air spaces - lined by Bronchiolar epithelium and filled with mucin.

vi. Smooth muscle hyperplasia - present in areas of fibrosis and honey combing.

(Usual Interstitial Pneumonia - For patients in whom lesion is idiopathic and not associated with another condition.)

Treatment

There is no effective therapy for IPF.

1. Hypoxemia (PaO_2 55 mmHg) at rest and / or with Exercise - supplemental O_2.
2. Cor pulmonale - diuretics, other treatment.
3. Pulmonary Rehabilitation.
4. Lung Transplantation
    1. Pathologic and Radiologic evidence of UIP AND
    2. Any of the following criteria
        a. $DLCO_2$ < 39%.
        b. Decrement in FVC ≥ 10% during 6 months of follow up.
        c. Decrease in SpO_2 below 88% during 6 min - walk test.
        d. Honey combing on HRCT

Patients with IPF and co-existant emphysema (COPD) develop pulmonary hypertension early and have a worse outcome.

Acute deterioration of IPF & Acute Exacebration

1. Acute deterioration secondary to :
    a. Infection
    b. Pulmonary Embolism
    c. Pneumothorax
    d. *Accelerated clinical course*

    Exacerabation of IPF - Criteria for diagnosis
        i. Worsening dyspnea within few days to 4 weeks
        ii. New developing diffuse ground glass opacity and / or

        Consolidation superimposed on background reticular or honey comb pattern consistent with UIP pattern.
        iii. Worsening hyponemia.
        iv. Absence of infections, pneumonia, sepsis and heart failure.

Treatment

i. No effective treatment
ii. Mechanical ventilation often required
iii. If patient survives - recurrence common and usually results in death.

Table 4.10 : Differences between Collapse and Fibrosis

	Collapse	Fibrosis
1. Onset	Acute	Chronic
2. Chest wall	Flattened	Retracted
3. Breath sounds	Absent	Feeble but never absent

6 Pneumothorax

Definition: Pneumothorax refers to air within the pleural space.

Causes

A. **Primary Spontaneous Pneumothorax (PSP)**

It is a pneumothorax that occurs without a precipitating event in a person who does not have known lung disease. Usually most individuals with PSP have unrecognized lung disease, with the pneumothorax resulting from rupture of a subpleural bleb.

Risk Factors

1. **Smoking** : Cigarette smoking is a significant risk factor. Respiratory bronchiolitis, a form of airway inflammation associated with cigarette smoking, may contribute to the development and recurrence of PSP.
2. **Family history** : Autosomal dominant, autosomal recessive, polygenic, and X-linked recessive inheritance mechanisms have all been proposed. The autosomal dominant Birt-Hogg-Dube syndrome, which predisposes patients to benign skin tumors and renal cancer, is associated with an increased incidence of PSP.
3. **Other**: Marfan syndrome, Homocystinuria.

B. **Secondary Spontaneous Pneumothorax (SSP)**

It is defined as a pneumothorax that occurs as a complication of underlying lung disease.

Etiologies

1. **Chronic Obstructive Pulmonary Disease**: 50 to 70 percent of SSP is attributed to COPD. Rupture of apical blebs is the usual cause.
2. **Cystic Fibrosis** : Usually due to rupture of

apical subpleural cysts. Factors associated with an increased risk of pneumothorax include infection with Pseudomonas aeruginosa or Aspergillus species or a prior episode of massive hemoptysis.

3. **Lung Malignancy** : Both primary and metastatic lung malignancy have been associated with SSP. The mechanism is endobronchial obstruction with air trapping.
4. **Necrotizing Pneumonia** : SSP can complicate the course of necrotizing pneumonia due to bacterial infection, Pneumocystis jirovecii, tuberculosis, and less often fungi.
   a. **Bacterial Pneumonia** : SSP has been associated with bacterial pneumonias caused by Staphylococcus, Klebsiella, Pseudomonas, Streptococcus pneumoniae, and anaerobic organisms. Extension of bacterial infection into the pleura can lead to development of empyema.
   b. **Pneumocystis jirovecii** : The pathogenesis of SSP in PCP is likely alveolar and pleural tissue invasion and rupture of large subpleural cysts that are caused by tissue necrosis.
   c. **Tuberculosis** : The pneumothorax is usually due to rupture of a tuberculous cavity into the pleural space.
5. **Catamenial Pneumothorax** : Refers to a pneumothorax occurring in association with menses due to thoracic endometriosis
6. **Less Common Causes** : Ankylosing spondylitis, asthma, histiocytosis X, interstitial lung disease (eg, idiopathic pulmonary fibrosis), lymphangioleiomyomatosis, Marfan syndrome, metastatic sarcoma, rheumatoid arthritis, and sarcoidosis.

III. **Traumatic and Iatrogenic**
   A. *Penetrating wounds:* Stab wounds, fractured ribs, crush injury.
   B. *Non-penetrating wounds:* Steering wheel impact against the drivers' chest.
   C. *Iatrogenic* : Central line insertion, surgery, lung biopsy, faulty tracheostomy.

IV. **Artificial:** It was induced in the past for severe tuberculosis (At present this is obsolete because of antituberculosis drugs).

Types

1. *Simple or closed Pneumothorax* : The opening in the lung is very small and heals rapidly. Therefore, there is no continuous communication between the lung and the pleural cavity. The pleural pressure on the affected side remains sub-atmospheric. A simple pneumothorax usually has only modest repercussions unless the patient has limited respiratory reserve or is being mechanically ventilated. Radiographically, simple pneumothoraces tend to be small and without mediastinal shift to the contralateral side.
2. *Open Pneumothorax* : The opening between the lung and the pleural cavity remains patent. Pressure in the pleural cavity is equal to that of the atmosphere. It occurs when a traumatic chest wall defect persists, through which air enters the pleural space during inspiration (ie, a "sucking wound"). As a result, the mediastinum shifts toward the normal side during inspiration and the lung on the injured side remains collapsed. During expiration, air exits the pleural space through the chest wall defect and the mediastinum swings back. Expiratory air from the normal lung (ie, "pendulum air") fills the collapsed lung. The "mediastinal flutter" may cause respiratory failure. Radiographically, an open pneumothorax is characterized by a visible chest wall defect and by expiratory mediastinal shift towards the injured side.
3. *Tension Pneumothorax* : The opening between the lung and the pleural caity is "valvular" - air can enter the pleural cavity during inspiration but cannot escape during expiration. Therefore, a positive pressure (exceeding atmospheric pressure) occurs on the affected side. This rapidly leads to respiratory failure and a is a medical emergency. Radiographically, tension pneumothorax shows a distinct shift of the mediastinum to the contralateral side.

4. *Others:*
   a. *Pneumothorax ex vacuo* : This rare type of pneumothorax forms adjacent to an atelectatic lobe. It is seen preferentially with atelectasis of the right upper lobe and is the result of rapid atelectasis producing an abrupt decrease in the intrapleural pressure with subsequent release of nitrogen from pleural capillaries. Treatment consists of bronchoscopy rather than chest tube drainage. Radiographically, pneumothorax ex vacuo is suggested when an atelectatic lobe or lung, particularly right upper lobe atelectasis, is surrounded by a focal pneumothorax.
   b. *Bilateral Postoperative Pneumothorax*: Bilateral pneumothoraces are seen after cardiac surgery, particularly in recipients of heart–lung transplants. They are a consequence of extensive mediastinal dissection allowing a unilateral pneumothorax to propagate to the contralateral hemithorax. A single thoracostomy tube is able to evacuate both pleural cavities. This type of pneumothorax has been dubbed "buffalo chest," since these animals have pleural spaces that communicate anteriorly and, as a result, they are susceptible to bilateral pneumothorax .

Conditions Mimicking Pneumothorax

1. **Bullae** : Large subpleural bullae can mimic a loculated pneumothorax . Both bullae and pneumothoraces usually have a straight or convex pleural contour laterally, but only bullae typically have a medial border that is concave to the chest wall.
2. **Trauma** : Herniated Stomach following trauma

Diagnosis

Symptoms

1. Primary spontaneous pneumothorax (PSP) usually occurs when the patient is at rest. Patients are typically in their early 20s, with PSP being rare after age 40.

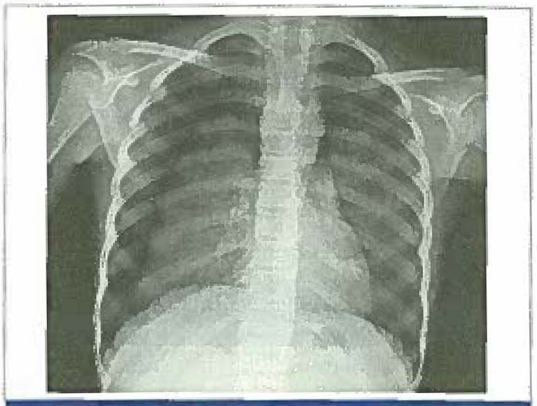


Fig 4.29 : Bilateral pneumothorax

2. Symptoms due to SSP are generally more severe than those associated with PSP, presumably because patients with SSP have less pulmonary reserve due to underlying lung disease.
3. Sudden onset of dyspnea and pleuritic chest pain. The severity of the symptoms is primarily related to the volume of air in the pleural space.
4. Evidence of labored breathing and hemodynamic compromise (eg, tachycardia, hypotension) suggests a possible tension pneumothorax, which necessitates emergency decompression.

Signs

A. ***Closed pneumothorax***
   1. Reduced chest movement
   2. Hyper-resonant note on percussion
   3. Absent air entry
   4. Mediastinal shift to opposite side
   5. Coin Test
   6. ↓TVF, VR

B. ***Open pneumothorax***

   All the signs of closed pneumothorax, plus —
   1. Crackpot sound on percussion
   2. Amphoric breath sounds
   3. Voice and cough sounds may be heard with metallic echo.

C. ***Tension pneumothorax***

   All the signs of closed pneumothorax, plus —
   1. Displacement of the mediastinum with respiration

2. Increasing breathlessness, cyanosis and tachycardia, ↑RR, ↓BP, ↑TVP
3. Respiratory failure

Differential Diagnosis

I. Table 4.11 : Differences between a Large Pulmonary Cavity and Pneumothorax

	A large pulmonary cavity	*Pneumothorax*
1. Onset	Insidious	Acute
2. Movements of chest	Restricted or diminished at apex only or normal.	Absent on the whole of the affected side
3. TVF	Increased	Reduced
4. Breath	Cavernous/sounds	Absent / amphoric
5. Coin sound	Rare	Present
6. Mediastinum	Central	Central / Pushed

II. Table 4.12 : Differences between Eventration of Diaphragm and Pneumothorax

	Eventration of Diaphragm	*Pneumothorax*
1. Symptoms	Usually absent or referable to gastrointestinal or circulatory system.	Symptoms of respiratory system
2. Movements	Increased inspiratory ascent of costal margin because of lack of opposition of paralyzed diaphragm	Movements diminished on the affected side.
3. Screening X-ray	Diaphragm high in chest with paradoxical movements	Radiolucency seen with razor sharp edge of the collapsed lung.

III. Table 4.13 : Differences between Congenital Large Cyst and Pneumothorax

	Congenital Large Cyst	*Pneumothorax*
1. Mediastinum	Central	To opposite side
2. X-ray	No collapsed lung at hilum.	Collapsed lung at hilum

Imaging

1. **Chest radiographs (Refer to Chapter 9)**

Main Features :

i. Hyper translucency between lung and thoracic cage.
ii. Razor sharp border of the collapsed lung (white visceral pleural line).
iii. Shift of mediastinum to the opposite side.

A pneumothorax may be identified on an upright, supine, or lateral decubitus chest radiograph. The lateral decubitus view tends to be the most sensitive, while the supine view is the least sensitive.

Upright

i. Most pleural gas accumulates in an apicolateral location.
ii. The visceral pleural line appears either straight or convex towards the chest wall.
iii. As little as 50 mL of pleural gas may be visible on a chest radiography.
iv. The collapsed lung preserves its transradiancy because hypoxic vasoconstriction diminishes the blood flow to the collapsed lung.

Supine

i. Most pleural air accumulates in a subpulmonic location.
ii. Gas in this location outlines the anterior pleural reflection, the costophrenic sulcus (creating the "deep sulcus" sign), and the anterolateral border of the mediastinum . In rare instances, pleural gas can also accumulate in the phrenicovertebral sulcus.
iii. The visceral pleural line may be seen at the lung base and has a concave contour.
iv. Approximately 500 mL of pleural gas are needed for definitive diagnosis of a pneumothorax on a supine chest radiograph.
v. The transradiancy and size of the entire hemithorax may be increased on the side of a pneumothorax.
vi. A hydropneumothorax in a supine patient

can produce a veil-like opacity, more opaque than a pure pneumothorax and less opaque than a pure hydrothorax .

Lateral decubitus

i. A pneumothorax can be most easily detected with a lateral decubitus view. In this position, most pleural air accumulates in the non-dependent lateral location.

ii. The visceral pleural line appears either straight or convex towards the chest wall.

iii. As little as 5 mL of pleural air may be visible on a lateral decubitus chest radiograph.

2. **Computed Tomography**

This is the most accurate imaging modality for the detection of pneumothorax. Even small amounts of intrapleural gas, atypical collections of pleural gas, and loculated pneumothoraces can be identified by CT. In addition, complex pleural pathology (eg, pleural effusion, pneumothorax) can be optimally displayed by CT scanning.

Pleural interventional procedures are also facilitated by CT guidance.

3. **Ultrasound** : Ultrasound of the chest is sometimes used to evaluate situations in which the diagnosis must be made emergently at the bedside, such as an ICU patient or a trauma patient in the emergency department, so-called point-of-care ultrasound.

In the presence of a pneumothorax, smooth, horizontal echogenic lines are seen above and below the pleural line and there is absence of lung sliding and B lines.

Treatment

Initial management is directed at removing air from the pleural space, with subsequent management directed at preventing recurrence.

Initial management : The choice of procedure depends on patient characteristics and clinical circumstances:

1. If cardio-respiratory embarressment:
   a. Supplemental oxygen
   b. Treatment of shock
   c. Aspiration of pneumothorax:
      - Chest Tube Insertion (Tube Thoractostomy) or
      - With the patient in sitting position, a Needle (14 guage) is inserted into the pleural cavity in the second space in the mid-clavicular line or in the fifth space in the axillary line. The other end of the needle is connected to the underwater seal.
2. If there is no cardiorespiratory embarrasment :
   a. If pneumothorax is small (≤ 3 cm between lung and chest wall) : Supplemental oxygen and observation.
   b. If pneumothorax is large (> 3 cm between lung and chest wall):
      i. Needle Aspiration.
      ii. Tube Thoracostomy (Chest Tube Insertion) : if needle aspiration fails.
      iii. Thoracoscopy (VATS) : See below.
      iv. Chemical Pleurodesis : If air leak persists.
   c. Recurrent Pneumothorax / Hydropneumothorax : Chest Tube insertion and Thoracoscopy. Chemical Pleurodosis may be performed.

Supplemental oxygen : administered to facilitate resorption of the pleural air.

Aspiration : Aspiration is most easily accomplished with a commercially available thoracentesis kit. Once no more air can be aspirated, the catheter can be removed or left in place attached to a one-way valve (Heimlich Valve).

Tube thoracostomy : Chest tube (≤22 Fr) or chest catheter (≤14 Fr) is connected to a water seal device, with or without suction and left in position until the pneumothorax resolves. The chest tube can be removed if the pneumothorax has not reaccumulated.

Thoracoscopy : Video-assisted thoracoscopy (VATS) -With this procedure, pleurodesis is created by pleural abrasion or a partial parietal pleurectomy; when necessary, an endoscopic stapler can be used to resect bullae.

Persistent air leak : A more aggressive approach is needed if an air leak persists after three days. For patients whose lung has expanded >90%.

- A Heimlich valve can be attached to the chest tube.

- Autologous blood or tube can be infused into the pleural space for chemical pleuradesis
- Performing video-assisted thoracoscopy to oversew the area of leak and perform mechanical pleurodesis.

Failure of lung reexpansion : For patients who have a persistent air leak and whose lung is less than 90 percent expanded, the preferred procedure is VATS.

Recurrence prevention :

a. Pleurodesis via VATS or chemical pleurodesis via tube thoracostomy (talc, bleomycin, tetracyclin derivatives like doxycycline or autologus blood can be used).

b. Thoracotomy : The indications for open thoracotomy are the same as those for VATS. Thoracotomy is presently recommended only if thoracoscopy is unavailable or has failed. During thoracotomy, apical pleural blebs are oversewn and the pleura is scarified.

c. Smoking cessation : may help prevent recurrent pneumothoraces.

7 Pulmonary Cavity

Definition: Pulmonary cavity is an area of liquefaction necrosis within the lung parenchyma in communication with the bronchus. The cavity may remain empty or may be filled with secretions or infected material.

Pseudo cavity is appearance of a cavity radiologically which may be obtained with summation shadows of vessels, ribs and calcifications.

Causes

A. Infection

1. Tuberculosis
2. Hydatid Cysts
3. Fungal infection
4. Abscess

B. Neoplasms

1. Bronchogenic carcinoma
2. Metastasis
3. Lymphoma

C. Traumatic: Resolving hematoma

D. Congenital

1. Infected bronchogenic cyst
2. Sequestration

E. Immunological

1. Rheumatoid
2. Wegener's granulomatosis

F. Vascular: Pulmonary infarction

On CXR 3/4th of circumference should be well defined in order to call it a cavity.

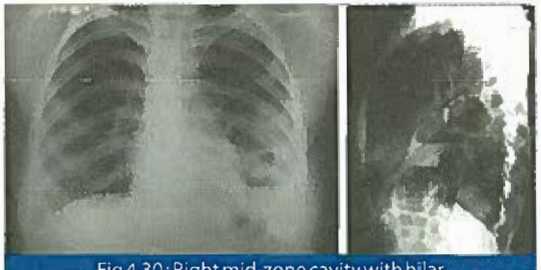


Fig 4.30 : Right mid-zone cavity with hilar lymphadenopathy

Table 4.13 : Types of Pulmonary Cavities

Thin shaggy walled	*Thin smooth walled*	*Thick walled*
Tuberculosis	Tuberculosis	Bronchogenic
Lung abscess	Lung cyst	carcinoma
Bronchogenic carcinoma	Emphysematous bullae	Lung abscess
	Hydatid cyst	
	Fungal infection	

Table 4.14 : Diagnosis of Pulmonary Cavities

		Empty	*Fluid filled*
1.	Movements over apex	Diminished	Diminished
2.	Retraction/Flattening of chest	Present	Present
3.	TVF/VR	Increased	Decreased
4.	Percussion note	Crack-pot sound	Diminished
5.	Breath sound	Amphoric/ Cavernous	Diminished
6.	Whispering pectoriloquy	Present	Absent
7.	Post tussive rales	Absent	Present

X-ray Chest: Ring shadows

8 Bronchogenic Carcinoma

Bronchogenic carcinoma must be considered in all cases, esp. > 40 years, or smokers presenting with respiratory involvement particularly with signs of:

I. Collapse
II. Consolidation
III. Cavitation
IV. Mediastinal obstruction
V. Pleural effusion
VI. Apical dullness, wasting of upper limb and Horner's syndrome

Table 4.15 : Differences between various types of Bronchogenic Carcinomas

	Epider-moid	*Adeno-carcino-ma*	*Anaplas-tic*	*Alveolar cell*
1. *Situation*	Central	Periph-eral	Either	Both
2. *Spread*	By conti-nuity	By all routes, especially blood	By all routes especially blood	Broncho-genic and by conti-nuity
3. *Onset*	Early	Late	Early	Early
4. *Association*	Cigarette smoking	Focal lung scars	—	—
5. *Sex*	Males	Females	Males	Females

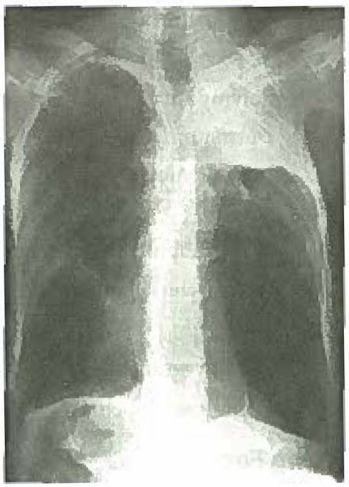


Fig 4.31 : Pancoast tumour

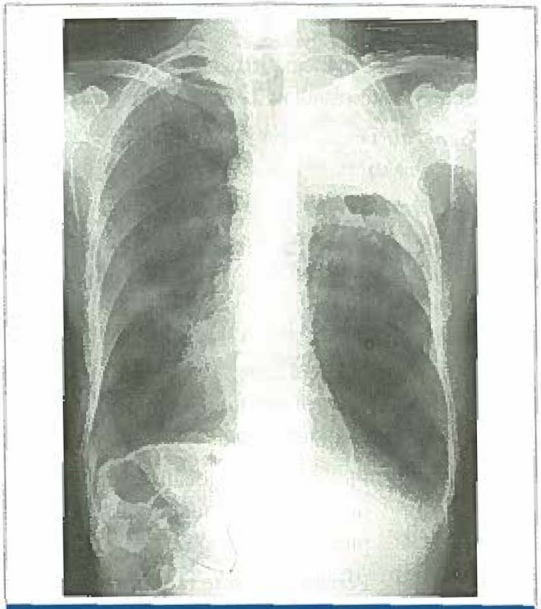


Fig. 4.32 : X-ray chest in a case of Bronchogenic carcinoma showing collapse L upper lobe with disseminated metastasis

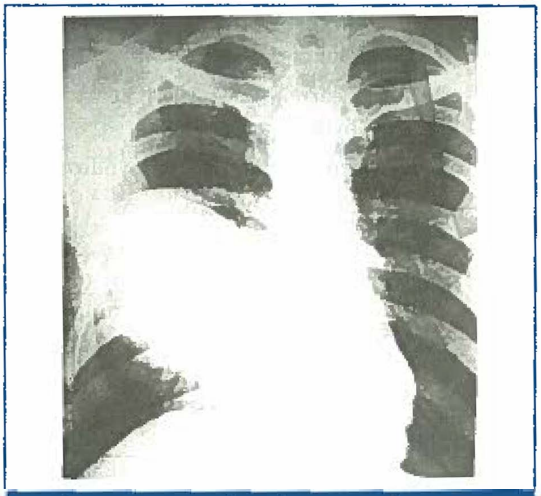


Fig. 4.33 : Brochogenic carcinoma showing nodular opacity on the right side

Types of Bronchogenic Carcinoma

1. Squamous cell or epidermoid carcinoma.
2. Adenocarcinoma
3. Anaplastic
4. Alveolar cell carcinoma

Symptoms

The patient may present with no symptoms, or the following symptoms:

I. ***General:*** Fever, malaise, anorexia, weight loss and weakness.

II. ***Respiratory:***

A. Cough with/without mucopurulent sputum.

B. Hemoptysis

C. Breathlessness

D. Stridor

E. Chest pain of various types:

1. Pleuritic due to localized pneumonia or carcinomatous involvement of pleura
2. Persistent severe radiating along the distribution of the intercostal nerves

III. ***Due to Local Spread:***

A. *Nerves:*

1. Phrenic: Hiccoughs, Paresis of diaphragm
2. Recurrent laryngeal: Hoarse voice, bovine cough
3. Sympathetic: Horner's syndrome
4. Vagus: Gastric symptoms
5. Brachial plexus: Weakness, wasting and sensory impairment over the ulnar border of the forearm and hand
6. Intercostal nerves

B. *Esophagus:* Dysphagia

C. *Blood vessels:*

1. Superior vena cava: Venous engorgement of head and neck
2. Azygous vein: Dilated veins over chest wall
3. Axillary vessels: Loss of peripheral pulsations and edema of the arm

D. *Thoracic duct:* Chylous effusion

E. *Erosion of ribs:* Local pain and tenderness

Invasion of heart and pericardium: CCF, arrhythmias, pericardial effusion.

IV. ***Due to Metastasis:***

A. Lymphatic: To mediastinal, cervical and axillary glands

B. Hematogenous: To brain, liver, skin, subcutaneous tissue, muscle, bone and breast

C. Bronchogenic: In the same or opposite lung

V. ***Paraneoplastic or Non-metastatic Manifestations***

A. *Endocrine*

1. Cushing's syndrome (excess ACTH)
2. Hypercalcemia (excess PTH)
3. Hyponatremia (excess ADH)
4. Hypoglycemia (excess insulin-like substance)
5. Carcinoid (excess serotonin)
6. Polycythemia (excess erythropoietin)
7. Gynecomastia (excess sex hormone)

B. *Skeletal:* Clubbing

C. *Skin*

1. Acanthosis nigricans
2. Pruritus
3. Eczema

D. *Neurological*

1. Neuropathy
2. Amyotrophy
3. Myelopathy
4. Encephalopathy

E. *Muscular*

1. Polymyositis
2. Dermatomyositis
3. Myasthenia

F. *Vascular:*

1. Thrombophlebitis migrans
2. Non-bacterial endocarditis

G. *Hematological:*

1. Hemolytic anemia
2. Thrombocytopenia

Predisposing Factors

1. Cigarette smoking

2. Occupational exposure to chromium, arsenic, nickel, coal gas, beryllium, iron and iron oxides
3. Air Pollution
4. Radiation
5. Chronic scarring

Radiology

1. There may be no radiological abnormality.
2. Unilateral enlargement of hilar shadows.
3. Peripheral shadows: Nodular and irregular homogenous or non-homogenous densities.
4. *Due to complications:*
   a. Cavity, collapse or consolidation.
   b. Pleural or pericardial effusion.
   c. Unilateral elevation of diaphragm.
   d. Pathological fracture of rib.
5. *Thoracic inlet tumour:*
   a. Dense irregular crescent at the apex.
   b. Destruction of the first three ribs.
   c. Bilateral hilar enlargement.
   d. Lymphangitis carcinomatosis.

Useful Investigations

1. X-ray and CT scan of chest
2. Bronchoscopy and mediastinoscopy
3. Lung scan
4. Sputum cytology
5. Scalene node biopsy
6. Lung biopsy
7. Tapping and examination of fluid - if there is pleural effusion.

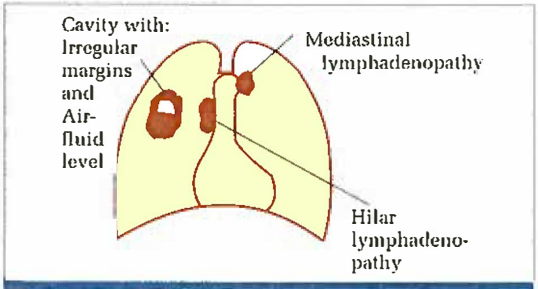


Fig. 4.34: Radiological appearances in bronchogenic carcinoma

Treatment

Curative treatment is achieved by surgical resection. If the tumour has spread, palliation can be achieved by radiotherapy and chemotherapy.

I. *Surgery*

Few patients are treatable by surgery. Even if the tumour is localized, results of surgery are poor in undifferentiated and poorly differentiated tumours, whereas in squamous cell carcinoma 5-year survival is as high as 50%.

Before surgery, staging of the tumour and pulmonary function tests (PFT) should be done. If PFT is poor there is high risk of post-operative complications and surgery is usually not considered.

II. *Radiotherapy*

It is not curative, but useful to relieve distressing complications like superior vena cava obstruction, hemoptysis and pain caused by chest wall invasion or skeletal metastasis. Undifferentiated and poorly differentiated tumours are more susceptible to radiotherapy.

III. *Chemotherapy*

Combination chemotherapy of 6 cycles at 3 weeks interval consisting of the following drugs is useful:

1. Doxorubicin 60 mg/sq.m. IV bolus- Day 1
2. Cyclophosphamide 750 mg/sq.m. IV infusion- Day 1
3. Etoposide 120 mg/sq.m. IV infusion - Day 1

They are useful in good prognosis group of patients (Age <70 years, Normal albumin and sodium and weight loss <10%).

In poor prognosis group, oral etoposide, 50 mg 12 hourly for 10 days every 3 weeks for 6 cycles offers good palliation.

In general, chemotherapy is less effective in non-small cell bronchial carcinomas.

IV. *Laser therapy*

Laser therapy via fiberoptic bronchoscope destroys the tumour tissue occluding the main bronchi and allows re-aeration of collapsed lung. It is essentially palliative.

9 › Pulmonary Tuberculosis

Tubercle bacilli gain entry into the body usually by inhalation or ingestion. Rarely they may gain entry through the skin, tonsils, conjunctiva and external genitalia. Sputum of the infectious patient is the commonest source of tubercle bacilli. The bacilli are scattered in the atmosphere mainly by coughing. (A single cough expels up to 40,000 tubercle bacilli). Droplets of sputum containing the bacilli may be inhaled directly by those in the vicinity or they may fall on the ground and mix with dust. When the ground is swept, the bacilli rise with the dust and may be inhaled. A sputum positive patient infects upto 25 persons / year.

Primary Pulmonary Tuberculosis

Pathogenesis: On inhalation, the tubercle bacilli reach the respiratory bronchioles and alveoli where they are taken up by the macrophages. These macro-phages may carry the tubercle bacilli elsewhere. Within the macrophages, the tubercle bacilli may multiply.

After about 3-8 weeks the individual develops a hypersensitivity to tuberculoprotein through specific modification of thymus dependent lymphocytes. At this time the following changes occur:

1. Tuberculin test becomes positive.
2. Macrophages may rupture releasing tubercle bacilli.
3. Granulomatous lesion (tubercle) may form.

   It consists of:

   a. Epithelioid cells derived from macrophages.
   b. Langhans giant cells also derived from macrophages.
   c. Lymphocytes.
   d. Central caseation due to cheesy type of necrosis: Caseous tissues may liquefy to become purulent material, which may be discharged into the air spaces, or it may be calcified.

A number of such tubercles may merge to form an area of pneumonitis (which is commonly subpleural). The lymphatics draining this area of pneumonitis may become involved and a chain of tubercles may be seen along these lymphatics going towards the hilar lymph nodes, which also become caseous and enlarged. This is called the **PRIMARY COMPLEX (Ghon's Complex).**

In the first few months following the primary infection, the tubercle bacilli can enter the lymphatics and from there the blood stream via the thoracic duct. Usually primary infection is seen in infants or children. Younger children have greater chances of progression of tuberculosis and developing its complications.

Primary Complex Consists of:

1. Subpleural TB
2. Hilar Lymphadenopathy
3. Draining Lymphatics
4. Right middle lobe collapse (Brock's syndrome): rare and seen mainly in children.

Classification

1. *GHON'S focus* - subpleural (lung)
2. *Ashman's focus* - deep apical (lung)
3. *Simmon's focus* - subpleural upper lobe focus
4. Cerebral - *Rich's focus*
5. Blood vessel - (Intima) *Wigard's focus*
6. Liver - *Simmonds focus*
7. Primary splenic, intestinal, primary lymph node focus.

Fate of Primary Complex

1. It may heal completely with or without calcification.
2. It may remain dormant, reawakening when the body defenses decrease.

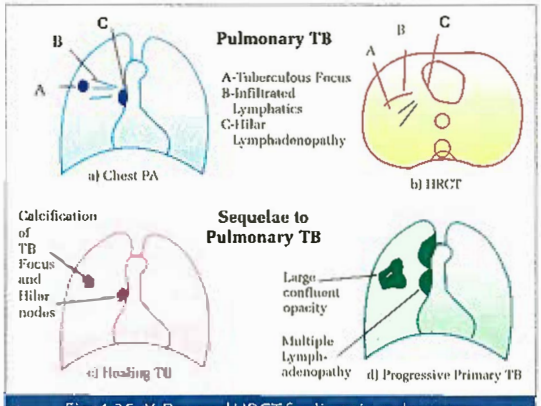


Fig. 4.35 : X-Ray and HRCT findings in pulmonary tuberculosis

3. It may actively progress merging into post-primary pulmonary tuberculosis.
4. It may lead to hematogenous spread of tubercle bacilli leading to miliary tuberculosis or tuberculous meningitis.

Clinical Features

A. Symptoms

1. There may be no symptoms
2. Fever for a brief period, which is often passed off as influenza. Evening rise of temperature.
3. Anorexia and weight loss
4. Cough and wheeze due to pressure of lymph nodes on bronchi

B. Signs

1. There may be no detectable physical sign.
2. General debility: A thin, pale, fretful child with loss of skin elasticity and less glossy hair.
3. Local areas of rales or rhonchi.

C. Radiology

In adults the pulmonary component is more obvious, whereas in children the glandular component is more obvious.

Radiological findings are:

1. Soft confluent shadow (suggesting exudative process)
2. Linear shadow (suggesting fibrosis)
3. Cavity: Initially irregular, later smooth walled
4. Thin walled bullae
5. Blocked cavity
6. Calcification
7. Bronchiectasis especially in the upper zones
8. Bronchial cold abscess: Elongated solid dense shadow
9. Enlarged hilar nodes
10. Miliary mottling
11. Tuberculoma
12. Primary complex

Complications

A. Pulmonary:

1. Epituberculosis: Dense homogenous density involving complete lobe yet the general condition of the patient is good. Prognosis is excellent. It may be due to inflammatory exudate, collapse or caseous pneumonia.
2. Bronchiectasis
3. Obstructive emphysema
4. Pleural effusion

B. Allergic

1. Erythema nodosum
2. Phlyctenular conjunctivitis

C. Due to hematogenous spread

1. Miliary tuberculosis
2. TB meningitis
3. Tuberculosis of bone, joints, kidneys and skin, any organ.

Post-primary Pulmonary Tuberculosis Pathogenesis

Post-primary pulmonary tuberculosis may rise in any one of the four ways:

1. Direct progression of primary lesion
2. Reactivation of the primary lesion when the individual's defenses have waned
3. Hematogenous spread of the disease from the primary focus
4. Exogenous superinfection with drug resistant bacilli.

The lesions of reinfection have the same basic tubercular pathology. Hyperallergy and immunity acquired as a result of first infection exert two opposing influences. As a result of hyper allergy there is a considerable tissue destruction and as a result of immunity there is a constant attempt at healing by localization and fibrosis. There is no tendency of involvement of draining glands.

When the immunity is high, exudative lesions are replaced by fibrotic lesions giving a nodular appearance. The lesions spread along the peribronchial lymphatics giving a typical X-ray appearance of infiltration - patchy opacities interspersed with normal parenchyma. In healing, the peribronchial granulation tissue is replaced by fibrosis, which leads to dilatation of bronchi by traction (post-tuberculous bronchiectasis).

When immunity is low and the tempo of activity high, tuberculous material may be aspirated through the bronchi into other parts of the same or the opposite lung producing fresh lesions. The caseous material liquefies and discharges into a bronchus so that a cavity forms. Cavity is a favorable breeding ground for the tubercle bacilli. (Caseous material has 1×10^4 bacilli / gm, Cavity has 1×10^9).

The common sites of tuberculous lesion are the posterior segment of the upper lobe or the apical segment of the lower lobe. This is mostly due to decreased blood flow and relatively good ventilation of the upper lobe in the upright position.

Clinical Features

Symptoms

1. *Due to toxemia:* General symptoms such as fever with evening rise of temperature, night sweats, anorexia, weight loss, tiredness and mental symptoms like irritability and difficulty in concentration.
2. *Local symptoms:* These are caused by the disease process in the lungs. The symptoms include cough with expectoration, pleuritic chest pain breathlessness and hemoptysis.
3. *Indirect symptoms:* Indigestion and dyspepsia due to stimulation of parasympathetic fibers. Amenorrhea often occurs in a young woman even without direct involvement of the reproductive organs.
4. *Symptoms from complications*
5. *Due to primary/associated disease e.g.* diabetes mellitus, HIV infection, alcoholism, COPD, immuno-suppressed individuals, patients on cortico-steroid therapy
6. *Psychological*: Anxiety neurosis, night sweats
7. Hemoptysis due to rupture of a hypertrophied bronchial vessel (Rasmusen's aneurysm).

Signs

1. *Due to toxemia:* Fever, tachycardia, tachypnea, loss of weight, loss of elasticity of skin and clubbing in chronic cases with purulent sputum.
2. *Local signs:* There may be no local signs in the chest or there may be signs of pleural effusion, pneumothorax, hydropneumothorax, consolidation, collapse, fibrosis or cavitation. Sometimes the only sign present may be localized rhonchi or post tussive rales especially at the apices.

Table 4.16 : Differences between Progressive Primary Complex and Post-primary TB

Progressive Primary Complex	*Post Primary TB*
1. Increased Hilar Lymph node	1. Absence of lymph node (usually)
2. Primary complex in any part of the lung	2. Usually apical fibrosis
3. Benign course, rarely cavitation, fibrosis is common	3. Tends to cavitate and progression common
4. Miliary TB common	4. Miliary TB uncommon
	5. Disseminated TB

Stigmas of TB: (evidence of present or past infection or disease)

1. Phlyctenular conjunctivitis
2. Erythema Nodosum: Erythematous raised subcutaneous nodules, painful, tender, seen on lower limb.
3. TB Lymphadenopathy: With or without scars and sinuses.
4. Thickened, beaded spermatic cord
5. Mantoux Test
6. Scrofuloderma (skin TB)
7. Localized gibbus, spinal deformity, paravertebral soft tissue swelling.

Investigations

1. **Laboratory Investigation**
   1. *CBC*: Anemia & leucocytosis: (Lymphocytes >75%. In treated TB, eosinophils increase. In miliary TB, neutrophils increase.
   2. *ESR* raised (non specific)
   3. *Mantoux Test* (Tuberculin test in select cases)
   4. *ADA* (Adenosine Deaminase) levels increased

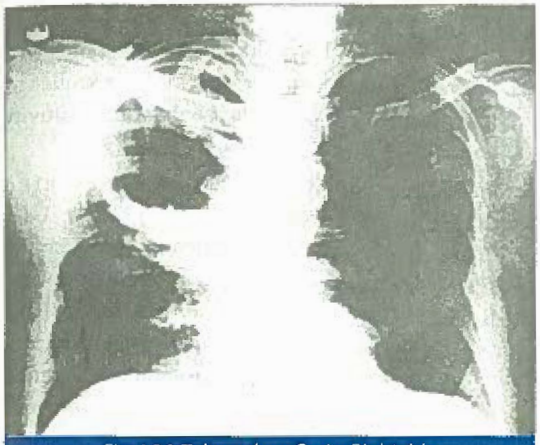


Fig. 4.36 : Tuberculous Cavity Right side



Fig. 4.37 : Tuberculous infiltration right apex with left sided pneumothorax

5. *Specimen Microscopy*
   a. Traditional method - Ziehl-Neelson Stain.
   b. Can detect upto 70% of culture positive samples with lower limit of detection of 5×10^3 organisms / ml.
   c. Modifications include
      i. Use of Bleach
      ii. Use of Guanidinium Hydrochloride
      iii. Fluorescent Microscope - Auramine and rhodamine stains.
   d. WHO 2010 guideline : Only two sputum sspecimens required. One sample should be an early morning sample.

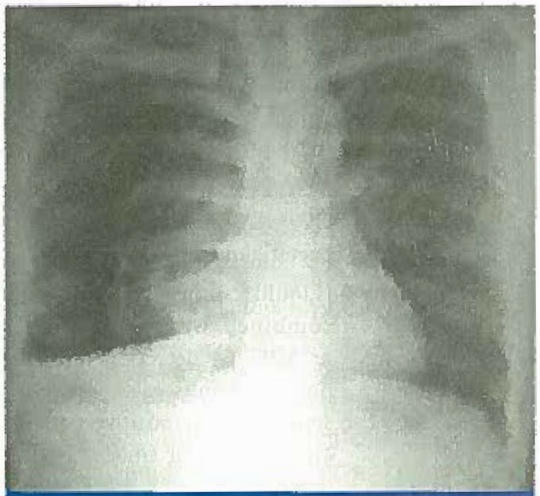


Fig. 4.38 : Tuberculous infiltration right apex with hydropneumothorax

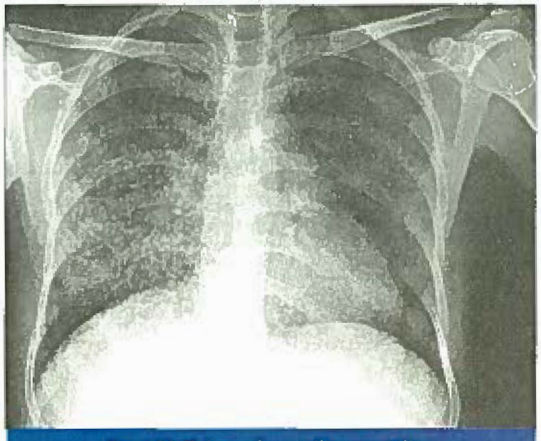


Fig. 4.39 : Tuberculous miliary mottling

6. *Culture Techniques*
   a. Conventional methods
      i. Agar based media takes 10-12 days.
      ii. Egg based Lowenstein Jensen Medium takes 18-24 days.

   More sensitive than smear examination and allows for biochemical identification of species enhancing specificity.
   b. Automated Liquid Culture Method:
      i. Mycobacterial Grower Indication Tube (MGIT) 960 TB
      - Employs fluorescent technology that enables result in 7-10 days.

- Used for isolation and accurate identification of mycobacteria.
- Employed for identification of culture positive isolates - PNB (para-nitro benzoic acid)

ii. MB Bact is based on a Colorimetric CO_2 sensor that is altered by bacterial metabolism.

[Liquid culture systems when combined with DNA probes or MPT 64 detection, produce positive results in 2 weeks for sputum smear positive patients and 3 weeks for smear negative specimens)

7. *Immunologic Methods*

1. Serological methods : Have poor sensitivity and specificity in endemic areas. WHO 2011 had issued a negative policy recommendation in July 2011 for the use of any commercial serological assay in the diagnosis of active tuberculosis.

2. Interferon Gamma Release Assay (IGRAs):

Used for diagnosis of latent TB. Antigens used - Early Secretory Antigenic Target - 6 (ESAT - 6) and Culture Filtrate protein - 10 (CFP - 10).

Quanti FERON GOLD assay - uses both ESAT - 6 and CFP-10; Whole blood is used.

T-SPOT TB - uses peripheral blood mononuclear cells (PBMC's) and detects the number of "spot forming T cells" by use of ELISPOT in response to above antigens.

WHO 2011 had issued policy that IGRAS should not be used for diagnosis of Active TB.

8. Molecular Techniques

A. Direct detection from clinical samples by Nucleic Acid Amplification.

Various PCR assays include

1. Polymerase Chain Reaction (PCR) : amplifies specific DNA sequence. Nested PCR enhances sensitivity of PCR
2. Transcription Mediated Amplifications (TMA) : Uses specific sequence of ribosomal RNA (rRNA) as target of reverse transcriptase. [False Positive reports are a concern. Presence of an organism in a clinical specimen does not necessarily indicate disease]

B. *Molecular Methods for detecting drug resistant TB:*

1. Genotypic Methods:

a. Soid Phase Hybridization techniques: Line Probe Assays for detection of resistance to rifampicin. Genotype MTBDR assay - for detection of resistance to Isoniozid and Rifampicin.

b. Real Time PCR technique.

2. Molecular Beacon Assays - based on a stem and loop structure with loop in the probe.
3. Microassays - also known as Biochips or DNA chips.

9. *Drug Susceptibility Tests (DST)*

A. Phenotypic methods

1. Absolute concentration method
2. Resistance Ratio Method
3. Proportion method
   - Standard methods require 3-6 weeks to report a susceptibility test from a positive culture.
   - BACTEC MGIT 960 1% proportion method is Gold standard for drug susceptibility testing for first line drugs.
   - Recently critical concentration methods for second line drugs have also been tested successfully for most drugs.

4. Direct Rapid Methods for screening MDR - TB:
   a. Nitrate Reduction Assay (NRA): Based on ability of M. tuberculosis to reduce Nitrate to Nitrite.
   b. Microscopic observation broth, drug susceptibility assay: Based on observation of characteristic cord formation of M. tuberculosis is complex that is visualized by inverted microscope.
   c. Thin Layer Agar (TLA) :
   - Short Turn around time of 11 days.
   - Microscopic Examination of growth on solid media using TH11 Middle Brook agar in quadrant petri plates containing isoniazid, rifampicin, PNB and one without additive.

   Indications of DST:
   1. Ideally should be done in all cases prior to start of Anti TB Rx.
   2. For definite diagnosis
   a. All previously treated cases.
   b. All cases of HIV with active TB
   c. Developing active TB after contact with MDR TB cases.
   d. All new cases in an area where level of MDR cases is >73% (In India it is < 3%).
   e. Treatment failure cases
10. Bronchoscopy- trans thoracic aspiration BAL.
11. Scalene Lymph Node Biopsy
12. Lung Biopsy

II. Imaging

1. X-ray chest: AP, PA, Lateral, Lordotic- to see apical area of lung
2. Fluoroscopy- outdated
3. Bronchography
4. CT Scan
5. MRI

Complications

1. Dry pleurisy, pleural effusion or empyema
2. Chronic bronchitis and laryngitis
3. Cor-pulmonale
4. Aspergillosis
5. Amyloidosis
6. Anemia
7. Tuberculosis of other organs

Treatment

I. Bed rest in a Sanitorium/ Hospital: In the past, pleasant rural or mountainous surroundings, fresh air, good food and graded exercises were the only modes of therapy. With chemotherapy, the results are as good without bed-rest as with it. However bed rest is advised for the following:
   1. Very ill patient with extensive disease
   2. Infectious cases with sputum positive for AFB or very extensive disease radiologically.

II. **Chemotherapy:**

Classification of Antitubercular drugs

- Bacteriocidal : Isoniazide, Rifampicin, Streptomycin, Pyranzinamide
- Bacteriostatic : Ethambutol, Thiacetazone, Para-amino salicylic acid (PAS), Ethionamide.

Case definitions (WHO Guidelines 2010)

1. *Tuberculosis suspect:*

   Any person who presents with symptoms or signs suggestive of TB.

2. *Case of Tuberculosis*

   A definite case of TB or one in which a health worker has diagnosed TB and has decided to treat the patient with a full course of TB treatment.

3. *Definite Case of Tuberculosis*

   A patient with Mycobacterium Tuberculosis complex identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay.

a. **New Patients :** New patients have never had treatment for TB, or have taken anti-TB drugs for less than one month.

b. **Previously treated patients** : Previously treated patients have received one month or more of Anti-TB drugs in the past, may have positive or negative bacteriology and may have disease at any anatomical site.

c. **Relapse** : Patients who have been cured previously from or completed treatment for TB and now have TB.

d. **Failure** : A patient whose sputum smear or culture is positive at 5 months or later during treatment. Also included are patients found to have a multidrug-resistant (MDR) strain at any point of time during the treatment, whether they are smear - negative or smear - positive.

e. **Default** : A patient whose treatment was interrupted for two consecutive months or more.

f. **Cured** : A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear or culture - negative in the last month of treatment and on atleast one previous occasion.

g. **Treatment Completed** : A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion.

h. **Treatment success** : A sum of cured and completed treatment.

i. **Smear Positive Pulmonary TB** : Based on the presence of at least one acid fast bacillus (AFB+) in atleast one sputum sample.

j. **Smear Negative PTB cases** should either

A. Have sputum that is smear negative but culture - positive for M. tuberculosis:

OR

B. Meet the following criteria

i. decision by a clinician to treat with a full course of anti - TB therapy; and

ii. radiographic abnormalities consistent with active pulmonary TB and

either

- Laboratory or strong clinical evidence of HIV infection

or

- If HIV - negative no improvement in response to a course of blood spectrum antibiotics (excluding anti-TB drugs and Fluocoquinolones and Aminoglycosides).

Previously TB patients were grouped under categories I -IV. The new grouping has been based on likelihood of patients having drug resistance which is a critical determinant in deciding treatment. Prior TB treatment confers an increased risk of multi drug resistant tuberculosis.

Treatment of New Patients

Table 4.17 : Recommended doses of First-Line Anti Tuberculosis drugs

Drug	Recommended Dose			
	Daily		3 times per week	
	Dose and Range (mg/kg B.W.)	Maximum (mg)	Dose and Range	Daily Maximum
Isoniazid	5 (4-6)	300	10 (8-12)	900
Rifampicin	10 (8-12)	600	10 (8-12)	600
Pyrazinamide	25 (20-30)	-	35 (30-40)	-
Ethambutol	15 (15-20)	-	30 (25-35)	-
Streptomycin	15 (12-18)		15 (12-18)	1000

Table 4.18 : Regimen for treatment of TB

Category of cases	Intensive Phase	Continuation Phase
New Cases	2 months of HRZE	4 months of HR
Previously Treated Cases		
• Failure cases (High Likelihood of MDR-TB)	Emperical MDR regimen for 6-9 months (modified after DST result)	18-24 months
• Relapse / Default (Medium / Low Likelihood of MDR-TB)	2 HRZES / 1 HRZE / 5HRE (modified after DST results)	

Standard Regimen

The 2 HRZE / 4HR is the standard regimen where

isoniazid (H), Rifampicin (R), Pyranzinamide (Z) and Etahmbutol (E) are given for 2 months (Intensive Phase). This is followed by HR for 4 months (Continuation Phase). Daily regimen during both phases is optimal. However alternative regimen with dosing 3 times per week is acceptable if administered via DOTS (Directly Observed Therapy - Short Term).

In settings where the level of Isoniazoid resistance among new TB cases is high and isoniazid susceptibility testing is not done before the continuation phase begins, following regimen is given: Intensive Phase - 2 HRZE and Continuation Phase 4 HRE.

Treatment of Extrapulmonary TB (EPTB)

A. HIV Testing is important in patients with or suspected of having EPTB.

B. EPTB is treated with same Regimen as for Pulmonary TB except :

- 9-12 months of Treatment for TB meningitis (because of risk of severe disability and mortality).
- 9 months of treatment for TB of Bones and joints (because of difficulties in assessing treatment response).

C. In TB meningitis Ethambutol should be replaced by streptomycin.

Tretment Regimens in special population

1. *Pregnancy and Breast Feeding*

   A. With the exception of streptomycin, first line Anti TB drugs are safe [STM is ototoxic to the fetus]

   B. No contraindication for Breast feeding. Should continue with full course of AKT.

   C. After active TB in the baby is ruled out, baby should be given 6 months of Isoniazid preventive therapy, followed by BCG vaccination.

   D. Pyridoxine supplementation is recommended for all pregnant or breast feeding women taking isoniazid.

2. *Liver disorders*

   A. Usual regimen can be given to following patients provided that there is no clinical evidence of chronic liver disease

      a. Hepatitis virus carriers

      b. P/H of Acute Viral Hepatitis

      c. Currentexcessivealcoholconsumption [Hepatotoxic reactions are more common].

   B. Unstable or Advanced Liver disease / ALT ≥ 3 times ULN following regimens used :

      a. Two Hepatotoxic drugs

         - 9 months HRE
         - 2 mths HRSE followed by 6 mths of HR.
         - 6 - 9 mths of RZE.

      b. One Hepatotoxic drug

         - 2 mths of HES followed by 10 months of HE.

      c. No Hepatotoxic drugs

         - 18 - 24 mths of STM, ETB and Fluoroquinolone.

3. *Renal Failure and severe renal insufficiency:*

   - Regimen - 2 mths of HRZE followed by 4 mths of HR [No dose adjustment of H&R required as they have biliary excretion. There is significant renal excretion of ETB and metabolities of PZA so dose adjustment is required].

     [STM avoided as there is increased risk of ototoxicity].

Note : All patients receiving Isoniazide, should receive pyridoxine supplementation to prevent peripheral neuropathy.

Management of Previously Treated Patients

Previous TB treatment is a strong determinant of drug resistance and previously treated patients comprise 13% of the Global TB.

Drug Resistant Tuberculosis is defined as a case of tuberculosis who are excreting bacilli resistant to one or more anti-tubercular drugs.

Multidrug Resistant - TB (MDR - TB) is defined as disease due to M. tuberculosis that is resistant to Isoniazid and Rifampicin with or without resistance to other drugs.

XDR - TB : MDR strains that are resistant to all fluoroquinolones and to atleast one of three second line injectable agents.

Table 4.19 : Standard Regimens for Previously Treated Patients

Drug Sensitivity Testing	*Likelihood of MDR*	
Likelihood of MDR	High (Failure)	Medium or Low (Relapse, Default)
Conventional method	While awaiting DST Results:	
DST Available	Empirical MDR* Regimen. (Regimen modified once DST results are available)	2 HRZES / 1 HRZE / 5HRE (Regimen modified once DST results are available)
DST Not Available	Empirical MDR* Regimen	2 HRZES / 1 HRZE / 5 HRE for full course of Rx
	(Regimen should be modified once DST results or DRS data are available)	

*Emperical MDR Regimen : Refer Pg. 167

Drug Sensitivity Testing (DST) : Rapid Molecular based methods with results available in 1-2 days to confirm / exclude MDR-TB and guide choice of regimen

Mono Resistance TB is defined as resistance to one Anti-tuberculosis drug.

Poly Resistance TB is defined as resistance to more than one Anti-tuberculous drug.

Monitoring during treatment

To Ensure cure, compliance. To monitor side effects

A. *Sputum smear microscopy in New Sputum Positive Pulmonary TB patients:*
   1. For smear positive pulmonary TB patients treated with first line drugs, sputum smear microscopy may be performed at completion of intensive phase of treatment.
   2. If smear - positive at month 2, (i.e. intensive phase) obtain sputum smear again at month 3. If smear remains positive at month 3, obtain culture and DST.
   3. Smear or Culture positivity at the fifth month or later (or detection of MDR - TB at any point) is defined as treatment failure and necessitates re-registration and change of treatment.

B. *Sputum smear microscopy in previously treated patients.*
   1. Smear is obtained at end of Intensive Phase i.e. at month 3.
   2. If smear positive at month 3, obtain culture and DST.
   3. Smear or Culture positivity at the fifth month or later (or detection of MDR - TB at any point) is defined as treatment failure and necessitates re-registration and change of treatment.

C. *New Pulmonary TB patients whose sputum smear microscopy was negative at start of treatment.*
   1. Recheck sputum smear at end of 2 months and if negative, no further sputum monitoring is required.
   2. Clinical monitoring is more importnat - Body Weight is the most useful indicator.

D. *Extra Pulmonary TB*

   Clinical monitoring is more importnat - Body Weight is the most useful indicators.

Management of drug - induced hepatitis

H, R, Z can all cause liver damage. Rifampicin can cause asymptomatic jaundice without evidence of hepatitis.

Management depends on

a. Whether patient is in intensive or continuation phase.
b. Severity of liver disease
c. Severity of TB
d. Capacity of Health Care Unit to manage side effects.

Treatment

1. All drugs should be stopped. If patient is severly ill, non-hepatotixc regimen of streptomycin, ethambutol and fluoroquinolone should be started.
2. It is necessary to wait for LFT to revert to normal and clinical symptoms to resolve before re-introducing anti-TB drugs. If not possible to perform LFT, advisable to wait for extra 2 weeks after resolution of jaundice and upper abdominal pain / tenderness before restarting TB treatment.
3. If hepatotoxicity does not resolve, non hepatotoxic regimen consisting of STM, ETB, FQ given for 18-24 months.
4. Once drug induced hepatitis has resolved, drugs are reintroduced one at a time. If symptoms recur or liver function tests become abnormal as

the drugs are reintroduced, the last drug added should be stopped. It is advised to start with Rifampicin because it is less likely than H or Z to cause hepatotoxicity and is the most effective agent. After 3-7 days H may be reintroduced.

5. Alternative regimen depending on drug implicated:
   a. If 'R' is implicated : 2 months of SHE followed by 10 months of HE.
   b. If 'H' is implicated : 6-9 months of RZE.
   c. If 'Z' is implicated : 9 months of HR.
   d. If neither R or H can be used : 18-24 mths STM, ET and fluoroquinotine.
6. When hepatitis with Jaundice occurs during the intensive phase of TB treatment with HRZE - once hepatitis has resolved, restart the same drugs except replace 'Z' with 'S' to complete the 2 months course of initial therapy, followed by R&H for 6 month continuation phase
7. When hepatitis with Jaundice occurs during the continuation phase: Once hepatitis has resolved, restart 'H' & 'R" to complete the 4 - month continuation phase of treatment.

Treatment of MDR-TB

Once MDR-TB is confirmed, patients can be treated with:

a. Standard MDR regimen (Standardized approach); OR

b. An individually tailored regimen, based on DST of additional drugs

General principles of designing MDR regimen

1. Use at least 4 drugs certain to be effective (Each drug from different class).
2. Do not use drugs for which there is possibility of cross resistance.
3. Eliminate drugs that are not safe.
4. Include drugs from Groups 1-5 in a hierarchical order based on potency. [For regimens containing fewer than 4 drugs, consider adding group 5 drugs. Regimen often contains 5- 7 drugs).

Regimen used in India :

Intensive phase - Pyranzinamide + Ethambutol + Karamycin + Levofloxacin / Ofloxacin + Cycloserine + Ethionamide

Continuation Phase : Ethambutol + Levofloxacin / Oflaxcin + Cycloserine + Ethionamide.

Table 4.20 : Groups of Drugs to treat MDR-TB

Group	Drug
Group 1 First Line Oral Agents	Pyrazinamide (Z) Ethambutol (E) Rifabutin (Rfb)
Group 2 Injectable Agents	Kanamycin (KM) Amikacin (AM) Capreomycin (CM) Streptomycin (S)
Group 3 Fluoroquinoles	Levofloxacin (Lfx) Moxifloxacin (Mfx) Ofloxacin (Ofx)
Group 4 Oral bacteriostatic Second-line agents	Para-aminosalicytic acid (PAS) Cycloserine (CS) Terizidone (Trd) Ethionamide (Eto) Protionamide (Pto)
Group 5 Agents with unclear role in treatment of drug-resistant TB	Clofazimine (Cfz) Linezolid (Lzd) Amoxicillin / Clavulanate (Amx/Cl) Thioacetazone (TLz) Imipenem / Cilastatin (Ipm/Cln) High - dose Isoniozid (high-dose H) Clarithromycin (Clr)

Duration of treatment for MDR - TB

1. Intensive phase - defined by the treatment duration with injectable agent. It should be continued for a minimum of 6 months, and for atleast 4 months after the patient first becomes and remains smear or culture negative.
2. Continuation phase - Minimum of 18 months after culture conversion. Extension of therapy to 24 months may be indicated in chronic cases with extensive pulmonary damage.

Monitoring MDR - TB patient

1. Sputum smears and culture should be performed monthly until smear and culture conversion [conversion is defined as two consecutive negative smears and cultures taken 30 days apart].

2. After conversion, bacteriological monitoring is recommended monthly for smears and quarterly for cultures.
3. Monitoring by clinician should be at least monthly until sputum conversion, then every 2-3 months.
4. Weight should be monitored monthly.
5. Such large number of smear and culture for follow up is not possible at least 5 smears and cultures must be done at follow up (4, 6, 12, 18 and 24 months).
6. X-ray should be done every 6 months.

Adjuvant Therapies for MDR - TB

1. Surgery: Resection Surgery - indicated in patients who remain sputum positive, with resistance to large number of drugs, and localised pulmonary disease. Chemotherapy to be given 2 months prior and continued 18-24 months post surgery.
2. Collapse therapy : Reversible surgical therapy which involves collapse of lung by artificial pneumoperitoneum or pneumothorax - used for cavity containing diseased lung.
3. Laser therapy
   a. Tried in some countries.
   b. Effective in multicavitatory disease with heavy bacterial load.
   c. Thought to have a role in rapid killing of bacteria; increases and improves penetration of Anti TB drugs in walled off lesions and helps in early closure of cavities. It is of proven benefit in tracheal and endobronchial growth.
4. Immunotherapy and Immunomodulation.
   a. Use of Mycobacterium Vaccine.
   b. Enchancing pro-inflammatory cytokines - IL2, IL-12, IFN-γ, TNF-α, Inhibiting anti-inflammatory cytokines IL-4, 5, 10.
   c. Use of Thalidomide, Transfer factor, Indomethacin, Levamisole.
   d. Mycobacteriumw (Immuvac) - has been used in Leprosy.
5. Gene Therapy :
   - To detect drug resistance before start of treatment and develop new drugs that target these specific genes.

Factors influencing response to treatment

1. *Adequate Chemotherapy*
2. Regular Intake of Drugs (Compliance)
3. Optimal Duration
4. Severity Of Disease
5. Rest
6. Diet
7. Nursing
8. Climate
9. Psychological Factors

III. Corticosteroids: Corticosteroids are useful in tuberculosis because they exert anti-inflammatory, anti-allergic and anti-collagenous effects. Indications:

1. Tuberculous meningitis
2. Miliary tuberculosis
3. Tuberculosis of adrenal glands with Addison's disease
4. Tuberculosis of serous sacs, ureter, fallopian tubes.
5. Drug hypersensitivity

Corticosteroids are given in the dose of 40-60 mg/day of prednisolone for 6-8 weeks, and tapered over the next 2-3 weeks. They are to be given only under the cover of anti-tuberculous therapy, otherwise there may be flaring up of tuberculosis.

10 › Chronic Obstructive Pulmonary Disease (COPD) (Emphysema and Chronic Bronchitis)

Definition

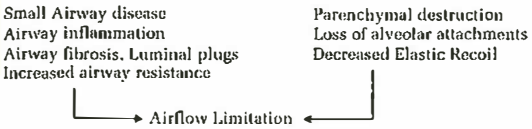
Emphysema is characterized by enlargement of the airspaces distal to the terminal bronchioles, either from dilatation or destruction of their walls.

Chronic bronchitis is clinically defined as chronic cough with expectoration for three months for two consecutive years, with other known causes being ruled out.

COPD is a common preventable and treatable disease, characterized by progressive airflow limitation associated with an enhanced chronic inflammatory response to noxious particles or gases.

Exacerbations and comorbidities contribute to overall severity on individual patients.

Mechanisms of Airflow Limitation in COPD:



Prevalence

1. Higher in smokers than non smokers
2. Higher in those over age 40
3. Higher in men than women.

Risk factors influencing disease development and prognosis

A. *Genetic predisposition* :
   1. α-1 Antitrypsin gene
   2. MMP 12 gene
   3. α-nicotine ACh receptor
   4. Hedge Hog interactivity protein gene

B. *Environmental factors*
   1. *Age*: Ageing itself is a risk factor for COPD.
   2. *Gender* : In past prevalence was more in men than women. But due to increase in smoking in women prevalence rates are now approaching equality.
   3. *Lung growth and development*
      a. Any factor that affects lung growth during Gestation and childhood has potential for increasing individual risk for COPD.
      b. Factors in early life termed "Childhood Disadvantage Factors" were as important as heavy smoking is in predicting in early adult life.
   4. *Exposure to Particles*
      a. Cigarette smoke
      b. Other types of tobacco (e.g. pipe, cigar, water pipe) and maijuana are also risk factor.
      c. Passive exposure to smoke - also known as environmental tobacco smoke.
      d. Smoking during pregnancy affects fetus by affecting lung growth and development of immune system.
      e. Occupational exposures, including organic and inorganic dust and chemical agents and fumes are appreciated risk factors.
      f. Wood, Animal during, crop residues and coal, typically burned in open fires or poorly functioning stoves or heating in poorly ventilated dwelling - important risk factor.
      g. Outdoor air pollution - in urban areas. Role is unclear, but is small compared to smoking. Air pollution from fossil fuel combustion is associated with decrement in lung function.
   5. *Socio economic status* : Poverty is clearly a risk factor but the components of poverty that contribute to this are unclear. Risk is inversely related to socioeconomic state.
   6. *Asthma / Bronchial hyper reactivity* :
      a. Asthma may be a risk factor but evidence is not conclusive.
      b. Bronchial hyper reactivity can exist without clinical diagnosis of asthma and has been shown to be an important predictor of COPD as well as an indicator of increased risk of decline in lung function in patients with mild COPD.
   7. *Infection*
      a. Severe childhood respiratory infection has been associated with reduced lung function and increased respiratory symptoms in adulthood.
      b. Susceptibility to infection plays an important role in exacerbation of COPD but effect on development of disease in less clear.

c. HIV - accelerate onset of smoking related emphysema.

d. TB is a risk factor for COPD.

Causes

I. **Localized**

A. Congenital

B. Compensatory due to lung collapse, scarring or resection

C. Partial bronchial obstruction

1. Neoplasm
2. Foreign body

D. MacLeod'syndrome

II. **Generalized**

A. Idiopathic

B. Senile

C. Familial (alpha-1-anti-trypsin deficiency)

D. Associated with chronic bronchitis, asthma or pneumoconiosis.

Diagnosis

A. *General condition:* Patient may be emaciated, cyanosed and edematous (blue bloater). JVP may show giant a-waves.

B. *Chest findings: Refer Pg. 134*

C. *Heart*

1. Apex beat may not be visible or palpable.
2. Right ventricular heave may be present.
3. Heart sounds may be diminished. Second sound may be loud. Gallop rhythm may be present. In marked emphysema, RV heave may not be visible or felt because the hyperinflated lung may cover it. In such cases, epigastric pulsations may be the only evidence of RV enlargement
4. Functional tricuspid regurgitation murmur may be present.
5. Hyperkinetic state with warm limbs and Waterhammer pulse may be present.

D. *Miscellaneous*

1. Liver may be enlarged.
2. Optic disc may show papilledema.

Investigations

A. Spirometry : Presence of post bronchodilator FEV_1 / FVC < 0.7 confirms the presence of persistent airflow limitation and thus of COPD. It is also used to grade the severity of COPD (given below).

B. Arterial Blood Gas : Retetion of CO_2 in Emphysema.

C. *X-ray chest*

1. Hyper translucency of lung fields
2. Widened intercostal spaces
3. Low flat diaphragm
4. Increased retrosternal translucency
5. Narrow vertical heart - Tubular heart
6. Large hilar shadows
7. Diminished peripheral vascular pattern
8. Bullae: Rounded areas of hypertranslucency with thin hairline shadow forming the margin

D. HRCT Chest is currently the definitive test to diagnose emphysema.

E. Serum α_1 AT Level to diagnose α_1 AT deficiency.

Table 4.21 : Differences between Pink-puffer and Blue-bloater

		Pink-puffer	*Blue-bloater*
1.	Course	Progressive dyspnea	Intermittent dyspnea
2.	Sputum	Scanty	Profuse
3.	Polycythemia	Uncommon	Common
4.	X-ray	Attenuated peripheral vessels	Normal peripheral vessels
5.	pCO_2	Normal	Normal
6.	Alveolar gas transfer	Reduced	Normal

Assessment of Disease

The degree of airflow limitation is an important prognostic factor. Global Initiative for Luung Disease (GOLD) criteria grades severity of COPD based on Spirometry. However a multifactorial index incorporating symptoms spirometry, exacerbations and excercise

performance has shown to be a better predictor of prognosis than only spirometry.

Treatment

I. **Of acute Exacerbation**

An acute event is characterised by worsening of patients respiratory symptoms that is beyond normal day to day variantions or leads to a change in medication. Frequent exacerbations are those occuring > twice a year.

It is precipitated by inection, allergic reactions, other systemic illness or air pollution.

A. *Chemotherapy:* Antibiotics are required as infection often precipitates acute attacks. One of the following drugs may be used:

If H. influenza, streptococci, staphylococci or Klebsiella is the cause:

1. Benzylpenicillin 10 lakh units 6 hourly with streptomycin 0.5 gm 12 hourly.
2. Ampicillin 0.5 gm 6 hourly.
3. Chloramphenicol 0.5 gm 6 hourly.

If there is Pseudomonas infection the following drugs may be used:

1. Gentamicin 80 mg 8 hourly I.M. or
2. Ciprofloxacin 0.5 gm 6 hourly orally or 200 mg IV 12 hourly.
3. Ceftazidime 1 gm IV 6 hourly.

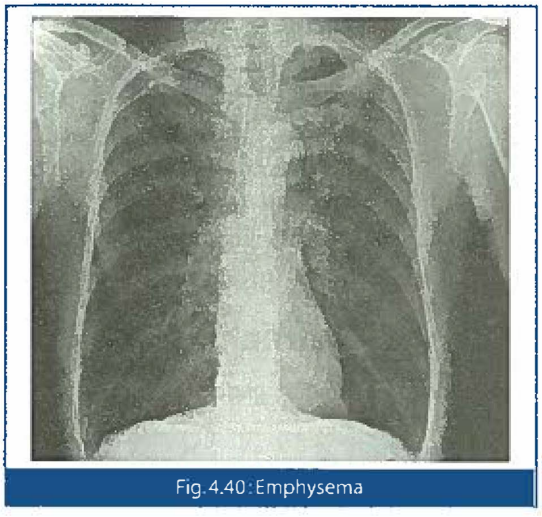


Fig. 4.40 : Emphysema

B. *Oxygen Therapy :* This is required to attain adequate oxygenation. However, in some patients with chronic obstructive airway disease and hypercapnia, the respiratory centre would have lost its normal sensitivity to carbon dioxide and would become dependent on the hypoxic drive to maintain respiration. In such cases oxygen must be given with care and preferably intermittently (Refer Chapters 7 and 11).

C. *Bronchodilators:* Aminophylline 0.25-0.5 gm. I.V. slowly not only relaxes the bronchial muscles but also stimulates the respiratory centre and assists in clearing the respiratory tract. Salbutamol inhalations are also useful as they are selective beta stimulants.

D. *Corticosteroids:* The role of corticosteroids in acute exacerbations is uncertain.

E. *For cor pulmonale:* If the patient is in cor pulmonale, diuretics like furosemide, digitalis and potassium salts must be given.

F. *Avoiding bronchial irritants:* Smoking must be avoided. Atmospheric pollution too must be avoided, but it may not be practical.

Table 4.22 : Gold Criteria

Gold Stage	Severity	Symptoms	Spirometry
0	At Risk	Chronic Cough, Sputum Production	Normal
1	Mild	With or without chronic cough or sputum production	FEV_1 / FVC < 0.7 and FEV_1 ≥ 80% predicted
2	Moderate	With or without chronic cough or sputum production	FEV_1 / FVC < 0.7 and FEV_1 50-80% predicted
3	Severe	With or without chronic cough or sputum production	FEV_1 / FVC < 0.7 and FEV_1 30-50% predicted
4	Very Severe	With or without chronic cough or sputum production	FEV_1 / FVC < 0.7 and FEV_1 ≤ 30% predicted OR FEV_1 < 50% predicted with respiratory failure or signs of right heart failure

However patient must stay indoors in foggy weather and sleep with closed windows.

G. *Expectorants and mucolytic agents:* A hot drink acts as a simple expectorant in clearing the airways. Bromhexine has been found useful in liquefying sputum and aiding airway clearance.

H. *Chest physiotherapy:* Postural drainage and proper breathing exercises, especially expiration, must be taught to the patient.

II. **Long term management:**

I. *Quit smoking*

II. A. *Bronchodilators*

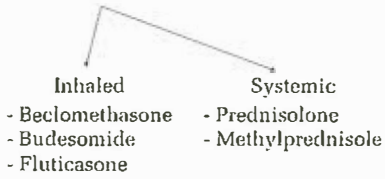
1. β_2 agonists - Shortacting - Fenoterol, Salbutamol, levosalbutamol. Longacting : Formoterol, Indacaterol, Salmeterol.

2. Anticholingergics - short acting - Ipratropium bromide oxitropium bromide. Long acting : Tiotropium.

3. Methylxanthines (minimal role now)

Aminophylline, Theophylline

B. *Steroids*



C. PDE - 4 inhibitors - Roflumilast

III. *Pulmonary rehabilitation - exercise training*

IV. Vaccines - H influenza and pneumococcal vaccine yearly.

V. *Home O_2* : >15 hr / day, in patients with chronic respiratory failure has shown to increase survival.

Indication

1. $PaO_2 < 55$ mmHg or $SaO_2 < 88\%$.

2. $PaO_2 < 60$ or $SaO_2 < 88\%$ with evidence of pulmonary HT, Peripheral edema suggestive of congestive cardiac failure and polycythemia

VI. *Non-Invasive Ventillation (BiPAP) :* is useful in those with pronounced daytime hypercapnia. Improves survival but not quality of life. If patient has concurrent OSA then there is a definite benefit.

VII. *LVRS (Lung Volume Reduction Surgery)* is a surgical procedure in which parts of lungs are resected to reduce hyperinflation, making respiratory muscles more effective by improving their mechanical efficiency (lengh / tension relationship).

Increase elastic recoil pressure → improves expiratory flow rates and reduces exacerbation.

It is more beneficial in predominant upper lobe emphysema.

VIII. *Bronchoscopic LVR* shows modest improvement: Increase chances of pneumonia, hemoptysis, COPD exacerbation

IX. *Lung Transplant*

- Criteria : any 1

a. History of exacerbation - associated with hypercapnia.

b. Pulmonary Hypertension or Cor pulmonale, despite O_2 Treatment.

c. $FEV_1 < 20\%$ predicted with DLCO < 20% with homogenous distribution of emphysema.

X. *Bullectomy* : in Bullous emphysema.

11 › Pneumonia

Definition: Pneumonia is inflammation of the parenchyma of the lung.

Etiology

1. **Bacterial:** Pneumococcus, Staphylococcus, Streptococcus, H. influenza, E. coli, Klebsiella, Pseudomonas, etc.
2. **Atypical:** Viral, Rickettsial, Mycoplasmal.
3. **Protozoal:** E. histolytica.
4. **Fungal:** Actinomycosis, Aspergillosis, Histoplasmosis, Nocardiosis.
5. **Allergic:** Loeffler's syndrome.
6. **Radiation**
7. **Collagenosis:** SLE, Rheumatoid arthritis, Polyarteritis nodosa.

8. **Chemical:**
   a. Aspiration of vomitus or due to dysphagia as in hiatus hernia and achalasia cardia.
   b. Toxic: Gases and smokes.
   c. Lipoid: Kerosene, paraffin and petroleum.

Predisposing Factors (Alter Host Defense)

1. Exposure to cold facilitates the passage of mucus containing pneumococci from the upper respiratory tract to the lower.
2. *Postoperative* especially after abdominal operations, because anesthetic agents suppress respiratory defenses, diaphragmatic movements are decreased and cough is limited due to pain and sedation.
3. *Smoking, chronic bronchitis, alcohol.*
4. *Infection* of the upper respiratory tract, sinuses and bronchi.
5. Debilitating illnesses and poor nutrition
6. Immunological deficiencies
7. Corticosteroid therapy
8. Uncontrolled diabetes
9. Chemotherapy and immuno-suppressive therapy

Organisms in Specific Situations

1. Young, previously healthy individual: Pneumococci, Mycoplasma, Legionella, Chlamydia, Coxiella
2. Elderly with chronic lung disease: Pneumococci, H. influenza, Legionella, Mycoplasma and Chlaimydia
3. Hospitalized patients: Pseudomonas, Proteus, Klebsiella, E. coli, Staphylococcus aureus, anaerobic organisms



Fig 4.41 : A case of Pneumococcal pneumonia showing herpes labialis around the lips. Incidentally he also has internal squint

Site of Pneumonia

1. *Right lung* is commonly involved because it is in continuity with the trachea
2. *Recumbent patient:* Posterior segment of upper lobe and superior segment of lower lobe are involved.
3. *In sitting up position:* Basal segments of lower lobe are involved.
4. *Apical:* Tuberculosis or Klebsiella

Clinical Features

A. **Pneumococcal**
   1. History of common cold or upper respiratory tract infection
   2. Fever with rigors
   3. Dry painful cough with rusty sputum
   4. Pleuritic pain
   5. Labial herpes simplex
   6. Patient may be flushed and cyanosed
   7. Temperature, pulse and respiration are raised

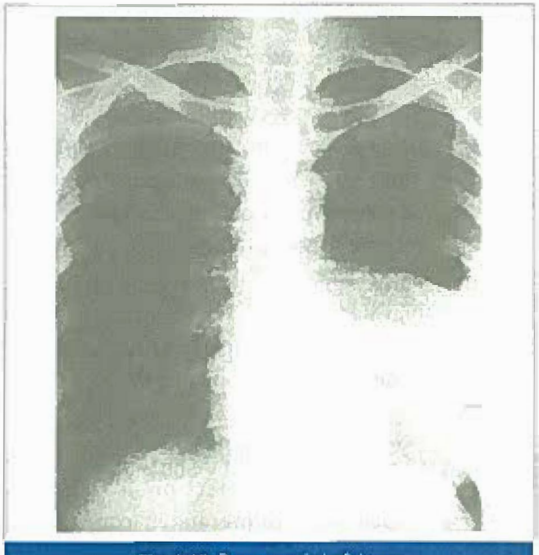


Fig. 4.42 : Pneumonia Left base

8. Signs of consolidation in the chest
9. Radiologically, hazy, relatively uniform density

B. Staphylococcal

1. It commonly occurs during epidemics of influenza.
2. Pneumonia can be very severe. It may be fatal within a few hours.
3. Abscesses, looking like a thin-walled cyst on X-ray are common. In children these may rupture to form pyopneumothorax.

C. Klebsiella

1. This is common in middle aged or elderly alcoholics.
2. It commonly involves the upper lobes or more than one lobe.
3. There is a strong tendency to abscess formation.
4. Sputum is viscid, jelly-like, blood stained, rusty or purulent.
5. It may clear up with or without residual fibrosis or may end fatally.

D. Gram-negative bacilli (H influenza, E. coli, Coliform bacilli, Proteus and Pseudomonas aeruginosa).

It arises mainly in hospitals in patients receiving corticosteroids or immunosuppressive drugs, those with tracheostomy, urinary tract infections or debilitating disease.

E. Viral

1. The presenting symptoms are headache, general aches, prostration and fever.
2. There may be no respiratory symptom or sign and it is often discovered when a routine X-ray of the chest is taken.
3. Paroxysmal cough and mucoid sputum may be present.
4. Localized diminished breath sounds and scattered rales may be present.

F. Legionella

1. Legionella is a small aerobic, gram-negative coccobacillus. Infection is acquired through water shower and air-conditioning system.
2. It is more common in males.
3. Febrile flu like illness with URTI for about 5 days is followed by cough, mucopurulent sputum and sometimes hemoptysis.
4. X-ray: Bilateral patchy involvement with pleural effusion.

G. Mycoplasma

1. It affects children of 5-15 years age.
2. There is mild fever with coryza.
3. X-ray shows patchy infiltration.
4. IgM cold agglutinin by ELISA or complement fixation test may be detected during first week of infection and up to 2-4 weeks.

Treatment

A. General Measures

1. *Position* should be most comfortable.
2. *Diet:* Initially light diet. With improvement the patient may gradually return to full diet.
3. *Fluids:* Copious fluid intake is advised as patient loses fluid from sweating and overbreathing.

B. Chemotherapy

1. *Pneumococci:* Procaine penicillin 8 lakh I.M. daily or Ampicillin or Tetracycline 0.5 gm 8 hourly orally.
2. *Staphylococci:* Crystalline penicillin 10 lakh IM 6 hourly or Cloxacillin 0.5 gm 6 hourly orally.
3. *Klebsiella:* Chloramphenicol 0.5 gm 6 hourly orally or Ciprofloxacin 500 mg 8 hourly orally or Cefotaxime 1 gm IV 6 hourly.
4. *E. coli, Proteus, Pseudomonas:* Carbenicillin 100-300 mg/kg/day in an IV drip or Gentamicin 80 mg IM 8 hourly or IV Ciprofloxacin 200 mg 12 hourly or IV Ceftazidime 1 gm 6 hrly.
5. *H. influenza:* Crystalline penicillin 10 lakh units I.M. 6 hourly with Streptomycin 0.5 gm IM twice a day.
6. *Legionella*
   1. Erythromycin 1 gm 8 hourly IV for

13 wks followed by 500 mg qds for 2 wks.

2. Doxycycline 100 mg twice a day orally for 3 weeks.
3. Rifampicin 600 mg twice a day orally for 3 weeks.

Other drugs are Ciprofloxacin and Co-trimoxazole. In Legionella endocarditis, the treatment with antibiotics has to be continued for 3-12 months.

C. **Symptomatic:** For pain, cough etc.

D. **Convalescence**

1. Once the fever subsides, the patient may sit up in the chair.
2. Breathing exercises must begin as soon as possible to clear the lungs of inflammatory products .

Complications

1. Herpes labialis
2. Pleural effusion and empyema
3. Lung abscess
4. Pneumothorax
5. Pericarditis, endocarditis
6. Peritonitis
7. Meningitis
8. Septic arthritis
9. Peripheral thrombophlebitis
10. Jaundice
11. Uremia
12. Circulatory failure

Prognosis

The following factors make the prognosis poor:

1. Staphylococcal, Klebsiella or type 3 pneumococcal pneumonia
2. Very young or very old people
3. Very high or very low WBC count
4. Positive blood culture
5. Jaundice

Recurrent Pneumonia

(Two or more attacks within a few weeks)

A. *Doubtful diagnosis of pneumonia:* Pulmonary infarction or eosinophilia

B. *Reduced resistance or local predisposing cause:* Chronic bronchitis, hypogammaglobulinemia, myelomatosis, lupus

C. *Recurrent aspiration:* Achalasia cardia, pharyngeal pouch, bronchial tumour or bronchiectasis

Unresolved Pneumonia

1. Staphylococci, Klebsiella or Tuberculosis
2. Neoplasm
3. Elderly
4. Uncontrolled diabetics

12 Bronchiectasis

DEFINITION: Bronchiectasis is an abnormal and permanent dilatation of one or more bronchi that involves lung in either a Focal or Diffuse Manner. It has classically has been characterized as Cylindrical, Tubular (most common), Varicose or Cystic.

Epidemiology

1. Varies according to etiology: e.g.
   a. Cystic fibrosis (CF) patients → clinically significant bronchiectasis present in late adolescence or early adulthood.
   b. Bronchiectasis → Classically affects Non-smoking patients, women older than 50 years of age.
2. In General
   a. Incidence increases with age
   b. More common in women than men.

Pathogenesis

A. Visious Cycle

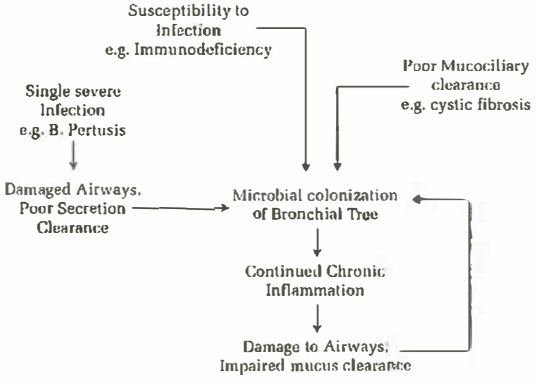


Table 4.23 : Etiology and Investigations

Pattern of lung involvement by bronchiectasis	*Etiology by categories (with example)*	*Investigations*
I. Focal	1. Obstruction (e.g. Aspirated foreign body; Tumors - Endobronchial, Carcinoids, Lymph nodes; Impacted Secretion)	a. Chest Imaging (CXR &/or HRCT) b. Bronchoscopy c. Induced sputum for AFB.
II. Diffuse	1. Genetic causes e.g.: a. cystic fibrosis; b. α_1 Anti Trypsin deficiency; c. Primary Ciliary dyskinesia (including Cartageners syndrome)	a. Measurement of sweat chloride levels b. α_1 Anti Trypsim levels c. Nasal or Respiratory tract Brush Biopsy d. Sperm analysis for sperm mortality e. Genetic Testing
	2. Infections (e.g. viral - Adenovirus, Influenza; Bacteria - S. aureus, Klebisiella, Pseudomanas, Anaerobes, B. pectosis, M. tuberculosis, M. arium complex (MAC)	a. Grams stain / cultures. b. Stains / cultures for AFB & Fungi c. Bronchoscopy with BAL (if no pathogen identified)
	3. Immunodeficiency (e.g. HIV; Panhypogamma Globulinemia; selective deficiency of IgG 2; Bronchiolitis Obliterans after Lung Transplant)	a. Complete Blood Count with differential b. Immunoglobulin levels c. HIV testing
	4. Autoimmune or Rheumatologic causes (e.g. Rheumatoid arthritis; Sjogrens Syndrome; Immune Mediated, Allergic Broncho-Pulmonary Aspergillosis (ABPA)	a. Clinical promination with careful joint examination b. Serologic testing (Rh. factor; Anti Ro/SSA) c. Skin reaction to A. Fumigatus antigen; increased specific IgE levels
	5. Recurrent Aspiration	a. Tests for swallowing function b. Oesophageal motility studies c. Neurological evaluation
	6. Miscellaneous (eg. yellow nail syndrome : Traction bronchietasis from Postradiation fibrosis or IPF	Guided by clinical condition
	7. Idiopathic	Exclusion of other causes

B. Others

1. Immune Mediated Reactions - Connective Tissue Disease, Allergic Broncho-pulmonary aspergillosis (ABPA).
2. Traction, Bronchiectasis, post radiation, fibrosis, Idiopathic Pulmonary Fibrosis (IPF).

Pathology

1. Destruction & Dilatation of walls of medium sized airways at level of segmental or subsegmental bronchi; and small airway inflammation.
2. Loss of elastic, smooth muscle and cartilage and replaced by fibrous tissue.
3. Dilated airways contain pools of thick, purulent material; while peripheral airways occluded by secretions or obliterated and replaced by fibrous tissue.
4. Microscopic features
   a. Bronchial & peribronchial inflammation and fibrosis; ulceration of bronchial wall; squamous metaplasia;, mucous gland hyperplasia.

Pathophysiology: Bronchiectasis is usually bilateral and commonly affects the lower lobes. The two main factors responsible for bronchiectasis are:

1. **Infection:** Infection causes chronic inflammatory changes in the bronchial walls. This destroys the muscular elastic tissues in the bronchi, which results in dilatation of the bronchi.
2. **Obstruction:** Results in collapse of the small bronchi, bronchioles and alveoli. There may be

accumulation of secretions, secondary infection and further weakening of the bronchial wall which is pulled apart due to negative pressure and this results in permanent dilatation of the bronchi.

Types

I. **Saccular or cystic:** affects major or proximal bronchi that end in large sacs by the fourth generation of branching

II. **Cylindrical or fusiform:** affects sixth to eighth generation of bronchi, probably less severe, clinically "dry"

III. **Varicose:** intermediate between saccular and cylindrical

Clinical Features

Symptoms

1. Persistent productive cough with ongoing thick, tenacious sputum production / purulent sputum.
2. Hemoptysis (40-70%) - due to bleeding from friable, inflammed airway mucosa; massive hemoptysis often due to bleeding from hypertrophied bronchial artery.
3. Bronchiectasis sicca – Patients are either asymptomatic or have a non productive cough associated with Dry Bronchiectsis of upper lobe.
4. Dyspnoea & wheezing – Reflects widespread parenchymal destruction or COPD.
5. Systemic symptoms – fatigue, wieght loss, myalgias.
6. Acute Exacerbation – (a) amount of sputum increases; (b) sputum becomes more purulent and often more bloody; (c) systemic symptoms like fever may be more prominent.

Signs

1. Combination of crackles, Ronchi, wheeze - reflect damaged airways contaning secretion.
2. Clubbing and cyanosis is the classical diagnostic finding is the presence of **coarse leathery rales** especially at the base of the lungs posteriorly.
3. **Wheezing** may be present due to associated asthma or bronchospasm.
4. Advanced Disease with Chronic Hypoxemia – patients may develop cor pulmonale and right heart failure.

Investigations

(Also see Table 4.23)

1. **Hemogram** will show neutrophilic leucocytosis during the acute infective phase.
2. **ESR** is raised.
3. **Sputum** will be thick and purulent with plenty of pus cells. The infective organism may be grown on culture.
4. CXR
   a. May be normal with mild disease.
   b. Saccular type - prominent cystic spaces with or without air fluid levels corresponding to dilated airways.
   c. Tram Tract appearance in longitudianl section & ring shadows in cross section - due to thickened and dilated airways.
   d. Opaque tubular or Branched Tubular Structure - due to dilated airways filled with secretion.
5. **HRCT :** Modality of choice
   1. Tram Track sign - due to airway dilatation and thickening.
   2. Signet Ring Sign - a cross sectional area of the airway with a diameter of 1.5 times that of adjacent vessel.
   3. Lack of Bronchial Tapering → including presence of tubular structures within 1 cm from pleural surface.
   4. Tree in Bud appearance → dilated airways + thickened walls & inspirated secretions.
   5. Cysts emanting from Bronchial wall → especially pronounced in cystic bronchiectasis.

Treatment : Major goals : Treat infection, decrease inflammation, clear airway, Treat cause.

I. *Antibiotics* : based on culture and gram stain. Empirical - Amoxicillin, Trimethoprim - Sulphamethoxazole, levoflox. Pseudomonas : oral quinolone or iv - aminoglycoside, carbapenem, 3rd generation cephalosporin.

Treatment for 10-14 days. Long term treatment is for recurrent / persistent infections

II. *Bronchial Hygiene*
   1. Hydration
   2. Drainage: Mechanical devices, appropriate position facilitate drainage.
   3. Pharmacological agens :
      a. 'Mucolytics for thin secretions
      b. Aerosolised recombinant DNAse are used for CF associated bronchiectasis
      c. Aerosolisation of Bronchodilators: used in case of hyperreactivity and proven reversability.
      d. Hyperosmolar agents (e.g. Hypertonic saline)

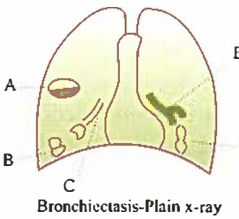
III. *Anti inflammatory Treatment*
   1. Inhaled Glucorticosteroids alleviate dysopnoea, increases need for inhaled B_2 agonists and reduces sputum production. But there is no differences in lungs function or exacerbation rates.
   2. Oral steroids → useful in ABPA, autoimmune condtion (e.g. RA, sjogrens).

IV. *Surgery*

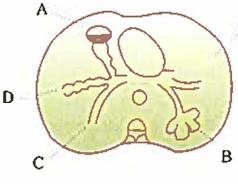
Indication :
   1. Localized disease not controlled on Medcial Management - Resection of involved lobe region.
   2. Lung Transplant

V. *Hemoptysis* : Medical Management - rest, antibiotics, Surgical - resection or coil embolisation.

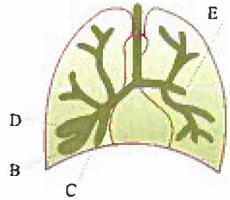
VI. *Vaccination* : for H. influenza, pneumococcal.



Bronchiectasis-Plain x-ray



Bronchiectasis-HRCT



A-Air-fluid level
B-Cystic,
C-Tubular,
D-Saccular Bronchiectasis
E-Bronchial cut-off due to mucoid impaction

Bronchiectasis-Bronchography

Complications

1. Recurrent pulmonary and pleural infections: pneumonia, lung abscess, empyema, broncho-pleural fistula.
2. Pericarditis
3. Cerebral abscess, meningitis
4. Osteomyelitis
5. Respiratory failure
6. Pulmonary osteoarthropathy
7. Amyloidosis

Prognosis : Depends on Etiology, frequency of excrerbain, specific pathogen involved.

Prevention : Correct immunodeficiencies, smoking cessation, suppressive antibiotic Rx, Bronchial Hygiene.

13 › Lung Abscess

Definition : Lung abscess is a localized collection of pus in the lungs caused by pyogenic organisms. It is usually subacute infection.

Causes

I. **Infections**
   A. *Pyogenic bacteria: Staphylococcus aureus,* Klebsiella, Gp. A Streptococci, Legionella sp., anaerobes
   B. *Mycobacteria: M. tuberculosis, M. kansasii, M. avium intracellulare*

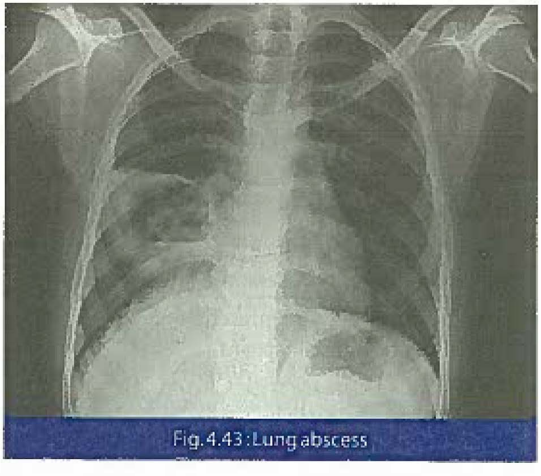


Fig. 4.43 : Lung abscess

C. *Fungi: Histoplasma capsulatum, Coccidiodes immitis, Aspergillus*

D. *Parasites:* Amebas, lung flukes

II. **Pulmonary Infarction**

A. Pulmonary thromboembolism

B. Septic embolism (Staphylococcus aureus, anaerobes, Candida)

C. Wegener's granulomatosis

III. **Neoplasm**

A. Metastatic malignancies (very common)

B. Bronchogenic carcinoma

C. Lymphomas

III. **Others**

A. Infected cysts and bullae

B. Silicosis

C. Coal miner's pneumoconiosis

Pathophysiology

Lung abscess is more common in the right lung. It is a solid yellow mass of inflammatory tissue surrounded by necrotic wall. As the disease progresses, the solid mass may be transformed to liquid pus. Microscopic-ally it consists of dense infiltration of polymorpho-nuclear leucocytes. Alveolar walls are destroyed.

Clinical Features

It presents within 1 - 2 weeks.

Symptoms

1. **Onset:** Insidious, acute or chronic
2. **Cough:** Most common feature with copious expectoration of foul smelling, greenish yellow and mucopurulent sputum. It may be rusty and blood-stained.
3. **Pyrexia:** High remittent fever with shivering and sweating
4. **Chest Pain:** Pleuritic pain if pleural surfaces involved
5. **Generalized symptoms:** malaise, lassitude, loss of weight, anorexia

Signs

1. **Temperature:** Very high with tachycardia
2. Clubbing of fingers
3. **Dullness on percussion & few coarse crepitations** during early phase
4. **Signs of cavity or local consolidation** may occur when pus is expectorated out
5. **Signs of pleural effusion** may mask other signs

Investigations

1. **CBC:** Polymorphonuclear leucocytes
2. **Sputum:** Pus cells, causative organisms on staining and culture.
3. **Chest X-ray:** Large homogenous opacity or a cavity showing a fluid level may be seen. Associated involvement of pleura may be noted by obliteration of CP angle.
4. **Fiberoptic bronchoscopy:** to rule out bronchogenic cause of lung abscess
5. **CT Scan** if necessary

Complications

1. Dry pleurisy
2. Empyema
3. Pneumothorax
4. Brain abscess
5. Hemoptysis

Treatment

1. **Chemotherapy:** Appropriate antimicrobial therapy
2. **Postural drainage and percussion therapy**
3. **Bronchoscopic aspiration**
4. **General measures:** Bed rest, oxygen, high protein diet, breathing exercises
5. **Surgery:** Surgical resection may be required if there is no response to above measures or there is massive hemoptysis, localized malignancy or bronchiectasis.

Prevention

The most common mode of acquiring lung abscess is following aspiration following tonsillectomy, oral surgery, nose-throat operations, following inhalation of vomitus during general anesthesia or coma or iatrogenic due to intermittent positive pressure breathing and nebulization. Care should be taken to prevent all of the above.

14 Solitary Pulmonary Nodule (SPN)

A SPN is a lesion that is both within and surrounded by pulmonary parenchyma. The size at which a nodule becomes a mass is arbitrary, although 3 cm is typically used .

Prevalence of SPNs varied from 8 to 51 percent, usually detected incidentally on a chest radiograph or computed tomographic (CT) scan

Differential Diagnosis

The causes of a SPN can be categorized as benign or malignant.

Malignant Etiologies

Common causes of a malignant SPN include-

1. *Primary lung cancer* - Adenocarcinoma(most common), followed by squamous cell carcinoma and large cell carcinoma. Rarely, lymphomas can present as a SPN.
2. *Carcinoid tumors* - Carcinoid tumors tend to be centrally located endobronchial lesions. These tumors are generally well circumscribed radiographically.
3. *Metastatic cancer* - malignant melanoma, sarcomas, and carcinomas of the colon, breast, kidney, and testicle.

Benign Etiologies

1. *Infectious granulomas* - cause approximately 80 percent of benign nodules . Endemic fungi (eg, histoplasmosis, coccidioidomycosis), mycobacteria (either tuberculous or nontuberculous mycobacteria, nontuberculous mycobacterial disease, Pneumocystis jirovecii infection
2. *Hamartomas* - They cause approximately 10 percent of benign nodules,gives characteristic appearance of a hamartoma on a chest radiograph is a SPN with "popcorn" calcification.
3. *Dirofilariasis* - Pulmonary infestation with the dog heartworm, Dirofilaria immitis, is a rare but well-recognized cause of a SPN .

Diagnostic Evaluation

The clinical features, radiographic features, and quantitative models are used to determine the likelihood that a nodule is malignant or not. In all cases, every attempt must be made to secure old imaging studies because size comparisons can be used to determine stability versus growth.

Clinical Features

Layer associated with an increased probability that a SPN is malignant include -

1. *Patient age* - The probability rises with increasing patient age
2. *Risk factors* - history of smoking, asbestos exposure, family history, previously diagnosed malignancy.
3. *Radiographic features* — that can be used to predict whether a nodule is malignant include -
   a. **Size** - Larger lesions are more likely to be malignant than smaller lesions.
   b. **Border** - Malignant lesions tend to have more irregular and spiculated borders, whereas benign lesions often have a relatively smooth and discrete border.
   c. **Calcification** - The presence of calcification does not exclude malignancy. As an example, "eccentric" calcification (ie, asymmetric calcification) should raise concern about carcinoma arising in an old granulomatous lesion (ie, a "scar" carcinoma).Certain patterns of calcification, however, strongly suggest that a SPN is likely benign eg. "popcorn" calcification, laminated (concentric) calcification, central calcification, and diffuse, homogeneous calcification
   d. **Density** - Increased density of a SPN argues against malignancy.
   SPNs may have a purely ground glass appearance (through which normal parenchymal structures, including airways and vessels, can be visualized). The typical histology for a malignant SPN with pure ground glass morphology is adenocarcinoma. Adenocarcinomas with a ground-glass appearance are often slow growing, such that apparent stability over time may be misleading.
   e. **Growth** - Lesions that are malignant tend

to have a volume doubling time between 20 and 400 days, where volume doubling of a nodule corresponds to an approximately 30 percent increase in its diameter. Volume doubling time also varies according to the CT appearance of malignant SPNs.

Management

An initial management decision should be made once the probability that the SPN is malignant has been assessed.

Solid solitary nodules

1. A nodule that has clearly grown on serial imaging tests should be biopsied or excised.
2. A solid nodule that has been stable for over two years can be considered benign.
3. For other solid SPNs not meeting these criteria, the risk of malignancy is determined based on the clinician's overall impression, after consideration of all clinical and radiographic features and is used to guide the following choices:
    a. A nodule that has a low probability of being malignant can be followed with serial CT scans.
    b. A nodule that is smaller than 1 cm and has an intermediate probability of being malignant can be followed by serial CT scans.
    c. A nodule that is 8 to 10 mm or larger and has an intermediate probability of being malignant should be evaluated by 18-fluorodeoxyglucose positron emission tomography (FDG-PET). Nodules that are negative on FDG-PET can be followed with serial CT scans, while nodules that are positive should be excised
    d. A nodule that has a high probability of being malignant should be excised.

Subsolid solitary nodules Subsolid nodules may be purely ground glass in appearance or may have a combination of ground glass and solid components (called part-solid). A subsolid SPN should be reassessed in three months to confirm continued presence, as a portion of these will resolve spontaneously.

a. If a subsolid SPN has increased in size or if it has a solid component that is ≥5 mm in diameter, it should be biopsied or surgically resected.
b. If a purely ground glass nodule is ≤5 mm, no further CT follow-up is required.
c. All other subsolid SPNs need serial CT scanning for a minimum of three years, due to the risk of low grade adenocarcinoma, which tends to be slow-growing.

Serial CT scans — A nodule that remained stable for two years or longer on a chest radiograph was traditionally considered benign.

Guidelines for solid nodules

1. For nodules ≤4 mm, serial CT scans are not required if the patient is low risk. Patients who are high risk should have a CT scan performed at 12 months with no further follow-up if the nodule is unchanged.
2. For nodules 4 to 6 mm, a CT scan should be performed at 12 months if the patient is low risk, with no further follow-up if the nodule is unchanged. Patients who are high risk should have a CT scan performed at 6 to 12 months and at 18 to 24 months if the nodule is unchanged.
3. For nodules 6 to 8 mm, a CT scan should be performed at 6 to 12 months and at 18 to 24 months if the nodule is unchanged and the patient is low risk. Patients who are high risk should have a CT scan performed at 3 to 6 months, 9 to 12 months, and 24 months if the nodule remains unchanged.
4. For nodules greater than 8 mm, a CT scan should be performed at 3, 9, and 24 months if the nodule remains unchanged, regardless of whether the patient is low or high risk.

Guidelines for ground-glass and part-solid nodules — For purely ground-glass (GG) nodules >5 mm and for part-solid nodules, a follow-up thin-slice chest CT scan be obtained after a three-month interval and the results used to direct the following strategy -

1. A nodule that is purely GG based on thin-slice (1 mm sections) chest CT and ≤5 mm in diameter does not need further CT follow-up.
2. A GG nodule that is >5 mm in diameter is followed by serial CT scans at 12, 24, and 36 months. If the nodule has not increased in

size after 36 months of observation, the need for further CT monitoring is determined on a case-by-case basis. For patients who are suitable candidates for surgical resection and have a single GG nodule that is >10 to 15 mm in diameter and persists for >3 months, we typically offer the option of surgical resection, as some patients prefer resection to the anxiety associated with ongoing monitoring.

3. A part-solid nodule with a solid component <5 mm is followed by serial CT scans at 12, 24, and 36 months. If the solid component is ≥5 mm, then the nodule is biopsied or resected.

FDG-PET — 18-fluorodeoxyglucose positron emission tomography (FDG-PET) can help distinguish malignant and benign lesions because cancers are metabolically active and take up FDG avidly. It is indicated for patients with a solid or part-solid SPN that is 8 to 10 mm or greater in size and has an intermediate probability of malignancy, especially if the patient has increased surgical risk.

FDG-PET has high negative predictive value, but poor positive predictive value.

An additional benefit of FDG-PET is the acquisition of staging data if the nodule is malignant.

Nodule sampling — Sampling of the nodule can be performed by -

1. **Bronchoscopy** — Fiberoptic bronchoscopy is a reasonable approach for the diagnostic evaluation of large, central nodules and masses; however, it is much less useful for small or peripheral SPNs. The small amount of material provided by fiberoptic bronchoscopy is a limiting factor:
   - Combining cytology and fluorescence in situ hybridization (FISH) may improve the sensitivity compared to cytology alone, although the specificity is unaltered. This is applicable to both washings and brushings.
2. **Percutaneous needle aspiration** — Percutaneous needle aspiration (also called fine needle aspiration) of a SPN can be performed through the chest wall using either fluoroscopy or CT scanning to guide placement of the needle within the lesion. Its diagnostic yield is higher than fiberoptic bronchoscopy, since placement of the needle is more reliable. Percutaneous needle aspiration obtains material for cytology, but does not biopsy a core of tissue. As a result, it is more helpful for confirming malignancy than establishing a specific benign diagnosis Percutaneous needle aspiration may be complicated by pneumothorax, which can be clinically significant in patients with coexisting emphysema. Bleeding is a less frequent complication.
3. **Percutaneous needle biopsy** —. In this procedure, a core of tissue is obtained using a cutting needle. Up to 97 percent of patients with a malignant or benign lung nodule will obtain a definitive diagnosis using this procedure .
4. **Surgical resection** — Excision can be performed by thoracotomy or thoracoscopy (also called video assisted thoracic surgery or VATS) if the lesion is located close enough to pleural surface to allow VATS resection.

15 › Obstructive Sleep Apnoea

Obstructive sleep apnea (OSA) is a common chronic disorder, cardinal features of which include:

1. Obstructive apneas, hypopneas, or respiratory effort related arousals.
2. Daytime symptoms attributable to disrupted sleep, such as sleepiness, fatigue, or poor concentration.
3. Signs of disturbed sleep, such as snoring, restlessness, or resuscitative snorts.

Severe untreated OSA has been associated with increased all-cause and cardiovascular mortality.

Risk Factors

Definite risk factors for OSA include:

1. Obesity
2. Craniofacial abnormalities
3. Upper airway soft tissue abnormalities
4. Heredity
5. Smoking
6. Nasal congestion:

Clinical Features

History

1. Most patients with OSA first complain of daytime sleepiness, or the bed partner reports loud snoring, gasping, snorting, or interruptions in breathing while sleeping.
2. Other associated symptoms and historical features include the following:
   a. Awakening with a sensation of choking, gasping, or smothering
   b. Awakening with a dry mouth or sore throat
   c. Moodiness or irritability
   d. Lack of concentration
   e. Memory impairment
   f. Morning headaches
   g. Decreased libido and impotence
   h. Awakening with angina pectoris
   i. History of hypertension, cardiovascular disease, cerebrovascular disease, or renal disease
   j. History of type 2 diabetes mellitus
   k. Nocturia
   l. Depression
   m. Symptoms of fibromyalgia.
3. Epworth Sleepiness Scale is used to quantitatively document the patient's perception of sleepiness, fatigue, or both.

Physical Examination

1. OSA is most common among males who are 18 to 60 years old, although it is also common at other ages and in women.
2. The physical exam is frequently normal, except for obesity (body mass index >30 kg/m2) and a crowded oropharyngeal airway.
3. Additional physical findings that are common among patients with OSA include the following:
   a. Narrow airway – Numerous conditions causing narrowing of upper airway include- retrognathia, micrognathia, lateral peritonsillar narrowing, macroglossia, tonsillar hypertrophy, an elongated or enlarged uvula, a high arched or narrow palate, nasal septal deviation, and nasal polyps.
   b. Large neck and/or waist circumference – OSA is more strongly correlated with an increased neck size or waist circumference than general obesity. OSA is particularly prominent among men who have a collar size greater than 17 inches and women who have a collar size greater than 16 inches.
   c. Elevated blood pressure – Approximately 50 percent of patients with OSA have coexisting hypertension, which is often most elevated in the morning.
   d. Signs of pulmonary hypertension or cor pulmonale (eg, peripheral edema, jugular venous distension) – Pulmonary hypertension and cor pulmonale are common sequelae when OSA coexists with either obesity hypoventilation syndrome or an alternative cause of daytime hypoxemia (eg, chronic lung disease).

Diagnostic Tests

1. **Polysomnography** :

   Full-night, attended, in-laboratory polysomnography is considered the gold-standard diagnostic test for OSA. It involves monitoring the patient during a full night's sleep. Patients who are diagnosed with OSA and choose positive airway pressure therapy are subsequently brought back for another study, during which their positive airway pressure device is titrated.
2. **Portable monitoring** — There are a variety of devices that are used for in-home, unattended, portable monitoring of cardiorespiratory parameters. Many have been validated against standard PSG, typically by testing the same patient with both modalities in the sleep laboratory.
3. Laboratory Tests

   Nonspecific abnormalities related to OSA occasionally found are:

   1. Proteinuria – Proteinuria is not common among patients with OSA (<10 percent of patients) but, when it occurs, it may be severe (ie, nephrotic range)

2. Hypercapnia – often present if obesity hypoventilation syndrome coexists.
3. Cardiac dysrhythmia – OSA is associated with nocturnal cardiac dysrhythmias, including bradycardia, atrial fibrillation, and asystole
4. Hypothyroidism – Hypothyroidism may cause or exacerbate OSA.

Diagnostic Criteria

OSA is confirmed if either of the two conditions exists:

1. There are 15 or more apneas, hypopneas, or respiratory effort related arousals per hour of sleep (ie, an apnea hypopnea index or respiratory disturbance index ≥15 events per hour) in an *asymptomatic patient*. More than 75 percent of the apneas and hypopneas must be obstructive.
2. There are five or more obstructive apneas, obstructive hypopneas, or respiratory effort related arousals per hour of sleep (ie, an apnea hypopnea index or respiratory disturbance index ≥5 events per hour) in a patient with *symptoms or signs of disturbed sleep*. More than 75 percent of the apneas and hypopneas must be obstructive.

Treatment

A. Behavior Modification

1. **Weight loss** — Weight loss improves overall health, decreases the apnea hypopnea index, improves quality of life, and probably decreases daytime sleepiness.
2. **Exercise** — modestly improves OSA even in the absence of significant weight loss.
3. **Sleep position**- Non-supine position(eg. Lateral recumbent), semi-recumbent position may be helpful.
4. **Alcohol avoidance** — All patients should avoid alcohol, even during the daytime, because it can depress the central nervous system, exacerbate OSA, worsen sleepiness, and promote weight gain.
5. **Medication selection** — Medications that should be avoided include medications that inhibit the central nervous system, such as benzodiazepines and benzodiazepine receptor agonists, as well as barbiturates, other anti-epileptic drugs, antidepressants, antihistamines, and opiates. Antidepressants that cause weight gain eg, mirtazapine.

B. **Osa-Specific Therapies**

1. **Positive airway pressure** — Positive airway pressure splints the upper airway open Positive airway pressure therapy is generally considered first-line therapy for OSA. It can be delivered as-
   a. Continuous positive airway pressure (CPAP),
   b. Bilevel positive airway pressure (BPAP),
   c. Autotitrating positive airway pressure (APAP),
   d. Adaptive servo-ventilation or end expiratory positive airway pressure.
2. **Oral appliances**

   Designed to either protrude the mandible forward (ie, mandibular advancement/repositioning splints, devices or appliances) or to hold the tongue in a more anterior position (ie, tongue retaining devices).

   Either design holds the soft tissues of the oropharynx away from the posterior pharyngeal wall, thereby maintaining upper airway patency.
3. **Pharmacological treatment**
   a. Drugs that are OSA-specificacetazol amide,donepezil,opiod antagonists, theophylline, progestational agents, nicotine, thyroxine, serotonergic agents.
   b. Drugs that target residual sleepiness-modafinil, methylphenidate, amphetamines.
4. **Surgery**
   a. Surgical treatment most effective in surgically correctable, obstructing lesion. e.g. tonsillar hypertrophy that is obstructing the pharyngeal airway.
   b. Uvulopalatopharyngoplasty (UPPP)-

involves resection of the uvula, redundant retrolingual soft tissue, and palatine tonsillar tissue.

c. Laser-assisted and radiofrequency ablation (RFA).

d. Other common surgical procedures for OSA include - septoplasty, rhinoplasty, nasal turbinate reduction, nasal polypectomy, palatal advancement pharyngoplasty, tonsillectomy, adenoidectomy, palatal implants (ie, Pillar procedure), tongue reduction (partial glossectomy, lingual tonsillectomy), genioglossus advancement and maxillomandibular advancement.

16 Hepatopulmonary Syndrome

Hepatopulmonary syndrome is considered present when the following triad exists:

- Liver disease
- Impaired oxygenation-**Orthodeoxia**
- Intrapulmonary vascular abnormalities, referred to as intrapulmonary vascular dilatations (IPVDs)

The unique pathological feature of hepatopulmonary syndrome is gross dilatation of the pulmonary precapillary and capillary vessels, as well as an absolute increase in the number of dilated vessels. A few pleural and pulmonary arteriovenous shunts and portopulmonary anastomoses may also be seen.

Causes

Hepatopulmonary syndrome (HPS) is a complication of liver disease.

1. It is most commonly associated with portal hypertension (with or without cirrhosis), although chronic liver disease of virtually any etiology can be associated with HPS.
2. Also some acute liver diseases are associated eg. ischemic hepatitis.

No specific type of liver disease, severity of liver disease, or laboratory abnormality predicts HPS.

Clinical Manifestations

Clinical features are the consequences of both hepatic and pulmonary dysfunction-

Hepatic findings — Most patients with HPS have symptoms and signs of chronic liver disease.

Many will have hemodynamic complications of liver dysfunction:

1. Spider nevi - Spider nevi are cutaneous lesions that may be a marker of intrapulmonary vascular dilatations directly connecting pulmonary arteries to veins (IPVDs).
2. Hyperdynamic circulation - A hyperdynamic circulation manifests as three major findings: elevated cardiac output at rest (often exceeding 7 L/min), decreased systemic and pulmonary vascular resistance, and a narrowed arterial-mixed venous oxygen content difference.

Pulmonary findings

1. **Dyspnea** may be accompanied by pulmonary findings that are more specific for HPS :
   a. *Platypnea* - Platypnea is an increase in dyspnea that is induced by moving into an upright position and relieved by recumbency.
   b. *Orthodeoxia* - Orthodeoxia refers to a decrease in the arterial oxygen tension (by more than 4 mmHg [0.5 kPa]) or arterial oxyhemoglobin desaturation (by more than 5 percent) when the patient moves from a supine to an upright position, which is improved by returning to the recumbent position. The presence of orthodeoxia in a patient with liver disease is strongly suggestive (present in 88% patients) of HPS, although it can be seen in other situations (eg, post-pneumonectomy, recurrent pulmonary emboli, atrial septal defects, and chronic lung disease).

   It is hypothesized that platypnea and orthodeoxia in HPS are caused by preferential perfusion of IPVDs in the lung bases when the patient is upright.

2. **Hypoxemia** - Severe hypoxemia (PaO_2 <60 mmHg) in the absence of coexisting

cardiopulmonary disease is strongly suggestive of HPS.HPS-related hypoxemia is due to intrapulmonary vascular dilatations (IPVDs), which range in diameter from 15 to 160 microns. Shunting through the IPVDs leads to ventilation-perfusion mismatch and oxygen diffusion limitation.

Diagnosis

General approach — The diagnosis of hepatopulmonary syndrome (HPS) can be made when all of the following abnormalities have been confirmed:

- Liver disease
- Impaired oxygenation-orthodeoxia.
- Intrapulmonary vascular abnormalities, referred to as IPVDs

Impaired oxygenation

Detection of impaired oxygenation requires that arterial blood gases be drawn with the patient sitting upright at rest-

1. Elevated alveolar-arterial (A-a) oxygen gradient (most sensitive) - defined as ≥15 mmHg when breathing room air
2. An arterial oxygen tension (PaO_2) of <80 mmHg also indicates impaired oxygenation.
3. The right-to-left shunt fraction - measures degree to which oxygenation is impaired-calculate the shunt fraction using the following formula :

$$Qs/Qt = ([PAO_2 - PaO_2] \times 0.003) \div [([PAO_2 - PaO_2] \times 0.003) + 5]$$

where Qs and Qt refer to shunt and total blood flow, respectively, and PAO_2 and PaO_2 refer to the alveolar and arterial partial pressure of oxygen, respectively. A limitation of this formula is that it assumes that the cardiac output is normal, rather than increased.

Intrapulmonary vascular dilatations

Used to detect IPVDs :

1. **Echocardiography** — Contrast-enhanced echocardiography is performed by injecting a contrast material intravenously and then performing echocardiography. The contrast material is usually agitated saline (forms a stream of microbubbles 60 to 150 microns in diameter) or *iodocyanine green* dye. With an intracardiac shunt, contrast generally appears in the left heart within three heart beats after injection. In contrast, with an intrapulmonary shunt, contrast generally appears in the left heart three to six heart beats after its appearance in the right heart. In patients with liver disease, detection of an intrapulmonary right to left shunt is considered indicative of IPVDs.
2. **Nuclear scanning** — Technetium-labeled macroaggregated albumin scanning. It involves intravenously injecting albumin macroaggregates that should be trapped in the pulmonary capillary bed, since the 20 micron diameter of the macroaggregates exceeds the normal pulmonary capillary diameter of 8 to 15 microns. Scans that identify uptake of the radionuclide by the kidneys and/or brain suggest that the macroaggregates passed through either an intrapulmonary or intracardiac shunt .The proportion of radionuclide taken up by the kidneys and brain may be used to quantify the shunt.
3. **Pulmonary angiography** — Is invasive and is generally reserved for excluding alternative causes of hypoxemia, such as pulmonary embolism, pulmonary hypertension, and/or large direct arteriovenous communications.

Other diagnostic tests

1. *Chest radiography* - increased bibasilar interstitial markings, probably a manifestation of IPVDs.
2. *HRCT chest* - dilated peripheral pulmonary vessels and increased pulmonary artery to bronchus ratio.
3. *Pulmonary function test abnormalities* - normal expiratory flow rate and normal lung volume measurements; the diffusing capacity for carbon monoxide (DLCO) is typically mildly to severely impaired

Disease Severity

1. Mild – An alveolar to arterial (A-a) oxygen gradient ≥15 mmHg and an arterial oxygen tension (PaO_2) ≥80 mmHg while breathing room air

2. Moderate – An A-a gradient ≥15 mmHg and a PaO_2 in between ≥60 mmHg and <80 mmHg while breathing room air
3. Severe – An A-a gradient ≥15 mmHg and a PaO_2 in between ≥50 mmHg and <60 mmHg while breathing room air
4. Very severe – An A-a gradient ≥15 mmHg and a PaO_2 <50 mmHg while breathing room air; alternatively, a PaO_2 <300 mmHg while breathing 100 percent oxygen.

Treatment

There are no effective medical therapies for hepatopulmonary syndrome (HPS), although many approaches have been attempted to improve gas exchange and decrease hypoxemia. Liver transplantation offers the most promise for the successful treatment of patients with HPS.

1. **Medical therapies**
   a. Long-term supplemental oxygen is the most frequently recommended therapy.
   b. Various other medications- e.g. methylene blue, allium sativum (ie, garlic), terlipressin, somatostatin analogues (eg, octreotide), nitric oxide synthase inhibitors, cyclooxygenase inhibitors (eg, indomethacin), antibiotics, chemotherapy (eg, cyclophosphamide), glucocorticoids, beta blockers (eg, propranolol), and inhaled nitric oxide have been tried.
2. **Transjugular intrahepatic portosystemic shunt (TIPS)** placement - has been associated with improvement of HPS.
3. **Other medical interventions** - plasma exchange and the occlusion of intrapulmonary vascular dilatations (IPVDs) via spring coil embolization.
4. Agents tested in animal models and appear promising - pentoxifylline (inhibits nitric oxide synthesis) and quercetin (a flavonoid antioxidant).
5. **Liver transplantation** — Liver transplantation is indicated for patients with incapacitating hypoxemia due to HPS.

17 Allergic Bronchopulmonary Asperigillosis (ABPA)

ABPA results from allergic pulmonary reaction to inhaled spores of Aspergillos fumigatus; can also occur occassionally with other Aspergillosis species. [(Rare) Penicillium, Candida, Mycosis, Helminthosporium].

It is grouped under the syndrome of Pulmonary Infiltrates with Eosinophilia.

Major diagnostic criteria

1. Bronchial Asthma - Atopic
2. Peripheral Eosinophila (>1000/µl)
3. Pulmonary Infiltration → Transient, Recurrent, mostly involving upperlobes.
4. Central Bronchiectasis
5. Elevated serum IgE
6. Immediate wheel and Flare reaction to Aspergillous fermigates.
7. Serum preciptions to Aspergillus fumigation - classically low or undetectable.

Other diagnostic features

1. History of Brownish plugs in sputum - Eosinophils rich
2. Culture of A. fumigatus from sputum.
3. Elevated IgE (and IgG) class Antibodies specific for A. fumigatus.
4. Hemoptysis

Treatment

1. Bronchial Asthma : Treatment with Inhaled Corticosteroids and Oral steroid if there are signs of worsening or pulmonry shadowing is found.
2. Oral Itraconazole is helpful in preventing exacerbation.

Cardiovascular System

5

1 › Proforma

History

I. *Cardinal Symptoms*
   - A. Dyspnea on exertion or Breathlessness - including paroxysmal nocturnal dyspnea, orthopnea, platypnea and trepopnea
   - B. Chest Pain
   - C. Cough
   - D. Expectoration
   - E. Hemoptysis
   - F. Palpitation
   - G. Syncopal attacks

II. *Symptoms of Congestive Cardiac Failure (CCF)*
   - A. Exertional breathlessness
   - B. Edema of feet, puffiness of face, anasarca
   - C. Distension of abdomen and pain in right hypochondrium, anorexia, nausea, vomiting

III. *Symptoms of Rheumatic Heart Disease (RHD)*
   - A. Fever with sore throat
   - B. Fleeting joint pains and swelling
   - C. Involuntary movements (chorea)
   - D. Nodules under the skin (rheumatic nodules)

IV. *Symptoms of Infective Endocarditis (SBE)*
   - A. Pyrexia
   - B. Petechial hemorrhages
   - C. Pads of finger are tender (Osler nodes)
   - D. Palpable spleen
   - E. Phalangeal clubbing
   - F. Prolonged treatment with high doses of penicillin
   - G. Hemoptysis
   - H. Hematuria
   - I. Hemiplegia
   - J. Phlebothrombosis

V. *Symptoms Suggesting Congenital Heart Disease*
   - A. Cyanotic spells
   - B. Squatting episodes

VI. *Pressure Symptoms* (Due to Enlarged Left Atrium or Aneurysm of Aorta)
   - A. Hoarseness of voice (pressure on the recurrent laryngeal nerve), Ortner's syndrome
   - B. Dysphagia (pressure on esophagus)

VII. *Miscellaneous*
   - A. *Family History:* Hypertension, diabetes, coronary artery disease, hyperlipidemia, congenital heart disease, cardiomyopathies
   - B. *Past History of:* hypertension, diabetes, coronary artery disease, hyperlipidemia, obesity, recurrent lower respiratory infection, tuberculosis, syphilis, STD, HIV infection,
   - C. *History of hospitalization*
     1. Number of admissions
     2. Duration of each admission
     3. Investigations done e.g. ECG, X-ray, Echocardiography, cardiac catheterization
     4. Diagnosis reached, if known
     5. Drugs given e.g. diuretics, digitalis.
     6. Relief obtained or not
     7. Advised surgery/intervention or not
   - D. *History of cardiac surgery, angioplasty or valvuloplasty*

Physical Examination

General Examination

A. Build and nutrition

B. Nails and conjunctiva for pallor, icterus, clubbing, cyanosis.

C. Lymphadenopathy and thyroid swelling

D. Edema

E. Skin - for petechial hemorrhages, Osler nodes, rheumatic nodules, xanthelasmas (Fig 5.1), xanthomas

F. Skeletal system - Kyphoscoliosis, polydactyly, cubitus valgus, etc.

G. TPR, BP

H. Features of Marfan's syndrome - tall, thin person with long slender fingers, hyper-extensibility of joints, high arched palate, dislocation of lens

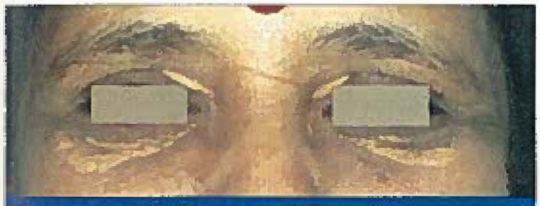


Fig. 5.1: Xanthelasma

Cardiovascular Examination

I. Peripheral

A. JVP - pressure and waves

B. Pulse - rate, rhythm, volume, character, equality, upstroke, downstroke, condition of vessel wall, apex pulse deficit and radio femoral delay, carotid bruit.

C. Blood Pressure - both arms, supine and upright

D. Peripheral signs of wide pulse pressure as in AI, PDA, etc. e.g., pistol shot sounds over the femorals, Duroziez murmur, Corrigan's sign, de Musset's sign, Quincke's sign, locomotor brachial.

II. Central

A. Inspection:

1. Precordium
2. Apex impulse
3. Other pulsations - Parasternal, epigastric, suprasternal, in the neck, in the second left space and on right side
4. Dilated veins
5. Scars, sinuses, etc.

B. *Palpation:*

1. Apex beat
2. Left parasternal heave
3. Diastolic shock (Palpable S2)
4. Thrills
5. Other pulsations

C. *Percussion:*

1. Left second and intercostal space dullness
2. Upper border
3. Right border
4. Left border
5. Lower sternal resonance
6. Liver dullness and Stomach tympany for situs solitus or inversus

D. *Auscultation:*

1. Heart sounds
2. Murmurs - Systolic, diastolic or continuous.
3. Other sounds e.g. pericardial rub, opening snap, ejection clicks, etc.

Relevant Examination of Other Systems

AS	RS	CNS
Liver	Basal rales	Pupils
Spleen	Pleural effusion	Reflexes
Ascites		Optic fundi

2 Examination

A: INSPECTION

I. Precordium

Precordium is the anterior aspect of the chest, which overlies the heart. Normally the precordium has a smooth contour, slightly

convex and symmetrical with part of the chest wall on the right side.

A. **Bulging:** Precordium may be bulging in:
   1. Enlarged heart
   2. Pericardial effusion
   3. Mediastinal tumor
   4. Pleural effusion
   5. Scoliosis

B. **Flattened:** Precordium may be flattened in the following conditions:
   1. Fibrosis of lung
   2. Old pleural or pericardial effusions
   3. Congenital deformity

II. **Apex Impulse** is the lowermost and outermost part of cardiac impulse seen. Normally it is in the fifth left intercostal space just inside the mid-clavicular line. The impulse may not be visible if it is lying just behind a rib. In such cases, it may be visible in the anterior axillary line, on turning the patient to the left lateral position. It may not be visible in cases with emphysema or pericardial effusion.

III. **Pulsations**

A. **Juxta Apical:** In ventricular aneurysm

B. **Left Parasternal:**
   1. Right ventricular enlargement
   2. Left atrial enlargement
   3. Aneurysm of aorta

C. **Epigastric:**
   1. Right ventricular hypertrophy
   2. Aneurysm of aorta
   3. Liver pulsations
   4. Aortic pulsation in a person with a normally thin chest wall
   5. Mass sitting on the aorta

D. **In the second left intercostal space:**
   1. Dilated pulmonary artery
   2. Aneurysm of aorta
   3. Hyperkinetic state
   4. Enlarged left atrium

E. **Suprasternal:**
   1. Aneurysm of aorta
   2. Aortic regurgitation
   3. Coarctation of aorta
   4. Hyperkinetic state
   5. Abnormal thyroidea ima artery
   6. Pulsating thyroid gland

F. **On the right side of the chest:**
   1. Dextrocardia
   2. Right atrial enlargement
   3. Shift of heart to the right side of aorta

G. **At the back:**
   1. Suzzman's sign in coarctation of the aorta.
   2. Pulmonary arteriovenous fistula

H. **At the right sternoclavicular joint:**
   1. Right-sided aortic arch
   2. Dissecting aneurysm of aorta
   3. Aortic aneurysm
   4. Chronic AR

I. **In the Neck:**
   1. Hyperkinetic state
   2. Aortic regurgitation
   3. Carotid aneurysm
   4. Subclavian artery aneurysm
   5. Exophthalmic goiter

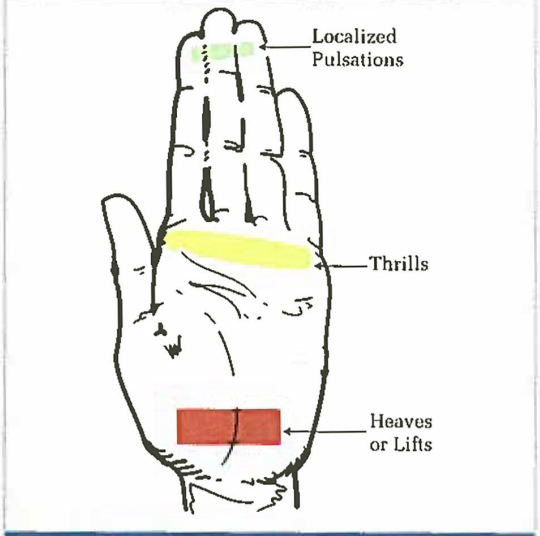


Fig. 5.2: Optimum Area in Hand for Palpation

IV. Dilated Veins Over the Chest Wall

Dilated veins over the chest wall may be present in the following conditions:

1. Intrathoracic obstruction
2. Superior and inferior venacava obstruction
3. Right sided heart failure

V. Scars and Sinuses: Scars of previous cardiac surgery may be present (e.g. horizontal lateral thoracotomy scar for closed mitral commissurotomy, repair of coarctation of aorta, B.T. Shunt Surgery, or ligation of PDA; vertical midline sternotomy scar of coronary artery bypass, open mitral commissurotomy or valve replacement). Sinuses were commonly seen in the past due to tuberculosis of spine.

B : Palpation

I. Apex Beat

Apex beat is the lower most and outer most point where maximum cardiac impulse is felt. It gives a gentle thrust to the palpating finger.

Normally, it is located in the fifth left intercostal space within the mid-clavicular line. It is normally confined to one intercostal space or less than 2.5 cm in diameter. It lasts for less than 50% of systole.

Abnormalities of Apex Beat

1. *Tapping Apex* : is the palpable first heart sound felt in mitral stenosis due to loud S_1 and right ventricular enlargement. It is a short and sharp systolic tap.
2. *Hyperdynamic Apex* : Is exaggerated in amplitude and lasts for less than 2/3rd of systole. It is seen in LV volume overload or diastolic overload eg.

   (a) aortic regurgitation; (b) mitral regurgitation; (c) high output states; (d) patent ductus arterosis, VSD; (e) A.V. fistulas; (f) Thin chest wall.
3. *Heaving Apex* : Is exaggerated in aplitude and lasts for more than 2/3rd of systole. It is well sustained. It is seen in LV pressure overload or systolic overload e.g. (a) aortic stenosis, (b) HOCM, (c) Coarctation of Aorta, (d) Systemic hypertension.
4. *Double Apical Impulse* : Felt in (a) LV Aneurysm; (b) Hypertrophic obstructive cardiomyopathy; (c) LBBB
5. *Diffuse Apex* : is > 3 cm in diameter or occupies more than one intercostal space. (a) LV Aneurysm; (b) Severe LV Dysfunction; (c) LV Dilatation, e.g. Aortic Regurgitation.
6. *Triple or Quadruple Impulse* felt in HOCM.
7. *Retractile Impulse* : is systolic retraction or indrawing of the apical impulse. It is called Broadbents Sign. It is seen in Constrictive Pericarditis.
8. *Absent Apex Beat* on the Left Side:

   Non cardiac causes (a) obesity, thick chest wall; (b) Emphysema; (c) Left pleural effusion with shift of heart to the right.

   Cardiac causes : (a) Dextrocardiac; (b) Pericardial Effusion; (c) Dilated cardiomyopathy; (d) LV Dysfunction e.g. : Coronary Artery Disease.

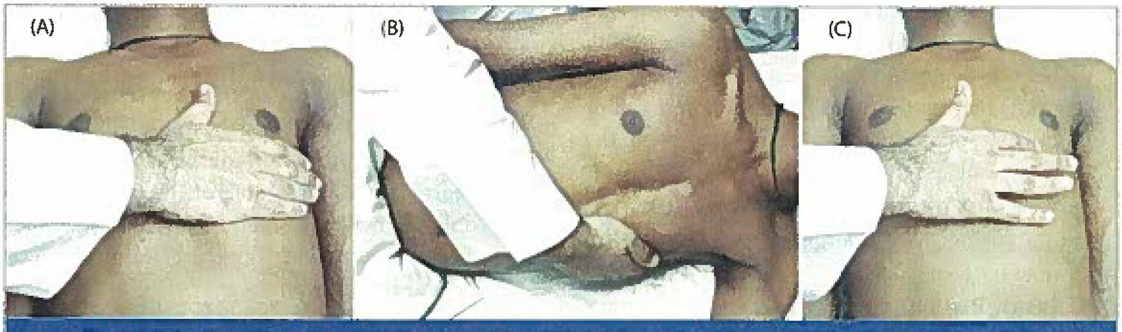


Fig. 5.3 : Palpation of Apex Beat (A) In Supine position, (B) In Left Lateral position and (C) Localization of Apex Beat

II. Parasternal Heave

Systolic impulse in the left parasternal region commonly felt in *right ventricular enlargement* is parasternal heave. It is assessed byplacing the ulnar border of the hand on the left parasternal area, with the patient in supine position.

AIIMS Grading of Parasternal Heave

Grade I: Just touches hand
Grade II: Palpable but compressible
Grade III: Palpable but not compressible

Sometimes an enlarged left atrium or an aneurysm of aorta may push the right ventricle up causing parasternal heave without right ventricular enlargement.



Fig. 5.4 : Palpation of Parasternal Heave

III. Diastolic Shock

This is the *palpable second heart sound.* Either the pulmonary or the aortic component may be palpable. A loud P_2 suggests pulmonary hypertension, whereas a loud A_2 suggests systemic hypertension or aortitis.

IV. Thrills

Thrills are *palpable* vibrations (like the purring of a cat that is felt by the hand) associated with heart *murmurs. They* are best felt with the palm of the hand. It is intensified if the chest wall is thin, site of production is near the surface of the chest wall and the blood flow is rapid.

Presence of a thrill is a definite evidence of the presence of an organic disease of the heart. They may be systolic (AS, PS, MR, TR, ASD, VSD, PDA), diastolic (MS, TS, AR) or continuous (PDA, rupture of sinus of Valsalva aneurysm, AV communication). The site and timing of thrill is given in the table below:

Table 5.1 : Timing and Site of Thrill

	Disease	Timing	Site
1.	Mitral stenosis	Presystolic	Apex
2.	Mitral Regurgitation	Systolic	Apex
3.	Aortic Stenosis	Systolic	Aortic Area / Neo-aortic Area
4.	Aortic Regurgitation	Diastolic	Aortic Area / Neo-aortic Area
5.	Pulmonary stenosis	Systolic	Pulmonary Area
6.	Aortic Stenosis	Systolic	Carotid Smudder over carotids.
7.	Patent Ductus Arteriosus	Continuous	Pulmonary Area or below left clavicle
8.	Ventricular Septal Defect	Systolic	3rd & 4th left intercostal space (Neo-aortic Area or Erb's Area)
9.	Arteriovenous communications	Continuous	Wherever it is situated in the body

C: Percussion

Percussion is mainly done to determine the boundaries of the heart. Percussion of the cardiac dullness has its limitations because fallacious results may be obtained due to greater part of the heart being surrounded by the resonant lung. The roots of the great vessels at the base of the heart produce a dull note that cannot be distinguished from cardiac dullness.

However, percussion is useful to detect pericardial effusion, aortic aneurysm, etc. rather than the size of the heart. Normally the right, left and upper borders are percussed. The lower border of the heart cannot be percussed because it cannot be distinguished from liver dullness.

I. Left Border: The patient must be percussed in the fourth and fifth space in the mid-axillary region and then medially towards the left border of the heart. The resonant note of the lung becomes dull. Normally the left border is along the apex beat. If it is outside the apex beat, it suggests pericardial effusion.

II. Upper border: The patient must be percussed

in the second and third left intercostal spaces in the parasternal line, which is the line between the mid-clavicular and the lateral sternal line. Normally there is resonant note in the second space and dull note in the third space. If there is a dull note in the second space it suggests:

1. Pericardial effusion
2. Aneurysm of aorta
3. Pulmonary hypertension
4. Left atrial enlargement
5. Mediastinal mass

III. **Right border:** The patient must be percussed anteriorly in the mid-clavicular line on the right side until the liver dullness is percussed. Then the percussion is done one space higher from the mid-clavicular line medially to the sternal border. Normally the right border of the heart is retrosternal. If the dullness is parasternal it suggests:

1. Pericardial effusion
2. Aneurysm of ascending aorta
3. Right atrial enlargement
4. Dextrocardia
5. Mediastinal mass
6. Right lung base pathology

To Determine Situs

Percussion of liver dullness on the right and Stomach tympany on the left is present in situs solitus. Liver dullness on the left and stomach tympany on the right indicates situs inversus.

D: Auscultation

The stethoscope consists of a dual chest piece, with a bell and a diaphragm. The Bell is used to auscultate Low Frequency sounds (80-150 Hz) such as S_3, S_4 and mid diastolic murmur of MS.

The Diaphgram is used to auscultate High Frequency Sounds (>300 Hz) such as S_1, S_2, OS, Clicks, Systolic murmur and early diastolic murmurs.

The tubing is usually 12 inches long.

Auscultation is done to describe

I. Heart Sounds

II. Murmurs

III. Other Sounds (opening snap, clicks, pericardial rub, pericardial knock, tumour plop).

I. Heart Sounds

Normally there are four heart sounds recorded phonocardiographically but clinically in majority of the cases only two heart sounds are usually audible. The heart sounds are auscultated in all the four areas of the chest, namely the mitral, tricuspid, pulmonary and aortic areas (see Table). The first heart sound is best appreciated in the mitral area whilst the second heart sound is best appreciated in the aortic and pulmonary areas.

Normally the first heart sound is single because the tricuspid and mitral components occur simultaneously. The second heart sound is normally split, because the

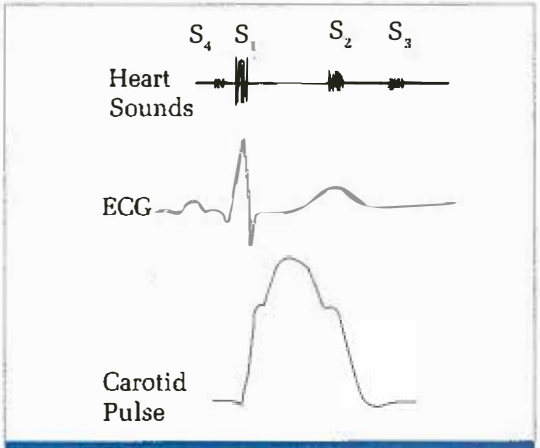


Fig. 5.5: Timing of Heart Sounds. It is important to simultaneously palpate the carotid pulse since S_1 immediately precedes it whereas S_2 follows the carotid pulse.

Table 5.2 : Areas of Chest Wall for Cardiac Auscultation

Area	Site
1. Mitral area	5th left intercostal space just inside the mid-clavicular line
2. Tricuspid area	Lower end of sternum near the ensiform cartilage
3. Aortic area	2nd Right intercostal area
4. Pulmonary area	2nd left intercostal area
5. Erb's area or Neo Aortic Area	3rd left intercostal area

aortic valve closes earlier than the pulmonary valve. This split of the second heart sound is best appreciated in the pulmonary area.

First Heart Sound (S_1)

It is produced by the closure of the mitral and tricuspid valves (M_1 & T_1 respectively). Normally the mitral valve closes before the tricuspid valve by 20-30 msec. Hence S_1 is appreciated as a single sound.

It is a high frequency sound heard best with the diaphragm of the stethoscope.

It is timed with simultaneous palpation of the carotid pulse. S_1 indicates the onset of systole

Abnormal First Heart Sound

I. Loud

II. Soft

III. Variable

IV. Widely Split

V. Reverse Split

I. *Loud First Sound*:

Due to increased excursion of the AV valves leaflets away from each other during their opening, there is a loud sound when they close (similar to a door which when open to a wider angle, closes with a louder sound).

A. Normal in children

B. Sinus tachycardia

C. Prolonged A-V filling due to A-V stenosis e.g. mitral stenosis, tricuspid stenosis

D. Increased A-V flow from high cardiac output, e.g. thyrotoxicosis, anemia, beriberi, A-V fistula.

E. Increased A-V flow from left to right shunt, e.g. PDA, ASD, VSD.

F. Short P-R interval

II. *Soft First Heart Sound*:

A. Poor conduction of sound through chest wall

1. Pericardial effusion
2. Emphysema
3. Thick chest wall
4. Obesity

B. Rigidity and calcification of A-V valve e.g. mitral stenosis with calcified valves

C. Mitral and tricuspid regurgitation

D. Prolonged P-R interval

E. Acute MI, LV aneurysm, cardiomyopathy

III. *Variable First Heart Sound*

A. Atrial Fibrillation

B. Complete Heart Block

C. A.V. Dissociation

IV. *Widely split first heart sound*:

Splitting of the first heart sound occurs when the Tricuspid valve closes late as compared to Mitral Valve.

In RBBB or VPC originating from LV, the LV systole starts first resulting in MV closing earlier. This is followed by RV systole which results in a late TV closure, thus causing a split S_1 (M_1-T_1).

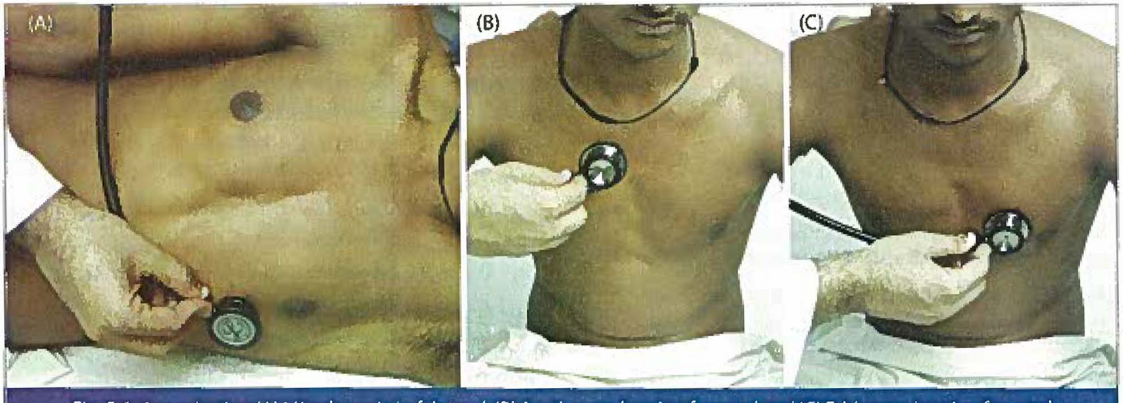


Fig. 5.6: Auscultation (A) Mitral area in Left lateral, (B) Aortic area, leaning forward and (C) Erb's area, leaning forward

A. *Electrical*
   1. RBBB
   2. VPCs originating from LV
   3. LV Pacing
   4. Idioventricular rhythms from LV

B. *Mechanical*
   1. TS
   2. Right Atrial Myxoma
   3. Ebsteins Anomaly (Sail Sound)

V. Reverse Splitting of First Heart Sound:

It means when M_1 occurs later than T_1.

A. *Electrical :*
   1. LBBB

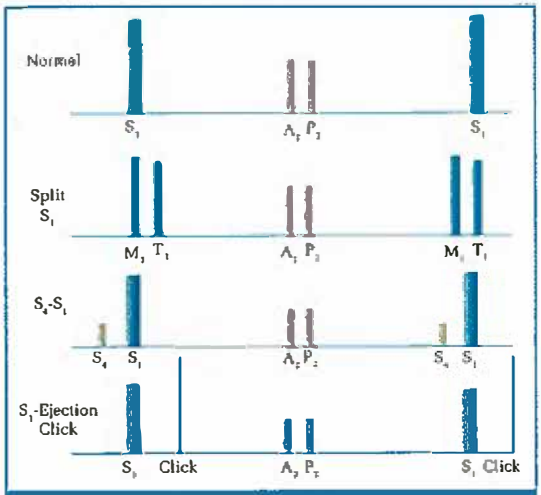


Fig. 5.7 : First Heart Sound

   2. VPC, originating from RV
   3. RV Pacing
   4. Idioventricular Rhythms originating from RV

B. *Mechanical :*
   1. Severe MS
   2. Left Atrial Myxoma

Splitting is best heard in the Lower Left Sternal Border. If it is heard well at the apex, it should be differentiated from a S_4 preceeding S_1 or a ejection click following S_1.

Second Heart Sound (S_2)

It is normally has two components, produced by closure of the aortic valve (A_2) and pulmonary valve (P_2). Normally, it is a high frequency sound, heard better in the aortic and pulmonary area.

It is normally split because the aortic valve closes before the pulmonary valve. The A_2 is normally louder than P_2. During inspiration, the splitting of A_2 P_2 becomes wider. During expiration the splitting of A_2P_2 is narrower and S_2 may be heard as a single sound.

The opposite occurs during expiration leading to Narrow Expiratory Split of S_2.

Abnormal Splitting of S_2

I. **Widely Split Second Heart Sound**

A. *Electrical*
   1. RBBB
   2. Left VPB
   3. LV Pacing

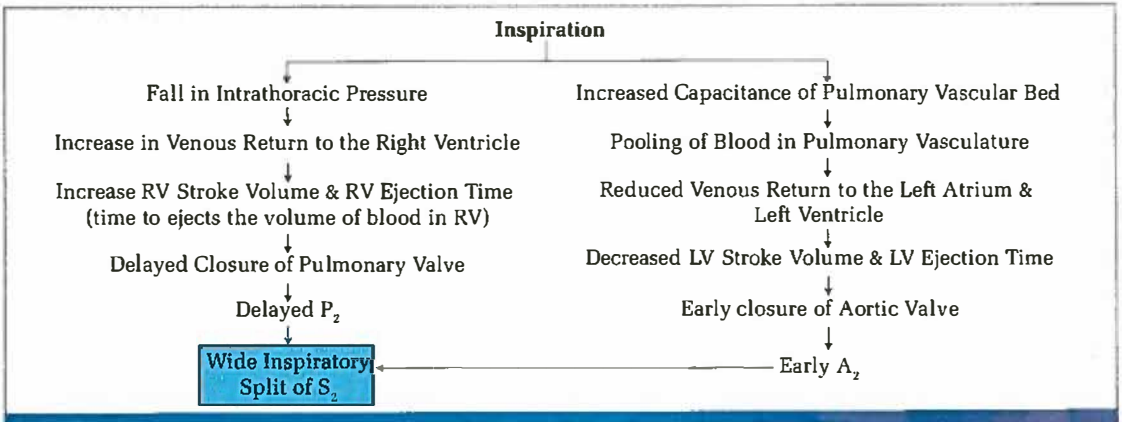


Fig. 5.8 : Mechanism of Normal Splitting of Second Heart Sound (S_2)

B. *Mechanical*

1. ASD (wide, fixed)
2. VSD
3. Pulmonary stenosis
4. RV Failure (Acute Pulmonary Embolism)
5. Severe MR

Mechanism

1. *Widely Split S_2* : Abnormal wide splitting of S_2 is defined as an audible *expiratory* split of A_2 P_2. It may occur due to delayed P_2 or early A_2. It is occasionally normal in children.

2. *Wide and Fixed Split S_2* : It is the hallmark of ASD (Ostium secundum type). The split of A_2 P_2 is wide due to delayed P_2, resulting from increased venous return, RV Stroke volume and RV ejection time during inspiration. Therefore, there is no left to right shunt across ASD during inspiration.

   During expiration, there is a reduced venous return to Right atrium but the left to right shunt across the ASD leads to increased RV filling, RV stroke volume and RV ejection time. This minimises respiratory variation of the RV volumes and leads to a *wide and fixed* split S_2.

   Another mechanism of wide and fixed split S_2 is related to pulmonary hangout interval. In ASD, there is increased pulmonary blood flow due to increased volume of blood in RV due to left to right shunt. This leads to increased capacitance of pulmonary vascular bed, during both phases of respiration (normally, an increase in capacitance of pulmonary vascular bed occurs during inspiration).

   The pulmonary valve is expected to close when the pressure in the RV falls below the pressure in the pulmonary artery. However, in reality the pulmonary valve closes later (the PV closes at the level of the incisura of the pulmonary artery tracing). The hangout interval is measured from the incisura on the pulmonary artery tracing (PV closes) to the same level of the RV pressure tracing (Figure 5.9).

   This hangout interval is determined by pulmonary capacitance and RV ejection time. It is normally 60-80 msec. In ASD, the hangout interval is prolonged and fixed due to increased pulmonary capacitance during both phases of respiration. This leads to a wide and fixed split second heart sound.

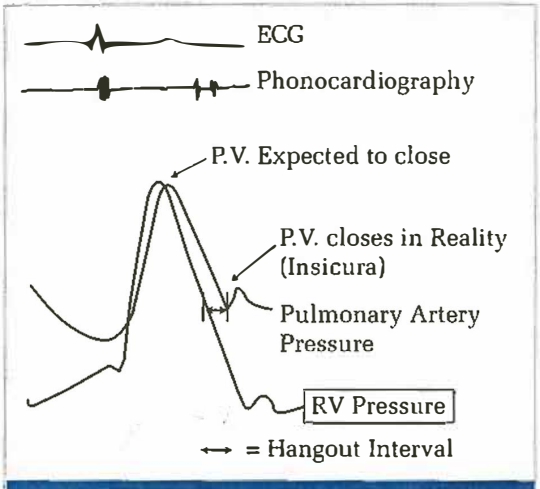


Fig. 5.9 : Pulmonary Hangout Interval

II. **Reverse Splitting of Second Heart Sound**

A single S_2 during inspiration and split S_2 during expiration is called Reverse Split of S_2. It occurs since pulmonary valve closes earlier than Aortic Valve. It occurs due to early closure of Pulmonary Valve (early P.) or delayed closure of aortic valve (late A_2).

A. *Electrical*

1. LBBB
2. Right VPB
3. RV Pacing
4. WPW syndrome

B. *Mechanical*

1. Aortic Stenosis
2. HOCM
3. Hypertension
4. Coarctation of Aorta
5. Large PDA
6. LV Failure

III. *Single Second Heart Sound*

A. Diminished Intensity of A_2 or P_2 :

1. AS
2. PS

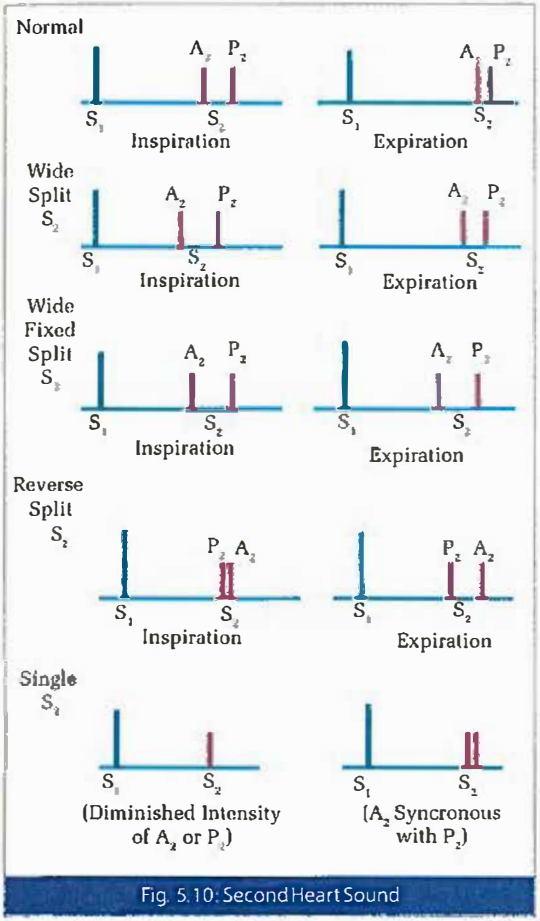


Fig. 5.10: Second Heart Sound

Normally A_2 - P_2 Interval
During Inspiration : 40-50 msec
During Expiration : <30 msec

3. Pulmonary Atresia
4. Tetrology of Fallot

B. P_2 synchronous with A_2
1. VSD
3. Single ventricle

C. Concealed by systolic murmur / Continuous Murmur

D. Others : Trunous Arteriosis

IV. *Narrowly Split S_2* : Pulmonary hypertension

Abnormality of Intensity of S_2

1. Loud P_2 : P_2 is called loud if it is louder than the A_2. It is loud in
   i. Pulmonary Hypertension
   ii. Pulmonary Artery Dilatation
   iii. A.S.D.
2. Soft P_2 : May be perceived as a single S_2
   i. Pulmonary stenosis
   ii. Tetrology of Fallot
   iii. Thick Chest Wall, COPD, Obesity
3. Loud A_2
   i. Systemic Hypertension
   ii. Aortic Aneurysm
   iii. Aortitis (Syphillitic aortitis produces "Tambour quality of A_2)
   iv. Hyperkinetic circulatory states
4. Soft A_2 : May be perceived as a single S_2
   i. Aortic stenosis
   ii. Aortic Regurgitation

Third Heart Sound (S_3)

Normally only two heart sounds are audible. The third heart sound is heard in the following conditions:

1. Normal up to 30 years and in children, atheletes and pregnancy
2. MR
3. TR
4. CCF
5. Myocardial infarction
6. ASD, VSD, PDA
7. High output state
8. Dilated cardiomyopathy

Mechanism:

Normally the third heart sound is a low frequency sound, heard because of the first rapid filling phase of the ventricular diastole when blood flows from the atria into the ventricles.

- In MR and TR during systole some blood goes back into the atria and hence there is increased flow into the ventricles during the first rapid filling phase resulting in the third heart sound.
- In heart failure there is increased atrial pressure and hence increased first rapid filling results in the third heart sound.

It is important to note that in significant mitral stenosis the third heart sound is never heard because rapid filling of the ventricles is not possible because of a stenosed A-V valve.

Factors that prevent detection of third heart sound: are environmental noise, emphysema, obesity, failure to apply the bell properly and examining the patient in sitting position. It disappears on standing up. A latent third heart sound can be made audible by rolling the patient onto the bed from sitting position to lying position or by passive straight leg raising.

If the heart rate is over 100 beats/min, discrimination of third or fourth heart sound is not possible and the triple rhythm (gallop) is called *summation gallop.*

Right ventricular third heart sound is located at the left lower sternal border rather than the apex and often increases on inspiration. It may radiate to right supraclavicular fossa. It is commonly seen in *cor pulmonale.*

Table 5.3 : Third Heart Sound

	Right Ventricular S_3	*Left Ventricular S_3*
Site	Tricusped Area	Mitral Area (Apex)
Best heard in position	Supine	Left lateral
Increase with respiration	Inspiration	Expiration
Change with isometric hand grip	No change	Increases

Fourth Heart Sound (S_4)

It is a low frequency sound. It occurs due to rapid emptying of atrium into a non-compliant ventricle in late rapid filling phase due to atrial contraction; heard best with the bell of a stethoscope. Normally it is inaudible. It is heard in the following conditions:

1. Elderly > 60 years.
2. Myocardial infarction,LV failure (summation gallop, quadruple rhythm $S_1 - S_2 - S_3 - S_4$)
3. AS, HOCM
4. PS
5. Pulmonary or systemic hypertension
6. MR, AR, TR
7. Hyperkinetic states

Gallops

Triple Rhythm : 3 audible heart sounds - $S_1 + S_2 + S_3 / S_4$

Quadruple Rhythm : 4 audible heart sounds $S_1 + S_3 + S_3 + S_4$

Summation Gallop : S_3 & S_4 are merged due to tachycardia $S_1 + S_2 + (S_3 \& S_4)$

Palpable HeartSounds

I. **Palpable S2(P2) (Diastolic shock):** denotes pulmonary hypertension

II. **Palpable S1:** 'Tapping' apex beat of mitral stenosis

III. **Palpable S4:** 'Double' apex beat (HOCM), severe aortic stenosis

II. Murmurs

Murmurs are abnormal heart sounds caused by vibration of the valves or the wall of the heart or great vessels. Murmurs may be systolic (if it is between first and second heart sound) or diastolic (if between the second and first heart sound) or continuous. Levine grades systolic murmurs as follows:

Table 5.4 : Grading of Systolic Murmurs

Grade I	:	Very faint murmur only audible with effort
Grade II	:	Faint murmur but clearly and definitely audible
Grade III	:	Moderately loud murmur but no thrill
Grade IV	:	Loud murmur with thrill
Grade V	:	Louder with thrill and can be heard with stethoscope half lifted off chest wall
Grade VI	:	Murmur with thrill heard even if stethoscope is just lifted up from the chest wall.

Diastolic murmurs have only Grades I to IV.

Factors for production of murmurs.

1. Flow of blood through an abnormal orifice. e.g. in mitral stenosis or regurgitation.
2. High velocity flow through a normal orifice. e.g. in anemia, hyperkinetic states.

Innocent Murmurs

Soft systolic murmurs heard in patients without any cardiac abnormality are called Innocent murmurs.

Characteristics

1. More commonly heard in children (Still's murmur)
2. Usually heard in the pulmonary area

3. Usually not a loud murmur
4. No thrill
5. Variation of murmur on posture or respiration
6. Usually systolic, but may be continuous
7. Soft, short and blowing in nature
8. Heart sounds are normal
9. Usually localized

Differential Diagnosis

1. Pulmonary ejection murmur
2. Vibratory murmur
3. Supraclavicular arterial bruit
4. Venous hum
5. Mammary soufflé

Organic Murmurs

A. **Systolic Murmurs** are those which occur between the first heart sound and second heart sound and last during part or whole of systole.

1. *Mid-systolic or ejection systolic murmurs*

Table 5.5 : Mid-Systolic or Ejection Systolic Murmurs

Aortic	Pulmonary
1. AS	1. PS
2. Co-arctation	2. Fallot's Tetrology
3. H OCM	3. Pulmonary artery dilatation (function)
4. PDA (Functional)	4. ASD, VSD (functional)
5. AR (Functional)	5. High output state
6. Aneurysm	6. P.R. (Functional)

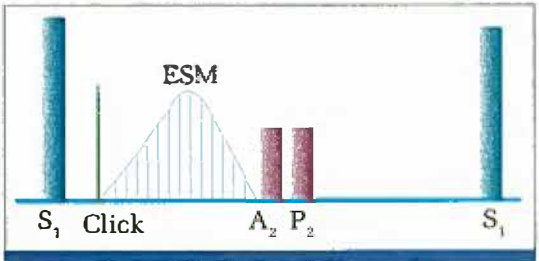


Fig. 5.11 : Ejection Systolic Murmur of AS

2. *Late Systolic Murmurs*
   1. Mitral Valve Prolapse (MVP)
   2. Tricuspid Valve Prolapse
   3. Hypertrophic Obstructive Cardiomyopathy (HOCM)
   4. Papillary Muscle Dysfunction (PMD)
   5. Coarctation of Aorta
   6. P.S.

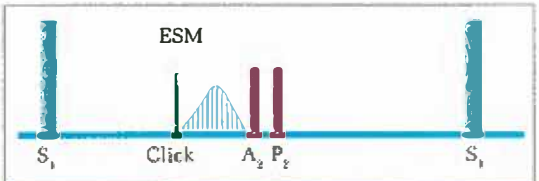


Fig. 5.12 : Late systolic murmur of MVP

3. *Pan Systolic / Holosystolic Murmurs*
   1. Mitral Regurgitation (MR)
   2. Tricuspid Regurgitation (TR)
   3. VSD

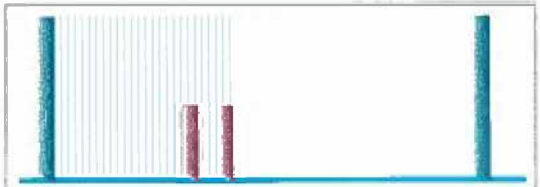


Fig. 5.13 : Pansystolic murmur of M.R./TR/VSD

4. *Early Systolic Murmur*
   1. Acute Severe MR
   2. Acute Severe TR
   3. Very small VSD or Large VSD with pulmonary hypertension

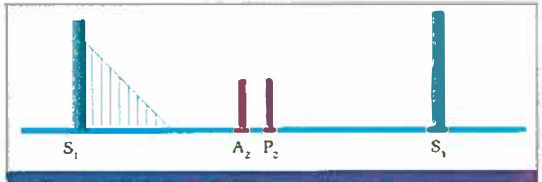


Fig. 5.14 : Early Systolic Murmur of Acute Severe MR/TR

B. **Diastolic Murmurs** : are those which occur between the second heart sound and the first heart sound, during any part of diastole.

1. **Early Diastolic Murmurs**
   a. Aortic Regurgitation (AR)
   b. Pulmonary Regurgitation (PR)

c. *Graham Steel's Murmur:* This is a functional, diastolic murmur best heard in the pulmonary area due to PR due to pulmonary hypertension.

2. **Mid Diastolic Murmurs**
   a. MS
   b. TS
   c. *Carey Coombs murmur:* This is the functional, apical, mid-diastolic murmur of mitral valvulitis.
   d. *Austin Flint murmur:* This is the functional, apical, diastolic murmur of free AI, without any lesion of the mitral valve.
   e. *Flow murmurs:* These occur because of increased blood flow, in diastole, across the mitral or tricuspid valves as in:
      i. ASD
      ii. VSD
      iii. PDA
      iv. MR
      v. TR
      vi. Aortopulmonary septal defect
      vii. Complete heart block (Rytands Murmur)

3. **Late Diastolic or Presystolic Murmurs**
   1. MS
   2. TS
   3. Left atrial myxoma
   4. Right atrial myxoma

C. Continuous Murmurs:

A Continuous murmur is one which begins in systole and continues through the second heart sound into part or whole of diastole.

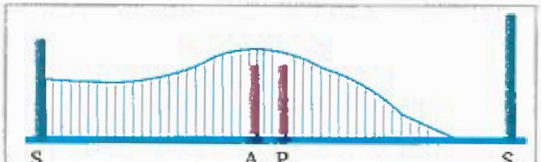


Fig. 5.15: Continuous Murmur

1. PDA
2. Aortopulmonary window
3. Ruptured sinus of Valsalva into the right side of the heart
4. Surgically produced shunts in TOF- Blalock-Taussig shunt
5. Co-arctation of aorta
6. Coronary/pulmonary/systemic A-V fistula
7. AS and AR
8. VSD with AR
9. Venous hum
10. Mammary soufflé
11. Anomalous origin of left coronary artery from pulmonary artery

VENOUS HUM: This is a low-pitched, soft, continuous murmur accentuated in early diastole and commonly heard in children and young adults. It occurs due to the flow of blood through the jugular veins and is best heard at the lower left border of the right sternomastoid muscle. It is best heard in the sitting position with the head turned towards the opposite side. It is obliterate by compression of the neck veins and Valsalva maneuver. It is accentuated by exercise.

MAMMARY SOUFFLE: This is a continuous murmur best heard over the mammary area and second interspaces during the third partum month. It is a soft, systolic or continuous murmur accentuated during systole. Firm digital pressure applied laterally obliterates it.

III. Other Sounds

A. Opening Snap

This is heard midway between the second and third heart sounds in cases of mitral or tricuspid stenosis. It is a high pitched, loud snapping or clicking, sharp sound due to sudden tensing of the cusps of the mitral (or tricuspid) valve as it tries to open during early diastole. It is best heard just inside the apex beat. It is not related to respiration or posture, but is accentuated with exercise and is best heard with the diaphragm of the stethoscope.

The interval between the onset of the second heart sound and the opening snap (A_2-OS interval) is a good guide to judge the severity of mitral stenosis. The shorter the A_2-OS interval, the more severe the mitral stenosis.

Table 5.6 : Differences between Opening Snap and Split Second Sound

	Opening Snap (A2-OS)	Split Second Sound (A2-P2)
1. Interval between the two sounds	Longer - 0.04 - 0.12 sec	Shorter - 0.04 - 0.05 sec
2. Area	Heard just inside the apex	Second and third Intercostal space
3. Character	Louder and sharper	Softer
4. Relation to respiration	None	The split increase on respiration.
5. Occurrence	In MS or TS	Normally present

Table 5.7 : Differences between Opening Snap and Third Heart Sound

	Opening Snap (A2 - OS)	Third Heart Sound (A2 -S3)
1. Sequence of sounds	0.04 - 0.12 sec after A2	0.12 - 0.17 sec after S2
2. Area	Heard just inside the apex	Heard at the apex
3. Relation to posture	Increase on standing	Disappears on sitting/standing
4. Physiological	Never	Upto 30 years
5. Occurrence	In MS or TS	In MR or LVF
6. Pitch	High Pitch	Low Pitch

A_2-OS interval can be 0.04 - 0.12 sec.

Opening snap is absent when there is:

1. Mild mitral stenosis
2. Calcified mitral valve
3. Mitral stenosis with associated mitral regurgitation

B. Systolic Ejection Clicks

They are produced due to opening of semilunarvalves. They are high pitched, click-like sounds that come immediately after the first heart sound and are best heard in the aortic or pulmonary areas. They are due to excessive ejection of blood from the ventricles into the blood vessels

1. **Pulmonary Ejection Click**

   This is best heard during expiration. It is the only right-sided event, which is increased on expiration.

   Causes

   a. Dilatation of pulmonary artery
   b. Pulmonary stenosis
   c. Pulmonary hypertension

2. **Aortic Ejection Click**

   This is transmitted to the apical area.

   Causes

   a. Aortic aneurysm
   b. Aortic regurgitation
   c. Aortic stenosis
   d. Coarctation of aorta
   e. Hypertension

3. **Midsystolic Click/Non-ejection Click**

   Produced by prolapse of AV valve leading to tensing of chordae tendineae.

   Causes:

   a. Mitral valve prolapse
   b. Tricuspid valve prolapse

C. Pericardial Rub

This is caused by slashing movements imparted by the heartbeat to the exudate within the pericardial sac. It gives rise to a to-and-fro type of sound due to forward and backward shifts of the exudate during systole and diastole.

Characteristics

1. Creaking, rasping, leathery or scratchy
2. Synchronous with the heart beat, both during systole and diastole, but louder during systole
3. Best heard anywhere over the precordium
4. Not transmitted

5. Varies from hour to hour or day to day
6. Louder in the upright than recumbent position and are accentuated by bending.
7. Intensity varies with pressure of the stethoscope.
8. Not affected by respiration.

Causes:

Pericarditis due to:

1. Acute MI
2. Dressler's syndrome
3. Acute RF
4. Uremia

D. Pericardial Knock

Heard in diastole in a case of constrictive pericarditis due to abrupt restriction of diastolic filling of ventricle due to the adherent pericardium.

E. Tumor Plop

Heard in left or right atrial myxomas (which are mobile in the heart) in diastole.

Table 5.8 : Differences between Pericardial Rub and Murmurs

	Pericardial Rub	*Murmurs*
1. In cardiac cycle	Does not coincide with systole or diastole	Coincides with systole or diastole
2. Character	Creaking, scratchy rasping or leathery	Blowing, rumbling or musical
3. Conduction	None	May be present
4. Variability	Present	Absent
5. Audibility	Sounds superficial	Sounds deeper
6. Pressure of stethoscope	Alters the intensity of the rub	Does not alter the intensity

IV. Dynamic Auscultation

Physiologic or pharmacological maneuvers carried out to change the circulatory hemodynamics and hence the quality of heart sounds and murmurs:

1. *Respiration:* Inspiration leads to increased venous return and therefore increased flow to right side of the heart.

   On the other hand, inspiration leads to increased pooling of blood in pulmonary vascular bed and therefore reduces the pulmonary venous return and reduces the flow of blood to the left side of the heart.

   The opposite occurs during expiration.

   Thus, Right Sided Murmurs are louder during inspiration. [TR murmur is accentuated in inspiration - Carvallo sign]. Conversely, Left Sided Murmurs are louder during expiration.

   Exception : (1) Mitral Valve Prolapse (MVP) - Inspiration reduces pulmonary venous return and flow of blood into left side of heart. This reduces the LV size. This increases redundency of Mitral Leaflets and increases the prolapse. Therefore the murmur of MVP is louder and longer and the click is earlier in Inspiration. (2) H.O.C.M. - During inspiration, the reduced LV size leads to increased sub-aortic obstruction. Therefore, the murmur is louder during inspiration.

2. *Valsalva maneuver:* In this manouver, the patient is asked to close his nose with her fingers and breathe forcibly through the closed mouth. This causes forced expiration against a closed glottis.

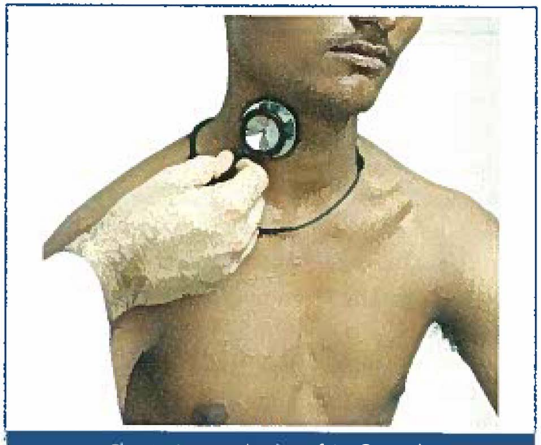


Fig. 5.16 : Auscultation of the Carotids

Table 5.9 : Phases of Valsalva Manouver

Phase	Heart Rate	Blood Pressure	Mechanism
Phase I (onset of strain)	No change	Increases	Increased Intrathoracic pressure & transient rise of LV output & arterial pressure
Phase II (maintenance of strain)	Increases	Reduces	Reduced Venous Pressure leading to reduced stroke volume & BP. Carotid baroreceptors stimulated to produce reflex tachycardia
Phase III (Release of strain)	No change	Reduces	Sudden increase venous return. Fall of intrathoracic pressure & transient drop of BP
Phase IV (Relaxation) or (overshoot)	Decreases	Increases	Increased venous return leads to increased stroke volume & BP. Carotid baroreceptors inhibited to produce reflex bradycardia

It has 4 phases summarized in Table.

Dynamic auscultation is described during changes in phase II (maintainance phase) of valsalva manouver. During this phase, there is increase in intra-thoracic presure and reduced venous return. This reduces flow on the right and left side of the heart. Therefore all murmurs are softer.

Exception : Since venous return is reduced, LV size is also reduced. Therefore the murmur of HOCM becomes louder and the murmur and click in MVP become louder and earlier

3. *Isometric Hand Grip or Exercise:* Left sided murmurs increase, except HOCM and MVP (decrease)
4. *Passive leg raising* → right-sided murmurs increase(due to increased venous return)
5. *Squatting* → It leads to sudden increase in venous return. All murmurs increase, except HOCM and MVP decrease
6. *Standing* → It leads to sudden reduction of venous return. All murmurs decrease, except HOCM and MVP increase.

Table 5.10 : Dynamic Auscultation

Manouver	Right Sided Murmur (eg. TR)	Left Sided Murmur (eg. MS)	HOCM	MVP
1. Inspiration	↑	↓	↑	↑
2. Expiration	↓	↑	↓	↓
3. Valsalva Phase II	↓	↓	↑	↑
4. Isometric Hand Grip / Exercise	-	↑	↓	↓
5. Passive Leg raising	↑	-	-	-
6. Standing	↓	↓	↑	↑
7. Squatting	↑	↑	↓	↓

3 Rheumatic Fever

Definition: Acute rheumatic fever (RF) is an inflammatory complication that may follow group A beta hemolytic streptococcal infection, manifested by one or more of the following: arthritis, carditis, chorea, erythema marginatum and subcutaneous nodules.

Pathogenesis: Following exudative streptococcal pharyngitis, rheumatic fever occurs after about 2 weeks. The exact pathogenetic pathway by which streptococcus leads to rheumatic inflammation is not known. Various mechanisms proposed are:

1. *Direct toxic action* by streptococcus, or its "L form" lacking the cell wall
2. *Allergic reaction* to the organism or its product
3. *Autoimmune reaction:* There is similarity between the carbohydrate of the streptococcus and some proteins of heart valves causing the immune reaction. This is the most accepted theory.

Pathology: Rheumatic fever can involve any or all the layers of the heart (pancarditis). Involvement of the valvular endocardium may lead to tiny vegetation on the valves and destruction and fibrosis of valve substance with fusion of cusps of commissures leading to stenosis. There is myocarditis and fibrinous pericarditis (bread-and-butter appearance). Both are self-limiting causing no permanent sequelae.

Microbiology: The hallmark of carditis is the "Aschoff" body which is a granulomatous lesion of the endocardium with fibrinoid necrosis. This area is

surrounded by cardiac histiocytes called Aschoff cells or Anitschoff cells. Mccullaris patch in chronic RF.

Clinical Features

Table 5.11 : Modified Jones Criteria for Diagnosis of Rheumatic Fever

Major Criteria	*Minor Criteria*
Carditis	**Clinical:**
Migratory polyarthritis	Fever
Sydenham's chorea	Arthralgias
Subcutaneous nodules	**Laboratory:**
Erythema nodosum marginatum	Elevated ESR or CRP
	Prolonged PR interval (ECG)

Essential Criteria: Evidence of recent Gp A Streptococcal infection	TO FULFIL JONES CRITERIA YOU NEED:
1. Positive throat culture or	- **2 MAJOR OR**
2. Elevated streptococcal antibody (anti-streptolysin O (ASO), anti-DNAase) or	- **1 MAJOR AND 2 MINOR**
	PLUS
3. Rapid antigen detection test or	**ANY ONE OF THE ESSENTIAL CRITERIA**
4. Recent scarlet fever	

1. Carditis
   a. Pericarditis: Chest pain, pericardial friction rub
   b. Myocarditis, tachycardia, soft S_1, Carey Coombs murmur
   c. Endocarditis: Murmurs of MS, MR, AS or AI. In adults, aortic valve is most commonly affected. In children, mitral valve involvement with MR is most common.
   d. Cardiac failure due to acute MR
   e. Cardiac enlargement
   f. Infective endocarditis (IE)
2. *Migratory polyarthritis* involving knees, ankles, elbows, wrists. No residual deformity.
   Course: Inflamed joint (red, warm, tender) —> completely resolves in 2 weeks —> another joint involved.
3. *Sydenham's chorea/St. Vitus Dance:* Late manifestation, mainly in females, 6 months after primary infection, self-limiting lasting 6 weeks to 6 months.
   Symptoms are initially irritability followed by uncoordinated spasmodic movements of hands, face and feet with facial grimacing.
   Signs:
   a. Tongue appears like a "bag of worms" due to continuous movements
   b. "Spoon-dish" hands due to hyperextension of MCP joints and flexion at wrist
   c. "Milkmaid" grip causing irregular repetitive squeezing on shaking hands.
4. *Erythema marginatum* is a non-pruritic, flat, circular or serpiginous rash on the trunk and thighs.
5. *Subcutaneous nodules* are firm, colorless, painless nodules 1-2 cm, in size, near the tendons or bony prominences of joints, especially elbows. They are a late manifestation.

Atypical Arthropathy in Rheumatic Fever

1. *Grisel's Syndrome:* Occasional involvement of Atlanto-occipital joint.
2. *Jaccoud's Arthropathy:* Chronic deformity of the hands after polyarthritis

Diagnosis

1. Antibodies to Streptococcus Gp A
   a. ASO positive > 200 Todd units. A rising titer is more significant.
   b. Others: Anti-deoxyribonuclease B, anti-hyaluronidase, Anti-streptokinase.
2. Rapid Antigen Detection Test: Latex agglutination or enzyme immunoassay on throat swab
3. ESR and CRP raised, Anemia, Leucocytosis
4. ECG: Prolonged PR (first degree heart block), Second degree or complet heart block
5. 2-D Echo

Management

1. Hospitalise or bed-rest if carditis
2. *Treatment of Streptococcal infection* (duration 10 days): Penicillin V 250 mg BD or erythromycin 250 mg qds orally or inj. Benzathine penicillin IM 1.2 million units single dose. Alternatives

for patients with penicillin allergy: Macrolides, : roxithromycin, azithromycin or sulfadiazine.

3. *Treatment of manifestations:*
   a. Arthritis: Anti-inflammatory agents: Salicylates: Aspirin 100 mg/kg/day in 4-5 doses or NSAIDs: Ibuprofen: 200-400 mg tds
   b. Carditis and cardiac failure:
      i. Steroids: Prednisolone 1-2 mg/kg/day or inj. Methyl prednisolone, if life-threatening for 2-3 weeks, then taper
      ii. Aspirin during tapering of steroids for 4-6 weeks
      iii. Rest, steroids, diuretics, digoxin, ACE inhibitors for cardiac failure
   c. Chorea: Self-limiting, no specific treatment. Drugs like diazepam, haloperidol can be used.

Prophylaxis (Secondary)

Drugs:

1. Benzathine penicillin 1.2-2.4 mega units IM every 3-4 weeks
2. Penicillin V 250 mg BD orally
3. Erythromycin 250 mg qds orally

Duration:

1. Patient with rheumatic fever without carditis – 5 yrs after attack or upto 18 yrs of age, whichever is later
2. Patient with rheumatic fever with carditisbut without valvular disease – 10 yrs after attack or up to the age of 25 yrs of age, whichever is later
3. Patient with rheumatic fever with carditis and valvular disease – upto 40 yrs of age; some advocate lifelong prophylaxis

4 Infective Endocarditis

It is a microbial infection of the heart valves or the endothelium in proximity to congenital or acquired cardiac defects.

Organisms

The common organisms are Streptococcus viridans, Staphylococcus aureus, Pneumococcus, group A Streptococcus, Gonococcus, Brucella and Rickettsia. They commonly follow tonsillectomy, dental extraction or suppurative cellulitis.

In narcotic addicts the endocarditis may affect the right side of the heart and the common organisms are Proteus, Pseudomonas and Klebsiella.

Following open-heart surgery fungal endocarditis is common with Histoplasma, Candida or Aspergillus.

Listeria endocarditis is common in patients on immunosuppressive therapy.

Pathogenesis

The characteristic lesions in endocarditis are vegetations over the valve leaflet. Sterile thrombotic vegetations form due to trauma to the endocardial cells. Thrombi may form over a sub-endocardial inflammatory reaction such as in acute rheumatic fever or myocardial infarction. When bacteremia occurs, the surface of the vegetation can become secondarily infected and converted to the typical vegetations of infective endocarditis. This results from deposition of platelets and fibrin over the bacteria. The vegetations then become a protective site through which phagocyte cells penetrate poorly.

Endocarditis occurs at a site where blood flows through a narrow orifice and at a high velocity, from a high to a low-pressure chamber. Lateral pressure is lowest and the velocity of blood greatest a short distance downstream from the opening between the chambers. A decrease in lateral pressure lowers perfusion of the intima, resulting in an area more susceptible to infection. This is the location where infective endocarditis initially develops. Hence it occurs on the right side in VSD and on the pulmonary artery in PDA. Endocarditis does not usually occur when there is only a small pressure gradient as in ASD or when the congenital defect is large enough to abolish the pressure gradient.

A high velocity stream of blood can produce satellite-infected lesions at distant points of impact. Hence, endocarditis occurs more frequently with incompetent than pure stenotic lesions and is characteristically seen on the atrial side in mitral valve and on the ventricular side in aortic valve lesions.

1. Vegetations may become extensive (as in fungal endocarditis) and completely occlude the valve orifice.

2. The valve tissues may be rapidly destroyed resulting in incompetence of the valve e.g. Staphylococcus aureus endocarditis.
3. Areas of healing may cause scar formation and consequent stenosis or insufficiency of the valve.
4. The infection may spread leading to conduction abnormalities, rupture of chorda tendineae, papillary muscles or the ventricular septum. This carries grave prognosis.

Clinical Manifestations

I. Signs of Infection

1. *Fever* with chills and rigors coming down with sweating. If there is associated cardiac failure, fever may be absent for as long as 4 months.
2. Progressive normochromic and normocytic *anemia.*

   N.B Microcytic, hypochromic anemia by itself can cause low-grade fever, petechiae, systolic murmur and splenomegaly.
3. *Tachycardia*
4. *Clubbing:* It takes 3-6 weeks to develop. It disappears once the patient is cured
5. *Splenomegaly:* Spleen enlargement is not gross. If spleen suddenly enlarges, is tender and a rub is present over the spleen, it suggests splenic infarction.
6. *Febrile proteinuria*
7. *Leucocytosis*
8. *Blood culture:* Usually organisms are grown on blood culture

II. Cardiac Signs

1. Signs of a pre-existing cardiac lesion is usually present except in patients with congestive cardiac failure, atrial fibrillation, renal failure or severe debility
2. Changing intensity of the cardiac murmur.
3. Appearance of new murmurs
4. ECG: Prolonged PR interval. AV block may be present if the septum is involved.

   There may be no cardiac signs especially if the right side of the heart is involved.

III. Signs of Embolic Episodes

1. *Petechiae:* This occurs due to embolic episodes, anemia or toxic damage to the vessel. It is found in the conjunctiva, palate, buccal mucosa and extremities. It is called splinter hemorrhage if it occurs under the nail.
2. *Osler nodes:* They occur singly or in crops, due to vasculitis. They are transient, tender, red nodules, the size of pinhead to pea, on the finger pads, the sides of the fingers and toes and thenar and hypothenar eminences. They disappear in few days. They may also be seen in SLE, typhoid, gonococcal infection.
3. *Janeway's lesions:* They are subepithelial microabcesses and are large non-tender macules over palms and soles. These are commonly seen in acute endocarditis.
4. *Peripheral vascular embolization:* This may involve larger vessels like carotids or radials, resulting in hemiplegia and painful fingers. If an embolus sits at the bifurcation of an aorta it will cause Leriche's syndrome that is characterized by acute onset of paraplegia, impotence and absent pulsations of lower limbs that become cold, cyanosed and later gangrenous.
5. *Pulmonary embolism:* This resembles hemorrhagic bronchopneumonia. Pulmonary embolism occurs if the vegetations are on the tricuspid or pulmonary valves or if there is a left to right shunt.
6. *Optic fundi:*
   a. *Roth's spots:* These are flame-shaped or canoe-shaped hemorrhages with central pallor. They are seen in severe anemia, leukemias and collagen vascular diseases in addition to infective endocarditis.
   b. Embolization of the retinal artery: This leads to blindness.
   c. Papilledema due to embolic cerebral infarction or renal involvement.

Investigations

1. **Hemogram:** Normochromic, normocytic anemia, leucocytosis and raised ESR.
2. **ECG:** Tachycardia, prolonged PR interval, atrioventricular block if septum is involved and signs of acute myocardial infarction if there is coronary embolism.
3. **Blood culture:** This usually grows the causative agent. It is negative in cases of endocarditis caused by Aspergillus, Histoplasma, Coxiella burnetii, anaerobic organisms and non-bacterial thrombotic endocarditis. It may also be negative if the patient is already on antibiotics or if there is faulty technique.
4. **Serum proteins:** Immunoglobulins are increased. IgM is selectively raised with rickettsial infection.
5. **Echocardiogram:** This may suggest the location of the vegetations.

Differential Diagnosis

The possibility of infective endocarditis should be suspected in any patient with a cardiac murmur and unexplained fever present for at least one week. Some clinical conditions, which have similar manifestations, i.e. fever, murmur and embolic episodes, are:

1. Acute rheumatic fever
2. Non-bacterial thrombotic endocarditis
3. Atrial myxoma
4. Systemic lupus erythematosus
5. Sickle cell disease

Hence a definitive diagnosis can only be made on positive blood culture though a negative blood culture does not rule out the possibility of infective endocarditis. Two-dimensional echocardiogram is also very useful.

Treatment

The cellular and humoral host defense mechanisms that normally eliminate organisms from other sites are not very effective in endocarditis. Hence, inhibition of the growth of the microorganism is not adequate for cure. In fact, the *bactericidal drug regimens* are necessary and the treatment must be continued for a long enough period of time to achieve sterilization of the vegetations. In addition, sufficient concentrations of antimicrobial agents must be reached in the serum to guarantee penetration of antibacterial concentrations into the vegetations.

I. Antibacterial Drugs

A. Streptococci: Penicillin and Streptomycin exert a more rapid action than does penicillin alone. Penicillin G 4 million units 6 hourly IV with Gentamicin IV 1mg/kg (max 80 mg) 8 hourly. If the patient is hypersensitive to penicillin then Ceftriazone IV 2 gm is given once daily. If allergic to penicillin and cephalosporin, give Vancomycin IV 30 mg/kg/day 12 hourly (max 2g/day).

B. Staphylococci: For Staphylococcus aureus only Penicillinase resistant penicillins (i.e. cloxacillin-nafcillin, methicillin and oxacillin) or Cefazolin (2 gm of either IV every 4 hourly) may be used, and continued for 6 weeks. For organisms resistant to these antibiotics, Vancomycin 30 mg/kg/day 12 hourly IV for 6 weeks may be given.

C. Enterococci: For enterococcal endocarditis, Penicillin G IV 4 million units 6 hourly with Gentamicin 1-1.5 mg/kg. 8 hourly. No alternate drug has been tested for efficacy in enterococcal endocarditis; hence if the patient is sensitive to penicillin, a desensitizing procedure should be tried. This involves a scratch test through a drop of penicillin G (100 units/ml). This is followed in 30-45 min. by graded amounts of penicillin intradermally, beginning at 0.001 units per 0.1 ml. of test solution and continued in tenfold increment every 30-45 min. With increasing amounts, administration is changed to the subcutaneous, intramuscular and finally the intravenous route. Epinephrine and diphen-hydramine should be on hand for emergency use during the procedure, if an anaphylactic reaction occurs. It is important to maintain continuous IV administration of penicillin throughout the course of treatment. If the IV infusion

is stopped it may be necessary to repeat the entire "desensitization".

If the patient still develops severe reaction, Vancomycin may be used as for streptococcal endocarditis.

D. Other organisms

1. *E. coli and Proteus mirabilis:* Penicillin, Ampicillin or cephalosporin
2. *Salmonella:* Ciprofloxacin or Chloramphenicol
3. *Klebsiella:* Cefotaxime
4. *Enterobacter, Pseudomonas and Proteus other than P. mirabilis:* Piperacillin, Ceftazidine, Amikacin or Ciprofloxacin.
5. *Fungal:* Amphotericin B 1 mg/kg/day IV and Flucytosine PO 150 mg/kg/day in 4 divided doses.

E. Emperic Therapy till culture report available:

Ampicillin IV 2 g 4 hourly + Nafcillin IV 2 g 4 hourly + Gentamicin IV 1mg/kg 8 hourly or Vancomycin IV 1 mg/kg/day 12 hourly (for penicillin-allergic patients) + Gentamicin 1 mg/kg 8 hourly.

Response to Therapy

1. The blood culture becomes negative within several days after the onset of therapy.
2. Regression of fever, weight gain and a fall in ESR occur soon, but may take several weeks.
3. Hematuria and proteinuria disappear along with the therapy.
4. Regression of clubbing takes several weeks.
5. Splenomegaly may persist for many months.
6. Although anemia may respond in several weeks, the rise in hemoglobin may be very slow.

Prognosis

With the antimicrobial therapy the prognosis for infective endocarditis is good. The factors that tend to make the prognosis poor are:

1. Non-streptococcal disease
2. Development of heart failure
3. Aortic valve involvement
4. Prosthetic valve involvement
5. Old age

Prophylaxis

Indications:

1. Prosthetic heart valves
2. Prior endocarditis
3. Unrepaired cyanotic congenital heart disease
4. Repaired congenital heart defects (for 6 months)
4. Valvulopathy developing after cardiac transplantation

Treatment:

1. Oral hygiene must be optimum.
2. *For dental manipulations* and other procedures in the oropharynx, prophylaxis is directed against *Streptococcus viridans.*

   Oral regimens: Amoxycillin 2 gm PO one hour prior to procedure.

   For penicillin allergic patients: Erythromycin or Clarithromycin 500 mg PO 1 hr before procedure or Clindamycin or Cephalexin.

   Parenteral regimens: Ampicillin 2 g IV within 1 hr before procedure or Clindamycin 600 mg IV 1 hr before procedure.
3. *For genitourinary or gastrointestinal tract* procedures or surgery, prophylaxis is directed against enterococci with Ampicillin 2 gm IV + Gentamicin 1.5 mg/kg IV or IM half an hour before the procedure followed by one dose of Amoxycillin PO 1.5 g 8 hours later.
4. *Cardiac surgery:* Prophylaxis is directed against staphylococci and consists of 2 gm Methicillin, Oxacillin, Nafcillin or Cephalothin IV every 4 hourly starting 1 hour before the procedure and continuing for several days.

5 › Ischemic Heart Disease

Definition: Ischemic heart disease (IHD) occurs whenever there is an imbalance between myocardial oxygen demand and its supply.

Causes: The commonest cause of IHD is atherosclerotic coronary artery disease. Other causes are:

I. *Atherosclerotic coronary artery disease*

II. *Other coronary artery diseases*
   1. Coronary artery spasm
   2. Coronary arteritis
   3. Embolism
   4. Coronary A-V malformation

III. *Valvular diseases*
   1. Aortic stenosis and regurgitation
   2. Mitral valve prolapse

IV. *Other cardiac disease*
   1. Hypertrophic cardiomyopathy
   2. Collagen disease
   3. Syphilis

V. *Increased demands*
   1. Thyrotoxicosis
   2. Anemia
   3. Beriberi

The exact cause for initiation and progress of atherosclerosis are unknown. However, certain factors may be responsible. These are called Coronary risk factors.

Table 5.12 : Coronary Risk Factors

Reversible	*Irreversible*
1. Tobacco smoking	1. Sex : Male
2. Hyperlipidemia	2. Family history of IHD
3. Diabetes	3. Type A personality
4. Hypertension	*Doubtful*
5. Obesity	1. Hypercalcemia, homocystenemia, fibrinogen, lipoprotein 'a'
6. Physical inactivity	2. Cardiac transplantation
7. Stress	3. Trace elements

Coronary Anatomy

There are 2 coronary arteries - left (LCA) and right (RCA) that arises from the aorta at the sinus of Valsalva.

The left main (LM) stem is short and divides into left anterior descending (LAD) - which supplies major part of the left ventricle (LV) and the anterior part of interventricular septum (IVS) - and the circumflex (CX) - which supplies the posterior and variable amounts of the inferior LV, sinoatrial (40%) and atrioventricular nodes and sometimes LV apex and posterior wall. RCA supplies the RV, sinoatrial node (60%) and posterior part of IVS.

The dominant circulation refers to the artery which gives rise to the "posterior descending artery" which supplies posterior part of IVS. Hence it may be either right dominant or left dominant circulation. Right dominant is more common.

Coronary Physiology

During stress, the coronary blood can be increased 5-6 times the basal values. This is regulated by coronary autoregulation mechanism. In the resting state, coronary blood flow is adequate until there is 75% or more narrowing of epicardial artery.

During stress, the perfusion pressure does not increase, but the increased flow is maintained by coronary vasodilatation, which is controlled by various metabolites like adenosine, prostaglandins, carbon dioxide and hydrogen ions. The coronary vascular resistance would fall to 20-25% of basal state in response to maximal demand on exercise. The ability to lower the resistance to flow at rest, even when there is an 80% reduction in the diameter of a large coronary artery, allows a patient to be asymptomatic in spite of large reductions in internal diameter of the artery.

Clinical Presentations

1. Angina - typical and atypical
2. Acute myocardial infarction
3. Ischemic cardiomyopathy
4. Cardiac arrest
5. Sudden cardiac death
6. Asymptomatic coronary artery disease detected on the routine medical checkup (Silent ischemia)

Angina Pectoris

Heberden in 1769 gave the first description of typical angina pectoris. It is substernal pain or heaviness, radiating to both arms or ulnar border of the left arm, jaw, teeth, occipital region or epigastrium.

Variation to the above may be 'gas' in the substernal

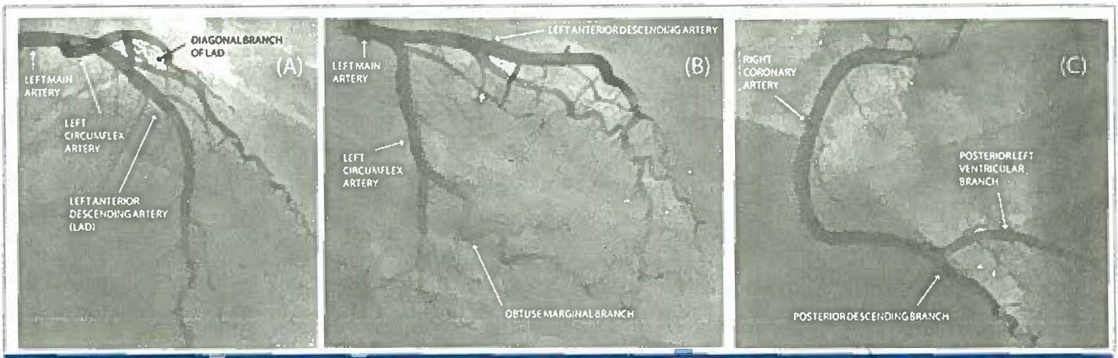


Fig. 5.17 : (A) Coronary Angiography of Left Coronary Artery in PA Cranial View; (B) Coronary Angiography of Left Coronary Artery in RAO Caudal view; (C) Coronary Angiography of Right Coronary Artery in LAO Cranial View

region or pain in the areas of radiation without substernal pain.

Sometimes there may be breathlessness or fatigue due to low cardiac output.

Types

1. **Stable:** It occurs with known physical effort and is relieved with rest and nitrates. Cold weather, smoking, emotional upset, high altitude, sexual intercourse and straining at stools can also aggravate it.
2. **Nocturnal:** Angina appears in the middle of the night due to left ventricular failure which may be precipitated by dreams causing release of catecholamines a full urinary bladder or transient hypoglycemia.
3. **Unstable:** This is also called Preinfarction angina as 20% of these patient develop myocardial infarction within 4 months.

   The following types of anginal pains are called unstable angina:

   a. Recent angina (less than 60 days)
   b. Stable angina in which symptoms are more severe in intensity, frequency and duration (Crescendo)
   c. Angina at rest and lasting > 10 minutes
   d. Angina not relieved by rest or nitrates
4. **Prinzmetal angina:** This was described by the early hours of morning associated with ST elevation on ECG. It responds to nifedipine or nitrates as it is caused by coronary spasm that can be induced by smoking or hyperventilation. Spasm may be caused by increased alpha-adrenergic activity during early hours of morning or due to platelet aggregation. Though coronary arteries can be normal on angiography, in 50% of patients there may be associated coronary artery obstructive disease. Beta-blockers may aggravate the spasm and hence are contraindicated.
5. **Post infarction angina:** Some patients with myocardial infarction develop angina 2 days to 8 weeks following the infarction. Most of them have multivessel disease and residual myocardial ischemic. They require early coronary angiography and appropriate treatment.

Table 5.13 : Assessment of Chest Pain

Modified Canadian Cardiovascular Society Criteria

Grade	
I.	Angina only on strenuous or prolonged exertion
II.	Angina climbing two flights of stairs
III.	Angina walking one block on the level
IV.	Angina at rest

* 1 block = 100 meters

Diagnosis

I. **Clinical:** A typical history of angina itself could give the diagnosis even in absence of any other abnormality on examination or investigation. Though physical examination in angina is often normal, certain clues to the presence of IHD may be present - Gallop rhythm (third heart sound), left ventricular enlargement, thickened blood vessels or absent pulses, systolic murmur

of mitral regurgitation or papillary muscle dysfunction or basal rales may be present.

Table 5.14 : Functional Classification of Fatigue, Palpitation, Dyspnea or Anginal Pain *[New York Heart Association (NYHA)]*

In a patient with established cardiac disease:
I. *No limitations to physical activity.* Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
II. *Slight limitation of physical activity:* Comfortable at rest. Ordinary physical activity results in fatigue, palpitation dyspnea, or anginal pain.
III. *Marked limitation of physical activity:* Comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea or anginal pain.
IV. *Symptoms at rest:* Inability to carry on any physical activity without discomfort. Symptoms of fatigue, palpitation, dyspnea or anginal pain may be present even at rest. It any physical activity is undertaken, discomfort is increased.

II. Diagnostic Tests:

1. *ECG:* In 50% of patients with angina, resting ECG may be normal at rest. During anginal episode, ST depression (stable/unstable angina) or elevation (Prinzmetal type) may be present. These may disappear with rest or following sublingual nitrates or nifedipine.
2. *Cardiac Enzymes (CK-MB, Trop T/Trop I):* In angina, cardiac enzymes are normal. In a patient with typical chest pain and ECG changes of ST depression, if enzymes are normal, then it is UNSTABLE ANGINA. If enzymes are raised, then it is a non-ST segment elevation MI (NSTEMI).
3. *Stress testing:* This is done with treadmill or bicycle ergometer using standard protocols like Bruce's. The workload is gradually increased by increasing the speed and elevation of the treadmill. The patient is exercised up to predicted target heart rate (220 - Age in years) or till there is ECG changes of ischemia, hypotension gallop, pain, fatigue, dyspnea or hypotension.

   This test though very popular can give both false positive and false negative results. It is contraindicated in unstable angina, acute myocardial infarction, heart failure, arrhythmias, A-V blocks, severe aortic stenosis and debilitating conditions.
4. *Thallium Stress Test:* This test is done by injecting Thallium whilst the patient exercises and then the regional myocardial perfusion is assessed by using a gamma camera. Thallium is picked up only by normal myocardium; ischemic areas would appear as perfusion defects. However, scans taken 2-4 hours after exercise may show reperfusion of Thallium in the ischemic zone signifying reversible ischemia. The necrosed area continues to remain cold. This has 85% specificity and sensitivity.
5. *Holter Monitoring:* Ambulatory ECG monitor may detect episodes of ST segment changes during normal activities. Some of the episodes of ST segment changes during normal activities. Some of the episodes of ST-T changes may not be accompanied by symptoms (Silent ischemia).
6. *Echocardiography and Doppler study:* This is helpful to judge the regional wall motion abnormality, left ventricular thrombus, ejection fraction and mitral and mitral regurgitation. Stress echocardiogram can identify regional wall motion abnormality immediately after exercise.
7. *Coronary angiogram:* This is a specific test to diagnose blockage of coronary arteries and its location and severity. It is usually indicated in severe angina not responding to medical treatment in whom revascularization through angioplasty or by pass surgery is planned.

Differential Diagnosis

I. Non-coronary cardiac causes

1. *Cardiomyopathy:* There is usually a gallop rhythm with systolic murmur of papillary muscle dysfunction. However, chest pain is more prolonged and not typically constricting. Echocardiogram identifies cardiomyopathy.

2. *Mitral valve prolapse:* The chest pain is rarely typical anginal, is usually prolonged, associated with anxiety and is more common in females. A mid-systolic click with a murmur may be present.

II. **Neuropsychiatric (anxiety state):** The pain is usually stabbing or jabbing without any relation to exertion. It also lasts longer and may be associated with palpitations, perspiration and cold limbs ECG is usually normal.

III. **Musculoskeletal**

1. *Costochondritis (Tietze's syndrome):* There is local pain and tenderness with swelling over costochondral junction, which may be mistaken as angina. ECG usually normal.
2. *Cervical Spondylitis:* There is usually radiating pain from the neck going to the arms and sometimes chest. It is associated with paresthesia ECG is normal and X-ray spine may show cervical spondylitis.
3. *Herpes Zoster:* In the pre-eruptive phase, herpes zoster of the left side of chest may mimic angina. However, it is usually in the distribution of the nerve root. Once eruptions appear as typical herpetic vesicles, the diagnosis is clear.

IV. **Pulmonary**

1. *Pneumothorax (Left-sided):* May cause chest pain, which may suggest IHD. However, there is shift of the mediastinum to the right and decreased breath sounds.
2. *Pneumonia:* Left sided pneumonia can cause chest pain, which can mimic angina. There is usually no relation to exertion but the pain is aggravated on inspiration. Fever and constitutional symptoms may be present.

V. **Gastrointestinal**

1. *Hiatus hernia:* The chest pain is usually a feeling of heartburn or indigestion, which occurs after meals on postural changes without any relation to effort. It can mimic nocturnal of postprandial angina. Stress test is usually normal and barium studies of esophagus may demonstrate the lesion.
2. *Achalasia Cardia:* There is squeezing pain in the substernal area radiating to the jaw or arm and precipitated by food. There may as associated dysphagia for liquids more than solids. ECG is normal and barium studies would show the spasm.
3. *Cholecystitis and Gallstones:* The pain is usually in the epigastrium or right hypochondrium with nausea and vomiting. Gallstones can be seen on sonographic examination of upper abdomen.
4. *Peptic Ulcer:* The pain has burning character and has no relation to effort. It also lasts longer.
5. *Splenic flexure syndrome:* Distension of splenic flexure of colon can cause precordial pain referred to the shoulder. The pain has no relation to efforts and is often relieved on passing flatus or stools.

Management

I. **Treatment of acute attack**

1. *Di-Nitrates:* Glycerine trinitrate 0.5 mg. or isosorbide dinitrate 5 mg sublingually relieves the attack in 2-5 minutes (Mononitrates are contraindicated). Rarely relief may nor occur or may be followed rapidly by a relapse. It may cause slight heaviness in the head and hypotension. It is also available as ointment to be applied on the skin.
2. *Beta-blockers or Calcium channel blockers:* May be used to decrease pain.

II. **Prevention of anginal attacks**

1. *Modification of life style:* Life style should be changed to avoid precipitating factors. Exertion, especially following meals, walking uphill against the wind must be avoided. Emotional disturbances like anger and anxiety must be avoided if possible.
2. *Rest and Exercise:* Bed rest is usually not required unless there are frequent attacks or there is angina decubitus. Exercise that does not cause pain or breathlessness may be allowed.
3. *Control of risk factors:* The risk factors must

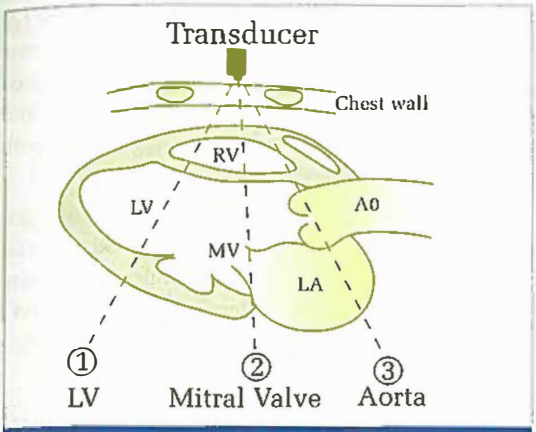


Fig 5.18: M mode echocardiography showing position of transducer and directions of ultrasonic beam. 1: Beam transverses left ventricle (LV) below mitral valve. Systole and diastole are indicated. 2: Beam demonstrates mitral valve (MV). 3: Beam transverses aortic valve (AV) and aorta (Ao)

be controlled if present. Hypertension, diabetes and hyperlipidemia (with statins) must be treated with drugs if required. Obese patient must be asked to reduce weight. Smoking must be strictly forbidden.

4. *Tranquilizers:* Diazepam 5-10 mg 6-8 hourly or Alprazolam 0.25 - 0.5 mg 8 hourly may be given to relieve anxiety.
5. *Coronary Vasodilators:*
   a. *Nitrates:* Isosorbide dinitrate 5 mg 6-8 hourly may be given sublingually for best effect. An extra dose may be given prior to an anticipated attack. 2% nitroglycerine ointment may be applied over the arm or chest 3-4 times a day. Mononitrates like Isosorbide mononitrate (20 mg) are usually given

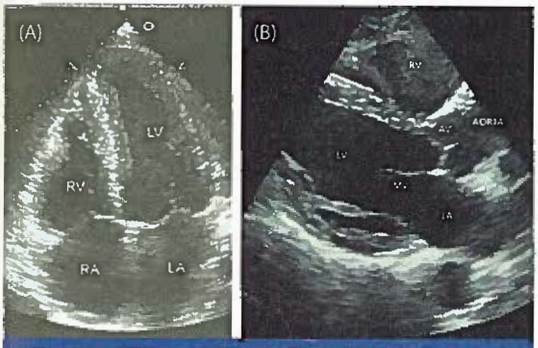


Fig. 5.19: (A) Normal Echocardiogaphy - Four Chamber View, (B) Normal Echocardiography - Parasternal Long Axis View

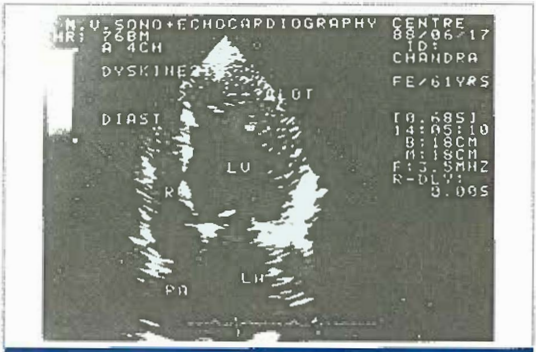


Fig. 5.20: Shows intact interventricular septum. There is dyskinesia of the lower septal and apical segments of the left ventricle. The LV cavity is dilated. There is suggestion of a clot at the LV apex.

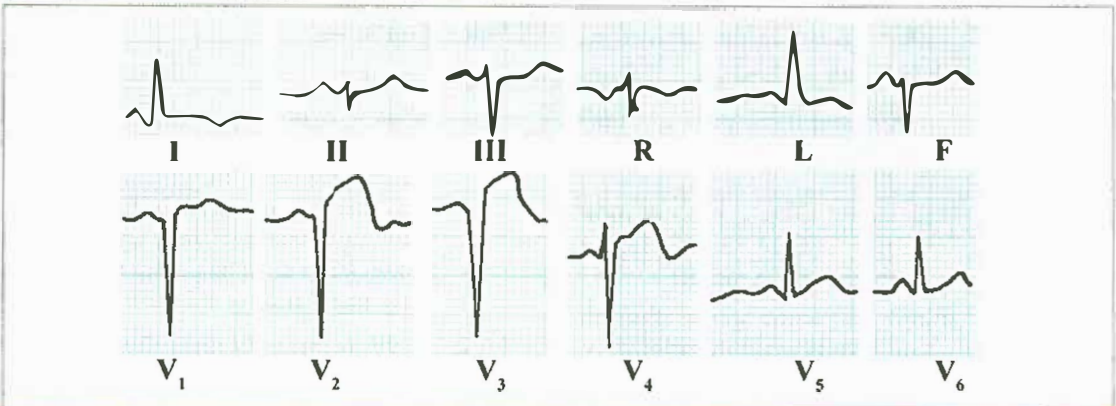


Fig. 5.21: ECG showing acute anteroseptal myocardial infarction. There are inverted T waves in leads I and aVL and QS pattern in leads V1, V2 and V3.

at 8 a.m. and 4 p.m. in an eccentric dosing fashion to avoid tolerance.

b. *Calcium antagonist drugs:* Nifedipine 10 mg, Diltiazem 30 mg or Verapamil 80 mg 4 times a day may be given to relieve angina.

6. *Beta-blockers:* Beta blockers reduce the oxygen requirement of the heart by reducing the heart rate, blood pressure and cardiac contractibility. Propranolol or oxprenolol 40 mg 6-8 hourly may be given. They are contraindicated in presence of associated cardiac failure, bronchial asthma or Prinzmetal angina. Atenolol or Metoprolol in small doses (50 mg daily) may be given in such situations, as they are cardio selective.

7. *Ace Inhibitors / Angiotensin Receptor Blockers* are useful in chronic IHD to prevent remodeling of heart. They are associated with decreased mortality (e.g. Ramipril, Lasartan).

8. *Antiplatelet drugs:*

a. *Low-dose Aspirin:* It acetylates cyclo-oxygenase and inhibits thromboxane A synthesis which causes platelet aggregation and is a potent vasoconstrictor. It is given in the dose if 75-150 mg per day.

b. *Dipyridamole:* It decreases platelet aggregation in the dose of 200-300 mg per day and has been used in angina. Combined with aspirin, the dose required is half.

c. *Ticlopidine:* This inhibits the final stage of platelet aggregation. It is not used any more.

d. *Clopidogrel:* Blocks platelet ADP receptor and decreases platelet activation. Dose 75 mg OD.

e. *Newer Antiplatelet agents:* Prasugrel 10 mg OD, Ticagrelor 90 mg BD, IV Cangrelov.

9. *Glycoprotein IIb/IIIa Inhibitors*; Abciximab 0.25 mg/kg bolus followed by 0.125 µg/kg/min. Eptifibatide, Tirofiban inhibit the Gp IIb/IIIa receptors on platelets and decrease platelet aggregation. They may be used instead of heparins in unstable angina, and for patients undergoing angioplasty with stenting procedure (Facilitated PTCA).

10. *Anticoagulation:* In unstable angina, unfractionated I.V. heparin 5000 units stat followed by 1000 units/hour can be given. Newer Low Molecular Weight (LMW) Heparins may also be used (See Ch. 15).

III. Definitive Treatment of Angina

Coronary Revascularization : A coronary angiography should be done to determine the coronary anatomy and to detect coronary artery disease. Revascularization is offered with percutaneous Transluminal Coronary Angioplasty (PTCA) or Coronary Artery Bypass Grafting (CABG) Surgery (Ref. to Pg. 217)

Myocardial Infarction

Myocardial infarction results from thrombotic occlusion (or sometimes prolonged spasm) of the infarct related blood vessel. Myocardial ischemia and necrosis occurs from subendocardial to subepicardial region. The entire process takes 6 hours to complete.

Types:

1. *S. T. Elevation MI:* ECG shows changes of S. T. Elevation & Elevation of cardiac enzymes.
2. *Non S.T. Elevation MI:* ECG does not shows S.T. Elevation but cardiac enzymes are raised.

Clinical Features

A. Symptoms:

1. *Pain in chest:* Pain in chest is a cardinal symptom of acute myocardial infarction. It is abrupt in onset. The site and radiation is like that of angina pectoris, but there may be no pain in chest even with extensive myocardial infarction, especially in long standing diabetics.
2. *Breathlessness:* Breathlessness is actually present with pain, but rarely it may be the only presenting symptom.
3. *Vomiting:* It is a common feature especially

in severe cases and is often associated with cardiogenic shock.

4. *Collapse:* The patient may be pale, ashen grey or cyanosed with intense perspiration. The patient may be restless, excited and rarely unconscious.

B. Signs:

1. *Pulse:* Fast and feeble pulse is usually present.
2. *BP:* Initially there is a rise in BP, which may be followed by a fall especially if cardiogenic shock occurs.
3. *Heart sound:* The heart sounds are usually muffled. A third heart sound gallop may be heard with a typical tic-tac rhythm.
4. *Lung signs:* The lungs may be normal or a few basal rales may be auscultated if there is left ventricular failure.
5. *Late signs:* On the second or third day mild fever of 38-39 C may occur. Pericardial rub may transiently appear around the same time.

Table 5.15 : Differences between Angina Pectoris and Myocardial infarction

	Anginapectoris	*Myocardial infarction*
Chest pain	Short duration often relieved by nitrates	Longer duration usually not relieved so rapidly by nitrates
Precipitating factors	Exertion or following meals or cold	May be absent
Breathlessness, vomiting, collapse and sweating	Absent	Present
Gallop rhythm	Absent	Present

Investigations

I. **Non-specific tests:** Polymorphonuclear leucocytosis with high ESR may be seen in the first week due to tissue necrosis.

II. **ECG changes:** The earliest change is ST segment elevation with the onset of pain. Q waves appear when transmural infarction occurs. By about 24 hours ST Segment reverts to normal and T wave becomes inverted.

In the leads opposite to the site of infarction there is ST depression even earlier than ST segment elevation (Reciprocal Changes).

Depending upon the area involved these changes are seen in respective leads:

1. *Anterior:* I, aVL, V_1 - V_6
2. *Lateral:* V_5V_6
3. *Antero-septal:* V_3-V_4
4. *Medial:* V_1-V_2
5. *Inferior:* II, III, aVF
6. *Right Ventricular:* ST deviation in V_1R
7. *Posterior:* ST depression with tall T and R in V_1 and V_2

New onset LBBB: May be sign of AMI requiring thrombolysis

III. **Serum Enzymes:** Myocardial necrosis leads to liberation of certain enzymes which may be elevated in blood, SGOT, LDH, Troponin and CPK levels rise. The isoenzymes Troponin and CPK (MB fraction) are more specific for myocardial infarction. The importance of these is as follows:

Table 5.16 : Serum Enzymes in Myocardial Infarction

Enzyme	*Normal Value*	*Earliest Rise in*	*Peak by*	*Normal by*
SGOT	0-35 U/L	8-12 hr	36-48 hr	7-10 days
LDH	45-90 U/ml	12-24 hr	24 hr	8-14 days
CPK	25-90 U/l	8 hr	24-30 hr	3-4 days
CPK-MB	4-6% of CPK	4-8 hr	18-24	3-4 days
Troponin T/I	<60 ng/h	4-12 hr	24-48 hr	7-14 days

IV. **Echocardiography:** This detects myocardial ischemia almost immediately by showing regional wall motion abnormality.

V. **Angiography:** Done when Primary Percutaneous Transluminal Coronary Angioplasty (PTCA) has to be performed.

Differential Diagnosis

1. **Pulmonary embolism:** Massive pulmonary embolism may mimic coronary artery disease. However, cyanosis and tachypnea is more.

Usually, it occurs in postoperative patient or those with prolonged immobilization. ECG would show typically prominent S wave in I and Q wave and inverted T wave in III (S1Q3T3).

2. **Acute pericarditis:** The pain is either precordial or substernal and radiates to the shoulder. However, it is not related to exertion or meals. Pericardial rub may be present. ECG shows ST elevation with concavity upwards.
3. **Pneumothorax:** Left sided pneumothorax may cause chest pain, which has no relation to exertion but increases in inspiration. There is shift of mediastinum to the opposite side and diminished breath sounds.
4. **Gastrointestinal hemorrhage:** Gastric hemorrhage patient may have epigastric and substernal pain with vomiting and cold limbs and this resembles acute myocardial infarction. Usually stools would be black and ECG would not show the changes of infarction.
5. **Acute pancreatitis:** Epigastrium pain usually goes to the back, but otherwise it may be confused with acute myocardial infarction. Here, serum amylase is usually high.

Management

I. General Measures:

1. *Coronary Care Unit (CCU):* Patients with a presumptive diagnosis of acute myocardial infarction (AMI) should be admitted to a CCU for continuous ECG monitoring. The CCU makes available trained personnel, facilities and equipment to deal with disturbance of cardiac rhythm and pump function. Uncomplicated patients can be transferred out of CCU after 3 days.
2. *Activity:* Bed rest must be given at least for the first 24-48 hours. The traditional approach is to prescribe prolonged bed rest because early ambulation may precipitate arrhythmias and heart failure, cause extension of the infarction and later lead to the development of ventricular aneurysm and rupture. With uncomplicated myocardial infarction, mobilization can be started by the second day and patient discharged after 7 days, without a higher risk of reinfarction, arrhythmias and sudden death. However, in patients with anteroseptal myocardial infarction and bundle branch block, the risk of late, in-hospital, death after being discharged from the coronary care unit is higher.

   The case against prolonged bed rest has been that it can lead to development of thrombophlebitis and pulmonary embolism. This risk is usually not commonly seen in our population, especially if the patient is on anticoagulants. Stool softeners or laxatives should be given to prevent straining while passing stools.
3. *Oxygen:* Oxygen (nasal mask) at the rate of 2 liters/min for at least 4-6 hours per day should be given initially. Patients with any degree of arterial hypoxemia whether resulting from acute pulmonary congestion or preexisting lung disease should receive oxygen and have serial arterial oxygen measurements to assess the efficacy of treatment.
4. *Diet:* Usually a diet of 1500 calories of soft food with increased bulk (to prevent constipation) and no added salt is given. Obese patients are made to lose extra fat during this time. Initially (for the first 24 hours only) liquids and fruits are advised. Feedings should be small and frequent i.e. 4-7 times a day. Oral fluid intake should be around 2 liters/day. Diet light in texture minimizes the risk of aspiration in case of cardiac arrest.
5. *Control of chest pain:*
   a. Sublingual nitroglycerine 0.3 - 0.4 mg should be repeated every 5-10 min until chest pain is relieved or tachycardia and hypotension occurs.
   b. Beta-blockers: Metoprolol 5 mg IV over 2 minutes. Repeated after 5 min for 3 doses.
   c. Morphine hydrochloride 15 mg SC or 2-4 mg IV slowly should be given if the chest pain is not relieved by

nitrates in 30 min. Morphine has vagotonic effects. Hence, in inferior wall infarction with conduction disturbances, pethidine 50100 mg IM is preferred. Pentazocin with diphenylhdramine is the alternative if morphine is not available.

6. *Prevention of ventricular fibrillation:* All patients were earlier treated with lidocaine to prevent ventricular fibrillation especially if there is no cardiac failure or shock. However, this is no longer indicated.

Reperfusion Therapy

I. During the first 12 hours (Hyperacute phase)

A. *Intravenous thrombolysis:* Thrombolysis should be given within 3 hours of infarction but can be given upto 12 hours. The agents used are:

i. Streptokinase: 7,50,000 to 15,00,000 units over 30-60 minutes.

ii. Urokinase: 15,00,000 units over 30-60 minutes.

iii. Fibrin Specific Agents:

1. Tissue Plasminogen Activator (tPA) (15 mg bolus IV followed by 50 mg IV over 30 min followed by 35 mg IV over 60 mins).
2. Tenecteplase (TNX) 0.53 mg/kg over 10 sec
3. Reteplase (rPA) 10 million units bolus over 2-3 min, which is repeated after 30 min.

B. *Mechanism of Action*

1. Streptokinase binds to plasminogen to form an activator complex that converts it to plasmin, which lyses the thrombus.
2. Urokinase, a product of human renal tubular cells acts as a direct activator of the fibrinolytic system. It is more clot-specific than streptokinase and causes less bleeding complication, reduction of fibrinogen and antigenicity.
3. Tissue-type plasminogen activator (tPA) and other fibrin specific antithrombolytics have greater clot selectivity than streptokinase or urokinase and tPA at therapeutic doses does not cause systemic fibrinolysis. Recently large quantities of tPA have been obtained by successful cloning and expression of human tPA gene in *Escherichia coli.*

Indications for thrombolysis:

Thrombolytic agents are indicated in the first 3 hours after onset of symptoms and are alternative to primary PTCA due to logistic difficulties with PTCA.

Contraindicated in patients with active bleeding, BP > 180 mmHg SBP, or >110 mmHg DBP, H/O hemorrhagic CVA at any time in the past, non-hemorrhagic CVA in last 1 year and aortic dissection. Relative contraindications are pregnancy, peptic ulcer, breathing diathesis, major surgery in last 2 weeks, use of streptokinase in last 2 years.

Side Effects : Allergic reaction to streptokinase, hypotension, bleeding

B. *Percutaneous transluminal coronary angioplasty (PTCA):*

It is the best therapy for patients with STEMI. It implies balloon dilatation of the stenosed infarct-related artery. It is usually accompanied by non-balloon techniques:

1. *Stents*: Bare-metal stents or Drug-

Table 5.17 : Types of PTCA

Type of PTCA	Indications
Primary PTCA or Primary Angioplasty in MI (PAMI)	AMI presenting > 3 hr after onset of pain or < 3hr, if PTCA facilities are readily available in hospital
Rescue PTCA	Thrombolysed patients who have persistent or recurrent chest pain/ ST elevation after > 90 min (Failure of Thrombolysis)
Elective PTCA	After thrombolysis, prior to discharge or on follow-up
Facilitated PTCA	Accompanied by use of GpIIb/IIIa inhibitors

eluting stents coated with taxol (paclitaxel), rapamycin (sirolimus), everolimus, zotarolimus or biolimus.

2. Thrombus aspiration devices to aspirate large thrombus burden in a STEMI.
3. *Atherectomy Devices* for coronary calcific deposits

C. *Pharmaco-invasive Therapy:* It is a combination of thrombolysis & coronary angioplasty (PTCA). It is used when there could be a delay in transfering the patient to a center where PTCA is possible. Thus full dose thrombolysis is given to the patient followed by immediate transfer to a PTCA centre. PTCA is planned within 2-12 hours of thrombolytic therapy.

D. *Coronary Artery Bypass Grafting (CABG):* CABG is a well-established and safe method to restore myocardial perfusion. It is rarely required in an emergency setting. It is useful in the following groups of patients:

1. Multivessel coronary disease (Triple vessel disease or > 2 vessels involved including proximal LAD)
2. Left main coronary artery stenosis
3. Patients in whom PTCA or thrombolysis are ineffective
4. Patients with mechanical complications like acute mitral regurgitation.

II. Between 12 hours and 3 days (Acute Phase)

During this phase the effort of the physician is to limit the infarct size by decreasing oxygen consumption and decreasing the incidence of cardiac arrhythmias and failure.

A. *Anticoagulation:* Administration of anticoagulants helps to reduce thrombophlebitis and pulmonary embolism. A mini-dose of heparin 2000-5000 units every 6-8 hourly initially and then given every 8-12 hours subcutaneously, for the first 4-5 days, is recommended. Now conventional heparins are being replaced by low molecular weight (LMW) heparins (See Management of Unstable Angina). Later, long-term anticoagulation for uncomplicated infarcts is controversial, but there is an agreement that anticoagulants must be administered only in the hospital. In patients of AMI, strokes resulting from embolization of left ventricular mural thrombi to the brain occur predominantly (23 times) in patients with high creatinine kinase levels (over 8 times normal). In such patients full dose heparinization may prevent the formation of large left ventricular thrombi and decrease the risk of cerebrovascular accident.

Anticoagulants are also useful to prevent AMI in unstable angina and occurrence of re-occlusion after thrombolytic therapy has restored perfusion of the artery.

B. *Anti-platelet Agents:* Aspirin 325 mg stat followed by 75-150 mg/day with Clopidogrel 300 mg stat followed by 75 mg/day. GpIIb/IIIa Inhibitors may be used in Facilitated PTCA.

C. *Beta-adrenergic blocking drugs:* Beta-blockers reduce myocardial oxygen consumption by reducing the heart rate, blood pressure and myocardial contractility. They redistribute blood to ischemic areas and augment collateral blood flow. In addition, they inhibit platelet aggregation and shift the oxyhemoglobin dissociation curve to the right. Patients with hyperkinetic circulation, anxiety and without cardiac failure, conduction disturbances or bronchospasm are ideal candidates for beta-blockers. Propranolol 1 mg IV is given every 5-10 min up to a total dose of 0.1 mg/kg. Oral therapy can then be started. Metoprolol or Atenolol can be given 5 mg every 2-3 min up to 3 doses followed by 100 mg BD orally.

D. *Calcium channel blockers:* In acute myocardial infarction, nifedipine not only does not decrease infarct size but may increase the ischemic damage due to decreased perfusion pressure and

reflex tachycardia. However, in cases with recurrent or persistent ischemia after myocardial infarction, especially where the pathogenetic mechanism is likely to be coronary vasospasm, it is useful. It is also used if beta-blockers or nitrates are not tolerated or are contraindicated.

E. *ACE inhibitors or ARB* decrease ventricular remodeling and therefore decrease mortality and are used in all AMI patients specially if associated with decreased KV function (e.g. Ramipril or Losartan (See Ch. 15 for details)).

F. *Nitroglycerine and Nitrates:* Nitrates reduce infarct size by reducing preload increasing collateral blood flow to the ischemic zone and relieving coronary vasospasm. Nitroglycerine (NTG) can be given sublingually or as ointment. For severe and recurrent angina I.V. NTG is given at 10 mcg/min., increased every 5 min. by 10 mcg/min. until angina is controlled or systolic BP is less than 100 mmHg or the dose has reached 200 mcg/min. If the patient's condition is stabilized for 48 hours and no re-infarction occurs. I.V. NTG is discontinued and the patient put on oral nitroglycerine or isosorbide dinitrate.

I.V. NTG is given to patients who are normotensive with left ventricular failure (Pulmonary wedge pressure > 16 mmHg and cardiacindex less than 2.5 L/min/M2).

G. *Nitroprusside (NP):* NP is useful for hypertensive patients, in the dose of 10 mcg/min and increased every 5 minutes by 5 mcg/min until angina is controlled or systolic BP is 120 mmHg. If there is no cardiac failure it can be combined with beta-blockers, which will prevent reflex tachycardia.

H. *Intra-aortic balloon counterpulsation (IABP):* This helps to maintain circulatory support for patients with cardiogenic shock. It favorably affects myocardial oxygen balance by decreasing demand (deflation of the balloon decreases the afterload) and increasing supply, (inflation of the balloon in diastole increase coronary perfusion pressure). However, because of the significant rate of complications and logistic difficulties associated with IABP, it is reserved only for very severe cases of angina not responding to other measures.

Prognosis

Bad Prognostic indicators in AMI

1. Old age, stress, history of diabetes
2. Previous myocardial infarction
3. CPK > 2000 IU/ml
4. ECG:
   a. Development of new intraventricular conduction defects
   b. Poor LV function
   c. Persistent heart block
5. Angiogram: Absent collaterals to jeopardized myocardium (non-patency of MI-related coronary artery)
6. Cardiogenic shock

Common Mechanisms of Death Following Myocardial Infarction

1. First few hours - Ventricular Fibrillation
2. First few days - Pump failure
3. First few months - Reinfarction

Treatment of Complications

Left Ventricular Failure

A. *Diuretics:* Furosemide 20-40 mg IV every 6 hourly is given if there is dyspnea or hypoxia, especially if pulmonary wedge pressure is over 18 mmHg. It favorable alters the myocardial oxygen supply by reducing left ventricular end diastolic volume and tension, which not only decreases myocardial oxygen demand but also increases coronary perfusion. However, it must be used carefully in mild failure brisk diuresis may reduce left ventricular filling pressure, activate renin-angiotensin system and arginine vasoconstriction, deteriorating the patient.

B. *Vasodilators:* Vasodilators like *nitroglycerine* (NTG) and *Nitroprusside* (NP) have beneficial hemodynamic effects in heart failure. They are most useful if the myocardial infarction is complicated by ventricular septal rupture or mitral regurgitation. The dose of these drugs should be adjusted such that pulmonary capillary wedge pressure is less than 20 mmHg and cardiac index greater than 2-5 L/min/M2. If blood pressure is less than 90 mmHg it must be combined with Dobutamine.

C. *Digitalis:* This is useful if there is cardiomegaly prior to ischemic episode or there is supra-ventricular tachycardia.

D. *Beta-adrenergic agonists:Dobutamine* is a synthetic sympathomimetic amine which does not alter the heart rate and blood pressure and does not increase the oxygen consumption of the heart. It is given in the dose of 2-15 mcg/kg/min. It increases the coronary and skeletal muscle perfusion over mesenteric and renal perfusion.

Dopamine, an endogenous catecholamine, exerts it inotropic effect directly on the myocardial beta-receptors and indirectly by releasing norepinephrine. It has a direct renal and mesenteric vasodilating effect in doses below 15 mcg/kg/min. It increases cardiac output and blood pressure. At higher doses it acts as arterial and arteriolar vasoconstrictor. Hence, initially dobutamine is the drug of choice. If hypotension does not respond, dopamine followed by norepinephrine is indicated.

Hypotension

A. *Hypovolemia:* Patients with acute myocardial infarction having peripheral hypoperfusion, in absence of pulmonary congestion and compensatory tachycardia should be given intravenous fluids. If blood pressure and peripheral perfusion normalize, no hemodynamic monitoring is required, otherwise it is required and fluids adjusted to achieve a pulmonary wedge pressure of about 20 mm Hg. If pulse rate is slow, intravenous atropine can be given to raise the heart rate of 90-100 beats/min.

B. *Right ventricular infarction:* This is seen with inferior or inferio-posterior infarction with hypotension in absence of pulmonary congestion. This is best treated with volume expansion, isoproterenol and dobutamine.

C. *Hypotension with normal systemic vascular resistance:* This is best treated with Dopamine.

Other complications

Arrhythmias, Pericarditis, LV aneurysm

6 Cardiac Failure

Definition

Cardiac failure is a condition where the heart fails to maintain an output sufficient for the needs of the body. It is usually a disturbance of ventricular function.

Classification

I. **Low Output or High Output**

1. **Low output cardiac failure:** There is primarily a lesion in the heart, which decreases the contractibility of the heart, and causes diminished cardiac output.
2. **High output cardiac failure:** There is primarily no lesion in the heart, but due to extra- cardiac conditions there is increased work load on the heart which causes cardiac failure with increased cardiac output.

Causes

I. Low output failure:
   - A. *Myocardial lesion:*
     1. Ischemic heart disease
     2. Rheumatic heart disease
     3. Myocarditis and cardiomyopathies
   - B. *Endocardial lesion:*
     1. Valvular lesion: Mitral, aortic, tricuspid and pulmonary stenotic or regurgitant defects
     2. Infective endocarditis
   - C. *Pericarditis* with or without effusion
   - D. *Congenital heart diseases:* PDA, VSD, ASD, etc.

E. *Vascular lesion:*
   1. Hypertension
   2. Aneurysm of aorta

II. High output failure

A. Thyrotoxicosis
B. Anemia and hypoproteinemia
C. Beriberi
D. AV Fistula
E. Cirrhosis of liver
F. Cor pulmonale
G. Paget's disease of bone

II. Left Sided or Right Sided Cardiac Failure (given below)

III. Systolic or Diastolic Cardiac Failure

1. Systolic Cardiac Failure : It results from impaired systolic function and reduced cardiac output. Usually seen in Ischemic Heart Disease. It is managed mainly by ionotropic agents e.g. Dopamine, Dobutamine and Digoxin.
2. Diastolic Cardiac Failure (Heart Failure with a normal ejection fraction (HFNEF) : It results from impaired diastole or reduced relaxation and ventricular filling. It is usually seen in systemic hypertension, constrictive pericarditis, restrictive cardiomyopathy and IHD. It is managed with vasodilators (ACE Inhibitors or Calcium Channel Blockers).

Clinical Features

I. Left Ventricular failure

A. Symptoms

1. *Due to back pressure effect:* Inability of the left ventricle to eject adequate blood leads to congestion in the pulmonary blood vessels. This causes exertional breathlessness. As the disease progress breathlessness increases and occurs even at rest. The patient may be comfortable only in the propped up position and increased vital capacity due to lowering of the diaphragm. Later the patient may be breathless even in propped up position (orthopnea).

   Paroxysmal nocturnal dyspnea and cough commonly occurs because of reduced vital capacity in supine position, reabsorption of tissue fluids from the lower limbs into the circulation and depressed respiratory center during sleep. The attacks are classically precipitated at night and may be characterized by sudden awakening with extreme suffocation, cyanosis, perspiration and air hunger. The patient may cough up frothy sputum, which may be pinkish (due to pulmonary edema). The episode may last from 5-20 minutes or more.
2. *Due to reduction in forward flow:* due to inadequate output of left ventricle. Blood flow to the vital organ suffers resulting in mental confusion, insomnia weakness and fatigue.

B. Signs

1. *Gallop rhythm:* Gallop rhythm or triple rhythm occurs due to the audibility of third or fourth heart sounds which resembles the sounds produced by galloping of horses. Normally in an adult only two heart sounds are heard. In cardiac failure, there is increased resistance to filling of left ventricle, hence blood flow through the atrio-ventricle valve is prolonged and results in the third or fourth heart sound. Associated with tachycardia it produces the classical tic-tac rhythm.
2. *Pulsus alternans:* Left ventricular failure alters the contractile forces of the heart, which may cause alternate large and small pulses without any change in rhythm.
3. *Basal rales:* Due to back pressure and congestion of the lungs, rales may be heard at both the lung bases initially and later throughout the lung fields. Fluid collection in the interstitial

spaces may cause rhonchi even in the absence of rales.

4. *Cheyne Stokes respiration:* This is alternate periods of apnea and hyperpnea, which occurs due to left ventricular failure. Signs of cardiac enlargement and of the causative disease may be present.

II. Right Ventricular Failure

A. Symptoms

1. *Due to back pressure:*
   a. *Pulmonary:* Cough, dyspnea and hemoptysis
   b. *Portal:* Anorexia, nausea, vomiting, abdominal fullness after meals and pain in the right hypochondriac region
   c. *Renal:* Nocturia and oliguria
   d. *Peripheral:* Edema of feet.
2. Due to diminished cardiac output: Weakness and fatigue

B. Signs

1. *Raised jugular venous pressure:* Normally at 45° position of the patient, the jugular veins are not visible. In cardiac failure, it is visible in the neck and at times may reach up to the angle of the sternum.
2. *Hepatomegaly:* Liver is enlarged and tender due to congestion; systolic pulsations may be present if there is tricuspid regurgitation.
3. *Edema:* Edema classically occurs over the legs and is pitting in character. If the patient has been continuously supine, edema may not be present over the legs but may be present over the sacrum because in that position, it is the most dependent part.
4. *Signs of TR and RV Enlargement:* Pansystolic murmur over the tricuspid area, increased in inspiration due to tricuspid regurgitation may occur. In late stages, cyanosis and cardiac cachexia may occur. Signs of right ventricular enlargement and evidence of the primary disease causing right-sided heart failure may be present.

B-Type Natriuretic Peptide (BNP): It is released by the ventricle in response to stretch or elevated filling pressures. It can be measured in the blood and is very useful in diagnosis, monitoring and prognosis of heart failure. BNP levels are very sensitive and specific for heart failure. BNP less than 100 pg/ml rules out cardiac failure.

Management

The treatment of cardiac failure aims at restoring the balance between the metabolic demands of the body and he heart's ability to meet these demands.

1. **Rest:** Complete bed-rest is the keystone of treatment. When the patient is dyspneic, bed-rest is given with the head end of the bed raised to 45°. The legs should be kept below the pelvis to prevent the fluid present in the legs to return to vascular system and precipitate pulmonary edema. Once weight loss and adequate diuresis occur, the patient may be allowed to sit on the bedside chair or use a bedside commode and he can be gradually mobilized. Prolonged bed-rest may predispose to venous thrombosis and pulmonary embolism, which can be prevented by leg exercise and elastic bandage wrapped around the legs.

2. **Diet:** The basic aim is to restrict sodium in diet. The amount of salt to be restricted depends upon the severity of cardiac failure. Normal diet contains 10-15 gm of sodium chloride or 46 gm of sodium. On avoiding salt in food and table salt this can be reduced to 2-4 gm of sodium/day and on completely avoiding salt in preparation, this can be further reduced to 1 gm sodium/day. Salt substitutes may be used to make the diet more palatable.

   Due to edematous gastrointestinal tract, digestion and absorption are poor. In addition, larger meal may cause pooling of blood to the gastrointestinal tract, thereby interfering with diuresis. Hence, instead of the traditional three meals, it is advisable to give frequent, small, liquid feeds.

If the patient is obese, loss of weight must be achieved by strict caloric restriction.

Usually fluid restriction is not required in cardiac failure. However, if edema is present with low serum sodium, fluids should be restricted.

3. **Diuretics:** In cardiac failure, there is always sodium and water retention. Hence diuretics are given to increase sodium extraction. Furosemide 40 mg orally or parenterally is a very potent and the most commonly used diuretic. Since the diuretic response is dose related, it can be increased if required. Since furosemide results in loss of sodium, chloride and potassium ions, the latter should be supplemented orally either as potassium chloride or as orange juice and coconut water, both of which are rich in potassium. Alternately, potassium sparing diuretics like spironolactone 25 mg four times a day, triamterene or amiloride hydrochloride can be used along with it.

   Other diuretics used are Torsemide, Hydrochlorthiazide, Chlorthalidone, Indapamide, Metolazone.

   Some patients with mild cardiac failure can be satisfactorily treated with a diuretic alone. Most patients will however require additional therapy. Failure of diuretic therapy may be due to high salt intake, electrolyte disturbances, inadequate renal perfusion or severe reduction in cardiac output.

   With the use of all diuretics it must be remembered that the compromised left ventricle is dependent on its preload to maintain the cardiac output.

4. **Digitalis:** Digitalis and the related cardiac glycosides have a direct cardiotonic action. They increase the force of myocardial contraction and decrease the work of the heart. Digitalis can be administered intravenously, intramuscularly or orally, rapidly or slowly. In rapid digitalization full digitalization is achieved within 24 hours and is usually given parenterally. If the patient is already on digitalis or has only recently stopped it, rapid digitalization parenterally may cause toxicity and hence it should be given orally. The commonly used drug is digoxin (0.25 mg tablets). The usual digitalizing dose is 1.5 mg. For maintenance 0.25 mg daily is adequate.

5. **Sympathomimetic amines:** Catecholamines stimulate the cardiac beta-adrenergic receptors and can be used to treat cardiac failure, but their effect increases the oxygen consumption and increases the work of the heart. Newer agents are free of these side effects and have been used in the treatment of acute and chronic cardiac failure.

   a. *Dopamine:* At low doses of 3-5 mcg/kg/min. dopamine increases the contractility of the heart by direct stimulation of the beta-adrenergic receptors cause vasoconstriction in all the vascular beds which increases arterial pressure, peripheral resistance and myocardial oxygen consumption. In severe cardiac failure dopamine can be combined with nitroprusside, which reduces afterload and thus increases cardiac output and decrease filling pressure.

   b. *Dobutamine:* It has a predominant effect on the cardiac beta-1 receptors with very slight activity on the vascular alpha and beta-2 receptors. At infusion rates of 2.5-15 mcg/kg min. it increases cardiac contractility and cardiac output, decreases filling pressure and causes minimal change in peripheral resistance. In acute myocardial infarction dobutamine increases cardiac output by 20% without altering the heart rate or blood pressure. Dobutamine increases collateral flow to the ischemic myocardium, thereby reducing the infarct size. The inotropic effects of dopamine do not persist beyond 24 hours whereas those of dobutamine persist. Both these drugs are complimentary and can be used together, dopamine is useful in hypotension, dobutamine is useful in low cardiac output because it causes reduction in filling pressures.

6. **Bipyridines:** These are non-glycoside positive inotropic agents that are affective both orally and intravenously. They reduce right and left ventricular filling pressures and systemic

vascular resistance with increase in cardiac output. This effect persists beyond 24 hours unlike dopamine. The two drugs useful in this group are Amrinone and milrinone.

Amrinone is given intravenously as a bolus of 0.75 mg/kg over 2-3 minutes followed by a maintenance infusion of 5-10 mg/kg/min. The side effects that can occur are fever, thrombocytopenia, nephrogenic diabetes insipidus, hepatitis and gastrointestinal disturbances.

Milrinone derived from amrinone, is more potent and with lesser side effects.

7. **Vasodilators:** In cardiac failure with loss of cardiac reverse, an increase in compensatory afterload results in increase in end-diastolic volume and pressure accompanied by a reduction in stroke volume. Vasodilators are useful by reducing afterload. They can be subdivided into those with a predominant action on the venous system (venodilators), those with a predominant action on the arterial system (arterial dilators) and those that have relatively equal effects on both the systems (balanced dilators).

   a. *Nitroprusside:* Sodium nitroprusside acts directly on the vascular smooth muscle and has a balanced dilator effect which reduces pulmonary congestion and increases cardiac output. It has a rapid onset of action and short half-life. It is given in the dose of 5-10 mcg/min and increased every 10-15 min by 5-10 mcg until the pulmonary wedge pressure has reduced to 18 mmHg or side effects occur.

   b. *Nitrates:* They act as predominant venodilators with mild effects on the arterial system and increase the cardiac output by about 18-25%.

      Sustained reduction in left ventricular filling pressure occurs for 4-5 hours with 20 mg of oral isosorbide, for 1-5 hours with sublingual administration and for 3-6 hours with cutaneous administration.

      IV nitroglycerine can be used in cardiac failure where predominant vasodilatation is needed with elevated filling pressures, an acceptable cardiac output and normal blood pressure. It is started at 5-10 mcg/min. and increased by 10 mcg every 10-15 min. to a total dose of 100-200 mcg/min.

   c. *Hydralazine:* It is an arterial dilator which produces slight decrease in BP, large decrease in systemic arterial resistance and 25-70% increase in cardiac output. Usually it is given in the dose of 25 mg 6 hourly and increased gradually up to 100 mg 6 hourly. In this dose lupus erythematosus may occur in 15% of patients. It is usually combined with nitrates or nitroprusside.

   d. *Prazosin:* This reduces the peripheral resistance by blocking the vascular alpha-I-adrenergic receptors. Decreases in arterial and left ventricular filling pressures, as well as systemic vascular resistance and increases in cardiac output result from both arterial and venous dilation.

      With acute use, heart size decreases and treadmill exercise performance improves. However, tolerance develops on continuous use, which does not improve by increasing the dose but by adding a diuretic. The initial dose is 1 mg increased gradually to a maximum of 10 mg/day.

   e. *Angiotensin-Converting Enzyme inhibitors:* Captopril is a balanced vasodilator that dilates both venous and arterial systems and thus reduces both the preload and afterload and increases cardiac output. Peak effects are observed within 90 min following oral administration. Renal perfusion is selectively increased out of proportion to the increase in cardiac output. Caution must be exerted if it is used with venous dilators like nitrates. The usual dose initially is 6.25 mg three to four times gradually increased to 50-100 mg four times. Other ACE Inhibitors include Enalapril, Ranipril, Lisinopril and Quinapril. They can lead to adverse reactions like dry cough, angioedema, hyperkalemia and raised creatinine.

In case patients are intolerant to ACE-Inhibitors, Angiotensin Receptor Blockers (ARBs) can be used. They include drugs like Losartan, Valsartan, Telmisartan, Olmisartan and Candisartan. They are less likely to produce cough as compared to ACE-Inhibitors.

f. Nesiritide : Recombinant BNP. It is a vasodilator used in refractory cardiac failure. It is given intravenously in a bolus of 2 μg/kg followed by an IV infusion of 0.01 μg/kg/min.

8. **Inodilator Levosimendan :** It is a calcium channel sensitizer. It has a positive ionotropic and vasodilatory effect. It is used in acute decompensated cardiac failure. It is given intravenously in a loading dose of 6-12 μg/kg/minute over 10 minutes followed by 0.05 - 2 μg/kg/min infusion.

9. **Oxygen:** Oxygen (through Woulfe's bottle) at the rate of 5-8 liters/min should be given especially in patients with lung disease, lung congestion or coronary heart disease.

10. **Miscellaneous**

a. *Tranquilizers:* Diazepam 2-5 mg three times a day or phenobarbitone 30-60 mg twice or thrice a day is useful to allay anxiety and achieve adequate sleep.

b. *Mechanical measures:* In cases of ascites or hydrothorax causing respiratory discomfort, aspiration of fluid is helpful. Massage of lower limbs to maintain peripheral circulation helps to prevent phlebothrombosis.

11. **Cardiac Re-synchronization Therapy :** Or Biventricular Pacing : It is used in patients with symptomatic refractory cardiac failure with conduction abnormality or Left Bundle Branch Block (LBBB). This therapy involves pacing the right atrium, right ventricle and left ventricle to improve synchrony of the cardiac chambers.

12. **Left Ventricular Assist Device (LVADs) :** Like Intra-aortic balloon pump. Impella device, Heart-Mate, Thoratic are considered when medical management fails. They are usually used as a bridge to cardiac transplant or CABG.

Management of Acute Left Ventricular Failure (LVF)

1. **Rest in bed** is given in a position that is most comfortable to the patient.
2. **Morphine:** 15 mg morphine or 100 mg pethidine I.M is given to relieve pain and allay anxiety. They also caused dilation of veins reducing the venous return to he heart.
3. **Oxygen:** 6-8 liters/min (through Wolfe's bottle) is given.
4. **Aminophylline:** 250-500 mg. I.V. improves cardiac contractibility and relieves bronchospasm.
5. **Digitalis:** Rapid digitalization is done intravenously unless contraindicated.
6. **Diuretics:** Furosemide 40 mg. I.V. is given. It may be given up to 100 mg. if required.
7. **BP Control:** Vasopressors are given if BP is low and hypotensives are given if BP is high.
8. **Diet:** Salt free diet is given till LVF improves. Later, restricted salt diet is given.
9. **Phlebotomy:** Removal of 500 ml of blood was done in the past. It reduces the load in the heart by reducing the venous return from the limbs to the right atrium.

7 Mitral Stenosis (MS)

Causes

A. *Rheumatic heart disease:* Mitral stenosis occurs usually after 5 years age and is the commonest cause of MS

B. *Congenital:* Mitral stenosis occurs early in life and may be associated with other congenital anomalies

C. *Lutembacher's syndrome:* Acquired MS + ASD.

D. *Atherosclerosis* in the elderly due to calcification and fibrosis of the valve, valve ring and chordae tendineae

E. *Endomyocardial fibrosis*

F. *Hurler's syndrome:* Due to deficiency of alpha-1-iduronidase. There is corneal clouding, growth and mental retardation, coarse features, multivalvular, coronary, great vessel disease and cardiomyopathy.

Pathophysiology

The essential fault is obstruction to the left ventricular inflow resulting in a rise in pressure in the left atrium and pulmonary circulation. For pulmonary blood flow, a pressure gradient of 10 mmHg must exist between pulmonary arteries and veins. As the pressure in the pulmonary veins increases, pressure in the pulmonary artery increases passively to maintain the gradient (*passive pulmonary hypertension*). When the left atrial pressure is above 20 mmHg, pulmonary artery pressure rises very rapidly due to arteriolar constriction (*active pulmonary hypertension*). The vasoconstriction affects the muscular arteries of the lower lobe, which show medial hypertrophy. The upper lobe arteries are normal or even enlarged.

The normal mitral valve area is 4-6 cm^2 and the pressure in the left atrium is normally 6-12 mmHg. When it is reduced to <1 cm^2 it is severe and critical mitral stenosis. To maintain adequate cardiac output, the left atrial pressure increases and left atrial dilatation occurs. The left atrial pressure may reach 30 mm or higher. As the effective osmotic colloidal pressure of plasma is only 25 mmHg pulmonary edema will appear unless it is partly prevented by capillary thickening and pulmonary arterial vasoconstriction. However, this leads to pulmonary hypertension, right ventricular hypertrophy and failure and tricuspid regurgitation.

Mechanism of Pulmonary Hypertension in Mitral Stenosis

1. Due to back pressure left atrial pressure increase causing an increase in pulmonary vascular pressure and subsequently passive rise in pulmonary artery pressure. This is *passive pulmonary hypertension.*
2. Above a mean left atrial pressure of 20 mm of mercury, pulmonary arterial pressure rises rapidly irrespective of left atrial pressure due to arteriolar constriction. This is *active pulmonary hypertension.*
3. Interstitial edema in walls of small pulmonary vessels

Pathological Types

1. *Leaflet type* - stiff, rigid, calcified
2. *Commissural type* - fusion of commissures, but no involvement of chordae or cusps
3. *Chordae type* - fused and thick chordae

Diagnostic Features

Due to Mitral Stenosis (uncomplicated)

A. *Tapping apex beat* occurs due to palpable first heart sound (accentuated S_1) combined with backward displacement of the left ventricle by enlarged right ventricle.

B. *Mid- diastolic presystolic thrill* in mitral area

C. *Loud first heart sound* because the cusps are kept open until the onset of ventricular systole. As the cusps become immobile, the loud first sound softens. Therefore a loud S_1 indicates pliable mitral valve.

D. *Opening snap* is the sound that appears in early diastole due to the opening of the mitral valve. It disappears when cusps become immobile. Normal A_2OS interval is 0.05 to 0.12 sec.

E. *Mid-diastolic murmur* with presystolic accentuation. It is localized low pitched, rumbling murmur best heard in the mitral area, with the bell, when the patient is in the left lateral position and holds the breath in expiration and is accentuated by exercise. It occurs due to turbulent flow of blood through the narrowed valve.

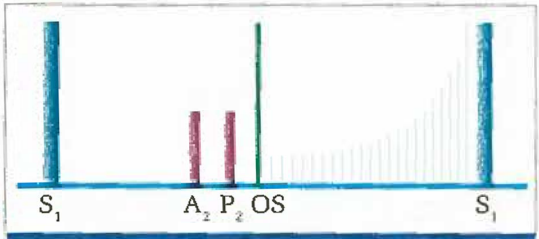


Fig. 5.22 : Mid-diastolic murmur with presystolic accentuation

Complications of Mitral Stenosis

A. **Due to back pressure**
   1. Left atrial enlargement
   2. Pulmonary edema
   3. Right ventricular hypertrophy and failure
   4. Tricuspid incompetence
   5. Right atrial enlargement

B. **Arrhythmias**
   1. Ventricular or atrial premature beats.
   2. Atrial fibrillation or flutter

C. **Infections**
   1. Subacute bacterial endocarditis
   2. Bronchopulmonary infections

D. **Embolism**
   1. Cerebral - hemiplegia, aphasia, etc.
   2. Pulmonary
   3. Renal hypertension
   4. Aorta - Leriche's syndrome
   5. Coronaries leading to angina

E. **Pressure of enlarged left atrium**
   1. Ortner's syndrome - hoarse voice due to pressure on the recurrent laryngeal nerve
   2. Dysphagia due to pressure on the esophagus
   3. Collapse of the left lung due to pressure on the left bronchus

F. **Pulmonary hemosiderosis** in long-standing MS

G. **Syncope in MS**
   1. Atrial fibrillation
   2. Ball valve thrombus
   3. Severe pulmonary hypertension
   4. MS with AS
   5. Recurrent emboli

Clinical Features due to Complications of Mitral Stenosis

I. **Due to Pulmonary hypertension** (which commonly occurs in later stages)

   A. *Symptoms*
      1. Severe dyspnea
      2. Cough with frothy sputum
      3. Hemoptysis
      4. Eventually right heart failure

   B. *Signs*
      1. Precordial bulge
      2. Pulsations in left parasternal region
      3. Right ventricular heave
      4. Diastolic shock
      5. Systolic impulse and thrill in the pulmonary area
      6. Upper border of the heart in the second space
      7. Widely split second heart sound in the pulmonary area and a loud P2
      8. Soft systolic murmur in the pulmonary area
      9. Graham Steell murmur
      10. Mitral facies: Malar flush i.e. bilateral cyanotic discoloration of upper check due to arteriovenous anastomoses and vascular stasis.

III. **Due to associated Right heart failure**

   A. *Symptoms*

   Weakness, fatigue, edema of feet and pain in right hypochondrium

   B. *Signs*
      1. Prominent 'V' waves in JVP
      2. Enlarged tender liver
      3. Edema of feet
      4. Pansystolic murmur accentuated by inspiration in the tricuspid area due to tricuspid regurgitation

IV. **Due to associated Atrial fibrillation**

   A. *Symptoms*
      1. Palpitations or thumping in the chest
      2. Due to low cardiac output: Angina, weakness, syncope, etc.
      3. Due to embolism: Blindness, hemiparesis

   B. *Signs*
      1. Irregularly irregular pulse rate
      2. Apex pulse deficit
      3. Absence of 'a' wave or 'x' descent in JVP
      4. Varying intensity of first heart sound
      5. Absent presystolic accentuation of the diastolic murmur

V. **Due to associated Valvular lesions**
   1. *Mitral regurgitation:* Hyperdynamic apex, reduced intensity of first sound and pansystolic murmur
   2. *Aortic regurgitation:* Hyperdynamic apex,

Water-hammer pulse and early diastolic murmur

3. *Aortic stenosis:* Hyperdynamic apex, small volume pulse and ejection systolic murmur in aortic area

VI. Changing MS murmur

1. *IE*
2. *Acute RF*
3. *Rupture of valve*

VII. Soft S_1 in MS

1. *Calcification of Mitral Valve*
2. *Associated MR*

Mechanism of Hemoptysis or Bloody Sputum in MS

1. Chronic bronchitis
2. Pulmonary infarction
3. Pulmonary apoplexy (rupture of thin-walled bronchopulmonary veins due to increased LA pressure)
4. Pulmonary edema
5. Bronchial vein rupture
6. A-V malformations or microaneurysms

Investigations

I. X-ray chest: A patient of mitral stenosis may have a normal X-ray or may have any of the following features:

A. *Evidence of enlarged left atrium*

1. Left bronchus lifted up with widened carina
2. Double atrial shadow
3. Straightened left border
4. Esophagus curving around the dilated left atrium

B. *Evidence of enlarged right ventricle*

1. Increased cardiac size
2. In ROA, obliteration of retrocardiac space

C. *Enlarged pulmonary conus*

D. *Lung changes*

1. Pulmonary congestion
2. Pulmonary edema
3. Pulmonary Infarction
4. Pulmonary venous hypertension: Initially there is redistribution of blood to upper lobe making upper lobe veins prominent (inverted mustache sign). This may be followed by generalized haziness (due to interstitial edema) and then Kerley B lines: transverse white bands of 1-2 cm length at the bases due to interlobular septal edema. In late stages there will be Hemosiderosis.

E. *Calcification of the mitral valve*

II. ECG: The ECG may be completely normal in mitral stenosis in early stages. Later there may be:

1. Right axis deviation
2. Left atrial enlargement - wide and notched P-waves (P-mitrale) in lead II and biphasic P-waves in lead V_1. The P wave may be absent in atrial fibrillation
3. Right Ventricular strain pattern
4. Atrial fibrillation - absent P waves

III. Echocardiogram: This is one of the most valuable investigation to diagnose and assess the severity of mitral stenosis.

A. On M-mode

1. E-F slope is reduced due to decreased closure rate of the anterior leaflet of the mitral valve.
2. Reduced D-E amplitude due to diminished opening movements of the mitral valve

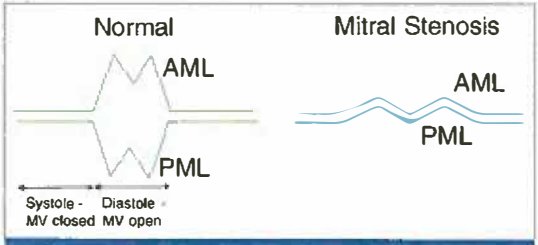


Fig. 5.23: M-Mode Echo showing paradoxical motion of PML with decreased EF slope. AML: Anterior mitral valve leaflet; PML: Posterior mitral valve leaflet

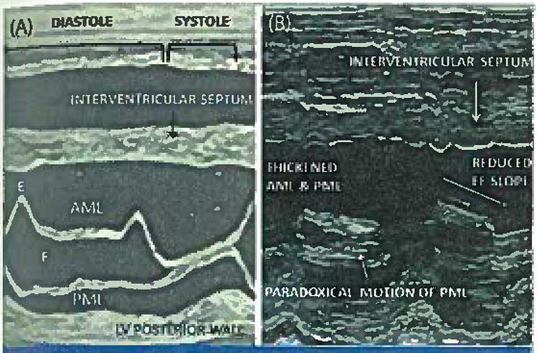


Fig. 5.24 : (A) Normal M Mode of Mitral Valve, (B) M Mode of Mitral Stenosis

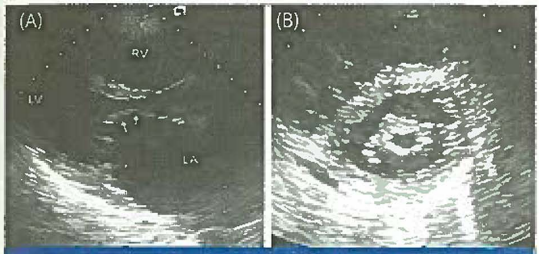


Fig. 5.25 : (A) Echocardiograhy of Mitral Stenosis with restricted motion of anterior mitral leaflet resulting in diastolic doming (arrows) and hockey stick appearance (parasternal long axis view), (B) Echocardiograhy of Mitral Stenosis in parasternal short axis view showing fish-mouth apperance.

3. Absent 'a' wave due to absence of second rapid filling phase
4. Anterior instead of posterior motion of the posterior mitral valve leaflet in diastole (paradoxical motion of PML)

B. On 2-D Echo

1. In parasternal long axis view, there is restricted excursion of the leaflet tips and prominent diastolic doming of the anterior leaflet into the left ventricular outflow tract (fish mouth appearance).
2. In parasternal short axis view at the level of the mitral valve, the valve area can be accurately measured (planimetry). Echo helps to show reduced valve area in MS.
3. Direct evidence of left atrial enlargement and pulmonary hypertension as well as indirect evidence of associated tricuspid regurgitation
4. Left atrial thrombus could be detected as also the close differential diagnosis, left atrial myxoma, can be excluded.
5. Secondary calcification, vegetations, subvalvular apparatus
6. *Wilkins Score on 2D Echo*

   16 points for Mobility of the valve, Thickness of the valve, Sub-valvular apparatus and Calcification (4 points each)

   >10 = C/I for Balloon Mitral Valvuloplasty (BMV)

   < 8 = BMV safe

C. Transesophageal Echo for atrial fibrillation to check for clots in left atrial appendage.

IV. Cardiac Catheterization: Pressure gradient between LA and LV

Conditions which Simulate MS

A. Tricuspid stenosis
B. Left atrial myxoma
C. Ball valve thrombus
D. Cor triatriatum

A. Table 5.18 : Differences Between Mitral and Tricuspid Stenosis

	Mitral Stenosis	*Tricuspid Stenosis*
JVP	Prominent 'a' wave if associated pulmonary hypertension. Prominent 'v' wave if associated TI	Giant 'a' wave, 'v' wave never prominent.
RVH	Often present	Never present
Pulmonary hypertension	Often present	Never present
Presystolic pulsation of liver	Never present	Often present
Location of murmur	Mitral area	Tricuspid area
Relation of diastolic murmur to respiration	None	Increases on inspiration

B. LEFT ATRIAL MYXOMAS are often diagnosed as mitral stenosis. Therefore, in a so-called 'mitral stenosis', left atrial myxoma may be suspected if there are:

1. Constitutional symptoms like fever, anemia, clubbing, weight loss, etc.
2. Postural syncope
3. Embolic episode in presence of sinus rhythm as a presenting symptom
4. Third heart sound heard
5. Tumor plop sound
6. Apical systolic murmur
7. Atrial fibrillation and left atrial enlargement is not common
8. Raised gamma globulins

Echocardiography helps to differentiate left atrial myxoma from mitral stenosis.

C. BALL VALVE THROMBUS: This mimics left atrial myxoma and can be differentiated by Echocardiogram.

D. COR TRIATRIATUM: There is obstruction to the inflow tract by a third chamber, which is demonstrated by echocardiogram. Opening snap and diastolic murmur is absent and usually systolic murmur is present.

E. ATRIAL SEPTAL DEFECT: Fixed split S_2 may be confused for OS and diastolic flow murmur across TV can be mistaken for MDM of MS. ECG shows RVH in both, but in ASD, split S_2 is fixed. 2-D Echo can differentiate them.

Indications of Severity

1. *Presence of NYHA Class III or IV symptoms*
2. *Signs*
   a. Length of diastolic murmur
   b. Proximity of opening snap to A_2 (A_2OS inversely related to severity of MS)
   c. Pulmonary hypertension or congestion
   d. Functional pulmonary regurgitation (Graham-Steell murmur) or tricuspid regurgitation.
3. *X-ray chest:*
   a. Left atrial or right ventricular enlargement
   b. Pulmonary hypertension and congestion
4. *ECG:*
   a. Atrial enlargement
   b. Right ventricular strain pattern
5. *Echocardiography:*
   a. *On M-mode:*
      Flattening of EF slope >30 mm/sec - mild; <10 mm/sec - severe
   b. *On 2-D Echo:* Cross-sectional valve area

Table 5.19 : Grading of MS based on Mitral Vlave Area

Mitral Valve Area	Grade of MS
4-6 cm^2	Normal Area of Mitral Valve
> 2.5 cm^2	Asymptomatic
1.5 - 2.5 cm^2	Mild/symptoms on exertion only
1 - 1.5 cm^2	Moderate
< 1.0 cm^2	Severe
< 0.8 cm^2	Critical

6. *Catheterization:*
   a. Mitral valve gradient
   b. Elevated right heart pressures
   c. Decreased cardiac output during exercise

Treatment

A. If asymptomatic Mitral stenosis:

1. *Advice for occupation:* The patient must have controlled work and avoid stress, exposure to dampness and overcrowding.
2. *Controlled exercises* within limits may be allowed.
3. *Marriage and pregnancy:* The patient may be allowed to marry. Females must be advised to restrict the number of children to two only with an interval of at least three to four years.
4. The patient must *avoid putting on excess weight* and, if obese, must be asked to reduce weight.
5. *Prophylaxis for rheumatic fever:* Up to the age 40 years (or life-long) the patient is advised to take one injection of benzathine benzylpenicillin (penidura) 1.2 mega units IM every 3-4 weeks.

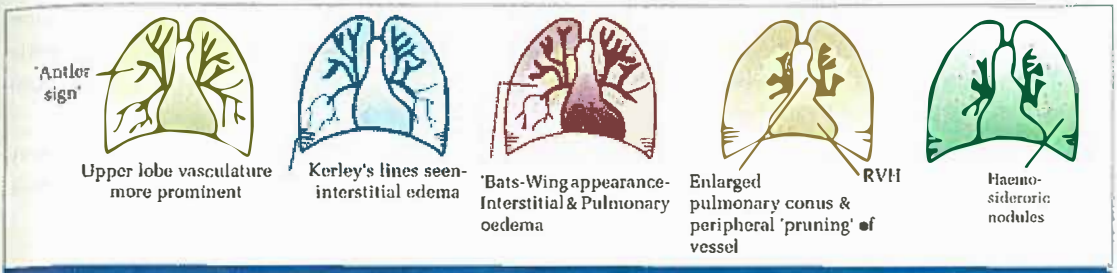


Fig. 5.26: X-ray chest: Mitral valve disease (MS and MR)



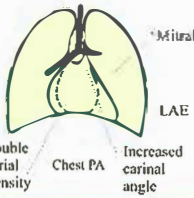


Fig. 5.27: X ray of Mitral Stenosis with Straightening of Left Heart Border. Double atrial shadow suggestive of Left atrial enlargement. Cephalization (Inverted Moustache sign or Antler Sign) also present in upper lung fields suggestive of Pulmonary Venous Hypertension



Fig. 5.28: Left atrium enlargement on barium swallow

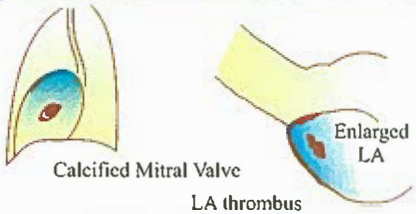


Fig. 5.29: Lateral chest X-ray and 2-D Echo in parasternal long axis view showing reduced Mitral valve area

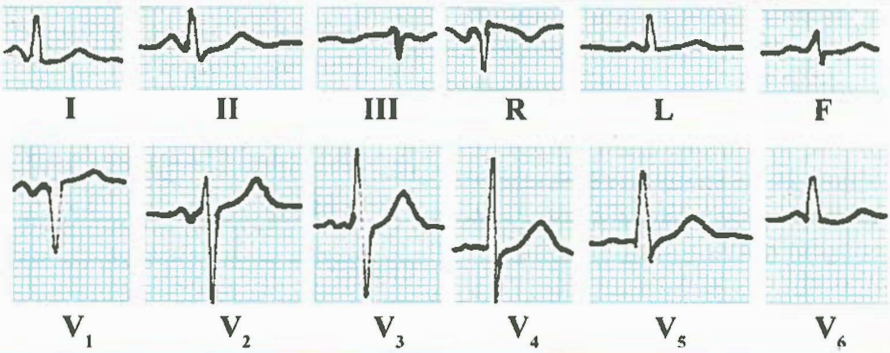


Fig. 5.30: ECG of a patient with mitral stenosis

6. *Prophylaxis for infective endocarditis:* Refer IE Pg. 208.

B. If symptomatic Mitral stenosis:

1. Medical Line of Treatment
   a. *Bed Rest*
   b. *Salt free diet*
   c. *Diuretics* like furosemide 40 mg/day
   d. *Digitalis* if there is congestive cardiac failure. Digoxin 0.25 - 0.5 mg is given daily. It also protects against fast ventricular rate, should atrial fibrillation occur. *Beta-blockers, calcium channel blockers (verapamil or diltiazem)* also used for decreasing ventricular rate.
   e. *Anticoagulants (warfarin)* if there is an embolic episode or recent atrial fibrillation (avoided if infective endocarditis is suspected).
2. Treatment of Complications
3. BALLOON MITRAL VALVULOPLASTY (BMV)

   Procedure: Catheter is inserted through femoral vein and passed into IVC, right atrium and trans-septally to left atrium. The balloon is inflated at the valve orifice to dilate the MV opening.

   Indications
   a. Uncomplicated MS with thin leaflets and no calcification (Wilkins score <6)
   b. Pregnancy with MS
   c. Elderly with operative risks

   Contra-indications
   a. Calcified valve, thickened cusps, sub valvular apparatus widening (Wilkins score >8)
   b. Clots in LA
   c. MS with moderate/severe MR

   Advantages: No scar and no open surgery

   Complications: Embolic events, MR, iatrogenic ASD
4. SURGERY
   a. Closed Mitral Commissurotomy (CMC)/Valvuloplasty

      Procedure: Left atrium is opened and the MV is dilated using special dilators or fingers. Done on a beating heart.

      Indications/Contra-indications: Same as for BMV

      Complications: Scar on LA may lead to atrial fibrillation, embolic events, MR

      Advantages: Cheaper than BMV
   b. Open Mitral Commissurotomy (OMC)/Valvuloplasty

      Procedure: Cardiopulmonary bypass is necessary. The MV commissures can be opened, LV clots removed, sub-valvular apparatus can be loosened.

      Indications: Clots in LA, MS with MR, MS with Wilkins score > 8
   c. Mitral Valve Replacement (MVR)

      Indications: Same as OMC + Calcified MV or IE with MS

   Prosthetic valves:
   - Bioprosthetic valves (porcine aortic valves, bovine pericardium, cadaveric valves) or
   - mechanical valves: Tilting disc valve (St Judes valve), Ball in Cage valve (Starr Edwards valve)

   Disadvantages: Bioprosthetic valves have a shorter life, whereas metallic valves need long-term anticoagulants

Normally Patient of MS never has LVH; if LVH Occurs, Suspect:

A. Associated MI, AS or AI
B. Hypertension due to renal embolism
C. Ischemic heart disease due to coronary embolism
D. Cardiomyopathy

8 › Mitral Regurgitation (MR)

Causes

A. Functional: Due to left ventricular dilatation as in
   1. Aortic valve disease

2. Hypertension
3. Ischemic heart disease
4. Cardiomyopathy
5. Myocarditis
6. Acute rheumatic fever

B. **Organic**

1. Rheumatic
2. Mitral valve prolapse
3. Infective endocarditis
4. Papillary muscle dysfunction
5. Endomyocardial fibrosis
6. Collagen disorder: SLE, Marfan'ssyndrome, Ankylosing spondylitis, Pseudoxanthoma elasticum, Hurler's, Ehler-Danlossyndrome
7. Ruptured chordae tendineae. Trauma, following myocardial infarction, primary chordal dysplasia
8. Congenital (endocardial cushion defect, parachute mitral valve with Ostium primum defect)
9. Following methysergide therapy
10. Iatrogenic: Post BMV, CMC

Pathophysiology

In mitral regurgitation, during systole, a portion of the left ventricular stroke volume is being ejected back into the left atrium rather than forward into the aorta. However, left ventricular function does not deteriorate till late. Since there is no obstruction to the flow across the mitral valve in diastole, left atrial pressure, is also not elevated in early stages and pulmonary venous and arterial hypertension too does not occur early.

In late stages, left ventricle dilates to accommodate the increased volume. The increased wall tension and the increased myocardial mass from ventricular hypertrophy increase myocardial oxygen demand and ultimately leads to left ventricular failure. As the left ventricular filling pressure rises, there is increase in left atrial and pulmonary venous pressure leading to pulmonary venous and later pulmonary arterial hypertension.

Symptoms

A. Fatigue, weakness

B. Dyspnea, orthopnea, PND

C. S/S of pulmonary hypertension, RVF or atrial fibrillation (Refer MS Pg. 225)

Diagnosis

A. Low, collapsing pulse (Water-hammer pulse)

B. Hyperdynamic apex

C. Systolic thrill in the mitral area

D. Muffled first heart sound

E. Loud third heart sound (0.12-0.17 sec after S_2)

F. Widely split second heart sound, even in the absence of pulmonary hypertension, because of early closure of aortic valve.

G. Pansystolic murmur best heard in the mitral area with the diaphragm and conducted to the axilla and back. It is increased on exercise and has no relation to respiration. Conducted to base of heart if posterior mitral leaflet involved.

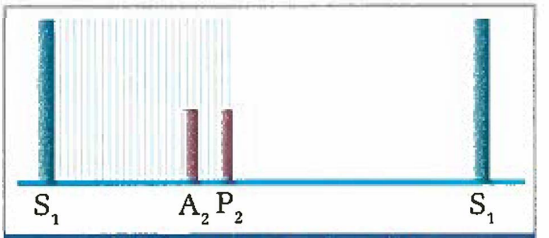


Fig. 5.31: Pansystolic murmur of MR

H. Flow murmur - Soft mid-diastolic murmur heard only in severe MR.

I. If pulmonary hypertension is present, features of pulmonary hypertension as mentioned with mitral stenosis are present.

J. 'Cooing' or 'musical' or 'seagull' quality of murmur in papillary muscle dysfunction or rupture of chordae tendinae

Investigations

I. **ECG:** The ECG may be normal in early stage.

1. Left atrial enlargement or overload pattern appears if the patient is in sinus rhythm.
2. Left ventricular hypertrophy occurs as regurgitation increases.
3. If pulmonary hypertension occurs biventricular hypertrophy pattern occurs.

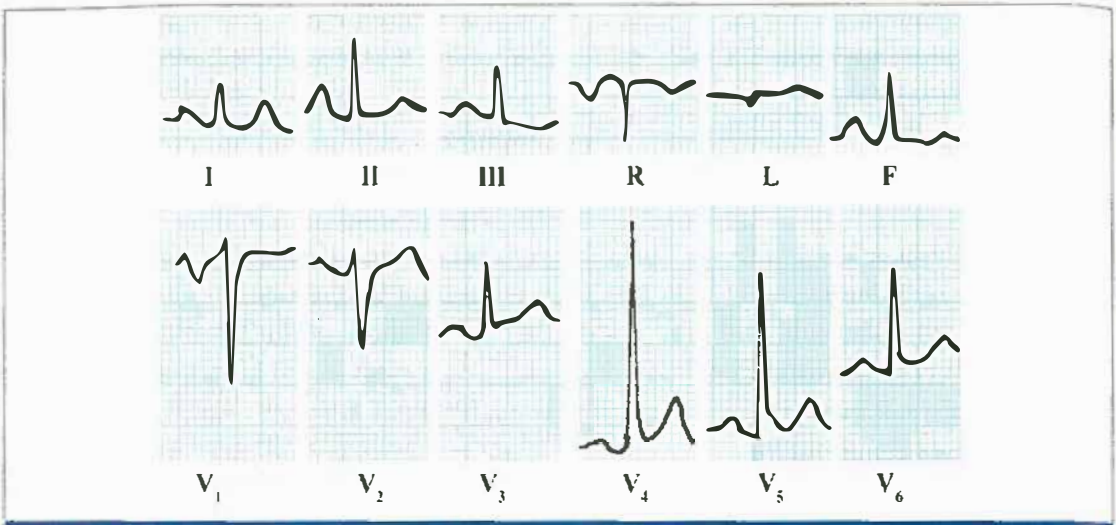


Fig. 5.32: ECG from a patient with mitral regurgitation showing left ventricular hypertrophy (sum of S wave in V_1 and R wave in V_6 more than 35 cm.), and left atrial hypertrophy (bifid p wave in lead II-p-mitrale and biphasic p-wave in lead V_1, with prominent negative wave.)

4. Atrial fibrillation present due to LA enlargement.

II. **X-ray chest: It is usually normal in mild mitral regurgitation.**

1. Initially there is left atrium enlargement, leading to straightening of the left heart border, and double density between both the main bronchi.
2. Later, left ventricular dilatation leads to cardiomegaly.

III. **Echocardiogram:** It gives valuable information, which aids in diagnosing and assessing the severity of mitral regurgitation (MR).

1. Increased left ventricular end-diastolic dimensions along with large atrium, hyperdynamic motion of the septum suggests mitral regurgitation.
2. The anterior mitral leaflet may be thickened or calcified.
3. Pulsed Doppler and Color Doppler would reveal mitral regurgitation flow and help to assess the severity.

Echocardiography helps to rule out others causes of mitral regurgitation like mitral valve prolapse, infective endocarditis, ruptured chordae tendineae.

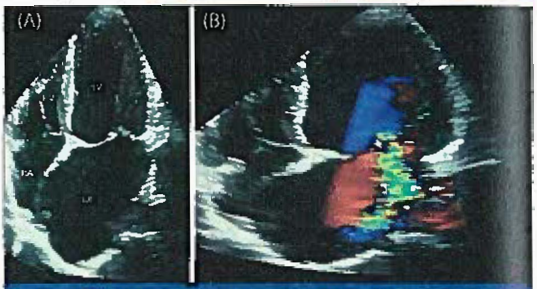


Fig. 5.33: (A) Echocardiography of Mitral Regurgitation with dilated LA and LV, (B) Echocardiography of Mitral Regurgitation

Differential Diagnosis

A. Table 5.20 : Differences between MR and VSD

	MR	VSD
1. History	History of fever with fleeting joint pains	History of palpitations and dizziness from early childhood
2. Systolic thrill	At the apex,	At left sternal edge
3. First sound	Muffled.	Normal
4. Third sound	Present	Absent
5. Pansystolic murmur	Best heard at apex and conducted to the left axilla and back	Best heard at left sternal edge and conducted to the right side
6. Enlarged left atrium	Present	Absent

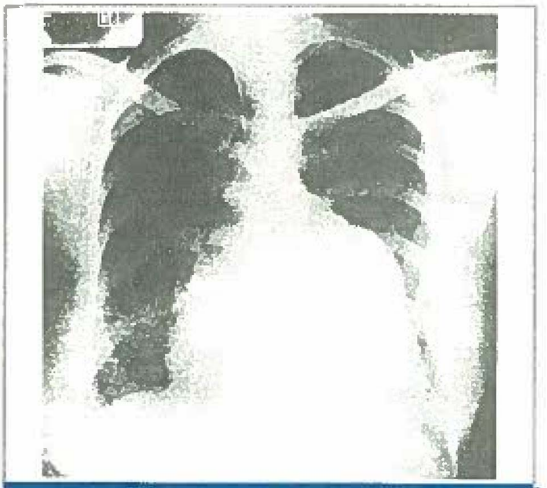


Fig 5.34 : Pentagon heart of mitral regurgitation

B. Table 5.21 : Differences between MR and TR

	MR	TR
1. JVP	Prominent 'a' wave if associated pulmonary hypertension	Prominent 'v' wave
2. Pulse	Normal or jerky	Normal
3. Palpation	LV heave	Left parasternal heave
4. LVH	May be present	Never present
5. Pulmonary Hypertension	Often present	Never present
6. Systolic pulsations of liver	Never present	Often present
7. Location of pansystolic murmur	In the mitral area conducted to axilla and back	In the tricuspid area and conducted to the mitral area
8. Relation of murmur to respiration	Increases on expiration	Increases on inspiration

C. Signs favoring Acute rather than Chronic MR

1. Sinus tachycardia
2. Large 'a' wave
3. Minimally displaced apex beat
4. RV heave with apical systolic thrill
5. Normal intensity S_1, S_4, loud P_2
6. Short (non-pansystolic) murmur radiating well to base.

Table 5.22 : Differences between Acute and Chronic MR

	Acute MR	Chronic MR
1. Symptoms	Sudden onset, dyspnea, orthopnea, PND	Gradual progression
2. Signs		
a. Apex beat	Minimally displaced	Displaced
b. S_1	Normal/soft	Soft
c. S_4	Present	Absent
d. PSM	Short/early	Pansystolic
3. ECG	Normal except if AMI	LAE, LVH
4. CXR	Normal heart size	Cardiomegaly
5. Causes	Infective endocarditis Post-MI – papillary muscle dysfunction, chordae rupture, Trauma, Acute rheumatic fever	See Causes above

Clinical Assessment of Severity

1. Degree of Left ventricular enlargement
2. Presence of S_3
3. Mid-diastolic flow murmur
4. Thrill
5. Loudness of murmur
6. Pulmonary congestion
7. Hypertension

Treatment

I. **If Asymptomatic:** Refer Mitral stenosis

II. **If Symptomatic:**

A. **Medical:**

1. *In mildly symptomatic cases:* Diuretics like furosemide 40 mg daily, along with digoxin 0.25 mg daily and salt restriction is advised to reduce volume overload and give inotropic support to the heart.
2. *In severe cases* with advanced functional disability vasodilators to reduce both preload and afterload are given. The former is done with nitrate and latter with captopril 75-150 mg/day or enalapril 10-20 mg/day.

B. Surgical:

Mitral regurgitation is well-tolerated lesion with slow progression. Surgical mitral valve repair (valvuloplasty or annuloplasty) or valve replacement is done in the following situation:

1. Severe mitral regurgitation (NYHA Class III or IV)
2. Severe pulmonary hypertension
3. Progressive increase in LV size demonstrated radiologically or by Echocardiogram and hemodynamic decompensation.
4. Ruptured chordae tendineae and resistant infective endocarditis.

9 › Mitral Valve Prolapse (MVP)

(Synonyms: Barlow syn., floppy mitral valve, systolic click murmur syndrome, billowing mitral leaflet syn.)

Mitral valve prolapse is commonly seen in young women with familial incidence. Usually posterior cusp prolapses. In Read's syndrome, both the anterior and posterior cusps prolapse and hence valve replacement is invariably required.

Causes

Its cause is unknown, but in some cases it may be a genetically determined collagen tissue disorder associated with:

1. Normal variant: Mild MVP is so common that it is regarded as a normal variant. It is often seen in patients with anxiety neurosis.
2. Rheumatic heart disease
3. Ischemic heart disease
4. Congenital heart disease, ASD (Secondum type), Ebstein's anomaly
5. Hypertrophied cardiomyopathy
6. Connective tissue disorders: Marfan's, Ehlers Danlos, SLE
7. Thyrotoxicosis

Pathophysiology

The mitral valve leaflets may be large Alternatively there may be enlarged mitral annulus, abnormally long chordae or disordered papillary muscle contraction. Myxomatous degeneration of the mitral valve may be present on histology.

During ventricular systole, a mitral valve leaflet prolapses into the left atrium that may cause abnormal ventricular contraction, and mitral regurgitation.

Clinical Features

1. Usually the patients are asymptomatic. There may be atypical chest pain, angina or palpitations.
2. Mid-systolic (non-ejection) click is heard due to prolapse of the valve and tensing of the chordae tendineae that occurs during systole 0.14 sec after S_1
3. Late systolic murmur due to mitral regurgitation may occur.
4. Click and murmur occur earlier with standing or Valsalva maneuver (decreased LV volume) and occur later with squatting or isometric handgrip or exercise (increased LV volume).

Complications

1. Severe MR
2. Endocarditis in patients with MR
3. Sudden death
4. Arrhythmias - ventricular and supraventricular
5. Chest pain
6. Embolic phenomenon
7. Transient ischemic attack (TIA)

Investigations

I. Chest X-ray: This is usually normal unless there is significant mitral regurgitation.

II. ECG: This may be normal or may show T wave inversion in inferior (II, III and aVF) and lateral (V_4 - V_6) leads.

III. Echocardiogram: This confirms the diagnosis by demonstrating both on M-mode and 2-D. posterior movement of one or both mitral valve cusps into the left atrium during systole.

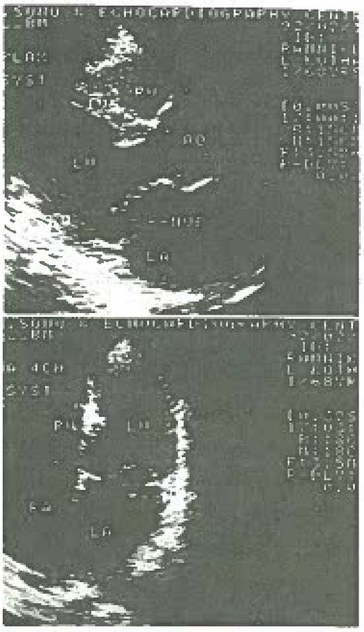


Fig. 5.35 and 5.36 : 2D Echo in left parasternal long axis view (upper one) & apical 4 chamber view (lower one) showing mitral valve prolapse

IV. Color Doppler studies

Treatment

1. Reassurance to asymptomatic patient
2. Beta blockers: Propranolol 10-20 mg twice a day or atenolol 50 mg daily is useful for atypical chest pain and palpitations.
3. Mitral valve plication or replacement may be required for severe mitral regurgitation.
4. Treatment of atrial fibrillation if present.
5. Antiarrhythmic agents if VPC or significant arrhythmias.
6. Prophylaxis against infective endocarditis, especially those with murmurs.
7. Low dose aspirin or anticoagulants for TIA

10 Aortic Regurgitation (AR)

Causes

A. Rheumatic fever
B. Syphilis
C. Infective endocarditis
D. Congenital disorders:
   1. Bicuspid aortic valve
   2. Marfan's syn., Ehler-Danlos syn.
   3. High VSD
   4. Coarctation of aorta
   5. Supravalvular aortic stenosis
   6. Aneurysm of sinus of Valsalva
E. Connective tissue disorders:
   1. Rheumatoid arthritis
   2. Ankylosing spondylitis
   3. Reiter's syndrome
   4. Systemic lupus erythematosus
   5. Pseudoxanthoma elasticum
   6. Takayasu's arteritis
F. Severe systemic hypertension
G. Traumatic rupture of the cusp
H. Dissecting aneurysm of the ascending aorta
I. Large ventricular aneurysm
J. Following methysergide therapy

Pathophysiology

In aortic regurgitation, blood flows back from the aorta into the left ventricle during diastole. To maintain adequate cardiac output, total amount of blood pumped into aorta must increase and hence left ventricular size increases. Angina occurs not only because of left ventricle enlargement leading to increased requirement of blood, but also because the coronaries are filled in diastole and in AR, blood leaks back into the ventricles in diastole. In addition, in syphilitic patients, there is coronary osteitis, which reduces the coronary filling.

Complications: Same as for MS

Diagnosis

A. *Blood Pressure:* High systolic BP, low diastolic BP (wide pulse pressure). Very often Korotkoff sounds do not disappear and can be heard with cuff deflated. In this case, the value at which the sounds get muffled (phase IV) is regarded as diastolic BP.
B. *Hyperdynamic apex beat*

C. *Diastolic thrill* in the aortic area and third and fourth left intercostal spaces in parasternal region

D. *Second sound* narrowly split with loud A2.

E. *Early diastolic murmur*, de crescendo, soft and blowing, in the aortic area, over the midsternum and to the left, transmitted to the apex, best heard with the diaphragm and the patient leaning forward and holding his breath in expiration. If the diastolic murmur is best heard to the right of the sternum (aortic area) it suggests A.R. due to dilatation of ascending aorta as in syphilis, Marfan's syndrome, ankylosing spondylitis and dissecting aneurism of ascending aorta. If the diastolic murmur is better heard in left 3rd intercostal space, it suggest A.R. due to pathology of aortic valve as in rheumatic heart disease, infective endocarditis etc.

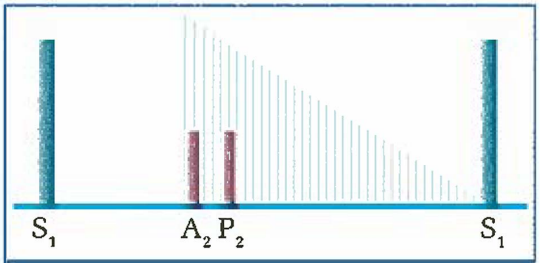


Fig. 5.37 : Early diastolic murmur of AR

F. *Ejection systolic murmur* in the aortic area due to increased stroke volume of left ventricle. It may be mistaken for aortic stenosis; however, in the latter the second sound is soft, whereas in pure aortic regurgitation it is often loud.

G. *Austin Flint murmur*: This is the functional, apical, diastolic murmur of free AR without any lesion of the mitral valve. It occurs sometimes in AR due to vibrations set up in the anterior mitral leaflet as it oscillates between blood coming from the left atrium and regurgitated from the aorta.

H. If *pulmonary hypertension* is also present there will be signs of pulmonary hypertension as mentioned for MS.

I. If there is *left ventricular hypertrophy* there is dilatation of the mitral valve leading to signs of mitral regurgitation.

J. *Peripheral signs of wide pulse pressure.*

1. *Water-hammer pulse* (Corrigan's pulse, collapsing pulse)

*If Water-hammer pulse is absent in a case of aortic regurgitation it suggests one of the following associated lesions:

1. Mitral stenosis 2. Aortic stenosis
3. Hypertension 4. Marked myocardial degeneration

2. *Corrigan's sign* (dancing carotids) - rapid upstroke collapse of carotid artery pulse bilaterally

3. *De Musset's sign:* To and fro motion of the head synchronous with the cardiac pulse

4. *Quincke's sign*: Increased capillary pulsations felt by applying gentle pressure on the nails or gently grasping the fingers

5. *Traube's sign:* Pistol shot sound over the femoral arteries

6. *Duroziez' murmur:* Diastolic murmur heard over the femoral artery when the diaphragm of the stethoscope is pressed distally

7. *Hill's sign:* There is increase in femoral artery pressure over the brachial artery pressure by more than the normal difference of 10 mm Hg. The larger this difference, the more severe is the aortic incompetence

Table 5.23 : Differences between Acute and Chronic AR

	Acute AR	*Chronic AR*
1. Onset	Sudden	Gradual, insidious
2. Blood pressure	Normal/↓	↑SBP, ↓DBP
3. Apex Beat	Normal	Hyperdynamic
4. Auscultation		
a. S_3	Present	Absent
b. EDM	Short	Long, high pitched
c. Austin Flint murmur	Absent	Present
5. Signs of wide pulse pressure	Absent	Present
6. ECG	Normal	LVH
7. CXR	LV normal Lung fields show prominent upper lobe vascularization	LV enlarged & dilation with dilatated aorta. Lung fields clear
8. Etiology	IE, Aortic dissection, trauma	Listed in Causes

(Mild AR: 20–40 mm Hg; Moderate AR: 40-60 mm Hg; Severe AR: >60 mm Hg)

Rare Signs

1. *Lighthouse Sign:* Blanching & Flushing of forehead.
2. *Landolfis Sign:* Alternate dilation & constriction of pupils
3. *Becker's Sign:* Pulsation of Retinal Vessels
4. *Muller's Sign:* Pulsation of Uvula
5. *Rosenbach Sign:* Pulsatile Liver
6. *Gerhard's Sign:* Pulsatile Spleen
7. *Mayer's Sign:* Diastolic Drop in BP > 15 mm Hg when arm is raised
8. *Lincoln Sign:* Pulsating Popliteal
9. *Locomotor brachialis*: Sign of atherosclerosis
10. *Dennisons sign* : Pulsative Cervix

Investigations

I. **Chest X-ray**
   1. LVH and dilatation
   2. Dilatation of the ascending aorta
   3. Ascending aorta wall calcification in syphilis

II. **ECG:** Left ventricular hypertrophy (volume overload) - Tall R waves and deeply inverted T waves in the left sided chest leads and deep S waves in the right-sided leads (LV strain)

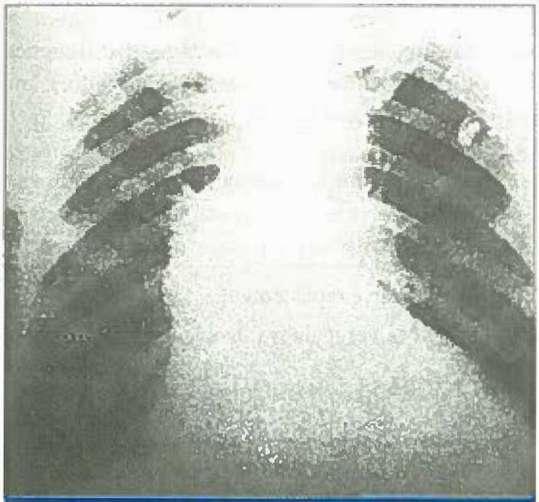


Fig. 5.38: Aortic Regurgitation

III. **Echocardiogram**
   1. Vigorous cardiac contraction and dilated left ventricular cavity

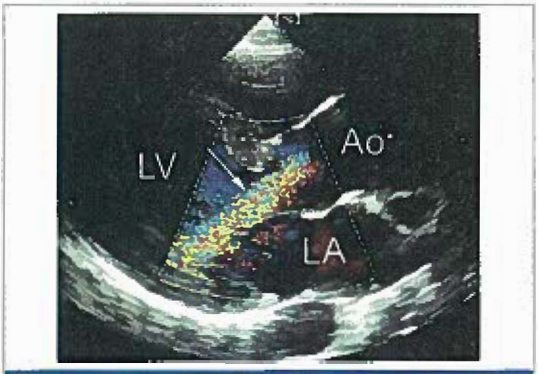


Fig. 5.39: Echocardiography in Parasternal Long Axis view with Aortic Regurgitation



Fig. 5.40: 2D Echo in parasternal long axis view showing enlarged LV and LA from a patient with AR

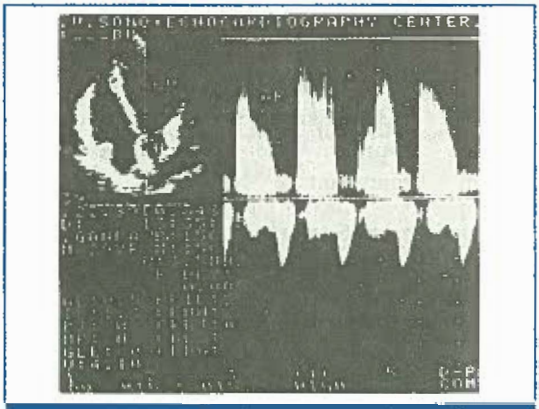


Fig. 5.41: 2D Echo with Doppler showing aortic regurgitation

Differential Diagnosis

A. Table 5.24 : Differences between AR and PR

		AR	PR
1.	Peripheral signs of wide pulse pressure.	Present	Absent
2.	Apex beat	Hyperdynamic	Normal
3.	Early diastolic murmur	Best in aortic area	Best in pulmonary area
4.	Relation of murmur to respiration	None	Increases on inspiration
5.	Ventricular enlargement	LVH	RVH

B. Table 5.25 : Differences between Austin Flint Murmur and AR with MS

		Austin Flint murmur	AR with MS
1.	Hemoptysis	Almost never	May be present
2.	Atrial fibrillation	Absent	May be present
3.	First heart sound	Normal	Usually loud
4.	Opening snap	Absent	Present
5.	Left atrial enlargement	Absent	Present
6.	Calcification of mitral valve	Absent	May be seen
7.	Echocardiography	Normal	Suggestive of MS
8.	Amyl nitrate inhalation	Murmur decreases	Murmur becomes louder

2. Vibrations of the anterior cusps of the mitral valve and the septum.
3. Pressure gradient can be detected by Doppler. Color Doppler can detect regurgitant jet.

Indications of Severity in AR

1. Signs of LV failure
2. Wide pulse pressure (> 60 mmHg):Hills sign
3. Soft S_2
4. Duration of EDM
5. Presence of LV S_3

C. Table 5.26 : Differences between Rheumatic and Syphilitic AR

		Rheumatic AR	Syphilitic AR
1.	History		
	a) Age	Before 30 years	After 30 years
	b) Past history	Rheumatic fever	Syphilis
	c) Duration	Long	Short
	d) Angina	Occurs late	Common or earlier
2.	Examination		
	a) Precordium	Prominent	Not Prominent
	b) Diastolic murmur	Third left space	Second right space
	c) Peripheral signs of A.I.	Not well marked	Very well marked
	d) Other valvular lesions	Common	Never present
	e) A2	Loud	"Tambour" quality
3.	Investigations		
	a) VDRL	Negative	Positive
	b) X-ray	No calcification or aortic irregularity	Calcification confined to ascending aorta and Aortic irregularity may be present

Management

Medical

1. Treatment of failure: Salt restricted diet, diuretics, digoxin. In severe cases ACE inhibitors and nitrates (vasodilators)
2. RF prophylaxis
3. IE prophylaxis

Surgical

1. Aortic valve replacement
2. Aortic valve repair by valvoplasty or annuloplasty

Indications of Surgery in AR

1. Symptoms of cardiac failure
2. Asymptomatic
   a. Reduced LVEF < 55% but > 20-30%

b. LV end-systolic volume > 55 ml/m²
c. LV end-systolic diameter >55 mm
d. Cardiomegaly on X-ray
e. LV Strain on ECG

11 Aortic Stenosis (AS)

Causes

A. *Valvular stenosis:*
   1. Rheumatic heart disease
   2. Atherosclerosis
   3. Congenital malformations – bicuspid AV
   4. Degenerative- sclerocalcific
B. *Subvalvular stenosis: congenital*
C. *Supravalvular stenosis* due to a ridge of fibrosis tissue just above the sinus of Valsalva, Williams' syn.

In a patient with aortic stenosis and aortic regurgitation, aortic stenosis is not significant if there is:

1. Rapid upstroke of pulse
2. Pulsus bisferiens
3. High systolic blood pressure
4. Absence of thrill

Pathophysiology

Obstruction to the left ventricular outflow in aortic stenosis leads to left ventricular hypertrophy. Myocardial ischemia may occur without coronary artery lesion due to increased requirement by the hypertrophied myocardium, which may lead to arrhythmias and sudden death. On exercise, the increase in cardiac output is not possible due to the obstruction to the left ventricular outflow and all the symptoms - dyspnea, angina and syncope are aggravated.

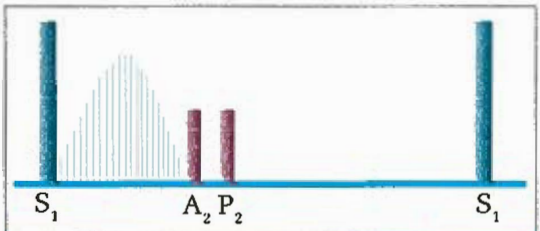


Fig. 5.42: Ejection systolic murmur of AS

Symptoms

Angina, syncope, exertional dyspnea, fatigue, pulmonary edema, sudden death

Diagnosis

A. *Pulse:* Small amplitude. Rises slowly and falls slowly. There may be anacrotic pulse or pulsus bisferiens.
B. *Blood Pressure:* Low systolic blood pressure with narrowed pulse pressure (systolic cut-off of BP)
C. *Apex beat* sustained and heaving in character, pushed outwards and downwards.
D. *Systolic thrill* in the second right interspace and along the carotids.
E. *Ejection systolic murmur* best heard in the aortic area and at the apex and conducted to the carotids. It is rough or harsh in character, rising to a peak in mid systole and tapering before the second heart sound. There is no relation to respiration (Crescendo-decrescendo). Gallavardin phenomenon – AS murmur conducted to apex.
F. *Second heart* sound is soft or absent with narrower reverse splitting.
G. *Ejection systolic click* may sometimes be heard just before the onset of the murmur due to the opening of a stenosed semi lunar valve. It disappears with the calcification of valve. (Valvular AS)

Indications of Severity in AS

1. Pulse character - slowly rising plateau
2. Pulse pressure - narrow
3. Signs of LVF
4. S_2 soft, single or paradoxically split
5. Presence of S_4, Thrill;
6. Long late-peaking murmur; later the peak, more the severity
7. Cardiac catheter-systolic transvalvular gradient > 60 mmHg

Investigations

I. **X-ray chest**
   1. It may be normal in mild cases

2. Prominent dilated ascending aorta with post- stenotic dilation
3. Aortic valve may be calcified
4. Left ventricular enlargement

II. ECG

1. Left ventricular hypertrophy with strain pattern (ST-T changes in leads I, aVL, V_5 and V_6)
2. Left axis deviation.
3. Arrhythmia, heart blocks or left bundle branch block may be present.

III. Echocardiogram

1. Thickened, calcified and immobile aortic valve cusps can be seen.
2. Left ventricular hypertrophy may be seen.
3. Doppler would record the gradient across the valve (Aortic valve area = 3-4 cm^2; Severe AS < 0.6 cm^2)

IV. Cardiac Catheterization

1. Valve gradient between LV and aorta
2. Coronary disease
3. Mitral and aortic valves

V. Coronary Angioplasty to rule out co-existing coronary artery disease

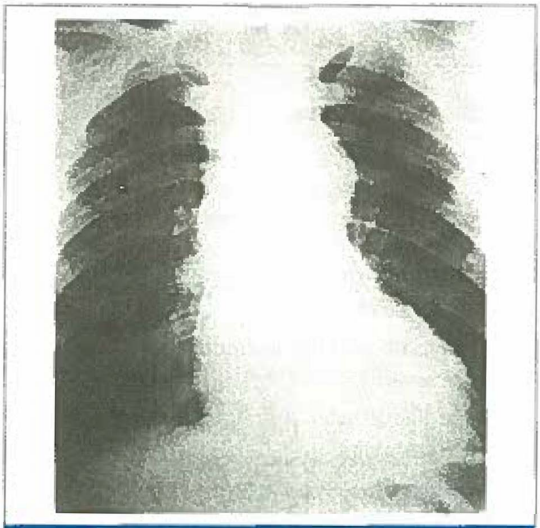


Fig. 5.43 : X-ray showing aortic stenosis

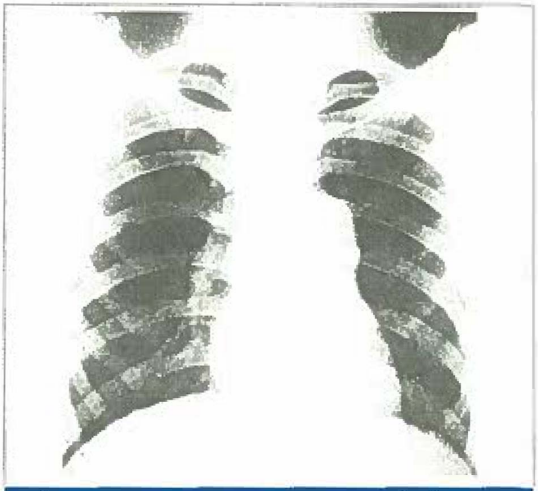


Fig. 5.44 : X-ray showing pulmonary stenosis with post-stenotic dilatation

Differential Diagnosis

A. Table 5.27 ; Differences between AS and PS

		AS	PS
1.	Pulse	Small amplitude, anacrotic or bisferiens	Normal
2.	Blood pressure	Low systolic	Normal
3.	Apex beat	Heaving	Normal
4.	Second sound.	A2 soft	P2 soft
5.	Splitting of 2nd heart sound	Reverse	Wide
6.	Site of systolic murmur	Aortic area, conducted to the carotids	Pulmonary area
7.	Relation to respiration	No change	Increase on inspiration

B. Table 5.28 : Differences between AS and Aneurysm of Aorta

	AS	Aneurysm of Aorta
Symptoms	Angina, syncope and dyspnea	Chest pain, dyspnea, dysphagia, hoarse voice, hemoptysis, cough and symptoms of compression myelitis
History of exposure	Absent	May be present
Second sound	Soft	Loud
Systolic murmur	Conducted to carotids	Not conducted to carotids

C. Table 5.29 : Differences between AS and Hypertrophic Obstructive Cardiomyopathy (HOCM)

		AS	HOCM
1.	Double apex	Uncommon	Common
2.	Presystolic gallop	Uncommon	Common
3.	Second sound	Paradoxical splitting	Single
4.	Systolic murmur	Second right space, conducted to the carotids	Along left sternal border and conducted to the apex
5.	Relation of systolic murmur to Valsalva maneuver or standing	Murmur softer	Murmur louder
6.	Associated AR	Common	Uncommon

D. Supravalvular AS

1. There are equal pulses. Right radial better than left.
2. No ejection click is heard.
3. Systolic thrill and murmur is transmitted to the carotids, suprasternal notch and along right sternal border.
4. Facies: Prominent forehead, depressed bridge of the nose, overhanging lips and deformed teeth.
5. Mental retardation, "elfin" facies, hoarse voice (Williams syn.)
6. Hypercalcemia

Complications

Same as mitral stenosis

Treatment

Medical

1. Patient with aorticstenosis must be advised to avoid strenuous exertion and competitive sports.
2. Angina is best treated with beta-blockers, ACE inhibitors, diuretics. Vasodilators and nitrites are avoided as they may precipitate syncopal attacks.
3. Prophylaxis against bacterial endocarditis must be given (see mitral stenosis)
4. Rheumatic fever prophylaxis
5. Treatment of cardiac failure

Surgical

1. Balloon dilatation of aortic valve gives temporary relief from obstruction.
2. Aortic valve replacement with a prosthetic or tissue valve should be done for everyone with aortic stenosis.

Mechanism of syncope in Aortic Stenosis

1. Due to reduced cardiac output there is reduced circulation to the brain. On exercise, vasodilatation occurs in the muscles due to utilization of metabolites, which further reduces the effective blood flow to the brain.
2. If calcification occurs in the aortic valve, it may also affect the Bundle of His, which is very near. This may lead to heart block and Stokes Adams syndrome.
3. If the patient is working at the peak of the Starling's curve, exercise would not increase the required increased cardiac output.

Prognosis

Life expectancy in patients developing angina is 4 yrs, syncope 3 yrs, dyspnea (LVF) 2 yrs.

12 Cyanotic Congenital Heart Disease

Cyanotic congenital heart diseases are caused by obstruction to the right heart outflow associated with either an intracardiac or a great artery communication proximal to the obstruction. The level of obstruction and associated shunt is given in the Table:

Eisenmenger's Physiology

Eisenmenger's physiology is defined as pulmonary to systemic resistance ratio equal to or greater than one or absolute elevation of pulmonary vascular resistance to greater than 960 dyne sec cm^{-5}

Clinical Features

1 In infancy patients present with failure to thrive,

recurrent respiratory infection and severe heart failure.

2. In adolescence, exertional fatigue, dyspnea and cyanosis develop. Hemoptysis is late and preterminal.
3. Infective endocarditis, cerebral abscess, clubbing and erythrocytosis causing dizziness, headache fatigue and blurred vision may occur.
4. Differential cyanosis and clubbing occur in PDA with right to left shunt. Reversed differential clubbing and cyanosis (clubbing and cyanosis of fingers with pink toes) occurs in PDA with right to left shunt and transposition of great vessels.
5. Supra-ventricular arrhythmias especially atrial fibrillation occurs late and suggests right ventricular failure. Syncope, sudden death or death from minor surgery is common with advanced pulmonary artery disease.
6. JVP shows prominent 'a' waves. If there is right sided failure V waves would be prominent due to tricuspid regurgitation.
7. Pulmonary second sound is loud. Fourth heart sound and ejection click may be heard. If there is right heart failure, third heart sound would be heard.
8. Soft systolic murmur in the pulmonary area along with Graham Steell's murmur replaces the left-right shunt murmur.
9. **ECG**
   a. There is right ventricular and right atrial hypertrophy with right axis deviation.
   b. Associated left ventricular hypertrophy occurs in patients with single ventricle, persistent truncus and a variant of Transposition of great vessels.
   c. Left axis deviation occurs in canal type of VSD and primum type of ASD
   d. First degree A-V block occurs in patients with A-V canal defects.
10. **X-ray chest:** This varies with the underlying lesion and duration and severity of pulmonary artery disease.
    a. Heart may be normal or show right ventricular and atrial enlargement.
    b. Pulmonary artery may be dilated and aneurysmal and in long-standing calcified with pulmonary oligemia peripherally.
    c. A prominent aortic knob suggests that the shunt is at great vessels level.
11. **Echocardiography:** This helps to diagnose the underlying cardiac defect, direction of shunt and presence of pulmonary hypertension.

Table 5.30 : Differential Diagnosis of Eisenmenger's Complex

	Patent Ductus Arteriosus	*Ventricular Septal Defect*	*Atrial Septal Defect*
1. Symptoms Dyspnea, Angina, Syncope	Rare	Common	Less common
2. Clubbing, cyanosis, polycythemia	Differential Cyanosis	Dates from infancy	Not until adult life
3. 'a' waves in neck	Very rare	Rare	Common
4. Chamber enlargement	LVH RVH	LVH RVH	RVH RAH
5. Second sound	Closely Split	Single	Wide fixed split
6. Murmur	Continuous	Pansystolic	Ejection systolic
7. ECG	LVH RVH	LVH RVH	RVH, RAH RBBB
8. X-ray	Enlarged aorta and pulmonary artery	Enlarged pulmonary artery	Enlarged right atrium and pulmonary artery

Treatment

1. Treatment of right heart failure, atrial fibrillation and prophylaxis for infective endocarditis.
2. Phlebotomy for erythrocytosis. This is done when hematocrit is above 65. About 250-500 ml only must be removed at one sitting and preferably simultaneous volume repletion is advisable to achieve hematocrit of about 50-60. Repeated phlebotomy may lead to iron deficiency, which must be adequately treated.
3. Hyperuricemia may be associated with

erythrocytosis and must be treated with allopurinol.

4. Acute hemorrhagic episodes may require platelet transfusion in patients with thrombocytopenia.
5. Pregnancy and oral contraceptives should be avoided as they lead to pulmonary thrombosis and embolism. Tubal ligation carries risk from associated vasovagal effects. Intrauterine devices may cause bleeding in these patients who have abnormal hemostasis and also may predispose to infective endocarditis.
6. For those with advance pregnancy and heart failure, bed-rest is necessary in last trimester. Oxygen may help. Spinal and general anesthesia should be avoided. Induced vaginal delivery and chemoprophylaxis for infective endocarditis must be given.
7. Heart-Lung transplant may help and offers some hope at least for the future.

Tetralogy of Fallot (TOF)

Tetralogy of Fallot is the most common cyanotic congenital heart disease presenting after 1 year of age. Fallot's tetrad consists of:

1. *VSD (infracristal type)*
2. *Infundibular pulmonary stenosis*
3. *Overriding of aorta*
4. *Right ventricular hypertrophy.*

Of these 4 features only the first two are of primary physiological importance.

Fallot's Physiology (Hemodynamics in TOF)

Pulmonary stenosis is the most physiologically important defect (It results in *RV hypertrophy*). PS causes right heart pressure to be higher than left heart pressure, which result in a "right-to-left" shunt across the *VSD*. The blood is also directly shunted into the *aorta* (which *overrides* the septum).

The VSD is large and hence produces no murmur. The blood flow through the PS results in ejection systolic murmur. More severe the PS, more the shunting of deoxygenated blood through the VSD and into the aorta, thus leading to more cyanosis.

Variants

1. In 5% of cases the left anterior descending coronary artery has an anomalous origin from the right coronary artery or from the right sinus of Valsalva
2. *ASD*or patent foramen ovale occur in 25% of cases *(pentalogy of Fallot's)*.
3. Aortic regurgitation, secondary to bicuspid aortic valve, infective endocarditis or aortic leaflet prolapse may occur.
4. **Acyanotic Fallot's:** In some cases of Fallot's tetrad, pulmonary stenosis is mild and hence right ventricular pressure is lower than left sided pressure. There is left to right shunt across the VSD and the patient is not cyanosed but pink.
5. ASD, PS with RVH (Trilogy of Fallot)

Diagnosis

A. *Central cyanosis, clubbing and polycythemia.* Cyanosis occurs because of overriding of the aorta and polycythemia because of hypoxia. Cyanosis may appear at birth or after

B. *Squatting episodes* relieve breathlessness or cyanotic spells because there is:
   1. Compression of femoral artery which increases the resistance to the left ventricular outflow and left ventricle, thus reducing the right to left shunt and hence more blood goes to the lungs to be oxygenated.
   2. Compression of femoral veins reduces the venous return thus reducing the right ventricular pressure and right to left shunt.
   3. Diminished right to left shunt by the above two mechanisms reduces the acid metabolites reaching the brain and depressing the respiration.

C. *Hypoxic/Cyanotic attacks and syncope:* Onset usually during crying or after exertion. These are characterized by crying, cyanosis, tachypnea, syncope, convulsions and sometimes death. It occurs due to systolic contraction of a hypertrophied pulmonary infundibulum, which causes cessation of pulmonary blood flow.

D. *Quiet heart:* There is no right ventricular heave in spite of infundibular stenosis because the right ventricle can empty freely into the aorta.

E. *Second heart sound* is single and never loud. Palpable A_2 due to large aorta.

F. *Pulmonary ejection systolic murmur* due to obstruction of the right ventricular outflow. It disappears during hypoxic spells.

G. *Continuous murmur* due to bronchopulmonary anastamosis (large aortopulmonary collaterals) better heard in the back.

Investigations

I. **ECG**

1. Right axis deviation.
2. Clock wise rotation.
3. Moderate right ventricular hypertrophy with upright 'T' waves in chest leads.
4. RVH with or without RBBB

II. **X-rays**

1. *Coeur en Sabot (boot-shaped) heart* because:
   a. Right ventricular hypertrophy lifts the apex clear off the diaphragm.
   b. Cap of the left ventricle above the apex of the right ventricle.
   c. Pulmonary bay is deep due to hypoplastic pulmonary artery.
2. *Unilateral rib notching.*
3. *Oligemic lung fields.*

III. **Echocardiogram**

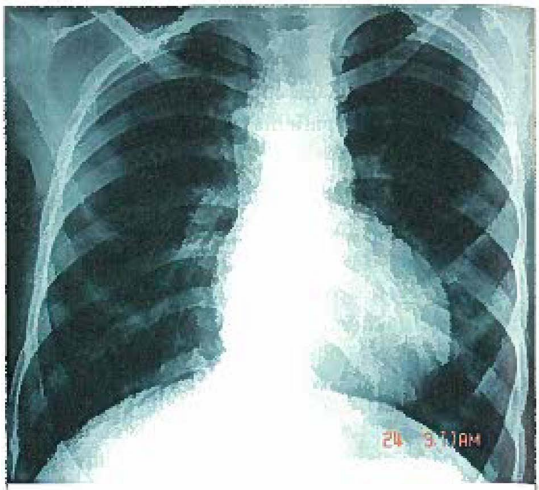
Two-dimensional echocardiography and Color Doppler helps not only to delineate VSD but also to diagnose associated ASD and/or PDA. Overriding of aorta can also be demonstrated.

Complications

A. Syncope from infundibular hypertonus and death.

B. Cerebral abscess occurs because:

1. Polycythemia leads to sludging.
2. Lung, which normally filters off bacteria, does not do so because of shunting.



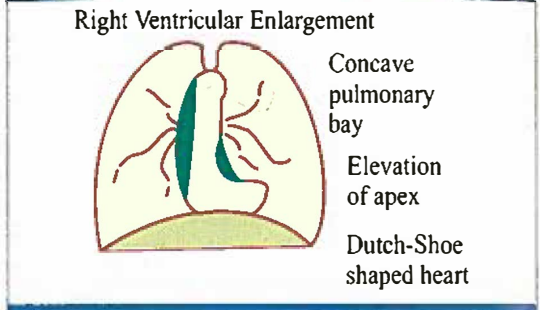


Fig. 5.45 : Chest Xray Tetrology of Fallot with Coren Sabot or Boot Shaped Heart

3. Paradoxical embolism is possible because of right to left shunting.

C. Cerebral thrombosis

D. Iron deficiency anemia

E. Epilepsy

F. Congestive cardiac failure usually is uncommon, but may occur if:

1. High VSD with AR
2. Infections – Pulmonary TB or IE
3. Associated cardiomyopathy
4. Associated severe anemia
5. Coronary thrombosis
6. Myocarditis

Treatment

A. **Medical line of treatment**

1. *Of Cyanotic Spells:*
   a. Knee chest position

Differential Diagnosis

A. Table 5.31 : Differences between Fallot's Tetrad and Eisenmenger's Syndrome

		Fallot's Tetrad	Eisenmenger's Syndrome
1.	Cyanosis	From birth	Later on
2.	Pulmonary artery-pulsations	Absent	Present
3.	P2	Soft	Loud
4.	Graham Steelle's murmur	Absent	May be present
5.	X-ray	Pulmonary oligemia	Pulmonary plethora

B. Table 5.32 : Differences between Fallot's Tetrad and Fallot's Triad (ASD, RVH and PS)

		Fallot's Tetrad	Fallot's Triad
1.	Cyanosis	From birth	A few years later
2.	Squatting	Common	Uncommon
3.	Facies	Not typical	Moon facies
4.	JVP	Small 'a' waves	Large 'a' waves
5.	Right atrial enlargement	Absent	Present
6.	Systolic murmur	Rarely loud	Usually loud with thrill
7.	ECG	'T' waves upright in chest leads	RVH, RBBB, RAH

C. Table 5.33 : Differences between Fallot's Tetrad and Acyanotic Fallot (VSD and PS)

		Fallot's Tetrad	Acyanotic Fallot
1.	Cyanosis	From birth	Later on
2.	'a' waves in JVP	Absent	Prominent
3.	RV heave	Absent	Present

b. Oxygen

c. Sodium bicarbonate if there is acidosis

d. Morphine 1 mg/kg to decrease the infundibular tone

e. Propranolol 5-15 mg to prevent a further attack

2. *Of Epilepsy:* Phenobarbitone or Phenytoin

3. Treatment of arrhythmia, right heart failure and infective endocarditis

B. Surgical line of treatment

1. *Total Correction:* This operation is deferred up to the age 5-6 years. It involves closing the VSD and resection of the Pulmonary or infundibullar stenosis.

2. *Palliative Shunt:* If pulmonary arteries are too hypoplastic, then before total correction, palliative shunt operations should be performed before 3 months. In Palliative Surgery, a systemic artery is anastomosed with the pulmonary artery to increase the blood flow through the pulmonary circulation for oxygenation. The following shunts can be done:

   A. Blalock Taussig Shunt - Subclavian artery to pulmonary artery anastomosis – preferred surgery

   B. Waterston's Shunt - Ascending Aorta to Right Pulmonary Artery anastomosis

   C. Pott's Shunt – Descending Aorta to Left Pulmonary Artery anastomosis

3. *Pulmonary Valvuloplasty:* is sometimes used before total correction.

4. *Percutaneous Infundibular Resection* of the infundibular muscle using modified atherectomy device is the latest technique.

Ebstein's Anomaly of Tricuspid Valve

In Ebstein's anomaly there is atrialization of the right ventricle, so that the tricuspid valve leaflets are displaced away from the tricuspid valve annulus. The A-V node and His bundle may be compressed causing A-V dissociation first degree A-V block and right bundle branch block.

Functional Effects

There is right ventricular inflow obstruction and tricuspid regurgitation. Due to increased right atrial pressure there is right to left shunt through an associated ASD with systemic desaturation.

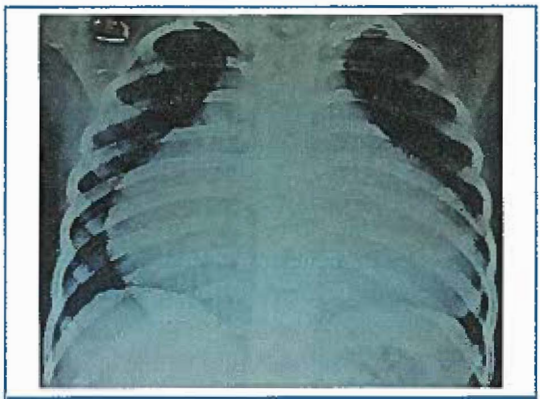


Fig. 5.46: Ebsteins Anomaly

Clinical Features

1. Dyspnea, fatigue and cyanosis
2. Right ventricular impulse is absent
3. First and second sounds may be split
4. A scratchy rub like mid-systolic ejection murmur may be heard in mid and lower sternum.
5. Murmurs of tricuspid insufficiency and relative tricuspid stenosis may be present.

Investigations

ECG

1. Right atrial enlargement
2. Right axis deviation
3. Wide bizarre and splintered QRS complex
4. First degree A-V block, right bundle branch block supra-ventricular tachycardia and type B WPW syndrome.

X-ray Chest

1. Enlarged globular cardiac silhouette
2. Right atrial enlargement
3. Straightening of upper left cardiac border due to leftward displacement of right ventricular infundibulum

Echocardiography

Demonstrates the anatomy of the cardiac defect.

Treatment

1. **Medical:** Similar to Fallot's tetrad
2. **Surgical:** Tricuspid annuloplasty or valve replacement with closure of ASD.

Tricuspid Atresia

DEFINITION: Tricuspid atresia is absence of orifice between the right atrium and right ventricle.

Both the atria are enlarged and thickened. In 40% there is patent foramen ovale and in the rest there is associated ASD. Mitral valve annulus is dilated with thickened valve leaflets. Left ventricle is enlarged and hypertrophied. Right ventricle is small or atretic.

Associated Lesions

1. Transposition of great vessels
2. Co-arctation of aorta
3. VSD

Clinical Features

1. First and second heart sounds are single. Second heart sound (aortic) may be loud.
2. Loud systolic murmur of VSD or Pulmonary stenosis may be present. Decrease intensity of this murmur with increasing cyanosis suggests VSD closure.
3. Mid-diastolic mitral flow murmur may occur
4. Continuous thoracic bruits due to systemic-pulmonary collaterals may be present.

Investigations

ECG

1. Left axis deviation
2. Biatrial and left ventricular hypertrophy

X-ray chest

Blunt elevated apex similar to Fallot's tetrad

Echocardiography

This confirms absence of tricuspid valve, small right ventricle, normal mitral valve and dilated annulus

Treatment

1. **Medical:** Similar to Fallot's tetrad
2. **Surgical:** To increase pulmonary blood flow, a *Rashkind balloon septostomy* or a *shunt (e.g. Glenn*

or Blalock) is performed. If pulmonary flow is too great, PA banding is done in the first year of life. Correction of the defect is done after 2 years age using *'Fontan' atriopulmonary connection.*

Persistent Truncus Arteriosus (TA)

Persistent truncus arteriosus consists of a single or common outflow trunk that arises from the base of the heart giving rise to systemic, pulmonary and coronary circulation. It is invariably associated with VSD.

Pathophysiology

If the pulmonary stenosis is not significant and VSD large, truncal pressure equals that of the ventricles and large pulmonary blood flow may lead to L.V. overload and cardiac failure. If however, there is significant pulmonary stenosis, pulmonary blood flow is decreased and there is hypoxia but normal heart size. The patients in between these two extremes may survive for many years with near normal function.

Clinical Features

1. Patient presents with cardiac failure and cyanosis
2. Wide bounding pulse may be present.
3. Second sound is usually single; split may be present due to extra-truncal vibrations. murmur with a thrill may be present.
5. High pitched diastolic decrescendo murmur of truncal regurgitation may be present.

Investigations

I. **X-ray chest**
   1. Marked rightward convexity with right aortic arch
   2. Cardiac pedicle is narrow due to absence of prominent pulmonary artery

II. **Echocardiography**

Absence of pulmonary valve and demonstration of the origin of the pulmonary artery from the truncus establishes the diagnosis.

Treatment

1. **Medical:** Treatment of cardiac failure
2. **Surgical:** VSD patch closure with placement of conduit from the right ventricle to the pulmonary artery and directing the left ventricle to the truncus.

Total Anomalous Pulmonary Venous Connections (TAPVC)

In TAPVC, the 4 pulmonary veins converge in a common collecting sinus, from where the blood is drained into the right atrium through an anomalous venous drainage.

TYPES: Supra cardiac, cardiac and infracardiac

Pathophysiology

Almost all patients with TAPVC have associated interatrial communication. Volume overload leads to right atrial, right ventricular and pulmonary hypertension. The clinical course depends upon whether pulmonary venous obstruction exists, the magnitude of right ventricular outflow resistance and size of the interatrial communication.

If there is obstruction to the pulmonary venous drainage, severe pulmonary edema or marked pulmonary hypertension occurs. If there is inadequate interatrial communication, right heart failure and pulmonary hypertension and pulmonary arteriolar disease ensues. Pulmonary stenosis may protect the individual from excessive pulmonary flow and heart failure.

Clinical Features

The clinical features resemble those of ASD associated with moderate cyanosis.

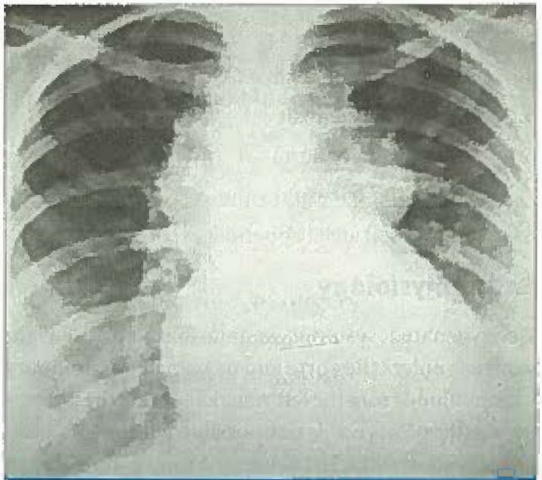


Fig. 5.47: X-ray of Supracardiac TAPVC with Snowman Appearance or Figure of 8 appearance

Investigations

I. **ECG:** Similar to ASD

II. **X-ray chest**

1. Normal heart size with pulmonary edema with figure of 8 silhouette
2. Increased heart size with dilated proximal pulmonary arteries and figure of 8 silhouette.
3. *'Cottage loaf' heart or 'snowman in a storm'* in the supra cardiac type TAPVC.

III. Echocardiogram

Suprasternal view would provide the definitive diagnosis.

Treatment : Surgical correction

Complete Transposition of Great Vessels (D Transposition, TGA)

Transposition of great arteries (TGA) consists of the following:

1. The great arteries arise from the wrong ventricles i.e. the aorta arises from the right ventricle and pulmonary artery arises from the left ventricle (D-loop).
2. The aorta is anterior to the pulmonary artery
3. The aorto-mitral continuity is absent.

Associated Lesions

1. PDA
2. VSD
3. ASD
4. Patent foramen oval
5. Pulmonary stenosis
6. Coarctation of aorta
7. Straddling tricuspid valve
8. Juxtaposed atrial appendages

Pathophysiology

Deoxygenated systemic venous blood from right ventricle enters the aorta and oxygenated pulmonary venous blood from the left ventricle enters the pulmonary artery. Survival is not possible without an additional ASD or VSD. The volume of admixture between the two circulations must be equal in each direction.

Clinical Features

I. **With intact septum**

1. Cyanosis is extreme with normal heart size
2. Loud second heart sound (because aorta is anterior)
3. Soft ejection systolic murmur

II. **With large VSD**

1. Cyanosis is mild but heart failure is common
2. Loud second and third heart sound
3. Long systolic murmur at the left sternal edge with mid-diastolic flow murmur.

III. **With large VSD and pulmonary stenosis**

1. Cyanosis is mild and heart failure infrequent
2. Loud second sound (aortic) with ejection click (pulmonary)
3. Loud systolic murmur
4. Thoracic bruits due to collaterals.

Investigations

I. **ECG:** Right atrial and ventricular hypertrophy

II. **X-ray chest**

Cardiomegaly with pulmonary plethora and venous congestion. The vascular pedicle is narrow *(Egg on a string appearance)*

III. **Echocardiography**

Helps to diagnose the anatomical lesions

Treatment

1. **Medical:** Treatment of cardiac failure
2. **Pacemaker:** For AV blocks
3. **Surgical:** Palliative treatment by balloon atrial septostomy/enlargement. Surgical correction may be possible.

13 Patent Ductus Arteriosus (PDA)

The ductus arteriosus is the vessel leading from the bifurcation of the pulmonary artery to the aorta distal to the left subcavian artery. It is open normally in the fetus but closes functionally in 1 -2 days after birth. It closes anatomically in 10 – 21 days. In PDA there is a failure of this vessel to close, resulting in a continuous AV shunt.

Associated Lesions

A. VSD
B. ASD
C. Aortic stenosis
D. Coarctation of aorta
E. Endocardial fibroelastosis
F. Pulmonary stenosis

Associated Syndromes

A. Downs Syndrome - Trisomy 21
B. Congenital Rubella Syndrome (Deafness, Cataract and PDA or Pulmonary Stenosis)
C. Fetal Hydantoin Syndrome due to phenytoin.

Diagnosis

Symptoms: Recurrent respiratory infection in childhood, dyspnea and angina.

Signs

A. Signs of *wide pulse pressure*
B. *Pulsations of pulmonary artery and pulsations in suprasternal notch*
C. *Heaving apex beat*
D. *Gibson's murmur:* It is a continuous murmur increased at the end of systole and early diastole and accentuated by exercise and expiration. It is best heard in the pulmonary area or higher up (below the clavicle in 2nd intercostal space). It is *'machinery' or 'train in tunnel'* in character. It is absent:
   1. Below the age of 3 years
   2. In heart failure
   3. If there is right to left shunt
E. *Mid-diastolic mitral flow murmur* may be heard.
F. If there is *pulmonary hypertension* there will be signs of pulmonary hypertension as described in mitral stenosis. In addition, there will be:
   1. *Differential cyanosis* i.e. cyanosis more in the lower limbs than upper limbs, more apparent after a hot bath
   2. Disappearance of Gibson's and mitral mid-diastolic murmurs

Investigations

I. **ECG**
   1. Normal in infancy
   2. Left ventricular and left atrial hypertrophy
   3. If associated pulmonary hypertension there will be right ventricular hypertrophy
   4. Prolonged PR interval
   5. Atrial fibrillation sometimes

II. **X-rays**
   1. Left atrial and left ventricular hypertrophy
   2. Marked pulmonary plethora
   3. Aortic knuckle prominent
   4. Notch between the aortic knuckle and the pulmonary artery is obliterated
   5. Calcified ductus

C. **Echocardiogram** would demonstrate the patent ductus and color Doppler would suggest the direction of flow.

Complications

A. Pulmonary hypertension
B. Infective endocarditis
C. Congestive cardiac failure

Differential Diagnosis

This includes all causes of continuous murmur as given above.

Treatment

A. Medical Treatment:Indomethacin – 0.1mg/kg/dose 12 hourly for 3 doses (if diagnosed within 2 weeks of birth)
B. **Surgical Treatment:** Ligation and excision of the ductus. All these cases require surgery unless contraindicated.

Contraindications of surgery

Absolute contraindications:

1. Eisenmenger's complex
2. Where ductus is compensatory alongwith:-
   a. Preductal coarctation
   b. Transposition of great vessels
   c. Tricuspid or pulmonary atresia

Relative contraindications:

1. Infective endocarditis (for 3 months).
2. Congestive cardiac failure.

C. **Trans-catheter closure** – using coils, plugs or umbrellas

14 › Ventricular Septal Defect (VSD)

Congenital VSD, the most common congenital heart disease, occurs as a result of incomplete septation of the ventricles.

Sites

1. **Peri**membranous (most common)
2. Muscular (apical, central, marginal, multiple-Swiss cheese pattern)
3. Inlet
4. Outlet(infundibular)

Associated syndromes

1. Trisomy 21, 18, 13
2. Cri du Chat syndrome
3. Fetal alcohol syndrome

Causes

A. Isolated

B. VSD is invariably present in:
   1. Eisenmenger's disease
   2. Fallot's tetrad
   3. Pulmonary atresia
   4. Common A-V canal
   5. Double outlet right ventricle

C. VSD is commonly present in:
   1. Tricuspid atresia
   2. Transposition of great vessels

D. VSD is coincidental in:
   1. Pulmonary and infundibular stenosis
   2. PDA
   3. ASD
   4. Coarctation of aorta
   5. Mitral valve deformities as in MS and MR.

Diagnosis

A. Recurrent respiratory infection of childhood and failure to thrive

B. Moderately collapsing pulse

C. Biventricular hypertrophy

D. Systolic thrill over 3rd, 4th left parasternal regions

E. Pansystolic murmur in the 3rd and 4thleft parasternal region, conducted to the right side

F. Mid-diastolic mitral flow murmur at apex

G. S_3 may be audible at apex

H. *Signs of pulmonary hypertension,* if present

Investigations

I. ECG
   1. Normal
   2. Biventricular hypertrophy
   3. Right bundle branch block

II. X-rays
   1. Normal
   2. Biventricular hypertrophy with equiphasic R & S waves in V3 & V4 (Kate-Watchel phenomenon)
   3. Pulmonary plethora

III. **Echocardiogram with Doppler** would define the ventricular septal defect and associated anomalies

Complications

A CCF at 30-40 yrs

B. Pulmonary hypertension (Eisenmengers)

C. Infective endocarditis

D. Arrhythmias (ventricular, supraventricular, complete heart block)

E. Recurrent respiratory infections or lung abscess

F. AR (if high VSD)

Differential Diagnosis

Mitral Regurgitation: Refer Pg. 232.

Management

1. 30-50% close spontaneously by 3 yrs (especially muscular or membranous types)

Table 5.34 : Differences between VSD and TI

		VSD	TI
1.	LVH	Present	Absent
2.	First heart sound	Normal	Soft
3.	Pansystolic murmur		
	a) Conduction	To the right	To apex
	b) Relation to respiration	Best in expiration	Best in inspiration
4.	JVP	Normal	'v' wave prominent
5.	Pulsatile liver	Absent	Present

Table 5.35 : Differences between VSD and PS

		VSD	PS
1.	JVP	Normal	'a' wave prominent
2.	Second heart sound	Loud P2	Soft P2
3.	Murmur	Pansystolic	Ejection systolic
4.	Middiastolic flow murmur	Present	Absent
5.	Ejection clicks	Absent	Present
6.	LVH	Present	Absent
7.	X-ray	Pulmonary plethora	Pulmonary oligemia
8.	ECG	BVH	RVH

2. **Medical treatment** of all complications.
3. **Surgery:** Ideal age < 2yrs. Closure with Dacron patch, through right atrium
4. Double Clamp shell device used to non-surgically close some muscular VSD.

Indications for Surgery:

1. Failure to thrive
2. Large defect (>1cm)
3. Left-to-right shunt
4. Cardiomegaly on chest X-ray
5. RV systolic pressure > 65%
6. LV systolic pressure if PVR > 8 units.
7. Pulmonary-to-systemic blood flow ratio is greater than 1.5:1
8. Pulmonary-to-systemic vascular resistance is less than 0.5:1.

15 › Atrial Septal Defect (ASD)

ASD is an acyanotic congenital cardiac anomaly in adults with a left-to-right shunt.

Types

1. **Secundum or Fossa ovalis defect:** This is commonest and is situated in the region of fossa ovalis.
2. **Sinus venosus defect:** This is crescent shaped opening near the orifice of superior vena cava. It is often associated with anomalous pulmonary venous drainage.
3. **Primum or partial atrioventricular canal defect:** Deficient tissue in the lower portion of the septum.
4. **Coronary sinus defects** are rare and involve posterior-interior surface of the septum.

Table 5.36 : Differences between Secundum and Primum ASD

		Secundum ASD	Primum ASD
1.	Incidence	70%	15%
2.	Associated MR	Late in life due to degenerative valvular disease	From birth due to associated left mitral leaflet Anomaly
3.	Right heart failure	Uncommon before fourth decade	May occur in infancy
4.	ECG		
	a) Axis	Right	Left
	b) Prolonged PR	Not common	Common

Diagnosis

A. *Right ventricular hypertrophy* – left parasternal heave

B. *Wide fixed split of second heart sound.* It is wide because due to left to right shunt at the atrial level

more blood has to flow across the pulmonary valve. Hence P_2 is delayed giving rise to a wide split. The split is fixed (i.e. split does not vary with respiration) because the shunt at the atrial level causes equal changes in pressure on both sides on inspiration. In addition, since the RV is fully loaded, inspiration cannot further increase the RV volume.

C. *Pulmonary ejection systolic murmur*, which increases on inspiration.

D. *Mid-diastolic tricuspid flow murmur.*

E. If there is *pulmonary hypertension* there will be signs of pulmonary hypertension as described with mitral stenosis. There will be:
   1. Absent tricuspid flow murmur
   2. Narrowing of the split of the second heart sound with loud P2
   3. Prominent 'a' waves in jugular veins.

F. **ECG**
   1. Right ventricular hypertrophy
   2. Right atrial enlargement
   3. Right bundle branch block (rSR' in V_1) with right axis deviation (secondum type)
   4. Sometimes atrial fibrillation
   5. First degree heart block with left axis deviation (primum type)

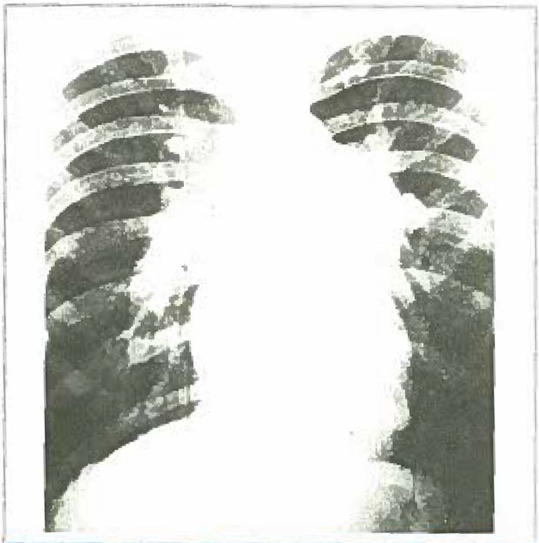


Fig. 5.48: X-ray in ASD with left to right shunt

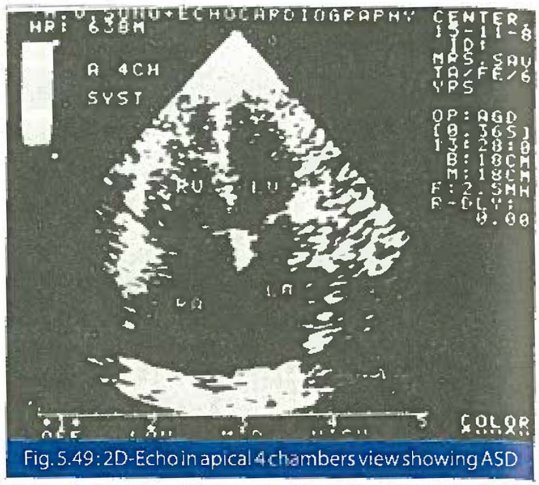


Fig. 5.49: 2D-Echo in apical 4 chambers view showing ASD

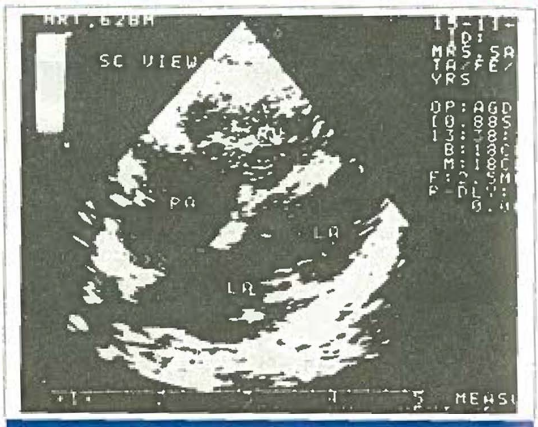


Fig. 5.50: 2D Echo in substernal view showing ASD

G. **X-rays**
   1. Marked dilatation of pulmonary trunk
   2. Right ventricular and right atrial hypertrophy
   3. Hilar dance on screening

H. **Echocardiogram (Transesophageal)** will demonstrate the defect in the septum.

Complications

1. Recurrent chest infections
2. IE
3. Pulmonary HT (Eisenmenger's complex)
4. Atrial fibrillation/SVT

Associated Lesions

A. Acquired Mitral stenosis *(Lutembacher's syndrome)*

B. Pulmonary stenosis *(Fallot's trilogy)*

C. Anomalous pulmonary venous drainage into right atrium

D. Skeletal defects like:

1. Marfan's syndrome
2. *Holt-Oram's syndrome:* Here ASD is associated with a hypoplastic thumb with an accessory phalanx

E. Trisomy21, Down's syndrome

F. Congenital Rubella syndrome

Cyanosis in ASD may be due to:

1. Pulmonary hypertension
2. Coronary sinus defect
3. Sinus venosus defect with a straddling superior vena cava
4. Secundum ASD with a large Eustachian valve, which allows inferior vena cava flow to enter the left atrium selectively

Management

Medical

1. Treatment of IE
2. Treat chest infections
3. Treat arrhythmias

Surgical

Management by operative repair at age 3-6 yrs

1. Pericardial or prosthetic patch
2. Percutaneous catheter device closure

Indications for surgery

1. Pulmonary:systemic blood flow greater than 1.5:1
2. Pulmonary:systemic valvular resistance <0.7:1

Contraindications

1. Small defects and trivial left-to-right shunts
2. Pulmonary hypertension
3. Associated malformations suspected
4. Coronary artery disease

Scimitar syndrome

1. Sinus venosus type of ASD
2. Partial anomalous pulmonary venous drainage in right atrium
3. Hypoplasia of the right lung
4. Secondary dextroposition and dextrorotation of the heart
5. Hemi-vertebrae

16 Coarctation of Aorta

Types of Coarctation

A. *Pre-ductal* (Infantile)between the fourth and sixth aortic arches – narrowed aorta proximal to left subclavian artery

B. *Post-ductal* (Adult or Juxtaductal) between the sixth aortic arch and the fusion of the two dorsal aortae – narrowing of aorta distal to left subclavian artery

C. *Pseudo-coarctation:* Tortuosity of the aorta in the region of the duct

Diagnosis of Post-ductal Coarctation

A. Symptoms

1. No symptoms
2. Symptoms due to hypertension like headache, epistaxis.
3. Intermittent claudication, coldness of feet and chilblains.
4. Due to dilated collateral: Shoulder pains.

B. Signs:

1. Upper part of the body may be well-developed and lower limbs underdeveloped
2. Radio femoral delay
3. Elevated upper limb blood pressure
4. Suprasternal pulsations
5. Suzzman's sign - palpable arterial collateral pulsations in the interscapular region
6. Left ventricular hypertrophy
7. Aortic ejection click:
   a. Aortic ejection systolic murmur at the base and apex due to dilatation of ascending aorta.

b. Late ejection systolic murmur in the interscapular region at second thoracic spine due to coarctation itself.

c. Systolic murmur over the large collaterals.

d. Mid-diastolic mitral murmur at the apex due to thickened mitral valve by concomitant fibroelastosis.

e. Early diastolic murmur due to associated aortic regurgitation.

f. Ejection systolic murmur at the aortic area, conducted to carotids due to associated aortic stenosis.

g Continuous murmur.

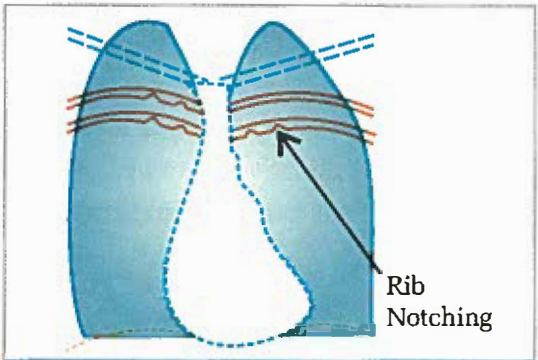


Fig. 5.51: Rib notching

C. X-rays

1. *Dock's sign* - Rib notching due to dilated collaterals. Rib notching does not involve the first and second ribs because first and second intercostal arteries are not involved in the collateralization process.
2. *Shallow figure of 3 silhouette* - upper notch is because of pre- and post-stenotic dilatation

D. ECG : In infants the ECG is usually normal. Left ventricular hypertrophy and left atrial enlargement may occur in adults. If it occurs in infants it suggests associated left ventricular outflow tract obstruction or endomyocardial disease. Right ventricular hypertrophy suggests associated VSD. RBBB is common.

E. Other tests

1. Echocardiography and Color Doppler in suprasternal and upper parasternal views helps to delineate the coarct and estimate the gradient. Left ventricle and its outflow tract, mitral valves and interventricular septum can be assessed.
2. Digital Subtraction Angiography helps not only to delineate the coarct but also helps to distinguish real from pseudo coarct.

Diagnosis of Preductal Coarctation

Features resemble those of post-ductal coarctation except:

A. Left arm is underdeveloped
B. Left radial is weak
C. Rib notching is only on the right side

Associated Anomalies

A. PDA
B. VSD
C. Bicuspid aortic valve
D. Congenital cerebral berry aneurysms
E. Secondary congenital endocardial fibroelastosis
F. Anomalous origin of right or left subclavian
G. Turner's syndrome
H. Male sex
I. Congenital AS

Complications

A. Infective endocarditis
B. Congestive cardiac failure
C. Hypertension and its complications
D. Ruptured berry aneurysm and subarachnoid hemorrhage
E. Aortic rupture
F. Premature coronary artery disease

Treatment

A. *Medical*

1. Sedation
2. Anti-hypertensives
3. Prophylaxis for infective endocarditis
4. Treatment of LVF

B. *Surgical*

Preferably between 5 and 20 years of age

1. Balloon angioplasty (dilatation) of the coarctation
2. Dacron or Teflon graft and end-to-end anastomosis
3. Aortic valve repair
4. Restrict energetic activities for six months post-operatively
5. Post-surgical hypertension is common.
6. Follow-up for Premature coronary artery disease

17 Aneurysm of Aorta

Definition: Aneurysm of aorta is an abnormal dilatation of aorta that involves all the three layers of the wall of the aorta. The basic defect is destruction of the elastic fibers in the media, which are replaced by fibrosis.

A false aneurysm of aorta consists of an encapsulated hematoma in communication with the lumen of the aorta.

Types

1. *Fusiform:* A segment of the aorta becomes diffusely dilated. Abdominal aortic aneurysms are usually fusiform
2. *Saccular:* A portion of the circumference is involved and consists of outpouching with a mouth. Thoracic aortic aneurysm is usually saccular.

Etiology

1. *Atherosclerosis*
2. *Syphilis*
3. *Connective tissue disorders:* Marfan's syndrome, Ehlers-Danlos syndrome, lupus erythematosus.
4. *Congenital diseases:* Bicuspid aortic valve, Turner's syndrome, Noonan's syndrome
5. *Iatrogenic:* Post cardiac surgery or post cardiac catheterization

Predisposing factors

Hypertension and Smoking

Clinical Features

I. **Thoracic Aortic aneurysm**

A. *Symptoms:* The patient may be asymptomatic or may have any of the following symptoms. Aneurysm of the arch of the aorta commonly presents with symptoms.

1. Chest pain: This may occur due to expansion or threatened rupture of aneurysm or due to compression and

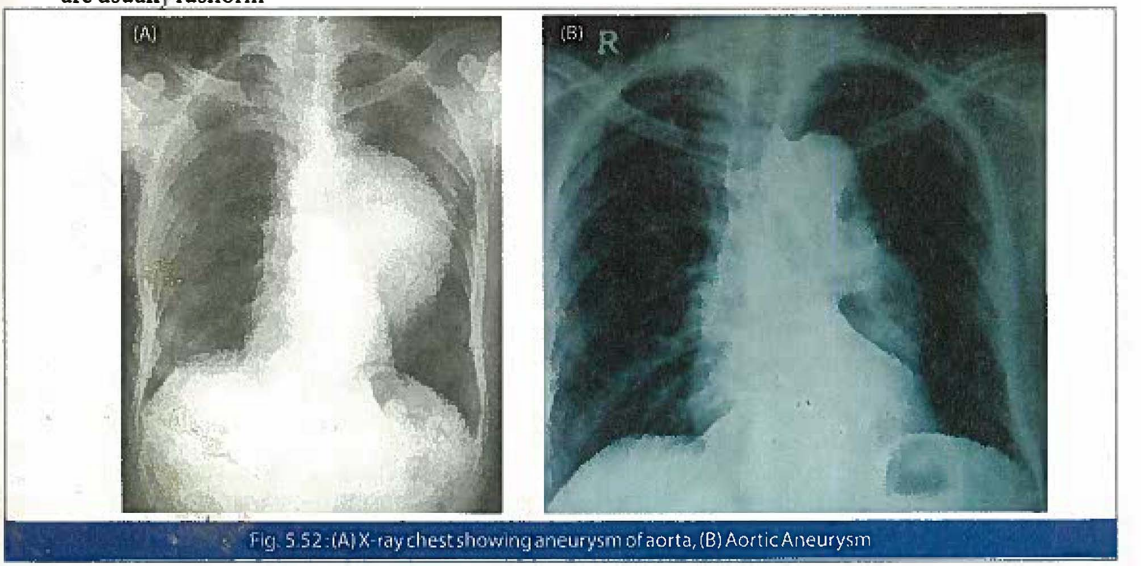


Fig. 5.52: (A) X-ray chest showing aneurysm of aorta, (B) Aortic Aneurysm

erosion of adjacent musculoskeletal structures. The pain may be steady, boring or throbbing.

2. Dyspnea: This may occur due to pressure on the esophagus.
3. Cough: This occurs due to pressure on the trachea. The cough has metallic quality and is called "Gander's cough".
5. Dysphagia: This may occur due to pressure on the esophagus.
6. Hoarseness of voice: This occurs due to pressure on the recurrent laryngeal nerve.
7. Compression myelopathy occurs when aneurysm erodes the bones and presses spinal cord causing spastic paraplegia.

B. *Signs:* Aneurysm of ascending aorta is also called aneurysm of signs

1. Signs due to aneurysmal sac
   a. Systolic impulse over the chest
   b. Systolic thrill over the area of impulse
   c. Systolic murmur over the area of impulse
   d. Parasternal dullness on the right side
   e. Loud tambour like aortic component of second heart sound
2. Signs due to compression:
   a. Superior vena cava: This causes puffy face, dilated veins over the chest and raised and fixed JVP.
   b. Sympathetic trunk: This causes Horner's syndrome characterized by ptosis, miosis, anhidrosis, enophthalmos and absent cilio spinal reflex.
   c. Right bronchus: This causes collapse of the right lobe of lung.
3. Other signs :
   a. *Oliver's sign: Tracheal tug i.e. pulsations are felt just below the cricoid cartilage*
   b. Difference in pulse and BP in both the extremities

II. Abdominal aortic aneurysm

A. *Symptoms:* Small stable aneurysms are asymptomatic. As it enlarges there may be deep continuous pain in the abdomen.

B. *Signs:*

1. Pulsating mass, free movable with expansile pulsations. Leakage of aneurysm may cause tenderness over the mass
2. Bruit may be heard
3. Femoral pulsations may be reduced.

Diagnosis

I. Thoracic

A. *Chest X-ray* and *screening* would show the dilated segment with expansile pulsations

B. *2D Echo:* This would demonstrate the aneurysm in suprasternal view.

C. *Aortography* helps of verify the presence and extent of aneurysm.

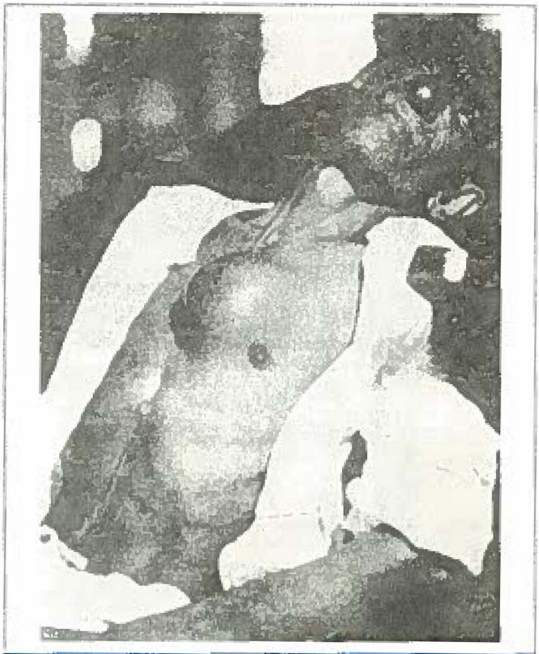


Fig. 5.53: A patient with rounded swelling over the chest wall due to aneurysm of aorta

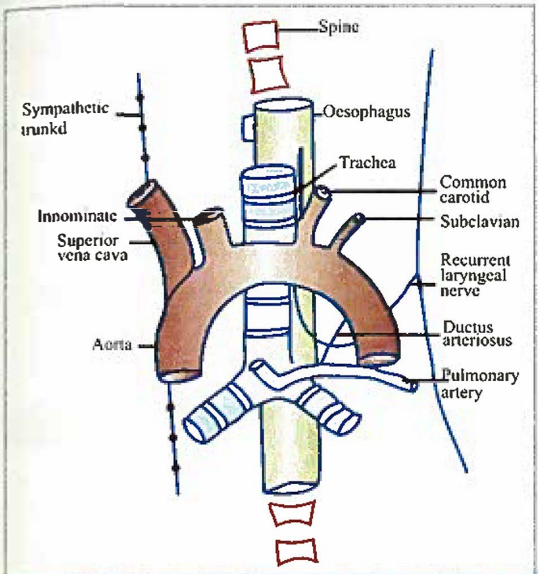


Fig. 5.54 : Diagramatic section of mediastinum showing relations of aorta with various important structures which are compressed

II. Abdominal

A. *X-ray abdomen:* A curvilinear or linear rim of calcification corresponding to the aneurysmal wall may be present. In an unruptured aneurysm, psoas muscle shadow is intact and there is gas in the bowel over the aneurysm.

B. *Sonography and CT scan:* This helps to evaluate the size of the aneurysmal sac as well as the thickness of its wall.

C. *Aortography:* This is helpful when the diagnosis is in doubt and also to evaluate the patency of the renal and iliac arteries. However, it is potentially hazardous and expensive.

Management

I. **Medical**

a. Treatment of hypertension and to avoid smoking and tobacco.

b. Role of anticoagulants with large clots

II. **Surgery:** Aneurysmectomy with replacement with synthetic prosthesis. This is particularly required if the size is more than 5 cms.

18 Pericardial Effusion

Causes

Common

1. Tuberculous
2. Rheumatic
3. Pyogenic
4. Viral
5. Uremia
6. Post-myocardial infarction
7. Malignancy of bronchi, breast or lymphatics
8. Amebic abscess rupturing into the pericardium

Uncommon

1. Traumatic
2. Collagen disease
3. Blood dyscrasias: Leukemia, purpura
4. Scurvy
5. Myxedema
6. Radiation therapy
7. Post-pericardiotomy syndrome
8. Ruptured aneurysm of aorta in pericardium
9. Fungal: Actinomycosis, histoplasmosis
10. Secondary to inflammation in surrounding tissue e.g. pleurisy

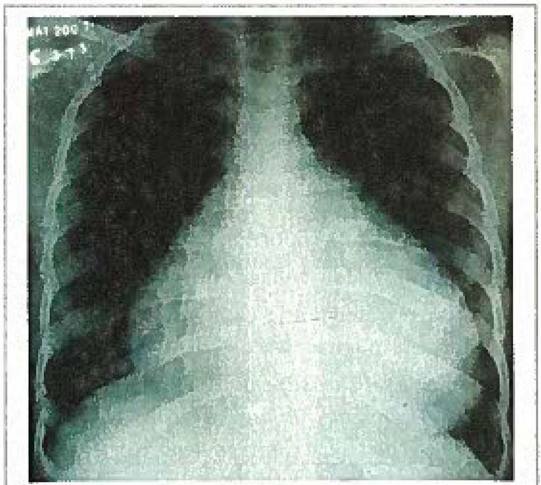


Fig 5.55 : X-ray chest showing Pericardial effusion

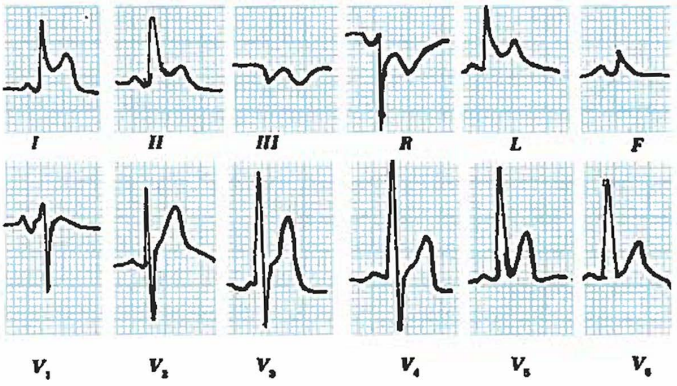


Fig. 5.56: ECG in acute pericarditis showing elevated ST segment with concavity upwards

Diagnosis

A. *Precordial pain* may be of 3 types:
   1. Typical precordial pain which is stabbing and increases on inspiration, coughing and body movements and radiating to the neck, arms and back
   2. Dull aching pain
   3. Pain in the right lower chest because of hepatic distension

B. *Constitutional symptoms* like fever, sweating, weight loss, dyspnea

C. *Pulse:* Pulsus paradoxus

D. *JVP: markedly elevated and increases on inspiration (Kussmaul's sign)*

E. Apex beat is not felt or very feebly felt

F. Increased cardiac dullness — upper border in the second space, right border parasternal and left border outside the apex

G. Heart sounds faint and muffled

H. Pericardial friction rub

I. Hepatomegaly

J. Ascites out of proportion to edema

K. ECG shows low voltage of the QRS complex

L. **X-ray:** Water bottle configuration in upright position

In any patient with hepatic enlargement and ascites one must always look for full jugular veins, especially on inspiration. If present, a clinical diagnosis of pericardial effusion must be made and the other signs of it must be looked for.

Treatment

I. **Treatment of cause**

II. **Supportive**
   A. Bed-rest
   B. Analgesics
   C. Adequate diet

III. **Steroids:** 60-80 mg. prednisolone tapered after 3 weeks if:
   A. Post-pericardiotomy
   B. Post-myocardial infarction
   C. Idiopathic.

IV. **Pericardial Aspiration:** This must be done if there is rapid accumulation of fluid or cardiorespiratory embarrassment.

V. **Pericardiectomy:**
   A. For chronic, recurrent effusions
   B. For thick pyogenic effusions

19 › Cardiomyopathy

Definition

Cardiomyopathies are diseases that involve primarily the myocardium and not the result of congenital, valvular, hypertension coronary, pericardial or arterial diseases.

Clinical Types

1. *Dilated (D) (Congestive):* Left & right ventricular

enlargement, impaired systolic function, cardiac failure, arrhythmias and embolization.

2. *Restrictive (R):* Endomyocardial scarring or myocardial infiltration result in right or left ventricular filling.
3. *Hypertrophic (H):* Disproportionate left ventricular hypertrophy involving the septum move than the free wall.

Causes

I. **Primary**
   1. Idiopathic (D,R,H)
   2. Familial (D,H)
   3. Eosinophilic endomyocardial disease (R)
   4. Endomyocardial fibrosis (R)

II. **Secondary**
   1. Infective (D): Viral, bacterial, fungal, protozoal, spirochetal, rickettsial, etc.
   2. Metabolic (D)
   3. Familial storage disease (D/R): Glycogen storage disease, mucopolysaccharidoses.
   4. Deficiency (D): Nutritional, electrolytes.
   5. Connective tissue disorders (D): SLE, rheumatoid arthritis, scleroderma, polyarteritis nodosa
   6. Granulomas (R,D): Amyloidosis, sarcoidosis, hemochromatosis, malignancy, etc.
   7. Neuromuscular (D): Muscular dystrophy, myotonia dystrophica, Refsum's disease, Friedreich's ataxia, (H,D), etc.
   8. Toxic (D): Alcohol, drugs, radiation, etc.
   9. Peripartum (D)
   10. Endocardial fibroelastosis (R).

Dilated (Congestive) Cardiomyopathy

In Dilated cardiomyopathy, there is impairment of systolic function of left and right ventricular. It is the end result of myocardial damage produced by a variety of toxic, metabolic and infectious agents.

Causes

1. Viral myocarditis (late sequel)
2. Toxic: Alcoholic
3. Pregnancy
4. Metabolic: Hypocalcemia, Hypophosphatemia
5. Selenium deficiency
6. Chronic uncontrolled tachycardia
7. Right ventricular dysplasia.

Clinical Features

The patients may present with

1. Cardiac failure
2. Angina
3. Systemic embolization from mural thrombus.

Investigations

X-ray chest: There would be cardiac enlargement, due to left ventricular enlargement. Lung fields show pulmonary venous hypertension and interstitial or alveolar edema.

ECG: This may show sinus tachycardia, cardiac arrhythmias and non-specific ST-T changes.

Echocardiogram: This may show LV enlargement and reduced ejection fraction.

Treatment

1. Treatment of cardiac failure with diuretics, digoxin and ACE inhibitors.
2. Immunosuppressive agents may benefit in a few patients who have evidence of myocardial inflammation.
3. Anti-arrhythmic agents: Most of these drugs are avoided for fear of pro-arrhythmias. Surgical interruption of arrhythmic circuit or implantable defibrillator may be used.
4. Cardiomyoplasty
5. Heart-Assist devices and Artificial heart
6. Cardiac transplantation may be tried in patients with advanced disease, refractory to medical treatment.

Restrictive Cardiomyopathy

This is characterized by abnormal diastolic function. The ventricular wall is rigid and impairs ventricular filling. It resembles constrictive pericarditis.

Causes

1. Idiopathic
2. Endomyocardial fibrosis
3. Eosinophilic endomyocardial disease
4. Amyloidosis, Hemochromatosis, Glycogen storage disease
5. Endomyocardial fibroelastosis
6. Neoplastic infiltration

Clinical Features

The partial obliteration of ventricular cavity by fibrous tissue and thrombus leads to increased resistance to ventricular filling. As a result of persistently elevated venous pressure, these patients have the following features:

1. Dependent edema, ascites and enlargement of liver (Resembling cirrhosis of liver)
2. JVP is raised and fixed. It may rise on inspiration (Kussmaul's sign).
3. Heart sounds are faint. Third and fourth heart sounds may be heard.

Investigations

X-ray chest: Normal or enlarged heart size would be present without pulmonary congestion. Pericardial calcification which occurs with constriction pericarditis never occurs.

ECG: This may show low-voltage and ST-T changes. Various arrhythmias may occur.

Table 5.37 : Differences between Restrictive Cardiomyopathy and Constrictive Pericarditis

	Restrictive cardiomyopathy	*Constrictive pericarditis*
Apex impulse	Easily palpable	Indistinct
Mitral regurgitation	Common	Uncommon
X-ray chest	No calcification	Pericardial calcification
MRI scan	Normal pericardium	Thick pericardium
Endomyocardial biopsy	Interstitial infiltration	Normal or fibrosis
Treatment	Cardiac transplant	Pericadiectomy

Echocardiogram: This may show symmetrically thickened left ventricular wall with normal or slight reduced systolic function (ejection fraction). On Doppler examination accentuated early diastolic filling is detected.

Hypertrophic Cardiomyopathy

This is characterized by left ventricular hypertrophy often with asymmetrical septal hypertrophy where upper part of the interventricular septum is preferentially hypertrophied and a dynamic left ventricular outflow tract pressure gradient occurs.

Genetics

In 50 % of patients, it is transmitted as an autosomal dominant trait. It is due to an abnormality of the beta myosin heavy chain, caused by a single point mutation on chromosome 14.

Clinical Features

Symptoms

1. Patients may be asymptomatic or may have Sudden death.
2. Dyspnea occurs due to stiff left ventricle and elevated left ventricular end-diastolic pressure
3. Angina pectoris
4. Syncope, fatigue or graying out spells

Signs

1. Double or triple apex impulse
2. Rapidly rising carotid arterial pulse
3. Fourth heart sound
4. Systolic murmur which is harsh, diamond shaped, blowing and best heard at the lower left sternal borders. It is increased by exercise, digitalis, nitrates, sudden standing and Valsalva manouvre. It is decreased by squatting, hand grip and passive leg raising.
5. Pansystolic murmur at apex due to mitral regurgitation.

Investigations

ECG: This may show left ventricular hypertrophy with broad Q waves and arrhythmias.

X-ray chest: There may be mild to moderate left ventricular enlargement.

Echocardiogram: This may demonstrate septal hypertrophy and systolic anterior motion of the mitral valve. The left ventricular cavity is small.

Treatment

A. ***Drugs***

1. *Beta-blockers:* Beta-blockers relieveangina and syncope in 33% patients.
2. *Calcium antagonists : Verapamil and Diltiazem* reduce the stiffness of the ventricles and reduce the elevated diastolic pressures.
3. *Disopyramide* has been used in some patients to reduce LV contractility and outflow gradient.

B. ***Dual chamber pacemaker*** reduces outflow gradient by altering the pattern of ventricular contraction

C. ***Surgery***

Myotomyormyectomy of the hypertrophic segment may improve the patient symptomatically.

D. ***Gene Therapy*** in the future.

20 Fitness for Surgery (Pre-operative Evaluation)

Table 5.38 : Cardiovascular Risk Factors in General Surgery

1. *Major*
a) Age > 70 years
b) Myocardial infarction in past 6 months
c) Clinical - Third heart sound, Elevated JVP
d) Catheterization data - Ejection fraction < 30%, Triple vessel or Left main disease
2. *Minor*
a) Duration of anesthesia > 3 hours
b) Thoracic or upper abdominal surgery
c) Aortic stenosis
d) Hypertension

Central Nervous System

6

1 › Proforma

History

I. **Name, Age, Sex, Occupation, Right or Left handed, Consanguinity**

II. **Motor symptoms**

A. *Power:*

1. *Upper limbs:*
   a) Proximal: Lifting the arm above the head, eating.
   b) Distal: Sewing, writing, buttoning, turning a key in a lock, etc.
2. *Lower limbs:*
   a) Proximal: Climbing stair up and down, squatting and getting up from squatting position.
   b) Distal: Slippers falling from foot
   c) Running, walking with or without support, standing without support, moving limbs in the bed or complete paralysis.

   Truncal : turning in bed.

B. *Nutrition*: Wasting of muscles (proximal or distal), atrophy, hypertrophy.

C. *Coordination:*

1. Unsteadiness (For cerebellar ataxia).
2. Difficulty in feeling the ground and unsteadiness increasing in the dark. (For sensory ataxia).
3. Difficulty in reaching the target.

D. *Involuntary movements:*
Chorea, athetosis, tremors, dystonia, hemiballismus, flexor spasms, fasciculations, titubation.

III. **Sensory symptoms**

A. Tingling, numbness, root pains

B. Feeling hot and cold water during a bath

C. Feeling the ground well or ground feels like cotton wool.

IV. **Sphincter disturbances**

A. *Bladder:*

1. Feeling the sensation of bladder fullness
2. Initiation of micturition immediately when desired
3. Control of micturition, once the desire to micturate has occurred
4. Complete evacuation of the bladder or a feeling of residual urine
5. Inability to pass urine at all
6. History of catheterization

B. *Bowel:* Constipation / Loose Stools

C. *Impotency:* In males

V. **Cranial nerves**

A. *Sensation of smell* - 1st CN

B. *Vision* — acuity and color - 2nd CN

C. *Diplopia, squint* - 3rd, 4th, 6th CN

D. *Sensations* (Tingling, numbness over the face, and difficulty in chewing) - 5th CN

E. *Facial asymmetry, dribbling of saliva from the angle of the mouth, stasis of food in the mouth*- 7th CN

F. *Vertigo, tinnitus, deafness* - 8th CN

G. *Hoarse voice, nasal twang, nasal regurgitation dysphagia* - 10th + 9th CN

H. *Dysarthria* - 12th CN

VI. **Higher functions**
- A. *Mental symptoms*
- B. *Speech disturbances*
- C. *Symptoms of raised intracranial tension:* headache, projectile vomiting, blurred vision, altered sensorium, photophobia, diplopia
- D. *Unconsciousness*
- E. *Convulsions:* Inquire for aura, tonic and clonic convulsions deviation of eyes, incontinence of urine and stools, tongue bite, fall and injuries. Post convulsion drowsiness or unconscious-ness. Sleep attacks.

VII. **For Etiology**
- A. Hypertension, diabetes, heart disease
- B. Tuberculosis, syphilis, HIV infection
- B. Trauma and fever
- C. Vaccinations, drugs or sera administered
- D. Alcohol, smoking, tobacco chewing, gutka, recreational drugs
- E. Similar episode in the past, in the family or in the surrounding

General Examination

I. Build, nutrition

II. Nails and conjunctiva: Pallor, clubbing, cyanosis, icterus

III. Lymphadenopathy, edema of feet, JVP

IV. TPR, BP - look for postural drop

V. Spine: For kyphoscoliosis

VI. Skin: For hypopigmented areas, hyperpigmented areas, cafe-au-lait spots, nodules, etc.

VII. Thickened nerves

Central Nervous System Examination

I. **Higher functions**
- A. Consciousness
- B. Behavior
- C. Intelligence
- D. Memory — past and present
- E. Orientation in time, place and person
- F. Hallucinations, delusions
- G. Speech

II. **Cranial nerves**
- A. *I CN:* Sense of smell in each nostril
- B. *II CN:* Acuity of vision, field of vision, color vision and fundus examination
- C. *III, IV, VI CNs:*
  1. External ocular movements on follow and command
  2. Pupils: position, shape, size, equality, reaction to light and accommodation and ciliospinal reflex
  3. Nystagmus
  4. Ptosis (IIIrd)
- D. *V CN:*
  1. Sensations over the face
  2. Masseters, pterygoids and temporalis muscles
  3. Corneal and conjunctival reflexes and jaw jerk
- E. *VII CN:*
  1. Eye closure, frowning, raising the eyebrows
  2. Blowing, whistling and showing the teeth
  3. Nasolabial fold, Platysma
- F. *VIII CN:*
  1. Hearing tick of the watch.
  2. Rinne's test
  3. Weber's test
- G. *IX, X CNS:*
  1. Uvula on saying 'ah' — central or deviated to one side
  2. Gag reflex
- H. *XII CN:*
  1. Tongue movements
  2. Wasting, fasciculations and fibrillations

III. **Motor system**
- A. *Nutrition:* Wasting or hypertrophy
- B. *Tone:* Normal, hypertonia or hypotonia
- C. *Power:* Graded from O to V

D. *Coordination:* By finger-nose test, knee heel test, rapid alternate movements at the wrist.

E. Involuntary movements.

IV. Sensory system

A. *Superficialsensations:* Touch, temperature, pain

B. *Deep sensations:* Position, joint and vibration

C. *Cortical sensations:* Tactile localization, tactile discrimination, tactile extinction and astereognosis

D. Calf tenderness or anesthesia of the calves

V. Reflexes

A: Superficial, B: Deep, C: Primitive.

Graded: Absent (--), depressed (+), normal (++), brisk (+++) and brisk with clonus (++++).e.g.

	BJ	TJ	SJ	KJ	AJ
Right	+++	+++	+	-	++++
Left	++	+++	+++	++	-

BJ : Biceps Jerk; TJ : Triceps Jerk; SJ : Supinator Jerk; KJ : Knee Jerk; AJ : Ankle Jerk

VI. Miscellaneous

A. Signs of meningeal irritation:

Neck stiffness, Kernig's sign, Brudzinski's sign.

B. S.L.R. and Lasegue's sign

C. Skull and spine

D. Gait including Romberg's sign

Relevant Examination of other Systems

I. CVS

A. Valvular heart disease: Heart sounds, murmur

B. Blood pressure in supine and standing position : For hypertension, postural hypotension.

C. Peripheral pulsations including carotid pulsations

D. Bruits: Over carotids or eyeballs

II. AS

A. Hepatosplenomegaly

B. Ascites

III. RS

A. Chest expansion

B. Dullness or hyperresonant note

C. Breath sounds

D. Foreign sounds

E. Vocal resonance

2 › Examination

A: Higher Functions

I. Consciousness

Consciousness is a state of awareness of one's self and one's environment.

Sleep: Sleep is a state of physical and mental inactivity from which the patient can be aroused to normal consciousness.

Catatonia: Catatonia is a state during which rigid plastic postures of limbs for long hours are assumed. The person is unresponsive, mute and immobile. It may occur in psychosis or with frontal lobe and hypothalamic lesions.

Akinetic mutism: Akinetic mutism is a state during which the patient remains immobile, making no sound, follows movements slowly with his eyes and allows himself to be fed and nursed. This is seen with lesions of diencephalon and brainstem.

Drowsiness: This is a pathological state that resembles normal sleep. Patient can be aroused with an external stimulus, but reverts back to his drowsy state on withdrawal of the stimulus.

Semicoma: Semicoma is a pathological state, which requires stronger stimulation to arouse the patient, though his reflexes are normal.

Stupor: Stupor is often considered synonymous to semicoma, whereas some doctors regard it as a state between drowsiness and semicoma.

Coma: This is the deepest level of unconsciousness. Patient is immobile, all the reflexes are absent and plantar response is extensor (See Ch. 7 & pg. 290).

II. Delirium

Delirium is the acute state of confusion with excitement and hyperactivity.

Causes

1. Infective: Septicemia, typhoid, cerebral malaria
2. Withdrawal state: Alcohol
3. Toxic: Overdose of aspirin, amphetamine, atropine, etc
4. Deficiency of thiamine and nicotinic acid
5. Metabolic: Renal failure, porphyria

III. Delusions

Delusions are false beliefs, which cannot be corrected in spite of evidence to the contrary.

Delusions have to be distinguished from superstitions, which are a part of the cultural traditions in certain societies.

Causes

1. **Holistic:** Delusions of disordered or diseased body, e.g. the body is riddled with cancer or his sex is changing. This is seen in schizophrenia or depressive illnesses.
2. **Delusions of guilt:** Patient may blame himself excessively for some trivial lapse and expect to be imprisoned or hanged for the same. This is seen in depressive states.
3. **Delusions of grandeur:** e.g. A patient who is a beggar may say that he is the richest man in the world, and is about to marry the Premier's daughter. This is seen in GPI mania and paranoid schizophrenia.

Significance: False beliefs on a background of a clear consciousness are of more grave significance than those occurring when consciousness is clouded.

IV. Hallucinations

This is false perception of sensations in the absence of any sensory stimulus e.g. humming in the ears when there is no sound or seeing somebody who does not exist. This has to be distinguished from illusion, which is altered perception to sensory stimulus, e.g. mirage in the desert.

V. Thought Content

1. Sudden onset of fear or depression before an epileptic attack points to temporal lobe origin.
2. Teichopsia preceding an attack of migraine represents occipital visual hallucinations.
3. Grandiose delusions are the hallmark of GPI (Neurosyphilis).

VI. Insight

Lack of insight is seen in:

1. Lesions of frontal lobe
2. With deteriorating intelligence

VII. Emotional State

Hostile, depressed or euphoric. Whether the emotions are appropriate or not.

Causes of Incontinence of emotions/ Emotional lability

1. Pseudobulbar palsy
2. Cerebral arteriosclerosis, multi-infarct state
3. Organic dementia - vascular
4. Multiple sclerosis

VIII. Memory

A. **Defect in registration:** This is largely due to inattention. It is seen in:
   1. Toxic delirium
   2. Manic states
   3. Senile dementia

B. **Defects in retention:** This is seen in organic cerebral disturbances like:
   1. GPI
   2. Frontal lobe lesion
   3. Senile dementia

C. **Defects in recall:** This is seen in:
   1. Post traumatic states
   2. Epilepsy
   3. Korsakoff's psychosis
   4. Ganser's syndrome
   5. Hysteria

Dementia is an acquired deterioration of cognitive abilities. It comes in the way of performing activities of daily living. Memory is most commonly affected.

Mini Mental State Examination (MMSE)

Used for screening and progression of dementia. The total score is 30. A score of < 21 in an educated person is severe dementia.

Table 6.1 : MMSE

Test for	Score
Orientation	
Time, Day, Date, Month, Year	5
Place, Floor, City, State, Country	5
Registration	
Name 3 objects and ask to repeat	3
Attention and Calculation	
Serial subtraction: 100 - 7-7-7-7-7	5
Recall	
Repeat all 3 objects named above	3
Language	
Name: Pencil, watch	2
Follow 3-step command (e.g. take paper, fold in half, put on table)	3
Copy intersecting pentagons	1
Repeat "Satara cha matara" or "No if's and's or but's"	1
Obey written command (e.g. 'close your eyes' written on a piece of paper)	1
Write a sentence (eg. Today is a sunny day)	1

Causes of Dementia

Treatable/Reversible

1. Drugs/Toxins: Alcohol, narcotic poisoning
2. Vitamin Deficiency: B1, B12, B3 (pellagra)
3. Infections: Syphilis, TB
4. Neoplasm: Primary or metastatic brain tumor
5. Trauma: Chronic subdural hematoma, normal pressure hydrocephalus
6. Endocrine: Hypothyroidism, Addison's syndrome, Cushing's syndrome, hyperparathyroidism
7. Miscellaneous: Vasculitis, liver/renal failure

Untreatable/Irreversible

1. Degenerative Diseases: Alzheimer's, Parkinson's, Huntington's disease
2. Infections: HIV, Sub acute Sclerosing Panencephalitis
3. Prion diseases: Creutzfeldt-Jacob disease
4. Multiple sclerosis
5. Multi-infarct dementia

IX. Language and Speech

Language includes all modes of communication between people. The various forms of language are:

1. **Listening to speech** which begins at about 6 months of age when the child hears some words or phrases and begins to associate them with appropriate objects or actions.
2. **Speaking or Spoken language** includes expression of thoughts in spoken words, phrases and sentences. It begins at about 9 months of age when the child begins to mimic the sounds he hears and begins to associate them with objects or meaning.
3. **Writing** implies ability to communicate by the written word. In mirror writing the letters or figures are reversed as seen in themirror. This is a normal feature in writings of children up to the age 6-7 years. Its persistence in later years is pathological and is seen in:
   a) Forced right-handedness.
   b) When a right-handed person with right hemiplegia attempts to write with his left hand.
   c) Developmental dyslexia: This is a

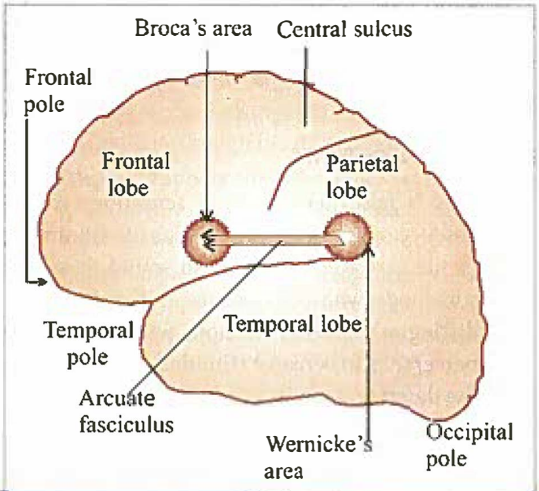


Fig.6.1 : The language areas

defect in learning to read. Hence here mirror writing is secondary to mirror reading.

4. **Reading** is the ability to communicate through the written word.
5. **Sign language** is ability to communicate by gestures.
6. **Touch language** is communication by the written word employed by the blind in reading.

Disorders of Language & Speech

The disorders of language and speech occur with lesions of the dominant hemisphere. About 90% of the population have left cerebral dominance i.e. they are right handed and 10% have right cerebral dominance i.e. they are left-handed. But among left handed people 60% have left cerebral dominance.

Dysphasia/ Aphasia

Definition: Dysphasia is difficulty with language function. It occurs due to lesions in the language areas of the dominant cerebral hemisphere.

Pathways: The main language areas are shown below:

Broca's Area (Inferior frontal region) (Area 44): This is concerned with generation of motor programs for the production of words or parts of word. Damage to this area causes reduced number of words, poorly articulated, non-fluent speech and grammatical errors. The speech has a tele grammatic quality.

Wernicke's Area (Posterior temporal lobe and adjoining parietal region) (Area 22): This is concerned with comprehension of language and selection of words to convey meaning. In lesions of this area, spontaneous speech is normal, fluent and articulation is normal. However the speech may contain incorrect words (verbal paraphasias), incorrect letters (literal paraphasias) and nonsense words (neologisms).

Occipitotemporal (lingual) gyrus is the visuopsychic area. The posterior part of the superior temporal gyrus is the auditory (auditopsychic) cortex. The final sensory pathway leads to the inferior part of the post central gyrus for coordination of the meaning of the information and the organization of any response that may be required. If any motor response is expected, then a relay of information goes to the precentral gyrus (the motor coordinating centre and from there, to the motor speech area if verbal response is expected.

Types of Dysphasia/ Aphasia:

Sensory (Wernicke's) dysphasia:

Auditory: The patient is unable to carry out simple verbal commands in absence of loss of hearing. The lesion is in the posterior part of the superior temporal gyrus (word deafness).

Visual: Inability to read in absence of loss of vision (word blindness). The lesion is in the medial occipitotemporal gyrus. It is associated with inability to write (dysgraphia).

Nominal: Inability to name objects. The lesion is in the left temporoparietal region.

Table 6.2 : Aphasias

	Fluency	Comprehension	Repetition	Naming	Reading	Writing
BROCA's (Non Fluent Aphasia)	Lost "Telegraphic"	Present	Lost	Lost	Lost	Lost
WERNICKE's (Fluent Aphasia)	Present verbal paraphasias Neologism	Lost	Lost	Lost	Lost	Lost
CONDUCTION	Present	Present	Lost	Lost		
ANOMIA	Word finding pauses	Present	Present	Lost	Present	Present
TRANSCORTICAL MOTOR	Lost	Present	Present	Present	Present	Present
TRANSCORTICAL SENSORY	Present	Lost	Present	Present	Present	Present
GLOBAL APHASIA	Lost	Lost	Lost	Lost	Lost	Lost
ISOLATION OF SPEECH AREA	Echolalia ++	Impaired	(No purposeful speech)			

Motor (Broca's) dysphasia:

The lesion is in Broca's area. The patient is unable to express himself. There may be difficulty in forming phrases and sentences. The emotional outbursts may be retained.

Central Dysphasia:

This results from a disorder of the central organization of written or spoken speech. The patient is unable to comprehend spoken or written language and even his own speech. This is usually associated with motor or expressive defects. The lesion is in the left temporo-parietal region (Arcuate fibers).

Conduction Aphasia : Speech output is fluent but paraphasic. Repitition is impaired, naming and writing are also impaired. Reading aloud is impaired but comprehension of read material is present, comprehension of spoken language is intact. Lesion is in perisylvian area with damage to fibres of Arcuate faciculus.

Transcortical Motor Aphasia features are similar to Broca's aphasia but repetition is intact. The lesion is anterior superior to Broaca's area.

Transcortical Sensory Aphasia features are similar to Wernicke's aphasia but repetition is intact. The lesion is posterior inferior to Wernicke's area.

Global Aphasia speech is nonfluent and comprehension is severely impaired. Naming, repetition, reading and writing are impaired. Lesion is usually large in middle cerebral artery territory or left internal carotid artery or a large hemorrhage or major trauma.

Isolation of Speech Area : This is a rare syndrome in which comprehension is severly impaired & no purposeful speech output. He may repeat like a parrot parts of heard conversation - "echolalia". It is seen in complete watershed zone infarctions.

Anomic Aphasia : There is minimal dysfunction only naming, word finding and spelling are impaired.

Most common language disturbance seen (Refer to Table 6.2).

Dysarthria

Definition: Dysarthria is indistinct speech due to weakness or impaired coordination of the orolingual muscles concerned with the production of consonants. However, the grammar is normal and comprehension of spoken and written language is retained.

Dysarthria commonly occurs due to mechanical factors such as ill-fitting dentures.

Types of Dysarthria:

1. **Spastic:** This results from bilateral upper motor neuron lesion. The tongue is small and spastic. There is difficulty in pronouncing 'b' 'p' and 't'.
2. **Monotonous:** This results from extrapyramidal lesions. The speech is slow, monotonous and lacking accents.
3. **Ataxic:** This results from cerebellar lesions. The speech is slurred and irregular in rhythm, tone and volume due to incoordination of muscles of respiration, larynx, pharynx and lips (scanning speech). This is called scanning speech when speech has explosive character and shining of consonants it is called staccats speech.
4. **Lower motor neurone:** This results from paralysis of the soft palate giving rise to nasal speech. There is failure to produce sounds like "b" and "g" correctly. e.g. "Egg" is pronounced as "eng". In myasthenia gravis, the force and volume of the words diminish as the patient speaks and may return to normal after some rest.

X. Other Higher Function Disorders

A. *Apraxia*

Inability to carry out learned voluntary movement in the presence of normal motor, sensory and cerebellar functions

Types

1. **Ideomotor Apraxia** : Inability to plan or complete motor actions. There is inability to pretend to use a tool e.g. pretend to brush ones hair when given a comb. The ability to spontaneously use tools is retianed e.g. brush one's hair in morning.
2. **Ideational Apraxia / Conceptual Apraxia** : Inability to conceptualizea task or complete a multistep task e.g. patient puts on shoes before socks, if given a screwdriver, the patient may try to write like it is a pen.
3. **Limb - Kinetic Apraxia** : Inability to make precise movements with an arm or leg.
4. **Dressing Apraxia** : Inability to dress or undress oneself.

5. **Constructional Apraxia**: Inability to draw or construct simple shapes e.g. intersecting pentagons.



6. **Orofacial Apraxia** : Inability to carry out movements of the face on demand e.g. lick lips, whistle.

Table 6.3 : Hemispheric Functions

Left Hemisphere : Verbal, Linguistic description, Mathematical, sequential, Analytical, linked to consciousness level

Right Hemisphere : Musical, geometrical, spatial, temporal synthesis, doubtful link to consciousness

B. Agnosias

Is anability to recognise objects in the presence of normal sensory, motor cerebellar functionals.

1. **Visual** : Patient is unable to name or describe use of objects shown.
2. **Tactile** : Able to describe the object but unable to give name or use even on seeing it.
3. **Auditory** : Unable to recognise sounds but can recognise them on sight or touch.

Details of Lobar Functions and Dysfunctions are given in Table 6.3 and 6.4.

Table 6.4 : Lobar Functions and Dysfunctions

Lobe	Function	Dysfunction
Frontal	Personality, emotional response, social behaviour	• **Dominant** : Apraxias : ideational, ideomotor, limbkinetic, difficult in performing similiar motor tasks. Contralateral hemiplegia • **Nondominant** : motor speech disorder with agraphia, loss of verbal fluency.
Prefrontal lesions		Abulia, akinetic mutism, lack of ability to solve problems, lack of attention, rigidity of thinking, bland affect, labile mood, sphincter incontinence. Release of primitive reflexes, utilization behaviours
Parietal	Calculation, Language, Planning, Stereognosis	• **Idiomotor, limb kinetic apraxias** • **Dominant** - Gerstman's syndrome (ataxia, acalculia, finger agnosia and left-right confusion) - Cortical sensory loss & sensory extinction - Homonymous inferior quadrantanopia - Ipsilateral opto kinetic nystagmus abolished - Graphesthesia - Asterognosis - Tactile agnosia • **Non dominant** - Visuospatial disorders - Geographical disorientation - Anosognosia - Dressing apraxia - Constructional apraxia
Temporal	**Dominant** : Auditory, speech, language, memory and **olfactional** **Non-dominant** : Music tone appreciation Non Verbal memory	• **Dominant** Homonymous superior quadrantanopian Wernicke's Aphasia, amusia, dreaminess with uncinate seizures • **Nondominant** Non verbal memory loss, Behavioural changes, Bilateral affection *Causes* : Karsakoff's amnesia, Kluver Bucy Syndrome
Occipital	Vision	• Homonymous hemianopia (sparing macula) • **Dominant** : Splenium of corpus callosum : alexia without agraphia, colour anomia. • **Non dominant** : Visual illusions, hallucinations • **Bilateral involvement** : Cortical Blindness, Anton's syndrome, Loss of perception of color, Prosopagnosia. Ballint's syndrome, failure to grasp / touch object under vision. Inability to scan peripheral fields.

B: Cranial Nerves

Refer Pg. 298

C: Motor System

I. Nutrition

A. Hypertrophy of Muscles: Some patients of muscular dystrophy may develop large muscles especially calves, buttocks and infraspinati. These muscles are weak in spite of their size. Hence they are called pseudohypertrophy.

B. Wasting of Muscles: Wasting of muscles may occur in several diseases as mentioned below. The wasted muscles are flabby, smaller and softer than normal. When there is associated fibrosis, the muscles feel hard, inelastic and shortened (contracture).



Fig. 6.2 : Hypertrophy of Calves



Fig. 6.3 : Wasting of small muscles of right hand compared to patient's normal left hand

C. Measurements:

For Upper limbs: Measure the circumference (10 cms) above and below the olecranon (elbow).

For Lower limbs: Measure the circumference 16 cms above patella and 10 cms below the tibial tuberosity (knees). A difference in the circumferences gives objective evidence of wasting.

Causes

I. Parietal Lobe Lesions

II. Vertebral Lesions

A. Craniovertebral anomalies

B. Vertebral metastasis

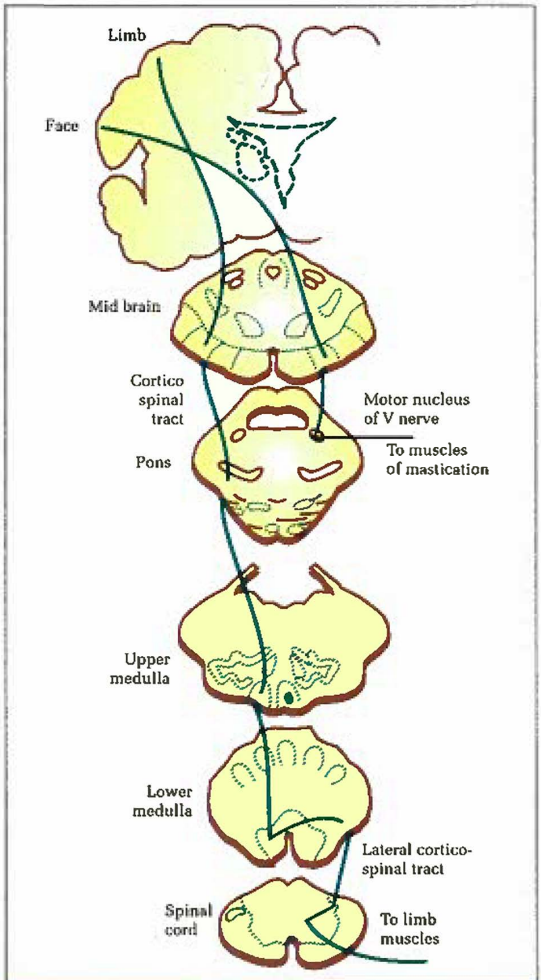


Fig. 6.4 : Pyramidal tracts

III. **Spinal Cord Lesions**
   A. Motor neuron disease
   B. Syringomyelia

IV. **Anterior Horn Cell Lesions**
   A. Poliomyelitis
   B. Peroneal muscular atrophy
   C. Progressive muscular atrophy
   D. Spinomuscular atrophy

V. **Root Lesions (Radiculopathy)**
   A. Cervical spondylitis
   B. Cervical cord tumor
   C. Cervical hypertrophic pachymeningitis
   D. Neuralgic amyotrophy

VI. **Peripheral Nerve Lesions (Neuropathies)**
   A. Leprosy
   B. Carpal tunnel syndrome
   C. Lead paralysis
   D. Diphtheria

VII. **Myoneural Junction**
   Eaton Lambert syndrome

VIII. **Muscle Diseases**
   A. Muscular dystrophy
   B. Polymyositis
   C. Myotonia

IX. **Disuse Atrophy**
   A. Therapeutic immobilization: Fracture
   B. Arthritic: Rheumatoid arthritis
   C. Post paralytic

X. **Systemic Wasting**
   A. Tuberculosis
   B. Malignancy
   C. Thyrotoxicosis
   D. HIV infection or AIDS
   E. Addison's disease

II. Tone

Tone is the resistance offered by normal muscles to passive movements. It is greatest in those

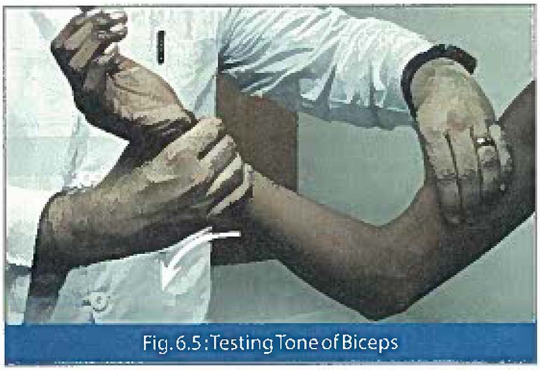


Fig. 6.5: Testing Tone of Biceps

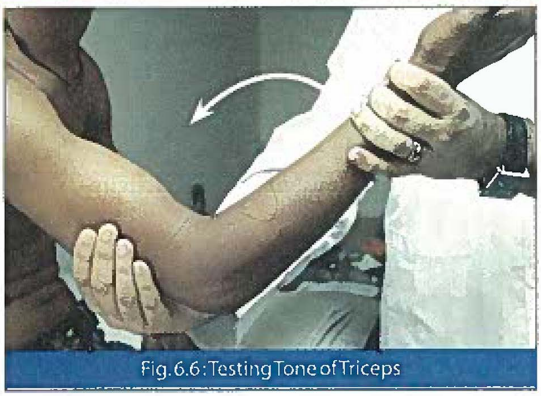


Fig. 6.6: Testing Tone of Triceps

muscles that maintain the body in position. These are the antigravity muscles, principally the flexors in the upper limbs and extensors in the lower limbs.

A. **Hypotonia (Flaccidity)**

Definition: It is characterized by flabby muscles, which offer less resistance to passive movements, leading to an increased range of passive movements and the limb is unable to maintain posture.

Causes

1. Lower motor neuron disease: Poliomyelitis, peripheral neuritis, tabes dorsalis etc.
2. Neuronal shock in upper motor neurone disease
3. Cerebellar disease
4. Rheumatic chorea

B. **Hypertonia**

Definition: Hypertonia is increased resistance to passive movements, a heightened salience of the muscles and increased firmness on palpation.



Fig. 6.7 : Decerebrate rigidity

Causes

1. Pyramidal disorders
2. Extrapyramidal disorders
3. Hysterical
4. Tetany
5. Tetanus
6. Decerebrate rigidity
7. Strychnine poisoning
8. Stiff man syndrome
9. Continuous muscle fiber activity (ISAAC disease)

Types

1. *Clasp knife spasticity:* There is increased tone in the flexors of the upper limbs. The resistance is increased only at the beginning or at the end of the passive movement. This is seen in pyramidal lesions.
2. *Lead-pipe rigidity:* There is increased tone, both in flexors and extensors. The resistance is present throughout the entire range of movement. It results from the failure of striatal regulation of tonus controlling centres in the mid-brain and brainstem. This is seen with extra pyramidal lesions.
3. *Cog wheel rigidity:* The increased resistance is throughout the entire range of passive movement and is rhythmically jerky because the static tremors which are masked by rigidity emerge faintly during manipulation.
4. *Decerebrate rigidity:* There is marked contraction of all extensor muscles. The limbs are stiff, extended, head is erect and the jaw is closed. The righting reflexes are abolished but the tonic neck and labyrinthine reflexes are retained, and the tendon reflexes are exaggerated.

   It results from the release of the vestibular nuclei from the higher extrapyramidal control and may result from lesions of the brain stem at any level between superior colliculi and vestibular nuclei.
5. *Hysterical rigidity:* It is of wide distribution

Table 6.6 : Differences between Spasticity and Rigidity

	Spasticity	*Rigidity*
1.	Pyramidal	1. Extrapyramidal
2.	Involves only anti-gravity muscles viz. flexors of upper limbs & extensors of lower limbs	2. Involves all groups viz. flexors & extensors.
3.	Present during beginning of movement	3. Present throughout the range of motion
4.	Plantars are extensors	4. Plantars are flexors

Table 6.5 : Differentiation of Motor Dysfunction

	Sensory neurone	*Lower Motor neurone*	*Pyramidal*	*Extra-Pyramidal*	*Cerebellar*
1. Nutrition	Normal	Wasting	Disuse atrophy (mild)	Normal	Normal
2. Tone	Decreased	Decreased	Increased (spastic)	Increased (rigid)	Decreased
3. Power	Normal	Decreased	Decreased	Normal but movements slow	Normal
4. Co-ordination	Normal with eyes open. Poor with eyes closed	—	—	Slow	Poor Intention tremor
5. Involuntary movements	Absent	Fasciculations may be present	Flexor spasm may occur	Tremors	Intention tremors
6. Superficial reflexes	Absent	Absent	Absent	Normal	Normal
7. Plantar reflex	Absent or flexor	Absent or flexor	Extensor	Flexor	Flexor
8. Deep reflexes	Absent	Absent	Increased	Normal	Pendular or swinging

and of long duration precipitated by alarm, excitement or fatigue with resistance usually increasing with increased force or passive movement of the limb.

6. *Reflex rigidity:* It is characterized by muscle spasm in response to pain e.g. board-like rigidity of the abdomen in peritonitis; neck rigidity in meningitis.
7. *Gegenhalten phenomenon:* Here there is stiffening of a limb in response to contact and a resistance to passive changes in position and posture. The strength of the antagonists increase as one increase s force to change the position of the limb. It can be mistaken for Hysterical rigidity.

   Causes: Encephalopathy, frontal lobe disorders toxic (manganese, carbon monoxide), drugs (reserpine, phenothiazines) and extrapyramidal (dystonia, athetosis and spasmodic torticollis)
8. *Myotonia:* There is increased muscle tone and contraction. There is tonic perseveration of muscular contraction and relaxation occurs slowly. Sudden movement may be followed by marked spasm and inability to relax. Repetition of movement often brings about ease of relaxation and gradual decrease in hypertonicity.

   Percussion myotonia can be elicited by mechanical stimulation: Abrupt tapping of the thenar eminence with hammer is followed by opposition of the thumb, which persists for several seconds before relaxation begins. It can be elicited by tapping on the tongue, deltoid or other muscular masses, which produces a "dimple" that disappears slowly.

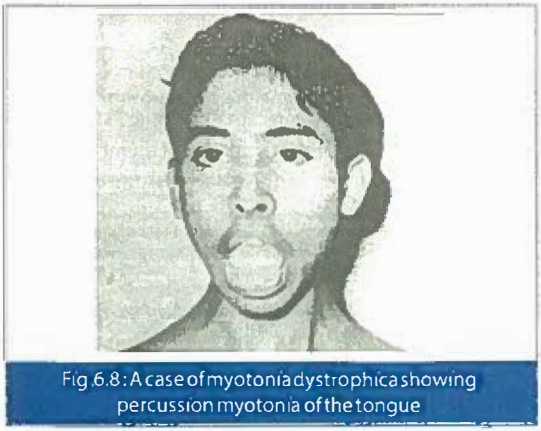


Fig 6.8: A case of myotonia dystrophica showing percussion myotonia of the tongue

III. Power

The power of all the muscles should be tested at each joint in both the upper and lower limbs both against gravity and against resistance. Power in individual muscles is graded as follows:

Table 6.7 : MRC Grading of Power

Grade 0 :	No power
Grade I :	Flicker of contraction only
Grade II :	Movement with gravity eliminated
Grade III :	Movement against gravity
Grade IV :	Movement against gravity & some resistance
Grade V :	Normal power



Fig 6.9: Testing Power of Biceps



Fig 6.10: Testing Power of Triceps



Fig 6.11: Pronator Drift

Table 6.8 : Muscles of Upper and Lower Limbs

No.	Muscle	Cord Segment	Nerve	Action
1.	Neck Muscles	C1 - C4	Cervical	Fl Ext Rot and Lat bending of neck
2.	Diaphragm	C3 - C5	Phrenic	Inspiration
3.	Scaleni	C3 - C5	Phrenic	Elev of Upper thorax
4.	Pectoralis Major and minor	C5 - T1	Pectoral nerve	Add of arm from behind to front
5.	Serratus anterior	C5 - C7	Long thoracic	Forward thrust of shoulder
6.	Levator scapulae	C3 - C5	Dorsal Scapular	Elev of scapula
7.	Rhomboids	C5	Dorsal Scapular	Add and Elev of scapula
8.	Supraspinatus	C5 - C6	Suprascapular	Abd of arm
9.	Infraspinatus	C5 - C6	Suprascapular	Lat rot of arm
10.	Latissimus dorsi	C6- C8	Thoracodorsal	Med rot and Add of arm
11.	Teres major	C5 - C6	Lower subscapular	Med rot and Add of arm
12.	Subscapularis	C5 - C6	Upp. & L. Subscapular	Med rot and Add of arm
13.	Trapezius	C1 - C5	Spinal part of accessory	Retract & Rot & Elev of scapula
14.	Subclavius	C5 - C6	To Subclavius	Stabilises clavicle during movement
15.	Deltoid	C5 - C6	Axillary	Abd of arm
16.	Teres Minor	C4 - C5	Axillary	Lat. rot of arm
17.	Biceps brachi	C5 - C6	Musculocutaneous	Fl and Sup of forearm
18.	Coracobrachialis	C5 - C6	Musculocutaneous	Add of arm and Fl. of forearm
19.	Brachialis	C5 - C7	Musculocutaneous	Flexor
20.	Flexor Carpiulnaris	C7 - C8	Ulnar	Ulnar Adductor of hand
21.	Flexor Digitorum profundus (Ulnar)	C8 - T1	Ulnar	Fl of terminal phalanx of ring and little finger fl of hand.
22.	Adductor Policis	C8 - T1	Ulnar	Add of thumb metacarpal
23.	Abd digit minimi	C8 - T1	Ulnar	Abd. of little finger
24.	Opponens digit	C7 - T1	Ulnar	Opposition of little finger
25.	Flexor digit minimi	C7 - T1	Ulnar	Fl of little finger
26.	Interossei	C8 -T1	Ulnar	Abd and Add of fingers
27.	Lumbricles	C8 - T_1	Ulnar & Median	Fl of proximal phalanx Ext. of distal phalanges
28.	Pronator teres	C6 - C7	Median	Pronation of fore arm
29.	Fl carpi radialis	C6 - C7	Median	Radial fl of hand
31.	Palmaris longus	C7 - C8	Median	Fl of hand
32.	Flexor digitarum sublimis	C7 - T1	Median	Fl of middle phalanx. Fl of hand
33.	Flexor policis longus	C7 - C8	Median	Fl of terminal phalanx of thumb
34.	Flexor digitorum	C7 - T1	Median	Fl of terminal phatanx of index and middle fingers.
35.	Abductor Policis brevis	C8 - T1	Median	Adb of metacarpal of thumb
36.	Flexor policies brevis	C8 - T1	Median	Fl of proximal phalanx of thumb.
37.	Opponens policis	C8 - T1	Median	Opposition of metacarpal- thumb
38.	Triceps and anconeus	C6 - C8	Radial	Ext of forearm
39.	Brachioradialis	C5 - C6	Radial	Fl of forearm
40.	Ext cappi radials	C6 - C8	Radial	Radial ext of hand
41.	Ext digitorum	C7 - C8	Radial	Ext of phalanges of little finger and hand.
42.	Ext carpi ulnanis	C7 - C8	Radial	Ulnar Ext of hand
43.	Supinator	C6 - C7	Radial	Supination of forearm
44.	Abd Policis longus	C7 - C8	Radial	Abd of metacarpal of thumb and

No.	Muscle	Cord Segment	Nerve	Action
				radial extension of hand
45.	Ext Policis brevis and longus	C7 - C8	Radial	Ext of thumb Radial ext. of hand
46.	Ext indices	C7 - C8	Radial	Ext of index finger and hand.
47.	Iliopsous	L1 - L3	Femoral	Fl and Ex of Hip.
48.	Sartorius	L2 - L4	Femoral	Fl and Ex of Hip.
49.	Quadriceps Femoris	L3 - L4	Femoral	Ext of leg
50.	Pectineus	L2 - L3	Obturator	Add of hip
51.	Adductor longus	L2 - L3	Obturator	Add of hip
52.	Adductor brevis	L2 - L4	Obturator	Add of hip
53.	Adductor magnus	L2 - L4	Obturator	Add of hip
54.	Gracilis	L2 - L4	Obturator	Add of hip
55.	Obturator externus	L3 - L4	Obturator	Add and Lat rot of hip
56.	Gluteus moximus	L5 - S2	Inferior gluteal	Abd of hip
57.	Gluteas meduis and minimus	L4 - S1	Superior Gluteal	Abd and Med rot of hip
58.	Tensor fasciae latae	L4 - S1	Superior Gluteal	Abd and Med rot of hip
59.	Piriformis	S1 - S2	Superior Gluteal	Fl of hip
60.	Piriformis	L5 - S1	Superior Gluteal	Lat rot of hip
61.	Obturatorinternus	L5 - S2	Br from Sacral plexus	Lat rot of hip
62.	Gemelli	L5 - S2	Br from sacral plexus	Lat rot of hip
63.	Quadractus	L4 - S1	Br from sacral plexus	Lat of rot of hip
64.	Priceps Femoris	L5 - S1	Sciatic	El of leg, Ext of hip
65.	Semitendinasus Semi menibra-nosus	L5 - S1	Sciatic	Fl of leg Ext of hip
66.	Tiabialis anterior	L4	Deep peroneal	Df & Inv of foot
67.	Extensor DigitorumLongus	L5 - S1	Deep peroneal	DF of foot Ext of II-V toes
68.	Extensor hallucdlongus	L5	Deep peroneal	DF of foot and Ext of great toe
69.	Extensor digitorum brevis	S1 - S2	Deep peroneal	Ext of great toe and 3 medial toes
70.	Peronei	L5 - S1	Superficial peroneal	PL F avoid EV of foot
71.	Gastrocnemius & plantaris	S1 - S2	Tibial	Plantar Fl of Foot & Fl of knee
72.	Soleus	S1 - S2	Tibial	Plantar Fl of Foot & Anti-gravity mus
73.	Flexor Digitorum Longus	S1 - S2	Tibial	Plantar Fl of 4 lateral toes
74.	Flexor Hallusis Longus	S1 - S2	Tibial	Fl of Great toes
75.	Tibialis Posterior	L4	Tibial	Add of foot

Fl = Flexor/Flexon Ext = Extensor/Extension Abd = Abductor/Abduction
Add = Adductor/Adduction Med = Medical Lat = Lateral Rot = Rotation

The various muscles of the upper and lower limbs, with their root value, nerve supplying and function are given in Table 6.2. The various movements of upper and lower limb muscles are shown in Fig. 6.6 to Fig. 6.27.

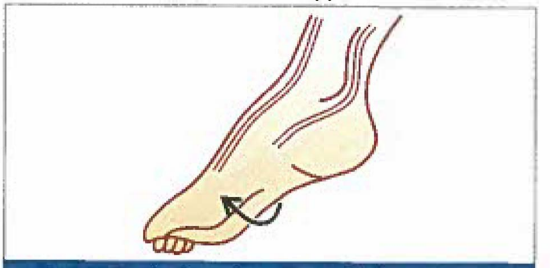


Fig. 6.12 : Testing inversion of foot - Tibialis anterior and posterior (Tibial and peroneal nerve) (L4)

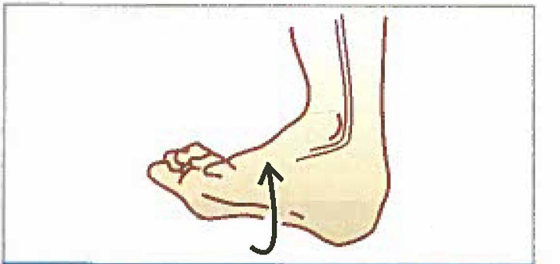


Fig. 6.13 : Testing Eversion of foot - Peronei longus and brevis, Extensor digitorum brevis (Peroneal nerve) (S1)

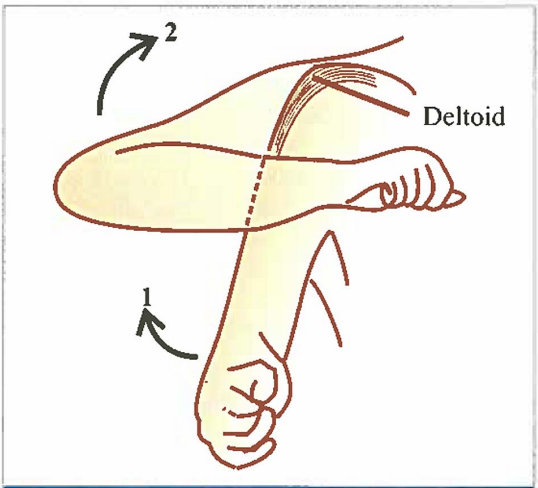


Fig. 6.14: Testing shoulder abduction: (1) First 30° by Supraspinators (Suprascapular nerve) (C5); (2) Between 30 and 90° Deltoid (Axillary nerve) (C5)

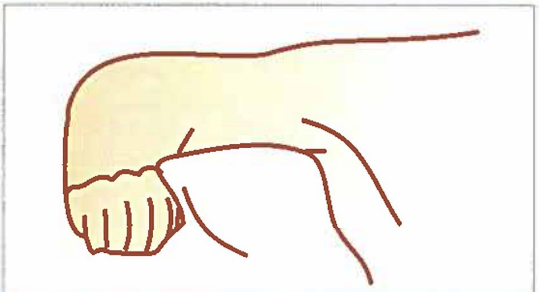


Fig. 6.15: Testing shoulder adduction - Latissimus dorsi and Pectoralis major (nerve to Lat. dorsi) (C7)

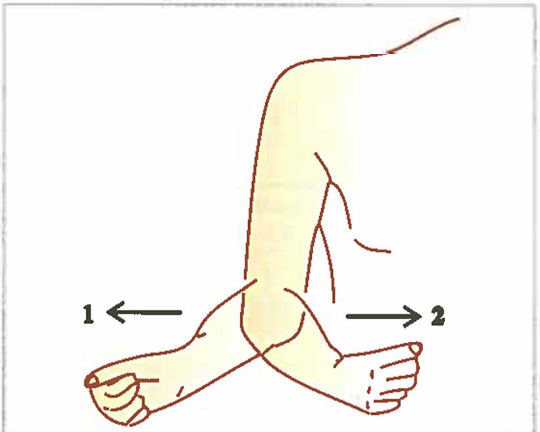


Fig. 6.16: Testing shoulder external and internal rotation: (1) External rotation Infra-spinators (Suprascapular nerve) (C5); (2) Internal Rotation Subscapularis and Teres minor (Subscapular nerve) (C5)

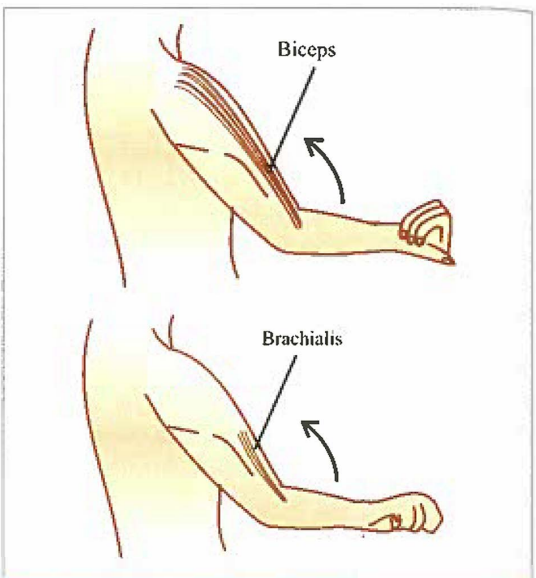


Fig. 6.17: Testing elbow flexion (fully supinated) - Biceps and Brachialis (Musculocutaneous nerve) (C5-6)

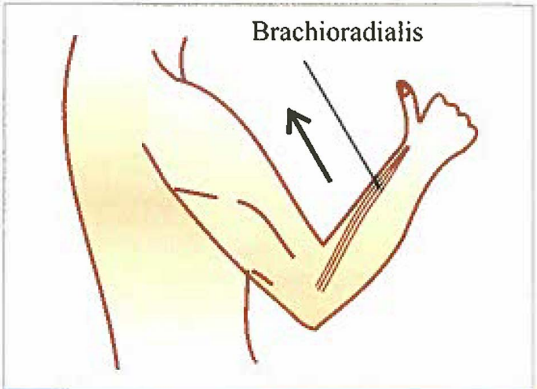


Fig. 6.18: Testing elbow flexion (half supinated) - Brachioradialis (Radial nerve) (C5-6)

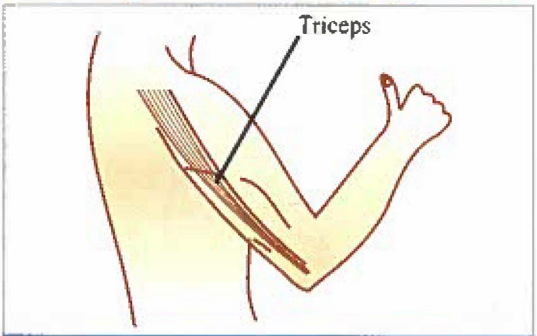


Fig. 6.19: Testing elbow extension - Triceps (Radial nerve) (C7)

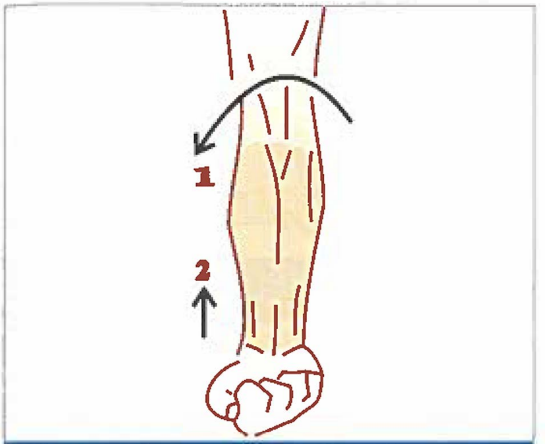


Fig. 6.20 : Testing : (1) Elbow supination Supinator muscle (Radial nerve) (C6) and (2) Wrist flexion - All forearm muscles (Median nerve) and Flexor carpi ulnaris (Ulnar nerve) (C7-8)

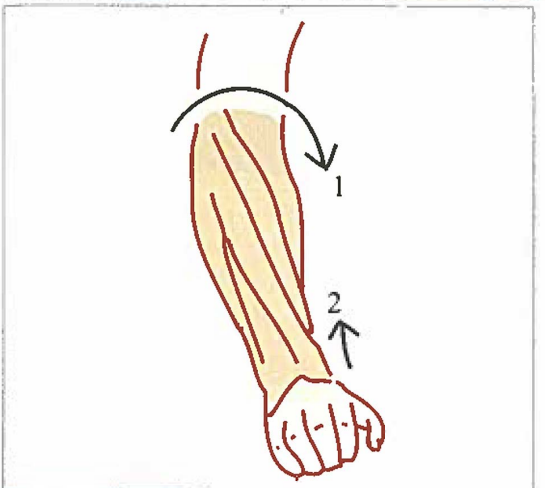


Fig. 6.21 : Testing : (1) Ebow pronation Pronator Teres and Pronator quadratus (Median nerve) (C6); (2) Wrist extension All extensor muscle (Radial nerve) (C6-7)

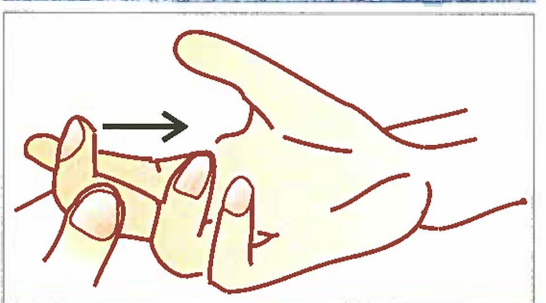


Fig. 6.22 : Testing finger flexion - Flexor digitorum profundus (Median and Ulnar nerve) (C8)

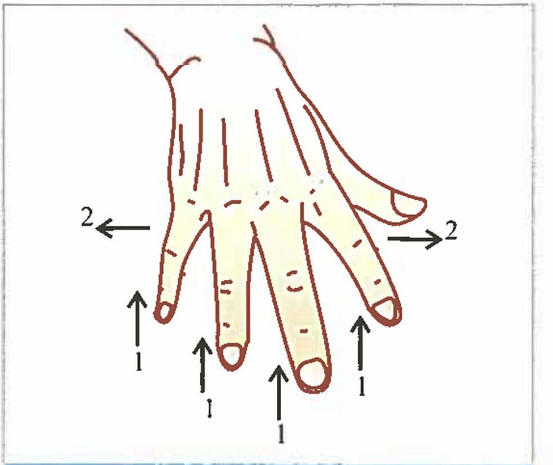


Fig. 6.23 : Testing : (1) Finger extension - All extensors (Radial nerve) (C8); (2) Finger abduction interossei and Abductor digitorum minimi (Ulnar nerve) (D1)

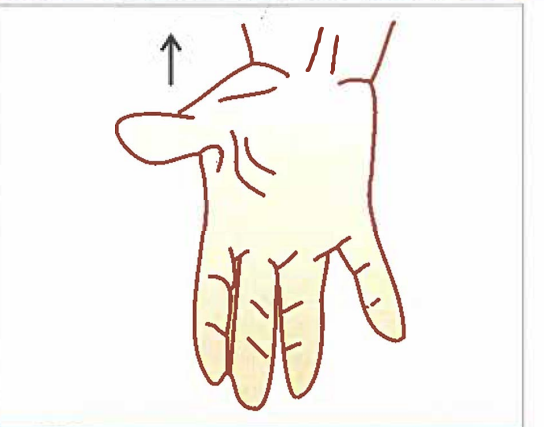


Fig. 6.24 : Testing Thumb Abduction - Abductor pollicis brevis (Median nerve) (D1)

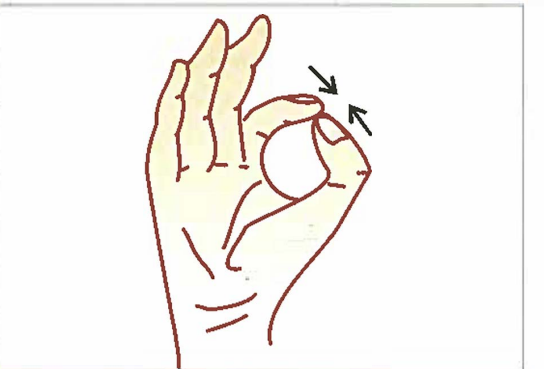


Fig. 6.25 : Pinching movement - Flexor pollicis longus and Flexor digitorum (Median nerve) (C8)

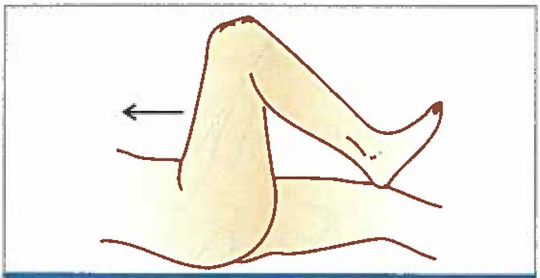


Fig.6.26 : Testing Hip flexioin - Ilio-psoas muscle (Femoral nerve (L2-3)

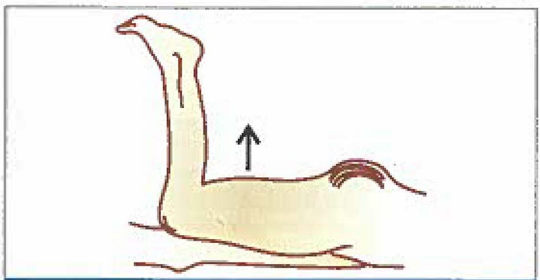


Fig.6.27: Testing Hip Extension - Glutei (Glutealnerve)(l4-5)

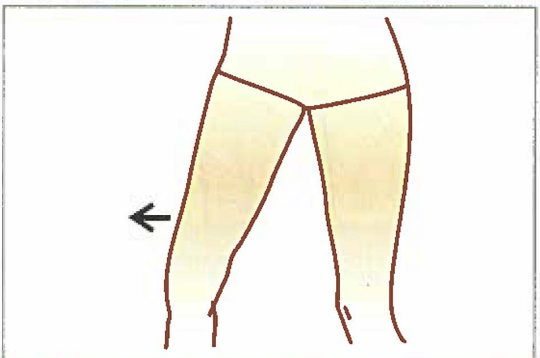


Fig.6.28: Testing Hip Extension - Glutei(Gluteal nerve)(l4-5)

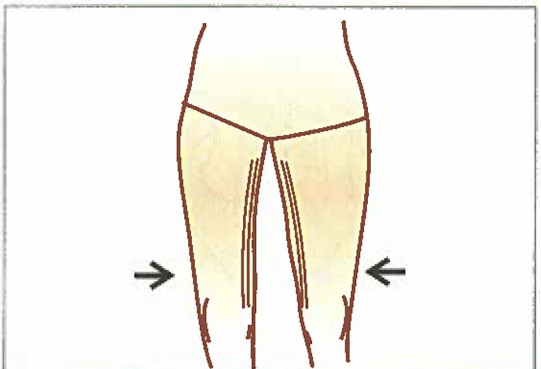


Fig.6.29: Testing Hip Abduction - Adductor group of muscles (Obturator nerve) (L2-3-4)

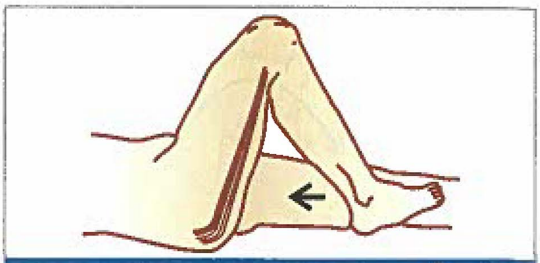


Fig.6.30 : Testing Knee Flexion - Hamstring muscles (Tibial and Peroneal nerve) (L5-S1)

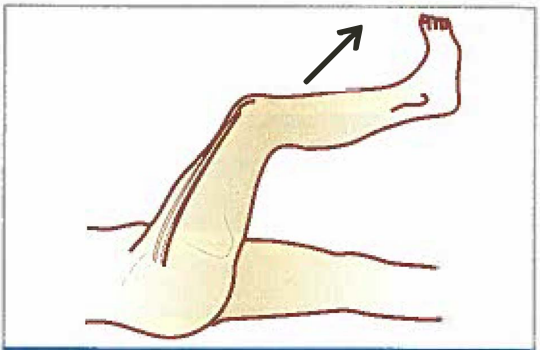


Fig.6.31 : Testing Knee Extension - Quadriceps muscles (Femoral nerve) (L2-3-4)



Fig.6.32 : Testing Plantar Flexion - Gastrocnemii muscles (Tibial nerve) (S1-2)

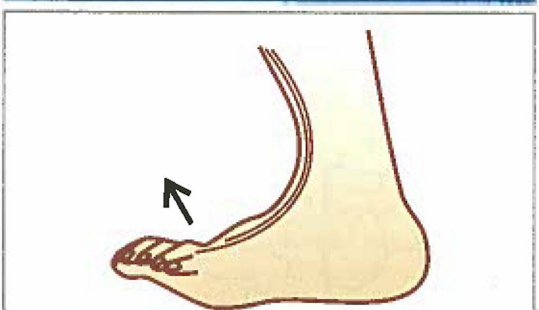


Fig.6.33 : Testing Dorsiflexion - Tibialis anterior, ext-ensor digitorum brevis muscle (Peroneal nerve) (L4-5)

Pronator Drift : This is a test used to detect mild arm weakness. It is a subtle sign of an upper motor neuron lesion. The patient is asked to hold both arms fully extended in front of him with the palms facing upwards and hold the position. When positive, the affected side arm tends to drift down and pronation occurs.

IV. Ataxia

Causes

A. *Cerebellar*
   1. Cerebellar tumor or abscess
   2. Vascular lesion
   3. Cerebellar degeneration
   4. Encephalitis
   5. Hereditary ataxias
   6. Drugs: Alcohol, eptoin, piperazine citrate, streptomycin
   7. Labyrinthitis

B. *Sensory*
   1. Peripheral neuritis
   2. Tabes dorsalis
   3. Posterior column lesions: Subacute combined degeneration of spinal cord
   4. Parietal lobe disorders

C. *Labyrinthine*
   1. Acute labyrinthitis
   2. Meniere's disease
   3. Drugs: Streptomycin

D. *Central:* Vascular lesion in medulla affecting vestibular nucleus

Tests

1. *Romberg's Test:* The patient is asked to stand with his feet closely approximated, first with his eyes open and then with his eyes closed.

   In *sensory ataxia* the patient is able to maintain the upright position while the eyes are open, but when the eyes are closed he sways. This is a *positive Romberg sign* (Fig. 6.29).

   In the vermis or mid-line cerebellar lesion, there is difficulty in standing erect and maintaining a steady position with the eyes either open or closed. If he falls it is generally backwards or forwards.

   In a unilateral cerebellar hemispheric lesion or in a *unilateral vestibular lesion* the patient will sway or fall *towards the involved side.* The head may be tilted towards the involved side with the chin rotated towards the sound side.

   In *hysteria* there may be a false Romberg's sign, often with marked unsteadiness, but

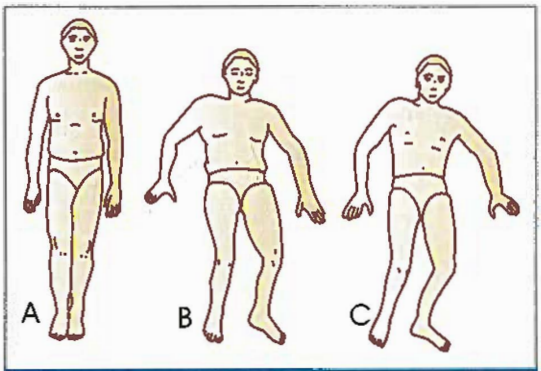


Fig. 6.34 : Romberg's Test for Position Sense : (A) Patient can stand with eyes open and legs together; (B) Patient unsteady when eyes are closed due to loss of position sense and (C) Patient with cerebellar lesion cannot stand straight with legs together, hands by the side and eyes open.

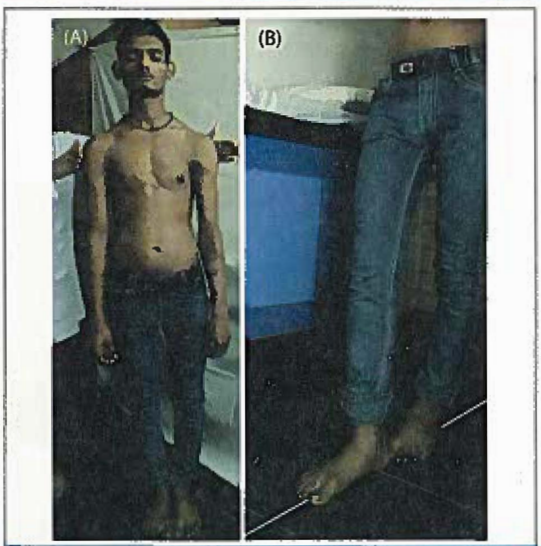


Fig. 6.35 : (A) Romberg's test and (B) Tandem Walking

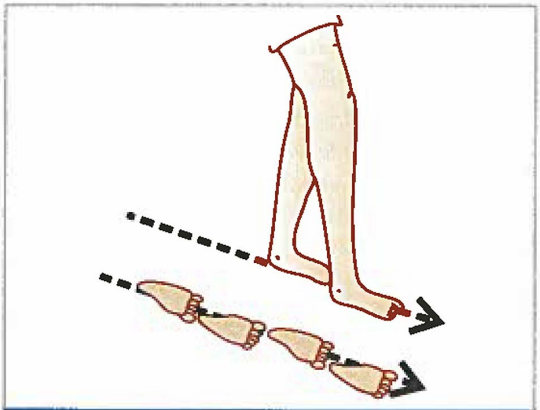


Fig. 6.36: Tandem walking

with swaying at the hips rather than the ankles.

2. *Tandem Walking:* The patient is asked to walk in a straight line by placing one heel directly in front of the opposite toes, both with eyes open and with eyes closed. (Fig. 6.30)

   In *sensory ataxia* the patient may walk fairly well with eyes open, but on closing his eyes he sways and staggers.

   In *vermis lesions* the patient sways with eyes open and tends to fall in any direction especially forwards or backwards. In unilateral cerebellar hemisphere lesion the patient deviates towards the side of lesion.

3. *Finger Nose Test:* The patient is asked to abduct and extend the arm completely and then to touch the tip of his index finger to the tip of his nose. The test is performed slowly at first, and then rapidly, with eyes open and then again with eyes closed.

   In *sensory ataxia* the patient may carry out the act without much difficulty while the eyes are open, but may be unable to find the nose when the eyes are closed.

   In *cerebellar ataxia* there may be intention tremors, dysmetria and dyssynergia. Intention tremors are characterized by hyperkinesis which becomes more marked, more coarser and more irregular as the finger approaches the nose.

   In *dysmetria* the patient may stop before he reaches his nose. In dyssynergia the act is not carried out smoothly and harmoniously but is decomposed into its constituent parts.

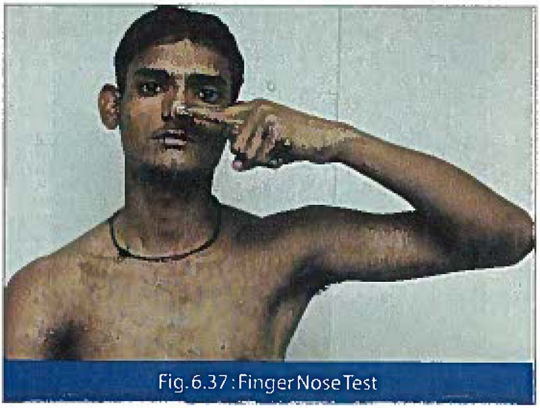


Fig. 6.37: Finger Nose Test

4. *Finger to Finger Test:* The patient is asked to abduct the arms to the horizontal and then bring in the tips of the index fingers in a wide circle to approximate them exactly in the mid-line. In unilateral cerebellar lesion the arm on the involved side will sag and undershoot so that the finger on that side will be below the one on the normal side.



Fig. 6.38: Finger to Finger Test

5. *For Dysdiadochokinesia:* The patient is asked to alternately pronate and supinate his hands, open and close his fists, pat his knees with the palms and dorsa of his hands alternately.

   In cerebellar lesion there is dysdiadochokinesia i.e. one movement cannot be immediately followed by its diametrically opposite movement because the contraction of the set of agonists and relaxation of the



Fig. 6.39: Testing for Dysdiadokokinesia

antagonists cannot be immediately followed by relaxation of the agonists and contraction of the antagonists. Hence the test is carried out slowly with pauses during transition between the opposing motions or it is done unsteadily, and irregularly with loss of rhythm.

6. *Rebound Test of Gordon Holmes:* It checks the ability to contract the antagonist muscles immediately after relaxation of the agonist. The patient is asked to flex his arm at the shoulder and forearm at the elbow and to clench his fist firmly. The examiner pulls on the wrist against resistance and then suddenly releases it. In the normal individual the contraction of the triceps checks the tendency towards flexion. In cerebellar disorders the patient is unable to stop the contraction of the flexors.

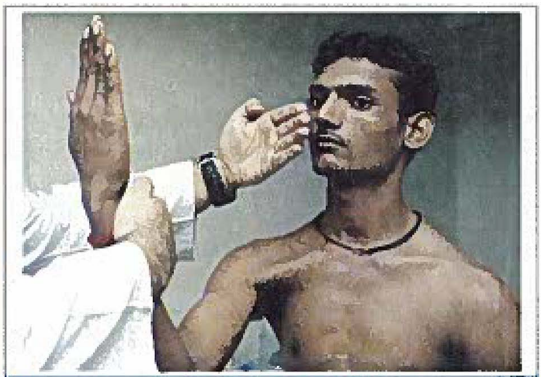


Fig. 6.40: Rebound Test

7. *Postural Holding In The Upper Limb:* The patient is asked to stand with both arms held at the horizontal level outstretched in front of him, with his eyes open and then with the eyes closed. In unilateral cerebellar disease the ipsilateral arm falls gradually and is deviated laterally.
8. *Knee-Heel Test:* The patient is asked to place the heel of one foot on the opposite knee and then push it along the shin in a straight line to the great toe. Dysmetria, dyssynergia and intention tremors as in finger nose test are looked for.



Fig. 6.41: Heel Knee Test

9. Pendular knee jerk - 2½ oscillations makes it pendular.
10. Hypotonia

V. Involuntary Movements

A. **Tremors:** They are regular, rhythmic contraction of agonist and antagonist.

Classification

1. *Type:* a. Simple b. Compound
2. *Site:* a. Unilateral b. Bilateral
3. *Rhythm:* a. Regular b. Irregular
4. *Amplitude:* a. Fine b. Moderate c. Coarse

Causes

1. *Static:* This is a coarse tremor that is present at rest and commonly occurs in one or both hands, jaw and tongue. It does not interfere with voluntary movement, which temporarily suppresses it. The causes are:
   a. Parkinsonism
   b. Senile
2. *Action/ Postural:* It is present when the limb is actively maintained in a certain position.
   a. Familial
   b. Anxiety
   c. Hyperthyroidism (Grave's disease)
   d. GPI (Syphilis)
   e. Delirium tremens (Post-alcohol)
3. *Intention:* It is fully expressed on performing an exacting precise willed movement, especially as the desired object is approached.
   a. Cerebellar
   b. Essential Tremor

4. *Hysterical:* It may simulate tremors in any of the limbs and if the affected limb is restrained by the examiner it may move to another part of the body.

B. **Chorea :** It is the disease of the caudate nucleus which is characterized by involuntary movements which are quasi purposeful, quick, brief, sudden, jerky, irregular in time, rhythm, character and place of occurrence which are flitting from one part to another. These increase during anxiety and are absent during sleep. It occurs more commonly proximally than distally and under the cover of hypotonia.

Causes

1. *Infections:*
   a. Rheumatic - Sydenham's chorea
   b. Bacterial: Scarlet fever, diphtheria, typhoid
   c. Viral: Chicken pox, encephalitis
   d. Spirochetal: Syphilis
2. *Hereditary:* Huntington's chorea
3. *Endocrine:* Thyrotoxicosis, hypoparathyroidism, hyperglycaemia.
4. *Collagen:* Rheumatoid arthritis, SLE
5. *Liver disease:* Wilson's disease
6. *Metabolic:* Porphyria, Neuroacanthocytosis
7. *Drugs:* L-dopa, lithium, atropine, amphetamine, oral contraceptives.
8. *Miscellaneous:* Polycythemia, anemia, pregnancy (Chorea Gravidarum), mental stress

Chorea variants

1. Hemichorea
2. Chorea mollis
3. Kinesogenic chorea
4. Familial paroxysmal chorea

C. **Athetosis:** It is a disease of the putamen, characterized by involuntary movement which are slow, rhythmic, writhing, more distally than proximally and under the cover of hypertonia.

Causes

1. Congenital
2. Birth injuries
3. Infections: Encephalitis
4. Vascular: Atherosclerosis
5. Toxic: Phenothiazine, *copper (Wilson's disease)*, manganese, carbon monoxide
6. Metabolic: Phenylketonuria, hyperuricemia
7. Cerebral anoxia, cerebral palsy
8. L-Dopa overdose
9. Post hemiplegia

D. **Hemiballismus:** It is the disease of the subthalamic nucleus of Luys which is characterized by unilateral rapid and continuous involuntary flinging movements with wide excursions affecting the proximal parts of the body. It is absent during sleep.

Causes

1. Congenital
2. Birth injury
3. Tumor
4. Vascular lesion

E. **Dystonia:** It is an abnormally increased muscular tone that causes fixed abnormal postures or shifting postures resulting from irregular, forceful twisting movements that affect the trunk and limbs. They increase during voluntary movement, nervousness and emotional stress and disappear on sleep.

Classification

1. Focal
2. Segmental/Multifocal
3. Generalized
4. Hemidystonia

Causes

1. *Primary torsion dystonia*
2. *Secondary — Generalized*
   a) Kernicterus

b) Cerebral hypoxia
c) Trauma
d) Vascular
e) Tumor
f) Infection: Encephalitis
g) Toxic: Iron, copper, phenothiazine
h) Drugs: Phenothiazine

3. *Segmental* (symptoms localized to one part)
   a) Spasmodic torticollis (Due to spasm of trapezius, sternocleidomastoid and other neck muscles)
4. *Focal*
   a) Blepharospasm
   b) Writer's cramp
   c) Hemifacial spasm
   d) Oromandibular dystonia
   e) Metabolic disorder: Amino acid disorders (homocystinuria), lipid disorders, Leigh's disease, Wilson's disease

Types

1. Dopa Responsive Dystonia
2. Myoclonic dystonia

F. **Myoclonus:** It is a brief shock-like muscular contraction, which may involve the whole muscle or a small number of muscle fibers. The contraction may be too slight to cause movements or may cause violent movements. It is decreased by voluntary relaxation. It usually disappears during sleep.

Lesion

1. Olivo dentate system
2. Cerebral cortex

Causes

1. Infections: Encephalitis lethargica, inclusion encephalitis
2. Degenerative: Cerebral lipidosis, subacute spongiform encephalopathy
3. Vascular
4. Tumor
5. Demyelinating: Disseminated sclerosis

G. **Fasciculations:** They are visible twitches of hyperirritable muscle fibers due to chronic degenerative disease of their anterior horn cells. Once the anterior horn cells are completely destroyed, the fasciculations cease.

Fasciculations are irregular and inconstant. They may be absent at rest, but they can be brought out by mechanical stimulation, fatigue and cold.

Causes

1. Motor neurone disease
2. Spinomuscular atrophy
3. Poliomyelitis
4. Intramedullary tumors
5. Syringomyelia
6. Syphilitic amyotrophy
7. Diabetic amyotrophy
8. Hypoglycemia
9. Hypoxia
10. Organophosphorus poisoning

H. **Fibrillations:** Fibrillations are contractions limited to a single muscle fiber or a small group of muscle fibers. Hence they are demonstrated only on E.M.G. and clinically they may be seen only if present on the tongue.

I. **Flexor Spasms:** In a patient with slow compression of the spinal cord due to an intact rubro-spinal tract which maintains the extensor tone of the lower limbs, the attitude of the patient is extension and the flexor withdrawal reflex is inhibited. This is paraplegia in extension. When the rubrospinal tracts are also affected, the extensor tone can no longer be maintained and the flexor withdrawal reflex cannot be inhibited. This gives rise to a sudden involuntary contraction of the flexors of the lower limbs in paraplegia. This is called flexor spasm. Once the rubro-spinal tracts

are totally damaged the patient assumes a flexion attitude of the lower limbs due to flexor withdrawal reflex and is said to be in paraplegia in flexion.

J. **Tics and Habit Spasms:** These are involuntary stereotype movements which, to start with, are voluntary as they serve some purpose (e.g. contraction of platysma with a tight collar) but later persist even though the stimulus that initiated the movement has ceased. They relieve tension. They can be inhibited by an effort of will, but re-appear when the attention is diverted. The severe form of the condition is Gilles de la Tourette's disease which is multiple convulsive tics.

Types

1. *Motor tics:* Simple (Clonic and Dystonic) and complex
2. *Vocal tics:* Simple and complex

K. **Myokymia:** They are transient or persistent, quivering or flickering movements which affect a few muscle bundles within a single muscle but usually are not extensive enough to cause movement at a joint. They are not limited to the muscle fibers and undulating and more widespread than fasciculations. They occur due to irregular discharge spreading to and through various muscle bundles. There is no associated muscle weakness and wasting. They are also called *false fibrillations.*

Causes

1. Physiological: Unaccustomed exercise, cold or when going to sleep
2. Anemia and debilitating conditions

L. **Titubation :** Involuntary nodding of head seen in lesions of vermis of cerebellum and old age.

D: Sensory System

Sensation can be divided into :

A. Superficial : Pain / temperature / superficial touch, carried by spinothalamic pathway.

B. Deep : Crude touch, joint position, vibration carried by dorsal, coloumn pathway.

C. Cortical : Can be tested only when other sensations are intact.

1. **Touch:** This is tested with cotton wool or the head of the pin on all the parts of the body (Fig. 6.42A).
2. **Pain:** Superficial pain is tested with a pin prick on all the parts of the body and any area where it is not felt adequately is noted. Deep pain is tested by pressing the calves, tendo Achillis or testes. It is lost in tabes dorsalis, whereas calves are tender in peripheral neuritis (Fig. 6.42B).
3. **Temperature:** Two test tubes, one containing

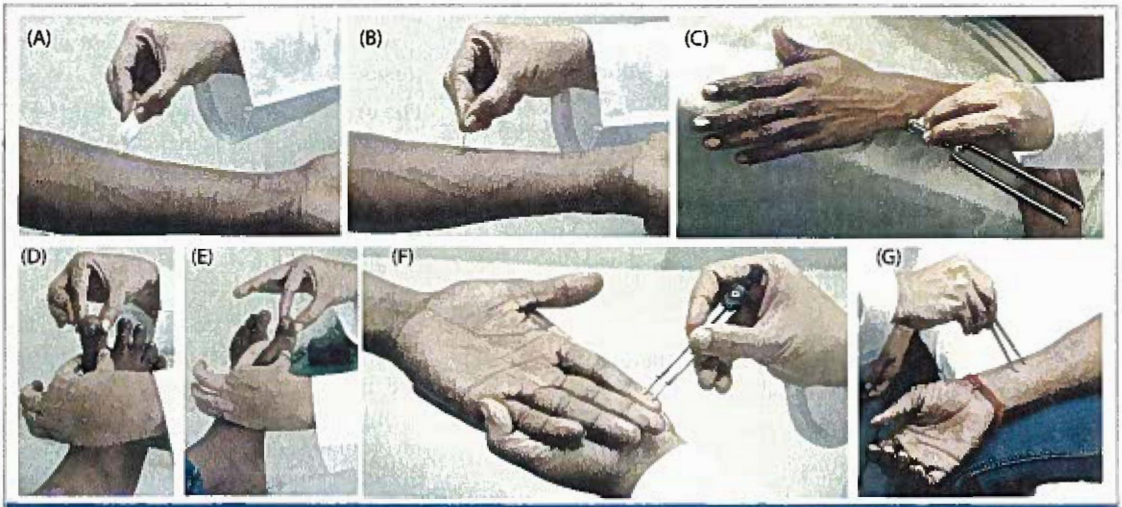


Fig 6.42 : Sensory System Testing (A) Touch, (B) Pain, (C) Vibration, (D and E) Joint Sense and (F and G) Two Point Discrimination

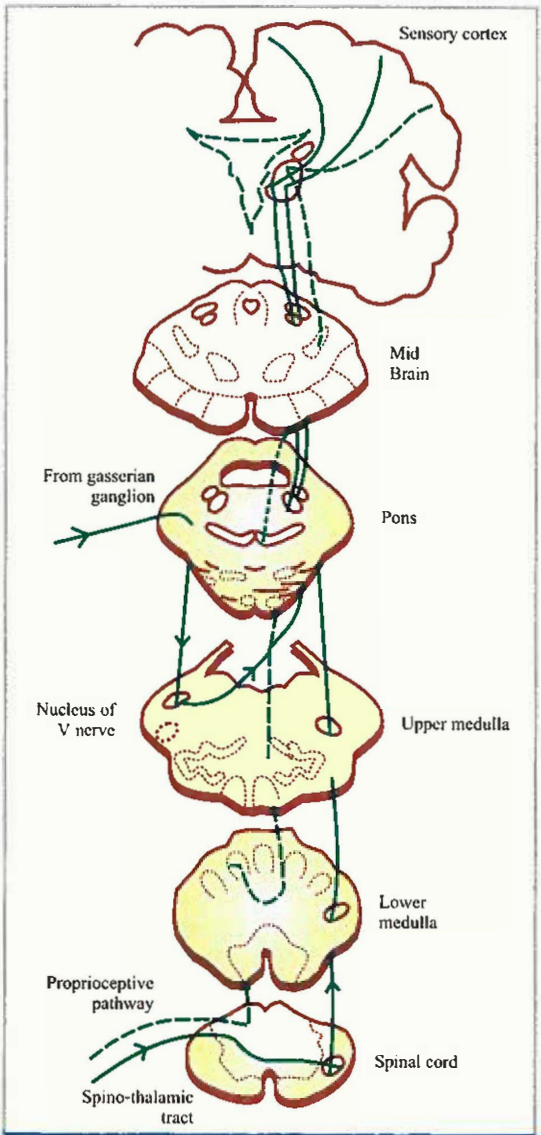


Fig 6.43 : Sensory Pathway

hot water and the other crushed ice is taken and placed on all the parts of the body. The patient is asked to denote if he feels the temperature.

4. **Position:** The patient is explained the procedure. With his eyes closed, a part of his limb / arm is placed in a definite position and then he is asked to denote the position or place the other limb in a similar position.
5. **Joint Sense :** Patients eyes remain closed. After fixing the joint, the finger / toe is moved at terminal interphalangeal joint, either up or down by holding the sides of digits. Pulp of finger is not touched. Patient is asked to tell the direction i.e. either up or down (Figs. 6.42 D and E).
6. **Vibrations:** A tuning fork of 128 vibrations per second is vibrated and placed on some bony prominence of the patient. The patient is asked to indicate if he feels the vibrations (see figure 6.42C).
7. **Cortical sense:** Tactile localization, tactile discrimination, tactile extinction and stereognosis 2 point discrimination and graphasthesia (see figure 6.42 F and G).

Sensory changes in various diseases are as below:

1. **Polyneuropathy:** Symmetrical glove and stocking anesthesia (affecting distal parts more) involving all the modalities of sensations. There is calf tenderness (Fig. 6.44).
2. **Cauda Equina and Conus Lesion:** Loss of all modalities of sensations involving especially lower sacral segments leading to perianal anesthesia (also Refer Pg. 336) (Fig. 6.45).
3. **Multiple Roots Involvement:** There are varying degrees of impairment of cutaneous sensations in the distribution of the nerve roots. Pain sensation is more affected than touch.
4. **Complete Section of Spinal Cord:** All forms of sensations are abolished below a particular level, with a narrow zone of hyperesthesia at the upper margin of the anesthetic zone. In some patients with high cord compression sacral fibers may be spared resulting in sacral sparing (Figs. 6.46 and 6.47).
5. **Hemi-section of Spinal Cord:** Pain and temperature is lost a few segments below a particular level on the opposite side whilst vibration, position and joint senses are affected on the same side (Fig. 6.48).
6. **Syringomyelia:** Loss of pain temperature sensation (fibers of which cross the cord in the anterior commissure). Touch, vibration, joint and position senses are normal. This is also called dissociate anesthesia (Fig. 6.49).
7. **Anterior Spinal Syndrome:** Loss of pain,

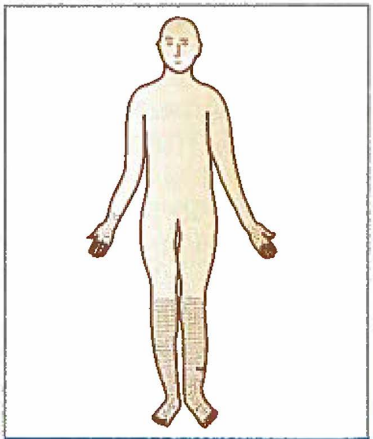


Fig. 6.44 : Glove and stocking anesthesia

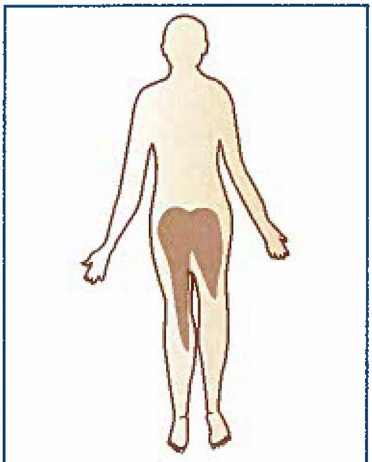


Fig. 6.45 : Perianal anesthesia

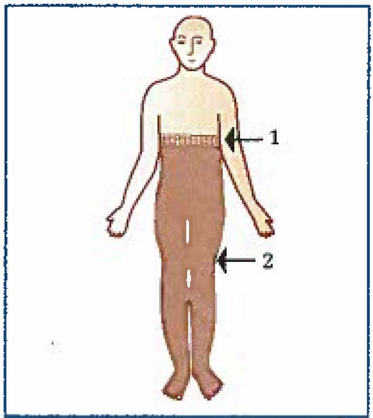


Fig. 6.46 : Complete section of spinal cord (1) Zone of hyperesthesia; (2) Loss of all modalities of sensations

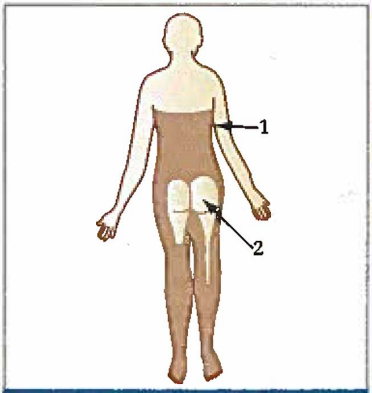


Fig. 6.47 : High cord compression showing sacral sparing (1) Loss of all modalities of sensations; (2) Sacral sparing

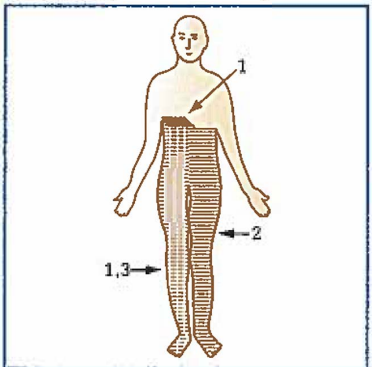


Fig. 6.48 : Hemi-section of the cord on right side (1) Hyperpathia increased perception of sensations; (2) Loss of pain & temperature; (3) Loss of touch vibration and joint senses

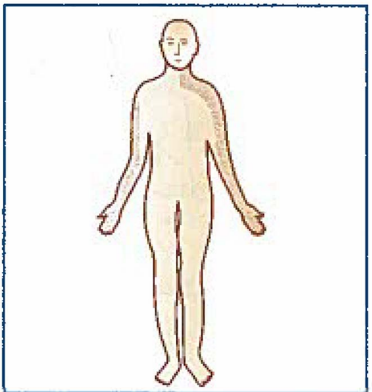


Fig. 6.49 : Dissociate anesthesia in Syringomyelia taking the form of a cuirasse involving both the upper limbs, the chest wall and the neck

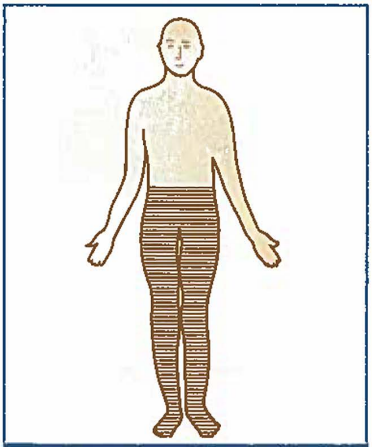


Fig. 6.50 : Loss of position and vibration sense (Posterior spinal syndrome)

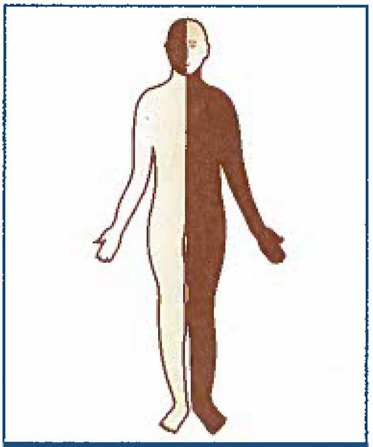


Fig. 6.51 : Contralateral loss of sensations (Brain-stem syndrome)

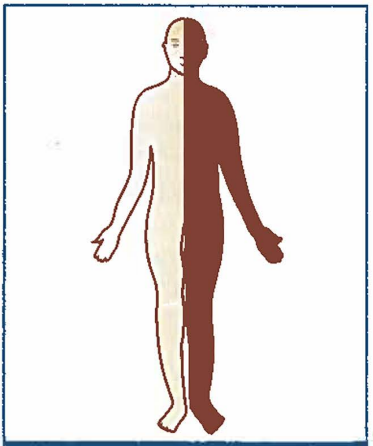


Fig. 6.52 : Ipsilateral loss of sensations (Thalamic syndrome)

temperature and touch below a level on both sides with preserved position, joint and vibration sense, e.g. Anterior spinal artery thrombosis.

8. **Posterior Spinal Syndrome:** Loss of position, joint and vibration sense below a level with normal touch, temperature and pain senses, e.g. Tabes dorsalis (Fig. 6.50).
9. **Brain Stem Syndrome:** Loss of touch, pain and temperature on same side of the face and opposite side of the body due to involvement of trigeminal tract or nucleus and lateral spinothalamic tracts (Fig. 6.51).
10. **Thalamic Syndrome:** Loss of all modalities of sensations on the opposite side of the body. Position sense is more affected than any other sensation. There may be spontaneous pain and discomfort (thalamic pain) of the most torturing and disabling type (Fig. 6.52).
11. **Parietal Lobe Syndrome:** There is loss of discriminative sensory function:
    A. *Loss of tactile localization:* Patient is unable to localize the site touched.
    B. *Loss of tactile discrimination:* When two stimuli are applied together, one near the other, the patient appreciates both as one stimulus.
    C. *Tactile extinction:* When two stimuli are applied simultaneously to two symmetrical portions of the body, the patient neglects the one on the opposite side of the lesion, though individually he appreciates the stimulus on both sides.
    D. *Astereognosis:* Patient is unable to appreciate objects (like coins, keys etc.) by touch alone.
    E. *Primary modalities of sensations* may be affected in deep-seated parietal lobe lesions.
    F. *Two Point discrimination (Figs. 6.42 F and G)* : This is performed with a divider. The patient is asked to distinguish the contact of 2 separate points of the divider when applied simultaneously. The distance at which the patient is unable to distinguish the two points as separate is measured. The minimum distance is different in different parts of the body which is normally:

       Finger pulp, lips : 3 - 5 mm
       Palm : 2 - 3 mm
       Sole : 4 cm
       Dorsum of foot : 5 cm
       Back : 5 cms.
12. **Hysterical:**
    A. Complete hemianesthesia with reduced hearing, vision, taste and smell as well as reduced vibration only over one half of the skull.
    B. Sharply defined sensory loss not confined to the distribution of the root or cutaneous nerve.
    C. Postural sense is rarely affected.

E: Reflexes

I. Superficial Reflexes

The superficial reflexes have, in addition to a spinal reflex arc, a superimposed cortical pathway, a "cerebral arc". Impulses ascend through the spinal cord and brain stem to the parietal areas of the brain and have connections with the motor centres in the pyramidal or the premotor areas. Efferent impulses then descend in the pyramidal tracts. Hence a lesion of the reflex arc or a lesion at a high level anywhere along the pyramidal pathway abolishes the superficial reflexes.



Fig. 6.53 : Flexor response and Extensor response

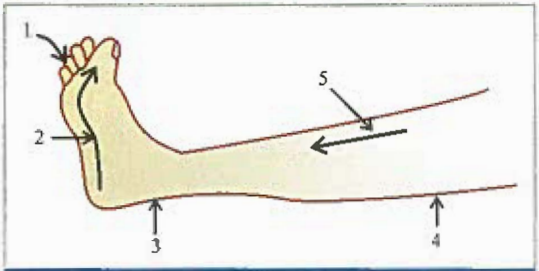


Fig. 6.54 : Methods of eliciting plantar reflex (1) Gonda (press down); (2) Babinski (stroke); (3) Schaefer (squeeze); (4) Gordon (squeeze); (5) Oppenheim (stroke)

There is believed to be a centre in the region of the red nucleus that inhibits the superficial reflexes, and a lesion of this centre leads to brisk superficial reflexes. It is seen in:

1. Extrapyramidal disease: Chorea, Parkinsonism
2. Amyotrophic lateral sclerosis
3. Psychoneurosis and hysteria

A. Plantar Reflex (S1)

Normally: Flexor response i.e. on stroking the lateral border of the sole, there is flexion of the big toe and all the toes.

Extensor plantar response: On stroking the lateral border of the sole, there is:

1. Fanning of the small toes
2. Dorsiflexion of the big toe
3. Dorsiflexion of the ankle
4. Contraction of tensor fascia lata
5. Flexion of knee and hip.

Causes

1. Pyramidal lesions
2. Deep sleep or coma
3. In infants it is normally present
4. Transiently following an epileptic fit
5. Hypoglycemia
6. Post-seizure
7. Metabolic encephalopathy
8. Anesthesia
9. Neuroleptics
10. Neurotoxins

Absent plantar response:

1. Loss of sensations of the sole (L5-S1)
2. Paralysis of the extensor hallucis
3. Lesion of the first sacral segment
4. Thick plantar skin
5. Cauda equina lesions

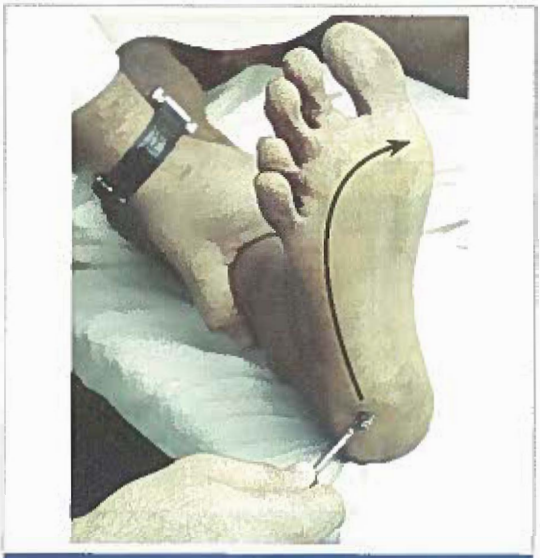


Fig. 6.55: Plantar Reflex

B. Abdominal Reflex (T7-T12)

Elicited by gentle stroking of the abdomen with a blunt object.

Response: Homolateral contraction of the abdominal muscles and retraction of the linea alba and the umbilicus towards the area stimulated.

Absent:

1. Marked obesity and abdominal distention
2. Multiparous women with lax abdomen
3. Lesions of local reflex arch of T7-T12
4. Pyramidal lesion (unilateral loss on same side as hemiplegia)
5. Typhoid perforation (segmental loss)
6. Herpes Zoster.
7. Post abdominal surgery
8. Lost early in Multiple Sclerosis.

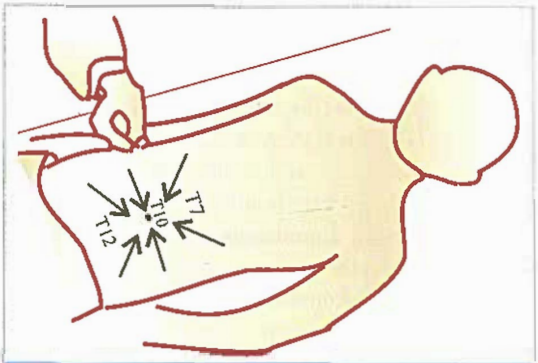


Fig. 6.56: Abdominal reflex



Fig. 6.57 : Abdominal Reflex

Note:

1. Abdominal reflex may be presented inspite of pyramidal lesions till late in motor neuron disease and cerebral palsy.
2. Beevor's sign in lesions at T10 level. There is loss of lower abdominal muscle contraction but retained upper abdominal muscle contraction. So on eliciting the abdominal reflex, the umbilicus gets pulled upwards.

C. Cremasteric Reflex (L1)

Elicited by stroking the skin on the upper, inner aspect of the thigh, from above downwards with a blunt point.

Response: Contraction of the cremasteric muscle with homolateral elevation of the testicle.

Absent:

1. Lesions of local reflex arch of L2
2. Pyramidal lesions
3. Hydrocele
4. Hernia

D. Bulbocavernous Reflex (S2-S4)

Elicited by pressing the glans penis.

Response: Contraction of the bulbocavernous muscle felt at the junction of the penis and the scrotum.

Absent:

1. Lesion of the local reflex arch of S2-S4
2. Pyramidal lesions

E. Anal Reflex (S4-S5)

Elicited by stroking or pricking the skin on mucous membrane in the perianal region.

Response: Contraction of the external anal sphincter.

Absent:

1. Lesion of the local reflex arch of S4-S5.
2. Pyramidal lesions.

F. Hoffmann's Sign

Method: The patient's hand is pronated and the observer grasps the terminal phalanx of the middle finger between his forearm and thumb. With a sharp flick, the phalanx is passively flexed and suddenly released. A positive response consists of a sharp twitch with adduction and flexion of the thumb and flexion of the fingers.

Significance: It is an index of muscular hypertonia rather than of pyramidal lesion as such. It is not always positive in presence of a pyramidal lesion. It may be elicitable in a nervous individual with no organic disease. If it is present on one side only, it is likely to be significant.



Fig. 6.58 : Hoffmans Reflex

H. Wartenburg's sign :



Fig. 6.59 : Wartenbergs Test

The patient's hand is supinated. Examiner pronates his hand and interlocks his fingers with the patients. The patient pulls his fingers away against the examiners resistance. Normally, the thumb extends. In pyramidal tract lesions the thumb adducts and flexes. This indicates early stage of pyramidal tract disease (this is equivalent to Babinski reflex in the lower limb).

II. Deep Tendon Reflexes

Physiology: The tendon reflex is the reflex contraction of muscle or part of a muscle in response to stretch. Hence the sudden stretch, brought about by tapping the tendon evokes a sharp muscular contraction.

Reinforcement of the tendon jerks may be achieved by clenching the fists or by pulling the flexed fingers of the two hands against each other (*Jendrassiks maneuver*), as these movements increase the activity of the gamma efferent system.

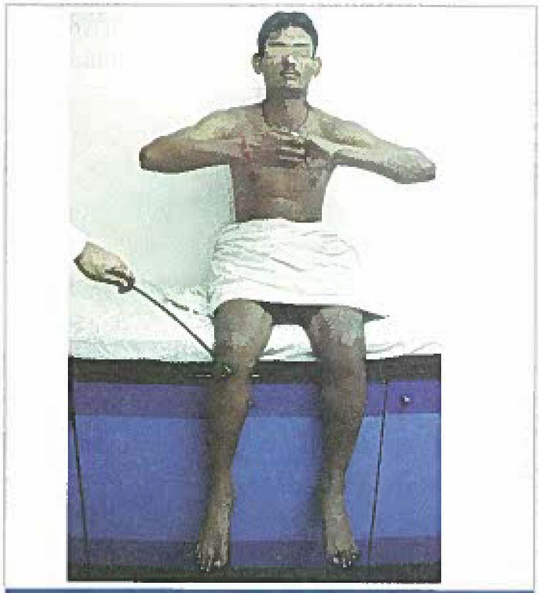


Fig. 6.60 : Jendrassiks Manouver

Finger Flexion Reflex:

Patients hand is supine with fingers relaxed and slightly flexed. Examiner's fingers are placed over the proximal part of the patients fingers and he strikes them with hammer. Normally there is slight flexion of fingers. *Positive* : brisk flexion of all fingers indicating a lesion of C6 - T1.

Table 6.9 : Deep Tendon Reflexes

Reflex	Nerve	Mode of elicitation	Response
Biceps C-5-6	Musculo cutaneous	Blow upon the biceps tendon	Flexion of the elbow
Supinator C-5-6	Radial	Blow upon the tendon of brachioradialis at the distal end of the radius	Flexion of the forearm with supination
Triceps C-7-8	Radial	Blow upon the tricep tendon	Extension of the arm
Finger Flexion C6-T1	Median and ulnar	Blow upon the palmar surface of the semiflexed fingers	Flexion of the fingers and thumb
Knee L3, 4	Femoral	Blow upon the quadriceps tendon	Extension of the knee
Ankle S-1-2	Sciatic	Blow upon the tendocalcaneous	Plantar flexion of the ankle

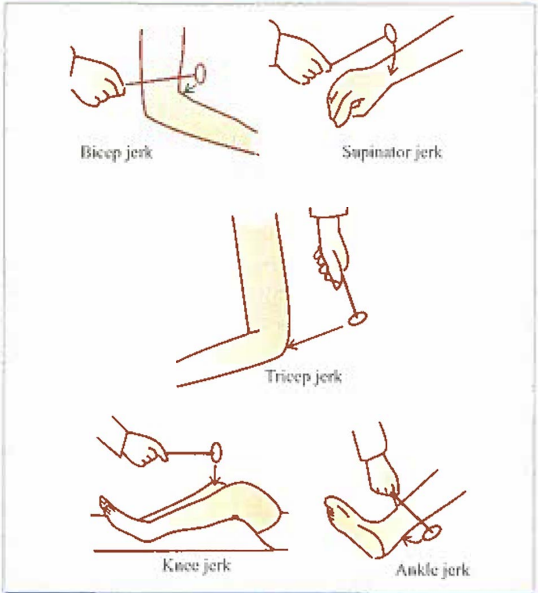


Fig. 6.61 : Deep reflexes

Exaggerated tendon reflexes

1. Pyramidal lesions
2. Tetanus poisoning
3. Hysteria
4. Fright
5. Strychnine
6. Hypercalcemia

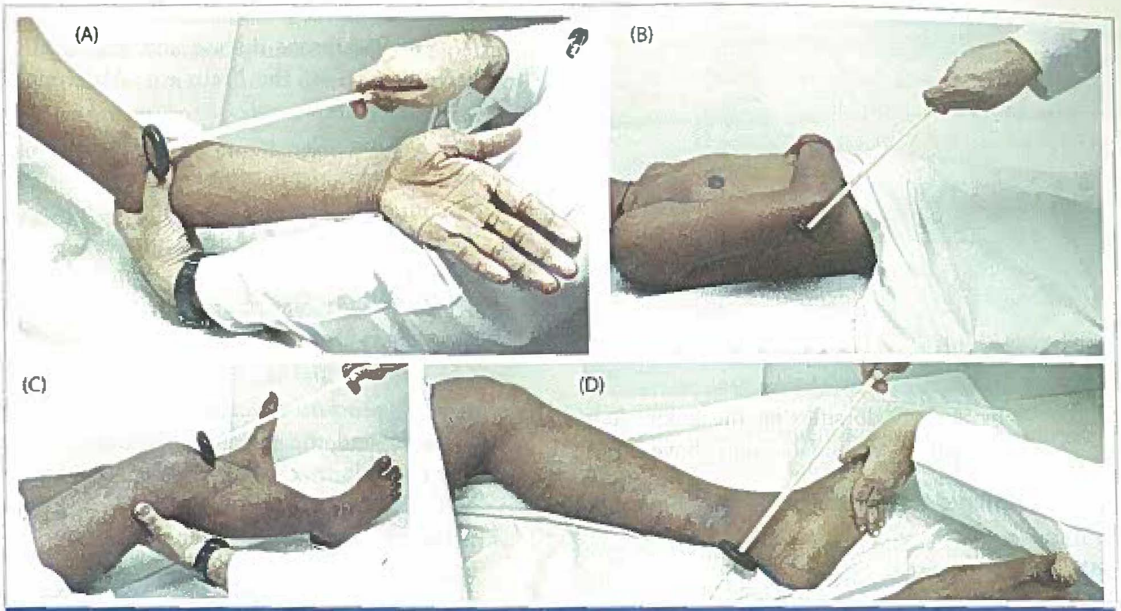


Fig. 6.62: Deep Tendon Reflexes (A) Biceps Jerk, (B) Triceps Jerk, (C) Knee Jerk and (D) Ankle Jerk



Fig. 6.63: Finger Flexion Reflex

Absent tendon reflexes:

1. Lower motor neurone disease
2. Neuronal shock
3. Marked spasticity and muscle contracture
4. Normal individuals unable to relax

Variations of deep tendon reflexes

1. *Paradoxic triceps reflex:* This consists of flexion instead of extension of the forearm following stimulation of the triceps tendon. This response appears when the arc of the triceps reflex is damaged e.g. in lesions of seventh and eighth cervical segments; in such cases the stimulus calls forth a flexor response unopposed by the triceps muscle.
2. *Inversion of the radial reflex:* In pyramidal lesions at the fifth and sixth cervical segments there may be contraction of the flexors of the hand and fingers without flexion and supination of the forearm. This is called inversion of the radial reflex.

   This occurs because there is exaggeration of reflexes sub served by segments below the fifth and sixth cervical segments. A tap on the styloid process stimulates both the contraction of the brachioradialis (which is served by C5-6 and hence abolished) and long flexors of the fingers (served by C7-8 and hence brisk).
3. *Clonus:* Clonus is a rhythmical series of contractions in response to the maintenance of tension in a muscle, associated with increased gamma efferent discharge. It is elicitable when tendon reflexes are brisk after a corticospinal lesion.

   Patellar clonus (of quadriceps) is best elicited by a sudden sharp downward displacement of the patella. It is present in pyramidal lesions above L-2. *Ankle clonus* is obtained



Fig. 6.64: Ankle Clonus

by sharply dorsiflexing the ankle. It is present in pyramidal lesions above S-1.

III. Primitive Reflexes

A. *Sucking/rooting Reflex:* Gentle stroking of the center of lips or corner of lips will result in sucking or rooting response, respectively, in direction of stimulus.

B. *Grasp Reflex:* Stroking in between thumb and index finger will cause grasping of finger. Stroking the back of the hand may release the grasp.

C. *Palmomental Reflex:* Stroking the palm will cause ipsilateral contraction of the chin (mentalis).

D. *Glabellar Tap:* Repeated tapping of patient's glabella with the index finger produces 2-3 blinks maximally in a normal person. It is said to be positive (abnormal) when blinking response is continuous. Seen in Parkinsons disease and degenerative diseases of the brain e.g. Alzheimer's dementia.

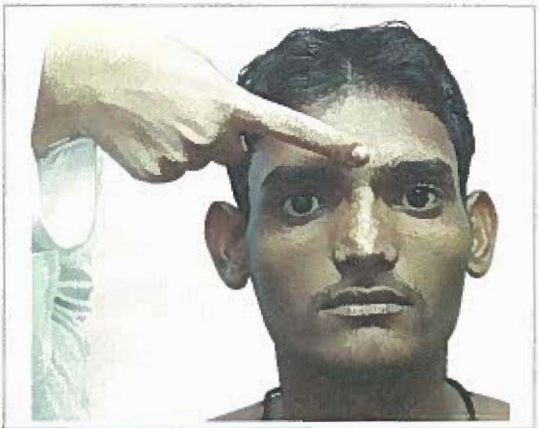


Fig. 6.65: Glabellar Tap

These are not normally present in adults but may be seen in Frontal Loss disorders.

F. Urinary Bladder

Anatomy

The bladder consists of both smooth muscles (the detrusor and the internal sphincter) and striated muscles (the external sphincter). The detrusor and the internal sphincter receive nerve supply from sympathetic (L 2,3 and 4) and parasympathetic (S, 2, 3 and 4) nerves. Both nerves have afferent and efferent fibers.

The parasympathetic afferent fibers which sub serve pain and stretch sensation from the bladder pass up the spinal cord in the spinothalamic tract, lying on its outer aspects. The parasympathetic efferent fibers contract the detrusor and relax the internal sphincter, thus stimulate emptying of the bladder. The sympathetic efferent fibers on the other hand relax the detrusor and contract the sphincter, thus inhibit emptying of the bladder.

The external sphincter is supplied by the pudendal nerve (S2-3). Its afferent fibers carry touch and pressure sensations from the urethra to the posterior column of the spinal cord, whilst its efferent fibers (which are from the anterior horn cells) are under the voluntary control so that it is possible to inhibit spontaneous emptying of the bladder. The supranuclear fibers of the efferent nerves lie close to the pyramidal tract. The paracentral lobule is the cortical centre for the control of voluntary activity of the bladder.

Physiology

The rise of intravesical pressure to about 25 cms of water sets off afferent impulses from the bladder wall stretch receptors. At the cortex they are recorded as "desire to micturate." If the circumstances are favorable, para-sympathetic efferents and pudendal

nerves are stimulated. Voluntary relaxation of the external sphincter and the perineal muscles initiate the act of micturition whereas contraction of the detrusor muscle and relaxation of the internal sphincter empty the bladder. If the circumstances are not favorable the sympathetic fibers are stimulated and parasympathetic inhibited which contracts the internal sphincter and relaxes the detrusor muscle. This increases the volume of the bladder and thus intravesical pressure falls and the urge to micturate disappears.

When more urine accumulates again, the intravesical pressure rises and the same sequence of events recur until the bladder can no longer expand to reduce the intravesical pressure and the urge remains till the patient passes urine.

Neurogenic Bladder vs Non Neurological Bladder

In elderly patients commonly due to Benign Prostatic hyperplasia (BPH), they face urinary symptoms. When predominant symptoms are urgency, hesitancy, poor stream / interrupted stream, post void dribbing, they arise from BPH (non-neurogenic bladder).

When Predominant symptoms are urgency, frequency, precipitancy, and episodes of involuntary passage of urine with a normal stream they indicate underlying neurolgical cause (neurogene bladder).

Neurogenic Bladder

Table 6.10 : Five types of neurogenic bladders

	Type	Lesion
1.	Uninhibited bladder	.. Cortico regulatory tract
2.	Reflex bladder	.. Spinal cord above S2
3.	Autonomous bladder	.. At S2, S3 and S4 level
4.	Motor atonic bladder	.. Motor efferents
5.	Sensory atonic bladder	.. Sensory afferents

A. Uninhibited Bladder

This occurs in cerebrovascular accidents, head injuries, brain tumors, etc. Here, since the lesion is in the cortico-regulatory tract, voluntary control of micturition is lost. Hence, when the circumstances are favorable and the patient wants to initiate micturition, he is not able to do so immediately. After sometime the micturition reflex arc is stimulated and the patient voids urine. This is called hesitancy. Again when the circumstances are not favorable, and the urge to micturate occurs, patient is unable to hold back the urine (because the voluntary cortical inhibitory control is lost) and patient may soil his clothes. This is precipitancy.

The treatment for precipitancy is to use a condom catheter and attach a bag to it.

Diagnosis: A positive diagnosis is made by cystometry only. It shows voiding contractions. To differentiate uninhibited bladder from chronically inflamed bladder 100 mg Banthine is given I.V. and cystometry repeated. In uninhibited bladder, the voiding contractions disappear as they are mediated via cholinergic fibers. In chronically inflamed bladder they persist as non-cholinergic fibers mediate it.

B. Reflex Bladder

Etiology

1. Transverse myelitis
2. Trauma
3. Neoplasms
4. Meningitis
5. Disseminated sclerosis

Pathogenesis

Acute transection of the cord causes retention of urine during the stage of spinal shock. If the urethral sphincter is unable to maintain the pressure of the urine in the bladder, it gives way and urine dribbles out causing retention of urine with overflow. Once a certain amount of urine has been passed, pressure within the bladder falls and the urethral sphincter tone prevents further evacuation of bladder. This leads to retention of residual urine. When more urine accumulates and

pressure builds up in the bladder, the urethral sphincter gives way and once again urine dribbles out.

When the stage of spinal shock passes, as a result of unopposed descending spinal impulses, reflex bladder activity begins since the local reflex arc is intact. The bladder can be stimulated by cutaneous stimuli or pressure over the hypogastrium and a complete evacuation of bladder occurs. This is called **automatic bladder.** This facilitated activity may involve the rectum causing mass evacuation of bladder and rectum.

Slowly developing and partial lesions of the cord do not cause spinal shock so that the initial retention with overflow does not occur. These lesions cause automatic bladder activity with precipitancy of micturition.

Diagnosis: Clinical examination will reveal spinal cord lesion and cystometry will show sudden and uncontrollable voiding.

Treatment:

1. *Catheterization of the bladder* must be done when there is retention of urine to prevent the bladder muscles from being over stretched. Again compression of the bladder wall by urine leads to ischemic necrosis of the bladder as the blood supply of the bladder lies within the bladder wall.
2. *Urinary antibiotics:* Urine examination for pus cells and RBCs and urine culture must be done. Usually urinary infection is a rule once catheterization is done and suitable antibiotics must be given.
3. *Aluminium hydroxide:* This is given once a catheter is put in the bladder to prevent the formation of phosphatic stones. Aluminium hydroxide prevents the intestinal phosphate absorption by combining with it and forming aluminium phosphate.
4. *Bladder washes:* In any patient with an indwelling catheter, bladder washes with antiseptic solutions like Condy's lotion must be given twice a day.
5. *Bladder exercise:* Once the stage of spinal shock has passed, the bladder muscles must be stretched, else they will atrophy and lead to a small capacity bladder. This is prevented by bladder exercises. The catheter is clamped for a few hours every day which is gradually increased so that urine accumulates in the bladder and stretches it. It can be evacuated by releasing the clamp once the sensation of fullness occurs or after a few hours. Once automatic bladder develops and the patient is well trained, catheter may be removed.

C. Autonomous Bladder

Etiology

1. Congenital: Spina bifida, meningomyelocele
2. Trauma: Gunshot, auto accidents
3. Infective: Arachnoiditis, radiculitis
4. Neoplasms of the cord
5. Surgery: Combined perineal and abdominal resection

Clinical Features

1. Loss of bladder sensation
2. Inability to initiate micturition normally. Patient learns to void urine by applying external force to the bladder.
3. Stress incontinence may occur if there is paralysis of periurethral striated muscles, which can no longer compress and elongate the urinary sphincter when the intravesical pressure is markedly elevated.
4. This is usually associated with saddle shaped anesthesia and absent bulbocavernous reflex.

Diagnosis: Cystometry — Absent sensation

and positive Urecholine supersensitivity test.

Treatment

1. Cutaneous vesicostomy
2. If there is continuous incontinence of urine
   a) Ureteroileostomy
   b) Diamond-shaped wedge to be constructed at the urethrovesical junction to narrow urinary sphincter

D. Sensory Paralytic Bladder

Etiology

1. Tabes dorsalis
2. Pernicious anemia
3. Diabetes
4. Disseminated sclerosis
5. Syringomyelia

Pathogenesis: There is loss of bladder sensation, which leads to overdistension of bladder. Initially there is normal capacity and complete emptying. Gradually the bladder capacity increases and residual urine appears.

Clinical Features: Initially these patients are asymptomatic. Gradually there is terminal dribbling, and later, overflow incontinence.

Treatment: The patient must be advised to void frequently even if he does not get bladder sensation.

E. Motor Paralytic Bladder

Etiology

1. Poliomyelitis
2. Polyradiculopathy
3. Congenital anomalies
4. Tumor
5. Trauma

Pathogenesis: Since the sensory nerves are intact, bladder if left alone, distends and decompensates.

Clinical features

1. Painful distension of the bladder and inability to initiate micturition.
2. Decrease in size and force of stream and interrupted stream.
3. Recurrent episodes of urinary infections.

Diagnosis: Cystometry — Normal sensations. No involuntary contractions of detrusor. Urecholine sensitivity test is positive.

Treatment

1. Urethral drainage
2. Parasympathomimetic agents

Meningeal Signs

I. Neck Stiffness: It is characterized by stiffness of the neck and resistance to passive movements, with pain and spasm on attempted motion. The chin cannot be placed upon the chest.

Causes

A. Meningitis
B. Subarachnoid hemorrhage
C. Tetanus
D. Strychnine poisoning
E. Hysteria
F. Cervical spondylosis
G. Meningism

In meningitis neck stiffness is absent in severe and terminal cases or in very young infants.

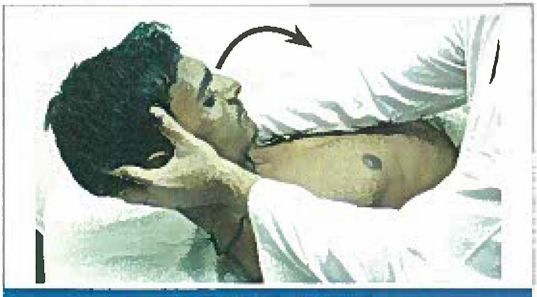


Fig. 6.66: Testing for Neck Stiffness

II. Kernig's Sign: With the hip flexed, the knee is extended. Normally it can be done up to 135°. In meningitis it is restricted due to spasm of the hamstrings. (Fig. 6.48)

III. Brudzinski's Sign:

A. *Neck sign:* On flexing the neck, there is flexion of the hips and knees.

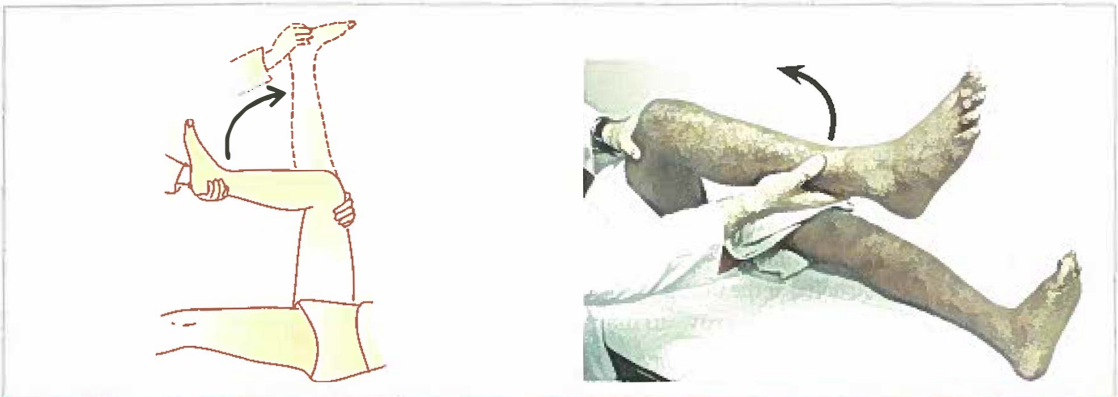


Fig. 6.67 : Testing for Kernig's Sign

B. *Leg sign:* On flexing one leg, the other leg also flexes. It is present in meningitis.

C. *Symphysis sign:* Pressure on symphysis pubis is followed by flexion of both lower limbs.

D. *Cheek Sign:* Pressure against the cheeks below the zygoma causes reflex flexion at the elbows, with an upward jerking of the arm.

IV. **Bikele's Sign:** The patient is seated with arms elevated extended and externally rotated and forearm flexed. The examiner attempts passive extension of forearm at the elbow. Resistance to extension occurs in brachial neuralgia and meningitis.

Straight Leg Raising Test (SLR)

With the patient supine and both legs extended, one leg is passively flexed at the hip keeping the knee extended. Normally it can be lifted up to 90°. It is restricted in meningitis and sciatica.

Lasegue's Sign:

Once the leg is raised at a particular level for the S.L.R. test and the patient gets pain at that level, the foot is dorsiflexed. If the pain worsens, it is due to Sciatica.

3 › Cranial Nerves

Can be divided into:

A. Pure Motor : III, IV, VI, XI, XII

B. Pure Sensory : I, II, VIII

C. Mixed : V, VII, IX, X

First (Olfactory) Nerve

Anatomy: The olfactory receptors in the nasal septum and lateral wall of the nasal cavity give central processes that form bundles, the filaments of the olfactory nerve which penetrates the cribriform plate of the ethmoid bone and enters the olfactory bulb and then to the olfactory tract in the sulcus on the orbital surface of the frontal lobe. Some of the fibers of the olfactory tract decussate with those from the opposite side and then they enter the piriform lobe of the temporal lobe (primary olfactory cortex) and then terminate in the amygdaloid nucleus, septal nuclei and hypothalamus.

Testing: The sense of smell is tested by asking the patient to sniff various non-irritating substances (like tea, coffee, clove oil, peppermint oil etc.) separately in each nostril and identify the odor. Irritating substances like ammonia are avoided because they stimulate, in addition, the trigeminal nerve. Each nostril is to be tested separately.

Anosmia

Causes

A. *Local disease* of the cribriform plate of ethmoid bone

B. *Subarachnoid hemorrhage*

C. *Neoplastic:*
   1. Tumors in the olfactory groove
   2. Frontal lobe tumors

D. *Infection:*
   1. Tabes dorsalis
   2. Meningitis

E. *Metabolic:*
   1. Refsum's disease
   2. Paget's disease
   3. Hypoparathyroidism

F. *Deficiency:* Zinc

G. *Hysteria*

H. *Idiopathic*

Parosmia and Cacosmia

Parosmia is perversion of smell and cacosmia is unplesant odors. These are rare phenomena and seen following head-injury or with psychiatric illness like depression. Cacosmia is seen in atrophic rhinitis.

Second (Optic) Nerve

Anatomy: The fibers of the optic nerve, from the retina, pass backwards to the optic chiasma, where the inner half decussate, whereas the outer half remain on the same side, forming on optic tract. Each optic tract passes backwards to the superior colliculus, from where part of the fibers goes to the lateral geniculate body, optic radiation and finally the occipital cortex around the calcarine sulcus (visual centre).

Test: The optic nerve can be tested by testing the visual acuity, visual fields and color vision.

1. **Visual Acuity:** The visual acuity is examined at bedside with finger counting at a distance of 1 meter. Detailed testing requires equipment not available at the bedside and cooperation of the patient, which is often lacking in patients with brain disorders.

   Visual acuity for distant vision can be measured by *Snellen's test types* which are a series of letters of varying sizes so constructed that the top letter is visible to the normal eye at 60 meters and the subsequent lines at 36, 24, 18, 12, 9, 6 and 5 meters respectively. Visual acuity is expressed as d/D. (d. = distance at which the letters are read — 6 metres and D. = distance at which the letters should be read). Each eye should be tested separately. The patient reads down the chart as far as he can. If only the top letter of the chart is visible, the visual acuity is 6/60. A normal eye should be able to read up to seventh line i.e. the visual acuity is 6/6.

   Visual acuity for near vision is tested by *Jaeger's chart.* The test types are of varying sizes. The near vision is recorded as the smallest type that the patient can read comfortably.

   Significance: Visual acuity is most often impaired by changes in the shape of the globe and in the refractory characteristics of the transparent media of the eye. Once refractory errors are excluded, changes in visual acuity are secondary to lesions in the macular region or its projection. All compressive and most of the non-compressive lesions of the optic nerve reduce visual acuity even before a field defect can be detected.

   Visual acuity is unimpaired in unilateral lesion dorsal to the optic chiasma.

2. **Visual Field**

   To test the field of vision by *confrontation method*, the examiner must sit opposite the patient at a distance of 2 feet. To test the right eye, the left eye of the patient is closed. He is asked to look fixedly at the left eye of the examiner, which should be at the same level as that of the patient. The examiner holds a pencil between the patient's face and his own and keeps it moving from outside towards the patient's eye in all the four directions. The patient is asked to indicate as soon as the pencil is visible in a particular direction. It is presumed that the examiner's field of vision is normal. Hence if the patient sees the pencil at the same time as the examiner, his field of vision in that direction in that eye is normal. If the examiner sees the pencil before the patient, the patient is likely to have restriction of field of vision in that direction. When any abnormality is suspected in the field of vision, accurate charts should be prepared by perimetry.



Fig. 6.68: Confrontation Test

Field Defects

I. **Concentric diminution:** Vision is restricted all round its periphery. It occurs in:
   1. Hysteria
   2. Papilledema
   3. Lesions of the anterior part of the cortical visual centres
   4. Retinal lesions

II. **Central scotoma:** Vision is lost in the centre of the visual field. It occurs in:
   1. Optic or retrobulbar neuritis
   2. Pressure on the optic nerves
   3. Lesions of the posterior part of the cortical visual centres
   4. Choroidal macular lesion

III. **Hemianopia:** Vision is lost in one half of the visual field. It occurs as follows:
   A. *Homonymous:* Blindness occurs in one half of both sides of the eyes due to lesions of the optic tracts or radiations on the opposite side.
   B. *Quadrantic:* Blindness occurs in a quarter of the normal visual field. It occurs in partial lesions of the optic radiations or lesions of the occipital lobes.
   C. *Bi-temporal:* Blindness occurs in the temporal halves of both the fields. It occurs due to lesions of the nasal halves of both the optic nerves as is commonly seen in pituitary tumors.
   D. *Binasal:* Blindness occurs in the nasal halves of both the fields. It can only be produced by bilateral lesions confined to the uncrossed optic fibers on either side. Hence it is rare.

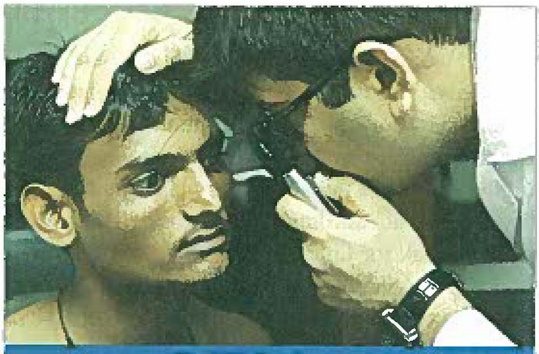


Fig. 6.70: Fundoscopy

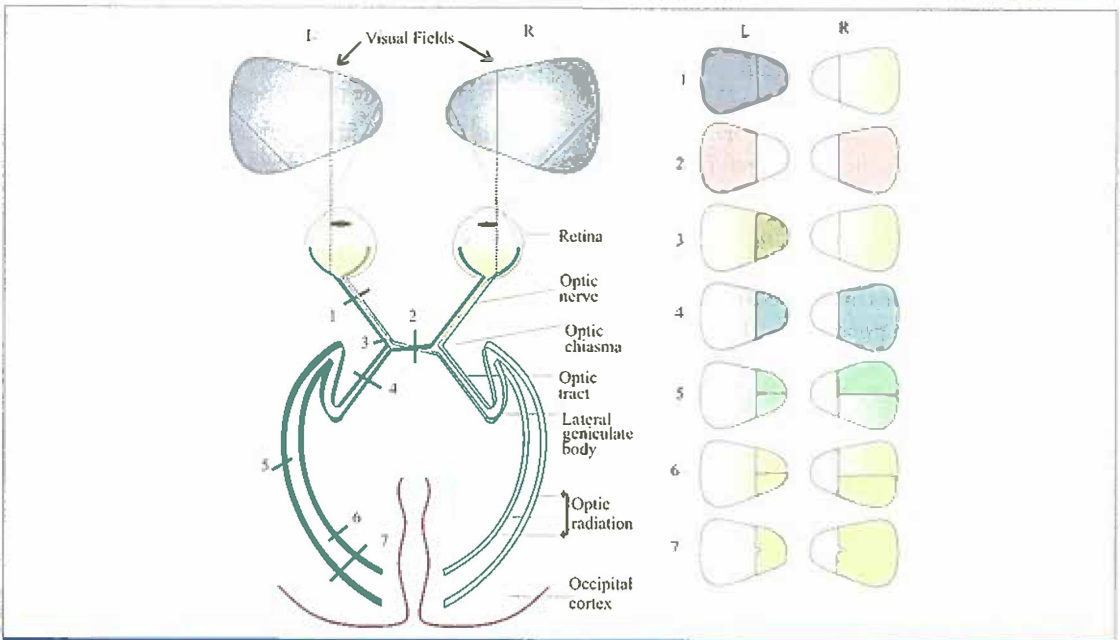


Fig. 6.69: Field defects associated with lesions of the optic pathways

3. Color Vision

Color vision is best tested by pseudoisochromatic plates of Ishihara. The plates are so constructed that a person with normal color vision will be able to read a number which a person with defective color vision will not.

Significance: Color vision loss usually parallels visual acuity loss, but in optic neuritis, color vision is much worse. Again, patients with bilateral lesions of the inferomedial occipital region often has color blindness with normal visual acuity.

The most common defect of color vision is red-green deficiency, inherited as a sex-linked recessive condition. Defect in color vision is not disabling, but is important in certain occupations like flying, driving etc.

Papilledema

Causes

A. *Raised intracranial tension:*
   1. Brain tumor
   2. Infections: Meningitis, cerebral abscess
   3. Vascular: Sub-arachnoid hemorrhage, intra-cranial sinus thrombosis
   4. Hydrocephalus
   5. Miscellaneous: Emphysema, tetany, hyper vitaminosis A

B. *Secondary to Optic neuritis and Retrobulbar neuritis*

C. *Vascular:*
   1. Arterial: Giant cell arteritis, malignant hypertension
   2. Venous: Thrombosis of central retinal vein, cavernous sinus, etc.

D. *Miscellaneous:*
   1. Guillain Barre syndrome
   2. Leukemias and reticulosis
   3. Pseudo tumor cerebri
   4. Anemia
   5. Emphysema
   6. SLE

Optic Neuritis

Causes

A. *Demyelinating diseases:*
   1. Disseminated sclerosis
   2. Devic's disease

B. *Infections:*
   1. Syphilis
   2. Tuberculosis
   3. Meningitis
   4. Encephalitis
   5. Herpes zoster

Table 6.11 : Differences between Papillitis (Optic Neuritis) and Papilledema

		Papillitis	Papilledema
1.	Pain in eyes	Marked	Absent
2.	Vision	Markedly diminished	Minimally affected
3.	Optic nerve	Edematous with exudates and hemorrhages early	Edema of disc with or without exudates and hemorrhages
4.	Pupillary reflexes	May be absent if blind	Normal
5.	Vitreous	May be cloudy due to inflammatory cells	Normal
6.	Perimetry	Central Scotomas	Enlargement of blind spot with concentric constriction of the fields
7.	Symmetry	Usually unilateral	Usually bilateral

Table 6.12 : Differences between Primary and Secondary Optic Atrophy

		Primary	Secondary
1.	Optic disc	Chalky white	Normal
2.	Disc margins	Clear cut	Hazy
3.	Veins	Normal	Dilated and tortuous
4.	Arteries	Mild attenuation	Markedly attenuated
5.	Hemorrhages	Absent	Present
6.	Exudates	Absent	Present

C. *Deficiency:* Vitamin B_1 and B_{12}

D. *Toxic:*
   1. Tobacco, alcohol
   2. Drugs: INH, chloroquine, ethambutol enteroquinol
   3. Metals: Lead, mercury, arsenic

E. *Metabolic: Diabetes*

F. *Vascular*

Optic Atrophy

Causes

A. *Familial*
   1. Cerebro-macular degeneration
   2. Hereditary ataxias
   3. Leber's hereditary optic atrophy
   4. Congenital optic atrophy
   5. Retinitis pigmentosa

B. *Secondary to papilledema*

C. *Secondary to optic neuritis*

D. *Optic conditions:*
   1. Trauma
   2. Retinitis
   3. Obstruction to central vein
   4. Glaucoma
   5. Tumour from optic nerve or its sheath
   6. Arachnoiditis affecting optic nerve

Pupils

The pupillary size is controlled by:

1. Constrictor fibers innervated by parasympathetic nervous system
2. Dilator fibers controlled by sympathetic nervous system

Since pupillary changes do not affect vision, majority of pupillary abnormalities are asymptomatic.

Parasympathetic Pathways

Light falling on the retina is conveyed via optic nerve, optic chiasma and then through both optic tracks to both lateral geniculate bodies. Fibers subserving light reflex are relayed via peri aqueduct to both Edinger-Westphal nuclei. Hence, light falling on either eye, constricts both pupils (basis of **consensual light reflex**)

When both medial rectus muscles are activated to converge the eyes, Edinger-Westphal nuclei are activated and constrict the pupils (**basis of accommodation reflex**).

The final relay of the pathway is in the ciliary ganglion in the posterior orbit from where it reaches the constrictor muscle of the pupil. This completes the light reflex pathway.

Types of Pupillary Changes

A. Pin-point pupils

Causes:

1. Poisonings
   a) Organophosphorous
   b) Morphine
   c) Barbiturates
   d) Alcoholic (Macewen's pupils)
   e) Carbolic acid
2. Iatrogenic: Overdosage of neostigmine in treating myasthenia gravis
3. Pontine hemorrhage
4. Hyperpyrexia: Sunstroke
5. Iritis
6. Miscellaneous:
   a) Syringomyelia
   b) Cavernous sinus thrombosis
   c) Transient after Gasserian ganglionectomy
   d) Apneic phase of Cheyne Stokes phenomenon

B. Dilated pupils

Causes

1. Parasympathetic paralysis
   a) Vascular accidents in mid-brain
   b) Tentorial herniation
   c) Aneurysm of carotid artery
2. Sympathetic stimulation
   a) Cervical rib
   b) Irritative lesions in neck
   c) Aneurysm of aorta
   d) Mediastinal tumor

3. Drugs
   a) Belladonna, atropine
   b) Adrenaline
   c) Cocaine
4. Miscellaneous
   a) Optic atrophy
   b) Epilepsy
   c) Anemia and neurasthenia
   d) Emotional excitement

C. ***Unequal Pupils***

Causes

1. Encephalitis
2. GPI
3. Third nerve lesion
4. Unilateral lesion of sympathetic trunk

D. ***Irregular Pupils***

Causes

1. Healthy subjects
2. Coloboma
3. Post-ophthalmic operations
4. Neurosyphilis

Clinical Lesions

1. In a ***completely blind eye*** there is no direct light reaction, but the resting pupil size is the same in both the eyes. If both eyes are blind, both pupils will be dilated and fixed to light if the cause is anterior to the lateral geniculate bodies. If bilateral blindness is due to occipital cortex lesion, the light reflex pathway will be intact and light reflex is preserved in both eyes.
2. ***Marcus Gunn Pupil***: When the normal eye is stimulated by bright light, there is no abnormality. When the affected eye is stimulated, the reaction is slower, less complete and so brief that the pupil may start to dilate again (pupillary escape phenomenon). It is best seen if the light is rapidly alternated from one eye to the other. This reaction is due to the reduction in the number of fibers subserving the light reflex on the affected side.
3. ***Parinaud Syndrome:*** Here pupils are dilated and fixed to light with loss of upward gaze. Convergence retraction nystagmus is seen. "Setting - sun" sign is seen. The lesion is either compressing or infiltrating the tectum - the area of superior collicular bodies in the periaqueductal area.
4. ***Hippus***

   Definition: Hippus is alternate rhythmic dilatation and constriction of pupils.

   Mechanism: Hippus has been said to be associated with respiratory rhythm; but is probably an evidence of imbalance of sympathetic and parasympathetic divisions of the autonomic nervous system.

   Causes:

   1. Recovery from III nerve paralysis
   2. Multiple sclerosis
   3. Syphilis
   4. Neoplasms
   5. Normal person
5. ***Argyll Robertson pupils***

   Features:

   a) Irregular
   b) Unequal
   c) Miotic
   d) No reaction to light
   e) Reaction to accommodation present
   f) Poor response to pain and mydriatics
   g) Absent ciliospinal response
   h) Atrophy of iris
   i) Normal media and optic nerve

   Causes

   a) Neurosyphilis: Tabes dorsalis, G.P.I. meningo-vascular syphilis
   b) Encephalitis
   c) Disseminated sclerosis
   d) Chronic alcoholism
   e) Diabetes
   f) Tumor in region of the third ventricle or aqueduct

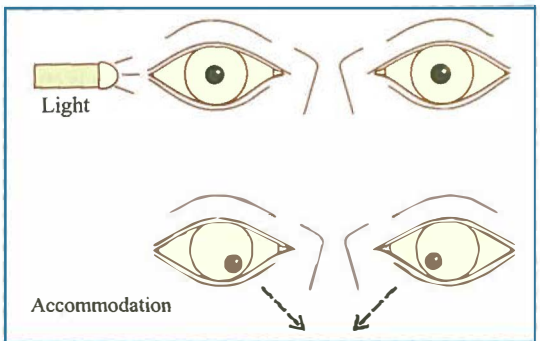


Fig. 6.71 : Argyll Robertson Pupils: (a) Miosis and no response to light; (b) Pupils constricts on accommodation.

g) Syringomyelia

h) Herpes zoster ophthalmicus

i) Chronic hypertrophic polyneuritis

j) Trauma behind the eyes

Site of lesion: This is not known.

Various theories are as follows:

a) Damage of fibers from pre-tectal region to the Edinger Westphal nucleus.

b) Damage at ciliary ganglion through which passes fibers for light reflex, whereas fibers for accommodation reflex pass below it.

c) Damage of ciliary fibers in iris.

d) Peripheral degeneration of the optic nerve and tract where pupillomotor fibers run.

6. ***Holmes-Adie Pupils***

Features

This is a widely dilated, circular pupil that reacts very slowly to bright light but reacts more definitely to accommodation because of a greater constrictive effect of accommodation. Both reactions are minimum and due to slow inhibition of the sympathetic activity and not due to any residual parasympathetic activity. It is often associated with loss of knee jerks and impairment of sweating. It is usually unilateral and more common in females.

Cause: Not known, but probably due to degeneration of the nerve cells in the ciliary ganglion.

Table 6.13 : Differences between Argyll Robertson and Holmes-Adie Pupils

		Argyll Robertson	*Holmes-Adie*
1.	Symmetry	Bilateral	Unilateral
2.	Sex	More in males	More in females
3.	Deep jerk	Knee jerk lost	Ankle jerk lost
4.	Size	Restricted	Widely dilated
5.	Sweating	Not impaired	Impaired

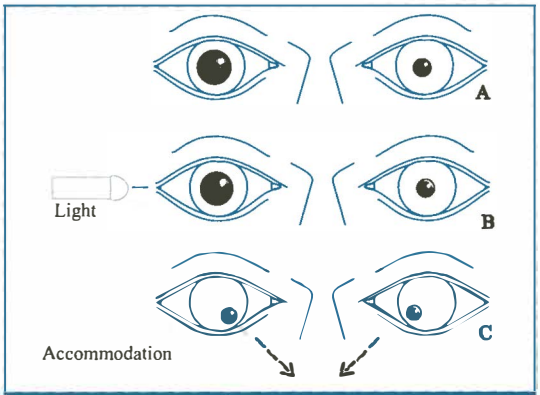


Fig. 6.72 : Holmes-Adie Pupils : (a) At rest wide dilated circular pupils; (b) Slow reaction to light not seen in this figure; (c) More definite response to accommodation.

Light Reflex

Afferent: Optic nerve

Efferent: Oculomotor nerve

Method: The patient should be asked to look at a distant object in order to eliminate contraction of the pupils on accommodation. The eye not being tested must be covered in order to eliminate *consensual reaction*. A direct source of bright light is focussed directly into



Fig. 6.73 : Consensual Light Reflex

the eye. Normally there is constriction of both pupils. The response of the pupil of the eye upon which the light falls is direct light reflex and that of the opposite pupil is the consensual light reflex, which occurs due to decussation of fibers both in the optic chiasma and Edinger-Westphal nucleus.

Significance:

In lesions of the second nerve, direct light reflex on same side and consensual light reflex on the opposite side is absent due to lesion in the afferent pathway.

In lesions of the third nerve, direct light reflex is absent on affected side but consensual light reflex is present.

Accommodation Reflex

Afferent:

1. Optic nerve
2. Proprioceptive fibers from extraocular muscles

Centre: Nucleus of Perlia

Efferent: Oculomotor nerve

Method: The patient is asked to look at a distant object and then at the examiner's finger which is gradually brought within 5 cms of the eyes. When the gaze is directed from a distant to a near object, contraction of the medial recti brings about a convergence of the ocular axes and along with this, accommodation occurs by contraction of the ciliary muscles and pupils constrict as a part of associated movement.

Significance: Accommodation reflex is lost in:

1. Diphtheria
2. Encephalitis
3. Reverse Argyll Robertson's pupils
4. Parkinsonism
5. Diabetes mellitus

Ciliospinal Reflex

Afferent: Cervical nerves

Efferent: Cervical portion of spinal cord

Method: A painful stimulus is applied on the neck and in a dim light pupils are noted. Normally there is mild dilatation of pupils.

Significance: This reflex is lost in lesions of the cervical sympathetic fibers.

Ptosis

Causes

A. Muscle diseases:
   1. Ocular myopathy
   2. Myasthenia gravis
   3. Myotonia dystrophica

B. Third nerve palsy

C. Sympathetic paralysis (Horner's syndrome)

D. Pseudoptosis due to eyelid tumors

Diagnosis

A. The patient should be asked to close the eyes (orbicularis oculi supplied by seventh nerve). If he is unable to do so, it is due to a muscle disease which would affect the muscles supplied by the third and seventh nerves.

B. If the pupils are dilated it is third nerve palsy. If they are constricted, it is Horner's syndrome.

C. In third nerve palsy, there will be ocular muscle palsies. In Horner's syndrome, there will be anhydrosis and enophthalmos.

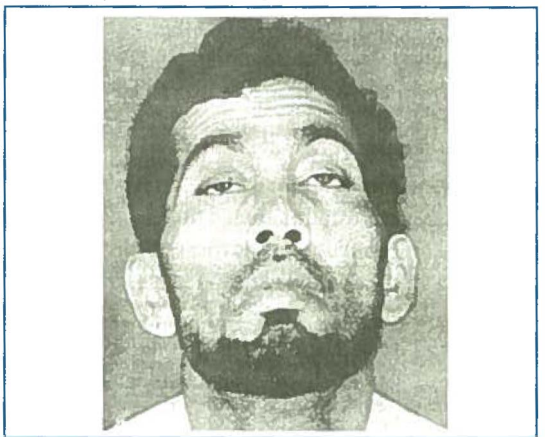


Fig. 6.74: Oculopharyngeal myopathy showing ptosis with hyperactivity of the frontal belly of occipitofrontalis muscle

Horner's Syndrome

Sympathetic Pathways

There are 3 neurons on the sympathetic pathways:

1. From hypothalamus to lateral grey mater in the thoracic spinal cord.
2. From spinal cord to the superior cervical ganglia.

3. From superior cervical ganglia to the pupils and blood vessels of the eye.
   a) Fibers carried in the third nerve innervate the levator muscle of the eyelid.
   b) Fibers in the nasociliary nerve traverse the ciliary ganglion without synapse to supply the blood vessels.
   c) Other fibers branch from the nasociliary nerve as the long ciliary nerves to innervate the pupils by passing around the eyes.

Definition: Horner's syndrome occurs due to paralysis of the sympathetic fibers which results in ptosis, miosis, anhydrosis, enophthalmos and absent ciliospinal reflexes.

Causes

I. Hemisphere lesion.

II. Brain-stem lesion: Since the sympathetic pathways in the brain stem lie adjacent to the spinothalamic tract. Horner's syndrome will be associated with loss of pain and temperature on the opposite side of the body.

Causes

A. Vasculitis
B. Encephalitis
C. Multiple sclerosis
D. Pontine glioma

III. *Cervical cord lesion:* Since the sympathetic fibers are centrally situated there will be usually bilateral Horner's syndrome with dissociate anesthesia and loss of deep reflexes in the arms.

Causes

A. Syringomyelia
B. Intramedullary gliomas or ependymomas

IV. *D1 Root lesion:*

Causes

A. Pancoast tumor
B. Cervical rib
C. Avulsion of lower brachial plexus

Features: Pain in the axilla with wasting of small muscle of the arm.

V. *Sympathetic chain:*

Causes

A. Neoplastic infiltration
B. Surgery on thyroid and larynx

Malignant disease in the jugular fossa at the skull base causes various combinations of Horner's syndrome and lesions of IX, X, XI and XII cranial nerves

VI. *Miscellaneous:*

Causes

A. Congenital
B. Migraine
C. Lesions in the orbit or cavernous sinus damage both sympathetic and parasympathetic fibers causing semi-dilated fixed pupils

Variants

1. Central lesion affects sweating over the entire head, neck, arm and upper trunk on the same side.
2. Lesions in the lower neck affect sweating over the entire face.
3. Lesions above superior cervical ganglion may not affect sweating at all as the main outflow to the facial blood vessels and sweat glands is below the superior cervical ganglion.
4. The presence of three neurons in the pathway leads to some useful pharmacological tests based on denervation hypersensitivity. Decrease in amine-oxidase due to lesion at or beyond superior cervical ganglion sensitizes the pupils to adrenaline 1:1000, which has no effect on the normal pupils. Conversely the effect of cocaine on the pupil depends on its blocking effects on the amine oxidase. Therefore cocaine has no effect on distally denervated pupil. It will only dilate the pupil in the Horner's syndrome if the lesion is below the superior cervical ganglion and there is amine oxidase at the nerve endings for it to block.

Nystagmus

Definition: Nystagmus is rhythmic oscillation of the eyes

Types

A. Vertical
B. Horizontal — jerky or pendular
C. Rotatory

Causes

A. *Retinal:*
   1. Amblyopia in childhood: Cataract, high myopia, ocular palsy or chorioretinitis
   2. Optokinetic
   3. Miner's

B. *Vestibular:*
   1. Otitis externa, otitis media, mastoiditis
   2. Blocked eustachian tubes
   3. Labyrinthitis, perilabyrinthitis, hydrops of labyrinth
   4. Tumors of internal ear

C. *Brain stem:*
   1. Encephalitis
   2. Vascular lesions
   3. Syringobulbia
   4. Brain stem tumors
   5. Multiple (Disseminated) sclerosis

D. *Cerebellar:*
   1. Encephalitis
   2. Vascular lesions
   3. Tumors
   4. Cerebellar abscess
   5. Cerebellar degeneration

E. *Ocular muscles:*
   1. Alcoholic polyneuropathy
   2. Myasthenia gravis
   3. Botulism

F. *Congenital and Familial*:
   1. Hereditary ataxia
   2. Spasm mutants

G. Hysterical

Diagnosis

When there is a lesion of the lateral and the medial vestibular nuclei there is horizontal nystagmus with a rotatory component. When there is a lesion of the superior vestibular nucleus there is vertical or oblique nystagmus.

Variants:

A. *Nystagmus retractorius*: Nystagmus with retraction of the eye or eyelids. Lesion is in the tegmentum.

B. *Ataxic nystagmus*: Defective inward movement of the adducting eye with fine nystagmus and a coarse nystagmus in the abducting eye. Lesion is in the medial longitudinal fasticulus commonly due to disseminated sclerosis.

C. *Seesaw nystagmus*: One eye moves upwards and the other moves downwards. Lesion is in suprasellar region anterior to the third ventricle.

D. *Convergence nystagmus*: Rhythmic oscillation in which slow abduction of the eye is followed by quick adduction of the eye (Parinaud's syndrome).

E. *Opsoclonus*: Sustained, irregular, dancing conjugate movements of the eye in any or all directions with cerebellar lesions.

F. *Oscillopsia*: Illusionary movements of objects in space with subjective awareness of nystagmus. Lesion is in and around foramen magnum.

Table 6.14 : Differences between Vestibular and Cerebellar Nystagmus

Vestibular Nystagmus	Cerebellar Nystagmus
1. Nystagmus is maximum when visual fixation is prevented.	Nystagmus is maximum when visual fixation is attempted.
2. Slow phase is towards the affected side	It depends upon the position of the eyes.
3. Nystagmus is more marked when the eyes are moved to opposite side	Nystagmus is more marked when the eyes are moved towards the side of lesion.
4. Usually accompanied by vertigo, vomiting tinnitus and deafness.	Accompanied by other cerebellar signs.

Third, Fourth and Sixth Nerves

The third, fourth and sixth cranial nerves are responsible for movements of the eyeball and hence if they are affected singly or together they cause defective ocular movements.

Anatomy of III, IV and VI Nerves

THIRD NERVE: The third nerve arises from the midbrain. The fibers from various nuclei course anteriorly,

traversing the red-nucleus, substantia nigra and the cerebral peduncle and exit from the anterior surface of midbrain. Various filaments of the third nerve unite to form the third nerve on each side. The third nerve emerges just above the pons and between the superior cerebellar and posterior cerebral arteries. It penetrates the dura anterior to the posterior clinoid processes and enters the cavernous sinus. It enters the orbit through the superior orbital fissure where it separates into superior and inferior divisions. The former supplies the superior rectus and levator palpebrae superioris, while the latter supplies the medial and inferior recti and the inferior oblique muscles and sends a short root to the ciliary ganglion from which postganglionic fibers go as the short ciliary nerves to supply the ciliary muscles and the sphincter pupillae.

The third nerve may also send some fibers to the orbicularis oculi and as a result some weakness of this muscle may be present in the third nerve lesions.

A third nerve paralysis need not always be complete. If the lesion is in the midbrain where the nuclear centres are still separated, or within the orbit after the nerve has redivided, only certain portions or functions may be involved. However, if the lesion is along the course of the nerve between its emergence from the midbrain and its division within the orbit, there is apt to be paralysis of all functions.

FOURTH NERVE: The nucleus of the fourth nerve lies in the midbrain just caudal to the lateral nucleus of the third nerve. The fibers curve posteriorly and caudally around the aqueduct and decussate in the anterior medullary velum. It is the only cranial nerve whose fibers emerge posteriorly. It encircles around the pons and cerebral peduncle. It penetrates the dura behind and lateral to posterior clinoid process, enters the cavernous sinus where it is lateral and inferior to the third nerve and enters the orbit through the superior orbital fissure. It terminates on the superior oblique muscle on the side opposite to the nucleus of origin.

The Sixth Nerve: It arises in the pons posterior to the nucleus of the facial nerve and crosses the internal auditory artery. It has a long intracranial course. It passes between the pons and clivus and pierces the dura at dorsum sellae where it lies close to the gasserian ganglion. It enters the cavernous sinus where it lies below and medial to the third nerve. It enters the orbit through the superior orbital fissure and supplies the lateral rectus muscle.

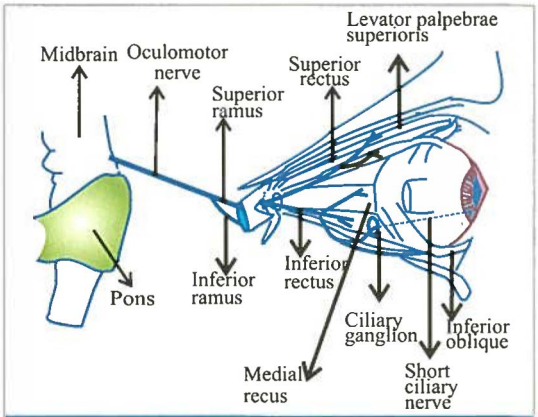


Fig.6.75 : Pathway of third Nerve

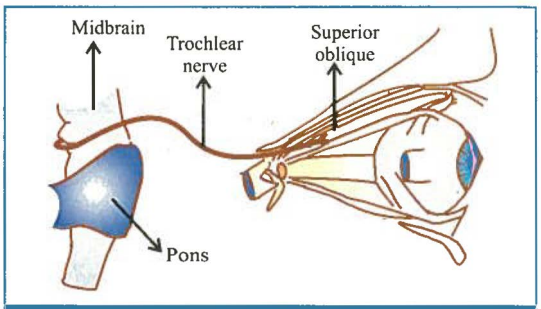


Fig.6.76 : Pathway of fourth Nerve

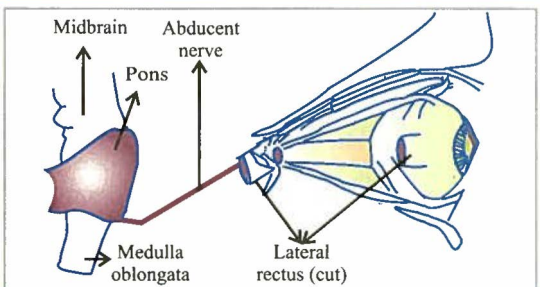


Fig.6.77 : Pathway of sixth Nerve

Cortical Control

The symmetrical and synchronous movements of the two eyes responsible for accurate binocular vision is called conjugate movement or gaze. It is controlled by centres in cerebral cortex and brainstem.

Area 8 in the frontal lobe is responsible for voluntary conjugate movements on command. These are rapid and jerky which are elicited reflexly when a sudden

Table 6.15 : Ocular Muscles

Names of the muscle	Action of the muscle	Nerve supplying the muscle
External		
1. Lateral Rectus	Abductor	Sixth
2. Medial Rectus	Adductor	Third
3. Superior Rectus	Adductor, Internal rotator, Elevator	Third
4. Inferior Rectus	Adductor, External rotator, Depressor	Third
5. Inferior Oblique	Elevator, External rotator, Abductor	Third
6. Superior Oblique	Depressor, Internal rotator. Abductor	Fourth
7. Levator palpebrae superioris	Elevator of the upper eyelid	Third
Internal		
Ciliary muscles	To constrict or dilate the pupils	Third

sound causes the eyes to move in the direction of stimulus. Parieto-occipital cortex is responsible for slower and smoother involuntary pursuit or following movements. This stabilizes the image of a moving object on the fovea. Ultimately all the pathways mediating rapid, pursuit and vestibulo-ocular movements converge via the pyramidal tract to the pontine centres for horizontal gaze. The pontine centre accomplishes conjugate lateral gaze by simultaneous innervation of the ipsilateral external rectus and contralateral internal rectus. The latter two are connected by medial longitudinal fasciculus.

Causes of Ophthalmoplegia

I. Within the brainstem

1. Encephalitis: Polio, diphtheria
2. Vascular lesions
3. Raised intracranial tension: Tumor, tuberculoma
4. Syringobulbia
5. Multiple sclerosis

II. In the Basilar area

1. Meningitis: Bacterial, tubercle, fungal, carcinomatous
2. Neoplastic infiltration from sinuses and the nasopharynx
3. Aneurysmal dilatation of the basilar and posterior communicating artery
4. Herpes zoster, syphilis

III. At the petrous tip

1. Mastoiditis
2. Lateral sinus thrombosis
3. Carcinoma of nasopharynx or the paranasal sinuses

IV. Around cavernous sinus

1. Cavernous sinus thrombosis
2. Intrasellar tumour
3. Aneurysm of intracranial portion of the carotid artery

V. At the superior orbital fissure

1. Trauma
2. Neoplasm

VI. In the orbit

1. Trauma
2. Infection
3. Neoplasm

VII. General

1. Diabetes
2. Syphilis
3. Migraine
4. Herpes zoster
5. Multiple sclerosis
6. Guillain Barre syndrome
7. Atherosclerosis

Isolated Third Nerve Lesion

1. Posterior communicating artery aneurysm. Carotid artery aneurysm.
2. Neoplasm at the base of the skull, sphenoidal wing or parasellar.
3. Upper midbrain vascular accidents.
4. Demyelinating lesions

Isolated Fourth Nerve Lesion

Cerebral peduncle lesion

Isolated Sixth Nerve Lesion

Raised intracranial tension

Clinical Features

Infranuclear and Nuclear Lesions:

III Nerve: In infranuclear paralysis, there is paralysis of the medial, superior and inferior recti, inferior oblique, levator palpebrae superioris and ciliary muscles resulting in:

1. Diplopia, squint and ptosis
2. Eyeballs deviated laterally (Lateral rectus action) and downwards (Superior oblique action). The normal downward movement of Superior oblique cannot be tested because the paralyzed Medial rectus does not allow the eye to adduct. Secondary action of the muscle is seen. The eyeball is depressed. If the patient makes a further attempt to look downwards, the eye will rotate inwards (Intorsion) because the Superior oblique pull sideways across the eye when it is in this position.
3. Inability to rotate the eye upwards or inwards
4. Dilated and fixed pupils.

In nuclear paralysis there is paralysis of individual extraocular muscles but without ptosis or internal ophthalmoplegia.

IV Nerve: In infranuclear paralysis there is paralysis of the superior oblique muscle resulting in:

1. Diplopia and squint.
2. Eyeballs deviated upwards and inwards on the same side.
3. Difficulty in reading or going downstairs due to inability to move eyes downwards and inwards.
4. As the patient tries to move the paretic eye downwards, there is absence of intorsion. The weakness of the muscle in primary position (looking straight ahead) allows the eye to rotate slightly outwards (Extortion).



Fig. 6.78: Right sided ptosis with ophthalmoplegia



Fig. 6.79: Right sided third nerve paralysis

5. A very slight slant of the image would make the patient tilt his head slightly away from the side of the affected eye to line up the image from the normal eye. Hence the head is tilted to the opposite shoulder (Bielschowsky's sign) which causes compensatory intorsion of the normal eye and ameliorates diplopia.

In nuclear paralysis, IV nerve is affected on the opposite side as the IV nerve decussates dorsally before leaving the brainstem.

VI Nerve: In infranuclear paralysis there is paralysis of the *lateral rectus* resulting in:

1. Diplopia and squint
2. Eyeballs deviated medially

In nuclear paralysis, in addition there is facial palsy and associated brainstem signs.

Supranuclear Lesion:

1. There is paresis of conjugate gaze rather than individual muscle paralysis.
2. There is no squint, diplopia or ptosis, as the visual axes remain parallel.



Fig. 6.80: Lateral rectus palsy

Conjugate Gaze Palsies

A. Lesion of the Frontal Cortex: This leads to paralysis of contralateral gaze. Hence the eyes are deviated to the side of the cerebral lesion and opposite to the side of hemiplegia.

B. Lesion of the Occipital Cortex: Voluntary movements are not affected but there is loss of follow and reflex movements.

C. Lesions of the Basal Ganglia:
   1. *Irritative*: Causes oculogyric crisis.
   2. *Destructive*: Attempted upward gaze causes jerky, vertical nystagmus, Parkinsonism and Huntington's chorea.

D. Lesions of the Collicular Area:
   1. *Superior colliculi*: Paralysis of the conjugate

upward gaze with loss of accommodation reflex.

2. *Inferior colliculi*: Paralysis of the conjugate downward gaze with loss of convergence reflex.

E. Lesions of Pons:

This leads to paralysis of ipsilateral gaze, hence the eyes are deviated to the opposite side i.e. same side as hemiplegia.

Oculogyric Crisis

Definition: Attacks of involuntary conjugate upward deviation of the eyeballs. Sometimes the eyes are deviated to one side.

Causes

1. Post-encephalitis
2. Parkinsonism
3. Petit mal epilepsy
4. Phenothiazine
5. Neurosyphilis
6. Head injury

Association

1. Weakness of upward gaze in between the attacks
2. Weakness of convergence

Impairment of Convergence

Lesion: Nucleus of Perlia

Causes

1. Disseminated sclerosis
2. Encephalitis
3. Trauma
4. Vascular

Localizing of Lesion:

I. Within the brainstem: There will be other features of brainstem lesions e.g. contralateral hemiplegia.

II. In the basilar area: There will be multiple or bilateral cranial nerve palsy:

The third nerve lesion occurs due to:

A. Compression by a posterior communicating artery aneurysm: Here the onset is acute with pain and dilated, fixed pupils.

B. Progressive damage by the prolapsing temporal lobe as in tentorial herniation. Here the patient becomes drowsy, with dilated pupils, ptosis and finally full third nerve palsy.

In third nerve lesion due to compression, pupils are dilated early because the pupilloconstrictor fibers are located peripherally.

The sixth nerve is usually involved in raised intracranial tension, which leads to tentorial herniation and pressure of sixth nerve against the petrous tip. Hence sixth nerve palsy does not have localizing value.

III. At the petrous tip:

A. *Mastoiditis*: This causes Gradenigo's syndrome – lesion of V, VI, VII and VIII nerves.

B. *Carcinoma of nasopharynx and paranasal sinuses*: It may infiltrate through the fissures of the skull and present as sudden painless sixth nerve palsy.

IV. Around the cavernous sinus:

A. Cavernous sinus thrombosis:
   1. Pain and edema over the eyelids
   2. Ophthalmoplegia with exophthalmos

B. Aneurysm of the intracranial portion of the carotid artery:
   1. Pain and edema over the eyelids
   2. Blindness
   3. Exophthalmos
   4. Third nerve palsy
   5. If at the posterior end of the cavernous sinus, there is associated VI nerve palsy and irritation of the ophthalmic division of the V nerve causes pain over the face.

V. At the superior orbital fissure:

A. Ophthalmoplegia without exophthalmos

B. Pain over the face and loss of corneal reflex (V nerve)

VI. In orbit:

A. Ophthalmoplegia with exophthalmos

B. Pain and redness of the eyes of Tolosa Hunt syndrome

VII. General:

A. *Diabetes*: Painful or painless ophthalmoplegia where pupils are always spared because diabetes causes infarction involving only the central portion of the nerve sparing the peripheral pupilloconstrictor fibers.

B. *Syphilis and Atherosclerosis* will produce painless ophthalmoplegia.

Internuclear Ophthalmoplegia (INO)

It occurs due to lesion in the Medial Longutidinal Fascicules (MLF). Normally, on voluntary conjugate gaze (looking to one side), the Ipsilateral eye abducts (ipsilateral VIth nerve) and simultaneously, the contralateral eye adducts (contralateral IIIrd nerve). This is possible because of the MLF which connects the IIIrd and VIth nerve nucleii (Fig. 6.81).

Internuclear ophthalmoplegia (INO) is characterized by (a) Failure of adduction on same side of lesion of MLF and (b) weakness of abduction with nystagmus of the other side (Figure 6.82). It is classically seen in Multiple sclerosis.

Variants of INO

1. Bilateral INO : pathognomic for Multiple Sclerosis.

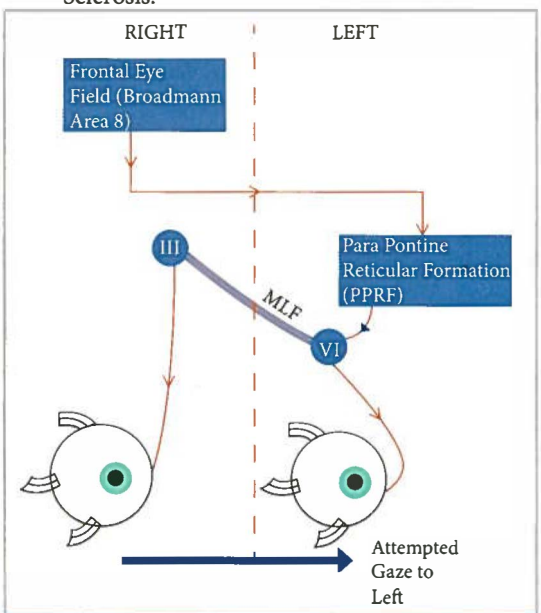


Fig. 6.81 : Pathway for conjugate eye movements

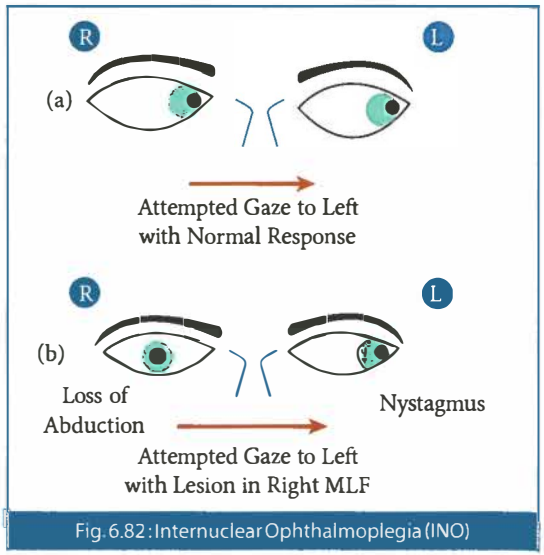


Fig. 6.82 : Internuclear Ophthalmoplegia (INO)

2. Anterior / Superior INO : features of INO + defective convergence (ipsilaterally). Lesion is near the midbrain.
3. Posterior / Inferior INO : features of INO but convergence is spared. Lesion is near the pons.
4. One and half syndrome : Lesion involves the MLF and PPRF. Total lack of horozontal eye movement ipsilaterally due to loss of function of ipsilateral III and VI nerves (PPRF). Contralateral eye cannot adduct due to lesion in MLF. The only movement possible is weak abduction of contralateral eye.
5. Eight and Half Syndrome : 1½ syndrome plus involvement of 7th nerve nucleus ipsilaterally.

Fifth Nerve

Anatomy

The motor nucleus of the trigeminal nerve is situated in the pons medial to the sensory nucleus. The motor root emerges from the anterolateral aspect of the pons and passes in the posterior fossa. It overlies the apex of the petrous bone and leaves the skull via foramen ovale to join the mandibular division (mandibular nerve). This supplies temporalis, masseter, pterygoids, tensor tympani, tensor veli palati, mylohyoid and anterior belly of the digastric muscles. The sensory root takes origin from the nerve cells in the Gasserian ganglion and enters the lateral surface of the pons. Fibers for

light touch and proprioception terminate in pons while those for pain and temperature terminate in the bulbospinal root that extends as low as the second cervical segment of the spinal cord. Distal to the Gasserian ganglion the nerve divides into 3 divisions.

The Ophthalmic (first) division supplies the conjunctiva (except that of lower lid), lacrimal glands, medial part of the skin of the nose, upper eyelids, forehead and scalp as far as the vertex. The maxillary (second) division supplies the cheek, front of temple, lower eyelid and its conjunctiva, side of the nose, upper lip, upper teeth, mucous membrane of the nose, upper pharynx, roof of the mouth, soft palate and tonsils. The mandibular (third) division supplies sensations to the lower part of the face, the lower lip, ear, tongue and lower teeth.

Testing:

1. The motor function can be tested by asking the patient to clench the teeth. Normally the *masseters* and temporalis on both sides stand out with equal prominence. If there is paralysis on one side, the muscles on that side do not become prominent (This can be better tested by palpating the muscles than on inspection).

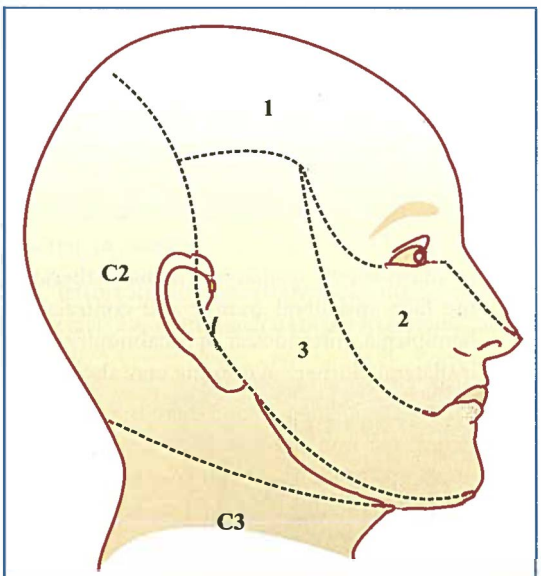


Fig. 6.83: Cutaneous distribution of the trigeminal nerve: (1) Ophthalmic division, (2) Maxillary division, (3) Mandibular division. C2 and C3 is second and third cervical root

The patient is asked to open the mouth. Normally the jaw is central. If there is paralysis on one side, the jaw will deviate to that side being pushed by the healthy lateral pterygoid muscle.



Fig. 6.84: Masseters

2. The sensory function is tested in all the three divisions separately, comparing both sides. Pain, temperature and light touch are tested.

   Lesions of individual divisions distal to the gasserian ganglion result in sensory loss confined to the cutaneous supply of the division. Lesions at or proximal to the Gasserian ganglion results in ipsilateral sensory loss of the whole face.

   Lesions within the brain stem and upper cervical cord results in an onionskin distribution of sensory loss (the lateral forehead, cheek and jaw are affected). Dissociation of anesthesia over the face (i.e. pain and temperature are affected and touch is spared) occurs with lesions affecting the spinal tract and nucleus of the trigeminal nerve.

   The cutaneous area over the angle of the mandible is supplied by the second and third cervical roots (greater auricular nerve) and not the trigeminal nerve. Hence, a hemifacial sensory loss that spares the angle of the jaw is organic, whereas one that includes this area may be hysterical.

3. The important reflexes conveyed by the trigeminal nerve are the corneal, conjunctival and the jaw jerk.

Conjunctival and Corneal Reflexes

Afferent: Ophthalmic division of Trigeminal nerve.

Reflex centre: Pons

Efferent: Facial nerve

Method

The patient should turn his eyes to opposite direction. The examiner should touch the cornea or conjunctiva from the side with a wisp of cotton. In response to this stimulus, normally there is blinking or closing of the same eye (direct response) and the opposite eye (consensual response).

Significance:

1. In unilateral trigeminal nerve lesion resulting in corneal or conjunctival anesthesia, stimulation of these structures fails to produce either the direct or consensual response, but stimulation of the opposite side elicits both responses.

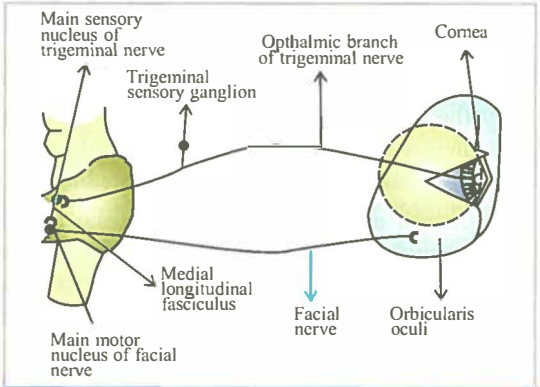


Fig. 6.85 : Corneal Reflex Arc

2. In unilateral facial palsy with weakness of orbicularis oculi, when either cornea is stimulated, response occurs only on the normal side but does not occur on the affected side. Hence, on stimulating the cornea on the affected side, direct response is absent but consensual response is present, whilst on stimulating the cornea on the unaffected side direct response is present but consensual response is absent.

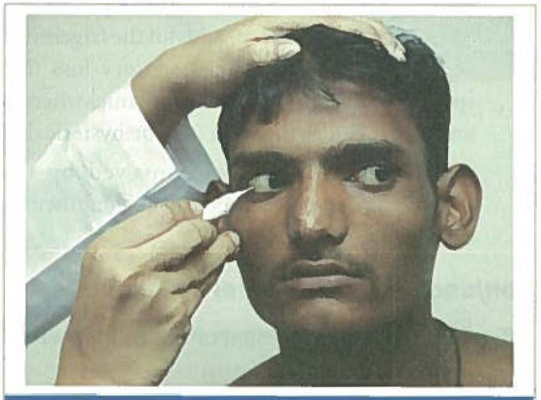


Fig. 6.86 : Conjunctival Reflex

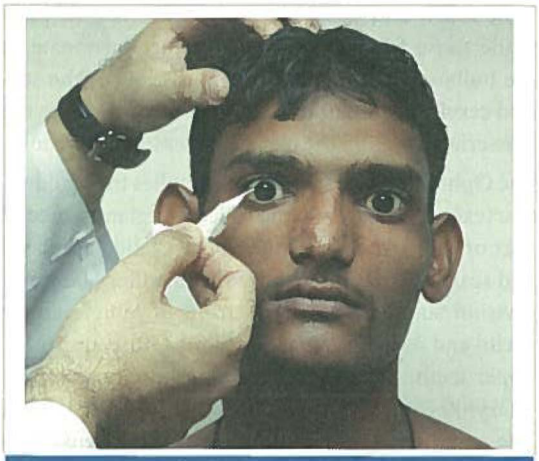


Fig. 6.87 : Corneal Reflex

3. The conjunctival response is less important clinically than corneal response as it may be absent in a few normal individuals and also in hysteria.

Lesions

1. *Supranuclear lesion*: Lesions interrupting the corticobulbar pathway on one side may cause contralateral trigeminal paresis. Bilateral lesion (pseudobulbar palsy) causes profound weakness of muscles of mastication and exaggerated jaw jerk. Thalamic lesion may cause contralateral anesthesia of the face.
2. *Nuclear lesion*: This is characterized by ipsilateral atrophy, paresis and fasciculation of muscles of mastication, ipsilateral hemianesthesia of the face, ipsilateral tremor and contralateral hemiplegia. Internuclear ophthalmoplegia and ipsilateral Horner's syndrome may also occur.
3. *Gasserian ganglion lesion:* There is severe pain, paresthesia and numbness on the face from the upper lip and chin to the anterior part of the ear with hemianesthesia of the face and weakness of muscles of mastication.
4. *Cerebello-pontine lesion*: Usually the ophthalmic division is commonly affected resulting in early loss of corneal reflex. There would be, in addition, lesion of the seventh, eighth and sixth cranial nerves.

5. *Gradenigo's syndrome*: The lesion is at the apex of the temporal bone. The osteitis or leptomeningitis may cause damage to the ophthalmic division of the fifth nerve and the sixth nerve causing pain and sensory disturbances in the ophthalmic distribution with ipsilateral lateral rectus palsy. There may be partial Horner's syndrome (ptosis and miosis) sometimes.
6. *Cavernous sinus syndrome*: Lesions within the cavernous sinus may damage the ophthalmic and maxillary division of the fifth nerve, the sixth, fourth and third nerves. Usually the mandibular nerve is spared.
7. *Superior orbital fissure syndrome:* There is affection of the sixth, fourth, third and ophthalmic branch of the fifth nerve with exophthalmos due to blockade of ophthalmic veins. Sometimes partial Horner's syndrome and blindness may also occur.

Jaw Jerk

Afferent: Sensory portion of Trigeminal nerve

Reflex centre: Pons

Method: The examiner places his index finger over the middle of the patient's chin, holding the mouth slightly open. He then taps his finger with the hammer. The normal response is slight and consists of closure of the mouth.

Significance

1. Since the normal response is slight, an absent jaw jerk is not always pathological.
2. Jaw jerk is absent in peripheral lesions of the trigeminal nerve.
3. It is brisk in supranuclear lesions of the pyramidal tracts above the nucleus of the trigeminal nerve.

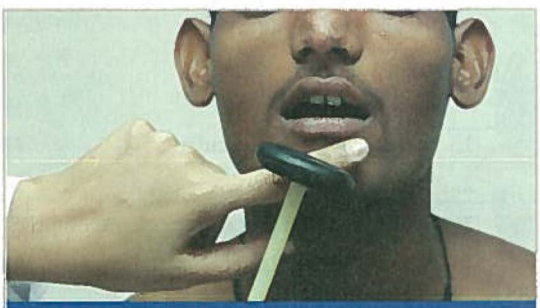


Fig. 6.88: Jaw Jerk

Seventh Nerve

Anatomy: The corticobulbar fibers controlling the facial movements arise in the lower third of the precentral gyrus and pass down through the corona radiata, the genu of the internal capsule and the medial cerebral peduncle to reach pons. In the pons, majority of the fibers decussate, ending in the facial motor nucleus on the opposite side. The ventral part of the facial nucleus, which innervates the lower two-thirds of the face, has a predominantly crossed supranuclear control. The dorsal portion, which supplies the upper third of the face, has bilateral supranuclear control. A separate supranuclear pathway for the control of involuntary movements originates in the globus pallidus, hypothalamus and thalamus and then descends through the internal capsule in their course to the facial motor nuclei.

The facial nerve nucleus is situated in the pons lateral to that of the sixth nerve. The facial nerve fibers wind around the sixth nerve nucleus and emerges out medial to the eighth nerve. It then enters the internal auditory meatus to the geniculate ganglion. Here it gives a branch, the greater superficial petrosal nerve which innervates the lacrimal glands. At the posterior aspect of the middle ear it gives a branch, the nerve to stapedius which supplies stapedius muscle, and another branch the chorda tympani which joins the lingual nerve and supplies taste fibers to the anterior two-thirds of the tongue. The facial nerve then exits through the stylomastoid foramen giving the posterior auricular nerve, digastric branch and the stylohyoid branch. It then pierces the parotid gland and divides into temporo-facial (temporal, zygomatic and upper buccal) and cervicofacial (lower buccal, mandibular and cervical) branches.

Test: The motor function can be tested by inspection of facial expression and tests of facial mobility. The patient is asked to raise the eyebrows (frontal head of occipitofrontalis), wrinkle the brow (nasociliary), close the eyes (orbicularis oculi), show the teeth and repeating a sentence with several labial consonants (orbicularis oris) blow out the cheek (buccinator) and retract the chin (platysma). Any asymmetry is noted. The stylohyoid, posterior belly of digastric, occipitalis and auricular muscles cannot be tested adequately. Weakness of stapedius may cause hyperacusis for

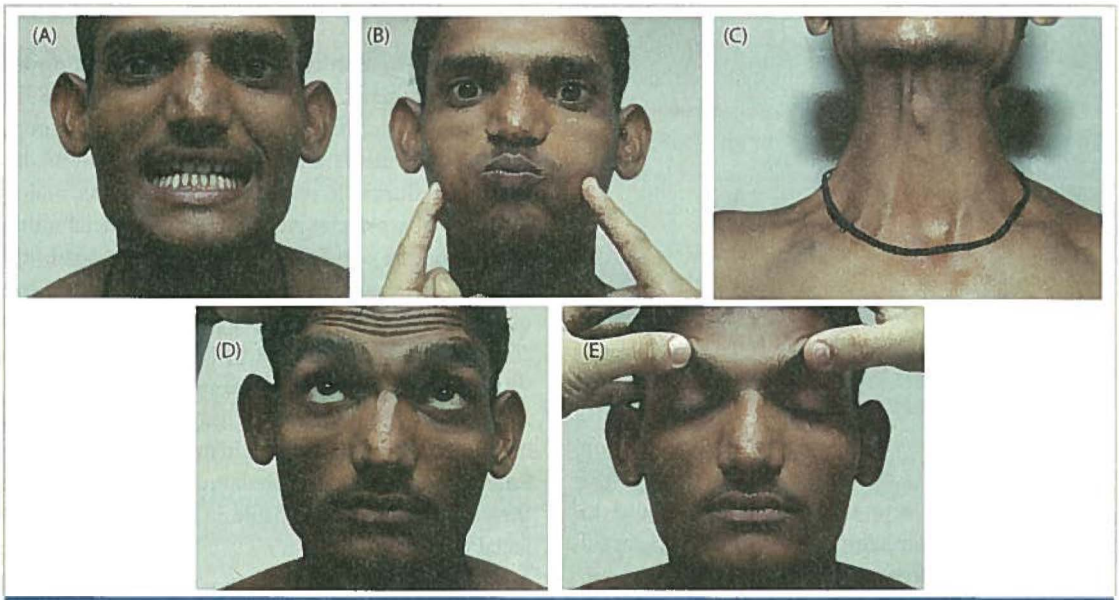


Fig. 6.89 : 7th Nerve (A) Showing Teeth; (B) Blowing Cheeks; (C) Platysma; (D) Frontalis; (E) Obicularis Oculi

low tones (because it no longer adequately tightens the ossicular chain that protects the inner ear from loud noise).

The sensory function to be tested is the taste sensation on the anterior two-thirds of the tongue. Each half of the tongue should be tested with the four fundamental tastes (sweet, sour, bitter and salty) and any asymmetry should be noted.

The reflexes to be tested are corneal, conjunctival and jaw jerk (Refer fifth nerve).

Diagnosis of Facial Palsy

A. Asymmetry of the face
B. Stasis of food in the mouth
C. Dribbling of saliva through the angle of the mouth
D. Inability to close the eyes

Signs: Due to paralysis of the following muscles:

A. *Orbicularis oculi:*
   1. Difficulty in closure of the eyes. On attempting eye closure eyeballs turn upwards and outwards (Bell's phenomenon).
   2. Involuntary blinking is abolished
B. *Nasociliary:* Frowning of the forehead is lost
C. *Frontal head of occipitofrontalis:* Wrinkling of the forehead is lost
D. *Orbicularis oris:* Whistling is not possible
E. *Buccinator:* Cheek puffs out with expiration
F. Muscles of facial expression:
   1. Flattening of nasolabial fold
   2. Drooping of the angle of the mouth on the affected side
   3. Crooked smile and laugh

Supranuclear Lesions of the Facial Nerve

A. Corticospinal lesion above pons

Features:

1. Upper motor neurone type of facial palsy
2. Ipsilateral hemiplegia

Causes:

A. Unilateral:

1. Cerebrovascular accidents
2. Cerebral tumors
3. Infections: Cerebral abscess, meningitis
4. Trauma affecting the facial area in the cerebral cortex

B. Bilateral:

1. Cerebrovascular accidents
2. Motor neurone disease

B. Mimic paralysis

Features: Weakness or abolition of emotional movements of the face selectively with normal voluntary movement of the face due to lesion in the anterior part of the frontal lobe.

Causes: Same as for corticospinal lesion, but affecting the anterior part of the frontal lobe.

In bilateral supranuclear capsular lesions producing double hemiplegia, only the corticobulbar fibers to the ventral nucleus are involved with affection only of the lower face on both sides.

Nuclear Lesions of Facial Nerve at the Pons

Features:

1. Lower motor neurone facial palsy.
2. Fifth nerve lesion giving ipsilateral loss of sensations over the face and paralysis of the masseter, temporalis and pterygoids. Loss of corneal reflex may often be the earliest sign.
3. Sixth nerve lesion giving rise to medial squint and difficulty in moving the eyeballs laterally.
4. Long tract sign — hemiplegia and hemianesthesia on the opposite side.

Causes:

1. Vascular lesions of the brainstem
2. Brainstem tumors
3. Polioencephalitis
4. Disseminated sclerosis

Infra-nuclear Lesions of the Facial Nerve

A. Cerebellopontine angle

Features:

1. Lower motor neurone type of facial palsy
2. Fifth nerve lesion
3. Eighth nerve lesion, giving rise to deafness, tinnitus, vertigo
4. Cerebellar signs
5. Pyramidal tract lesion — ipsilateral or contralateral hemiplegia

Causes: Cerebellopontine angle tumors e.g meningioma, acoustic neuroma, etc.

B. Near geniculate ganglia

Features:

1. Lower motor neurone type of facial palsy
2. Defective lacrimal secretion
3. Hyperacusis

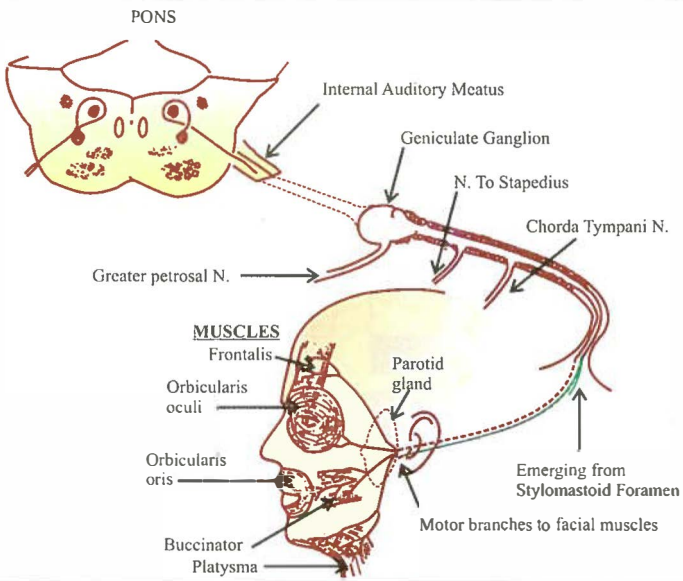


Fig. 6.90: Facial nerve pathway

4. Impaired salivary secretions and loss of taste over the anterior two thirds of the tongue.
5. Eighth nerve lesion — deafness, vertigo.

Causes:

1. Herpes zoster of the geniculate ganglia (Ramsay Hunt syndrome). In addition to the above features, vesicles may be present in the external ear and over the palate.
2. Spread of the infection from the middle ear.
3. Trauma



Fig. 6.91 : Right sided LMN fascial palsy



Fig. 6.92 : Loss of wrinkling of right forehead in LMN palsy



Fig. 6.93 : Bell's phenomenon in facial palsy

C. Between geniculate ganglion and nerve to stapedius

Features:

1. Lower motor neurone type of facial palsy
2. Hyperacusis
3. Impaired salivary secretions and loss of taste over the anterior two thirds of the tongue

Causes:

1. Spread of infection from the middle ear
2. Trauma

D. Between nerve to stapedius and chorda tympani

Features:

1. Lower motor neurone type of facial palsy
2. Impaired salivary secretions and loss of taste over the anterior two thirds of the tongue

Causes:

1. Spread of infection from the middle ear
2. Trauma

E. Between chorda tympani and stylomastoid foramen

Features: Lower motor neurone facial palsy.

Causes:

1. Bell's palsy
2. Tetanus
3. Infective polyneuritis
4. Otitis media
5. Following mastoidectomy

F. Extracranial (e.g. in parotid gland)

Features: Partial lower motor neurone facial palsy i.e. only a few muscles affected.

Causes: Trauma, inflammation or tumor of parotid gland

Bilateral Infranuclear Facial Palsy

Features:

1. Flattening of all the normal folds giving a fixed expressionless mask-like face
2. Paucity of movements of the facial muscles
3. Sagging of the angle of the mouth
4. Dysarthria
5. Bilateral Bell's phenomenon on attempted closure of the eyelids

Causes:

1. Acute infective polyneuritis
2. Leprosy
3. Sarcoidosis
4. Myasthenia gravis
5. Myotonia dystrophica

Ramsay Hunt Syndrome

Due to Herpes zoster infection of geniculate ganglion. Patient presents with vesicular lesion over external auditory meatus and pharynx. LMN VII nerve palsy, loss of taste, salivation, lacrimation and hyperacusis are present. VIII nerve may also be involved.

Mobius Syndrome

Congenital absence of VII nerve. Nucleus presents with LMN Facial Palsy.

Melkersson Rosenthal Syndrome

Recurrence unilateral LMN VII Nerve Palsy with facial edema and fissured tongue.

Eighth Nerve

Anatomy: The eighth nerve consists of two parts — the cochlear (hearing) and the vestibular (equilibrium). The auditory fibers from the cochlear ganglion are distributed to the dorsal and ventral cochlear nuclei in the pons. The vestibular fibers from vestibular ganglion terminate in a group of nuclei in the pons and medulla. The secondary auditory tract after partial decussation terminates in the inferior colliculi and medial geniculate bodies and then proceeds to the internal capsule and cortical centre for hearing. The vestibular nerve is connected with the cerebellum and then cerebrum.

Tests: The eighth nerve should be tested for both the auditory as well as the vestibular functions.

1. Auditory Function: Before testing the auditory function, wax, if present, must be removed from the ears. Hearing of slight sound in each ear must be tested either with the watch (tick of the watch) or rubbing fingers. If there is impairment of hearing the following tests are done to determine whether the disease is of the cochleovestibular system or of the middle ear.

A) *Rinne's test:* A vibrating tuning fork is placed in front of the ear (air conduction) and then on the mastoid bone (bone conduction). Normally air conduction is better than the bone conduction. In middle ear disease, bone conduction is better than air conduction. In nerve deafness air conduction is better than bone conduction but both are depressed.



Fig. 6.94 : Rinnes Test - Air Conduction

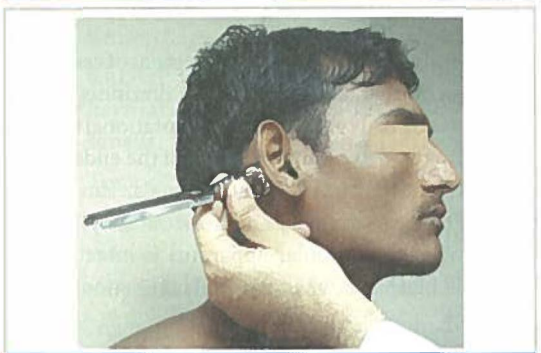


Fig. 6.95 : Rinnes Test - Bone Conduction

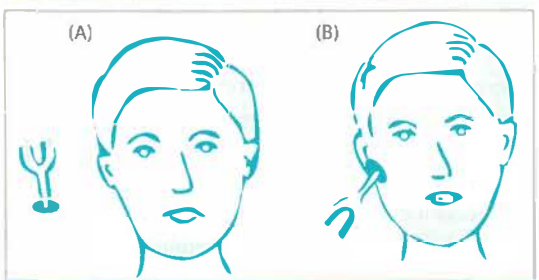


Fig. 6.96 : Rinne's test (A) Air conduction (B) Bone conduction

B) *Weber's test:* A vibrating tuning fork is placed over the forehead in the centre. Normally,

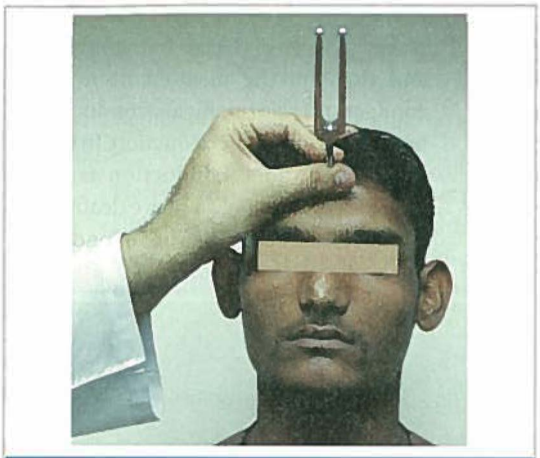


Fig. 6.97: Webers Test

vibrations are heard equally on both the sides. In middle ear disease, it is better heard on the affected side because external sound interfering with the vibration is less on the affected side. In nerve deafness, the vibrations are heard better on the healthy side.

2. Vestibular Function: Derangement of vestibular function usually causes vertigo, dizziness, nausea and unsteady gait. Calorie and rotational tests are employed to produce change in the endolymph current in the semicircular canals. This results in nausea, dizziness and horizontal nystagmus when the vestibular apparatus is intact. These will be absent when vestibular function is lost.

Ninth, Tenth and Eleventh Nerves

Anatomy: The ninth, tenth and eleventh nerves arise in that order from above downwards, in an elongated nucleus in the floor of the fourth ventricle. They emerge along the lateral aspect of the medulla. The spinal part of the eleventh nerve (accessory) from the lateral columns of the spinal cord passes up through the foramen magnum and joins the cranial part of the accessory nerve and emerges with it through the jugular foramen.

The ninth (glossopharyngeal) nerve supplies the sensations including the taste sensation to the posterior one-third of the pharynx. It also supplies the middle constrictor of the pharynx and stylopharyngeus muscle.

The tenth (vagus) nerve is motor for soft palate (except tensor palati), pharynx and larynx. It is sensory and motor for the respiratory passages, the heart and the abdominal viscera.

The eleventh (accessory) nerve is a pure motor nerve for innervation of the larynx, pharynx, sternomastoid and trapezius muscles.

Tests:

1. The **sensory** part can be tested by testing the superficial as well as the taste sensations over the posterior one third of the tongue.
2. The **motor** function is tested as follows:
   a) The patient is asked to open the mouth and say "ah" and palatal movements on both the sides are noted. Normally they are equal and uvula is in the centre. In unilateral palatal palsy, the median raphe is pulled to the normal side, as palatal movements on the affected side are absent. In bilateral paralysis, the whole palate remains motionless.
   b) The trapezius muscle is tested by asking the patient to shrug his shoulders against downward resistance. Normally both the sides are equal. In unilateral paralysis, there will be weakness on the affected side.
   c) The sternomastoid muscle is tested by asking the patient to rotate his chin to the opposite side. In unilateral paralysis, the chin is deviated to the affected side and there is impairment of rotation of the chin to the opposite side.
3. The **reflex** function is tested by examining the gag reflex.



Fig. 6.98: 11th Nerve - Testing for Trapezius



Fig. 6.99: 11th Nerve - Testing for Sternocleidomastoid

Gag Reflex

Reflex centre: Medulla

Efferent: Vagus

Method:

Stimulation of the posterior pharyngeal wall by a tongue blade or a cotton applicator results in elevation and constriction of the pharyngeal musculature accompanied by retraction of the tongue

Significance

1. The reflex may be absent or brisk in hysteria
2. The reflex is lost in lesions of the IX and X nerves.

Twelfth Nerve

Anatomy: The twelfth (hypoglossal) nerve arises from the hypoglossal nucleus in the floor of the fourth ventricle in medulla oblongata. The fibers of hypoglossal nerve emerge medial to the fibers of glossopharyngeal nerve and unite into two bundles that pass separately through the dura mater and the hypoglossal canal of the skull. After leaving the skull the two bundles unite and pass in the neck and then to the tongue to which it supplies the motor branches. The supranuclear control is through the corticobulbar fibers. The genioglossus is controlled by contralateral corticobulbar tracts whereas the other muscles have a bilateral supranuclear control.

Tests: The tongue should be observed at rest and on protrusion and various movements are noted. Unilateral lesion may cause paresis, atrophy, furrowing, fibrillations and fasciculations on the affected half of the tongue. On protrusion, the tongue deviates to the paralyzed side due to unopposed action of the contralateral genioglossus. Bilateral weakness in addition, causes dysphagia and dyspnea when the flaccid tongue falls back and obstructs the pharynx. Dysarthria especially for d and t phonemes occur.

4 Bulbar Palsy

Definition: Bulbar palsy refers to weakness of the lower cranial nerves with or without the affection of pyramidal, spinothalamic, proprioceptive and sympathetic fibers due to lesion in the medulla oblongata.

When the supranuclear fibers of these lower cranial nerves are affected due to a lesion in the pons, midbrain, internal capsule, corona radiata, basal ganglia or cerebral peduncles, the resultant weakness is referred to as pseudobulbar palsy.

Causes

I. **Trauma:** Basal skull fractures

II. **Infections:** Meningitis, encephalitis, bulbar, polio, diphtheria, syphilis, tuberculosis

III. **Vascular:** Thrombosis, embolism, aneurysm and hemorrhage

IV. **Raised intracranial tension leading to herniation of the medulla and cerebellar tonsils:**

Tumors, gumma, tuberculoma

V. **Degenerative:** Syringobulbia, Motor neurone disease

VI. **Demyelinating:** Multiple sclerosis

VII. **Congenital:** Craniovertebral anomaly

VIII. **Conditions mimicking bulbar palsy:**

1. Myasthenia gravis
2. Tetanus
3. Rabies

Clinical Features

I. **Due to lesions of cranial nerve nuclei:**

A. *IX, X cranial nerves:* Nasal twang, nasal regurgitation, hoarse voice, dysphagia, loss of sensations over the posterior one-third of the tongue, weak cough and absent gag reflex, weak cough reflex. In unilateral lesion, there is never a complete paralysis of deglutition or of articulation, but in

extensive or bilateral lesions there may be profound impairment of these functions.

B. *XI cranial nerve:* Weakness of trapezius and sternomastoid muscles.

C. *XII cranial nerve:* Dysarthria, wasting and weakness of tongue muscles and sometimes fibrillations over the tongue.

II. **Due to damage to fiber tracts:**

A. *Pyramidal tracts:* Since pyramidal tracts cross at the lower level of medulla, unilateral lesion causes crossed hemiplegia. Due to proximity of the two pyramidal tracts there may be paraplegia or decerebrate type of rigidity.

B. *Spinothalamic tracts:* Since the spinothalamic tracts are crossed tracts, unilateral lesion of these tracts lead to loss of touch, temperature

C. *Descending tract and nucleus of the trigeminal nerve:* This causes loss of touch, temperature and pain on the same side of the face.

D. *Spinovestibular and vestibulospinal tracts:* Ipsilateral nystagmus and other cerebellar signs.

E. *Spinovestibular and vestibulospinal tracts:* Vertigo.

F. *Sympathetic tract:* Ipsilateral Horner's syndrome.

G. *Medial lemniscus:* Ipsilateral loss of proprioceptive sensations.

H. *Medial longitudinal fasciculus:* Ipsilateral abducting nystagmus with weakness of adduction in the opposite eye.

III. **Vital functions:**

Involvement of the dorsal efferent nuclei of both vagus nerves or pressure on the medullary centres may lead to:

1. Bradycardia and hypotension.
2. Respiratory failure.
3. Disturbance in gastrointestinal function.
4. Hyperglycemia

Differential Diagnosis

1. **Supranuclear lesions:** Unilateral supranuclear lesions usually do not cause any neurological deficit because of bilateral corticobulbar input. However, bilateral lesions (pseudobulbar palsy) may cause severe dysphagia, explosive dysarthria, pathological laughter and crying, spastic tongue, severe retching and vomiting and exaggerated jaw jerk. The cough reflex is intact.

2. **Nuclear or Intramedullary lesions:** This may lead to involvement of ninth, tenth, eleventh and sometimes twelfth nerve damage with pyramidal signs and other brain-stem signs as mentioned above. The common causes are syringobulbia, motor neurone disease, demyelinating disease, vascular lesion, malignancy and bulbar polio. In bulbar polio, often the long tract signs are absent.

3. **Jugular foramen syndrome:** This consists of affection of the ninth, tenth and eleventh nerves. The common causes are glomus tumors and basal skull fracture.

4. **Retropharyngeal and retroparotid space lesions:** The lesions in this area may affect the ninth, tenth, eleventh and twelfth nerves with or without affection of the sympathetic chain and seventh nerve. The common causes are retropharyngeal carcinoma, abscess, lymphadenopathy, aneurysm, trauma or surgical procedures.

5 › Hemiplegia

Definition: Hemiplegia is paralysis of one half of the body i.e. upper and lower limbs of the same side. It may be associated with weakness of facial muscles on the same side (ipsilateral hemiplegia) or opposite side (contralateral hemiplegia). Hemiparesis signifies weakness.

Causes

Sudden Onset Hemiplegia

I. *VASCULAR:*

A. *Thrombosis:*

1. *Arterial*: Atherosclerosis, arteritis, syphilis, collagen diseases

2. *Venous*: Cortical thrombophlebitis, post partum or postoperatively

B. *Embolism usually from:*

1. *Heart*: Auricular fibrillation, myocardial infarction, infective endocarditis
2. *Arteries*: Detachment of an atheromatous plaque usually from the aorta or the carotid artery
3. *Veins*: Thrombophlebitis especially from the veins of the lower limbs and pelvis
4. *Miscellaneous*: Post cardiac surgery, Caisson's disease

C. *Hemorrhage: Rupture of —*

1. Berry's aneurysm
2. Atherosclerotic vessel
3. Angiomatous malformation

D. *Hypertensive encephalopathy*

E. *Arteritis/ Vasculitis*

II. *Intracranial Infections:*

A. Encephalitis

B. Meningitis

C. Congestive attacks of GPI

III. *Trauma - Depressed Fracture of Skull*

IV. *Todd's Paralysis (Post ictal)*

V. *Hysteria*

VI. *Metabolic : hypoglycemia, hypokalemia.*

Gradual Onset Hemiplegia

I. Cerebral tumor

II. Chronic subdural hematoma

III. Infections: Cerebral abscess, meningitis and encephalitis

IV. General paralysis of insane

V. Congenital defects e.g. cerebral agenesis

Transient or Recurrent Hemiplegia

I. Transient ischemic attacks

II. Hypertensive encephalopathy

III. Post epileptic

IV. Congestive attacks of GPI

V. Hysterical

VI. Multiple sclerosis

VII. Hemiplegic migraine

Hypertensive Encephalopathy

A. *Due to cerebral disturbances:*

1. Sudden onset of headache, vomiting, unconsciousness and convulsions

Differential Diagnosis

Table 6.16 : Differences between Thrombosis, Embolism and Hemorrhage

		Thrombosis	*Embolism*	*Hemorrhage*
1.	Age	Middle or old	Young or old	Middle or old
2.	Onset	Sudden or progressive (stuttering)	Instantaneous	Catastrophic and progresses rapidly
3.	Time	Early morning	After exertion	Post stress / anxiety
4.	Premonitory symptoms	May be present	Absent	Absent
5.	Signs of increased intracranial tension.	Absent	Absent	Usually present - headache, vomiting, unconsciousness
6.	Convulsions	Rare	Common	Usually absent
7.	Neck stiffness	Absent	Absent	Frequent
8.	Conjugate deviation of the eyes	Absent	Absent	Present
9.	B.P.	High	Normal	Usually high
10.	Leucocytosis	Absent	Absent	Common
11.	CSF	Usually Normal	Normal	Blood stained Increased pressure
12.	Recovery	Usual	Usual	Not so

2. Focal neurological signs e.g. cortical blindness, hemiplegia, speech disturbances, etc.
3. Meningeal signs like neck stiffness

B. *Evidence of severe hypertension:*
1. Diastolic pressure more than 130 mm Hg
2. Papilledema with retinal hemorrhages and exudates

Cortical Venous Thrombosis

1. Usually there is a history of recent delivery, abortion, operation (fracture etc.) or ingestion of oral contraceptives, dehydration, malignancy and coagulation abnormalities.
2. Sudden onset of headache, vomiting, convulsions and focal neurological deficits.

Encephalitis

1. *Mental change:* They are always present and may be the only manifestation
2. *Disturbances of sleep:* Insomnia, hypersomnia or reversal of sleep rhythm
3. *Parkinsonism:* Tremors and akinesia. Rigidity is usually absent and if present, is of catatonic type.
4. *Convulsions*
5. *Involuntary movements:* Tremors, chorea, athetosis, myoclonus, hiccoughs
6. *Ocular disturbances:* Conjugate ocular palsies, external ophthalmoplegia — Nuclear or supranuclear
7. *Pupillary changes:* Unequal or irregular pupils. Argyll Robertson pupils or reverse Argyll Robertson pupils
8. *Headache* with or without vomiting and pain in the back or limbs
9. Hypothalamic damage leading to obesity, diabetes insipidus and genital atrophy

Meningitis

1. Signs of meningeal irritation
2. Symptoms and signs of increased intracranial tension
3. Signs of septicemia
4. Signs of complications: Hemiplegia, blindness, deafness etc.

Hysterical Hemiplegia

1. Hemiplegia is often associated with blindness and deafness on that side and also with hemianesthesia but with sensory loss exactly up to the midline.
2. Wasting absent
3. *Deep reflexes* are never lost and plantars are never extensor.
4. *Hysterical gait*: The patient usually drags the leg and the characteristic circumduction of hemiplegia is absent.
5. *Hoover's sign*: The patient whilst lying on his back is asked to raise his leg against resistance. In a normal individual and in organic hemiplegia the back of the heel of the contralateral leg is pressed firmly down. This is absent in hysteria.
6. *Babinski's combined leg flexion test*: The patient with organic hemiplegia when asked to sit up without using his arms, involuntarily flexes the weak leg at the hip so that the heel of the affected leg is lifted from the bed, whilst the heel of the sound leg is pressed into the bed. This is absent in functional cases.
7. *Associated movements* are absent.
   a) Flexion of the arm results in an involuntary pronation of the same arm
   b) Flexion of one leg causes dorsiflexion and eversion of the same leg (*Strumpell tibialis sign*) and involuntary extension of the other leg
   c) Mirror movements.

Disseminated Multiple Sclerosis

1. More common in females between 20-40 years.
2. Relapses and remissions occur.
3. There is optic atrophy or temporal pallor of the disc.
4. Transient and recurrent paraplegia or hemiplegia
5. Charcot's triad — staccato speech, intention tremors and nystagmus
6. Colloidal gold curve is paretic but VDRL is negative

Cerebral Tumor

1. Symptoms and signs of raised intracranial tension
2. Focal symptoms e.g. hemiplegia, convulsions
3. Signs and symptoms of compression and infiltration to the surrounding tissues e.g. pituitary tumor pressing on the optic chiasma causing blindness

Cerebral Abscess

1. Symptoms and signs of septicemia
2. Symptoms and signs of raised intracranial tension
3. Symptoms and signs of compression

Subdural Hematoma

1. It follows an injury either immediately or following a latent interval of weeks, months or years. It is more common in alcoholics.
2. There is a gradual onset of signs of raised intracranial tension.
3. Convulsions are rare.
4. Focal symptoms are usually slight compared to the size of the hematoma.
5. Ocular symptoms: Transient ocular palsy, unequal pupils (large pupil with slight ptosis on the side of hematoma).

Todd's Post-epileptic Hemiplegia:

Transient paralysis following convulsions. Recovery occurs within 24-48 hours.

Determination of the Site of Lesion in Hemiplegia

If the hemiplegia is associated with cranial nerve affection on the same side (ipsilateral) then the lesion is above the brain stem.

If the hemiplegia is associated with cranial nerve involvement but associated with loss of vibration and joint sense on the same side and pain, temperature and touch on the opposite side (Brown-Sequard syndrome), then the lesion is in the spinal cord between C1 and C4 segments.

Ipsilateral Hemiplegia

A. *Cortical lesion.* If the patient has any one of the following features, cortical lesion is suspected:
   1. Mild hemiparesis or monoplegia
   2. Convulsions
   3. Cortical sensory loss — loss of tactile localization tactile discrimination and tactile extinction
   4. Astereognosis
   5. Aphasia (if dominant cortex is involved)

B. *Internal capsule:* This is the commonest cause of ipsilateral hemiplegia and in the absence of features suggesting cortical lesion, the lesion is localized at the internal capsule. *Hemiplegia* is always dense or complete because all the motor fibers are condensed in a small area. There may or may not be associated *hemianesthesia or hemianopia on the same side* as hemiplegia.

C. *Subcortical lesion:* Hemiplegia is incomplete or not dense and there are no features to suggest cortical involvement.

Contralateral Hemiplegia

A. *Midbrain lesion:*
   1. *Weber's syndrome:* Ipsilateral 3rd nerve paralysis with contralateral hemiplegia.
   2. *Benedikt's syndrome* (red nucleus affected): Third nerve affection on the same side with tremors, rigidity and ataxia on the opposite side.

B. *Pontine lesion:*
   1. *Millard-Gubler syndrome:* Nuclear type of facial palsy with contralateral hemiplegia.
   2. *Foville's syndrome:* Facial palsy, sixth nerve palsy and contralateral hemiplegia.
   3. If in addition, the tegmentum is also involved, there may be Horner's syndrome due to paralysis of the ocular sympathetic fibers.

C. *Medullary lesion:*

   Jackson's syndrome: Twelfth nerve paralysis with contralateral hemiplegia.

6 › Paraplegia

Definition : Paraplegia is paralysis confined to both lower limbs.

Causes

1. Due to upper motor neuron lesion
   a. Intracranial
   b. Spinal (myelopathy)
      i. Non compressive
      ii. Compressive
2. Due to lower motor neuron lesions
   a. Anterior Horn cells
   b. Roots
   c. Peripheral Nerves
   d. Myo-neural junction
   e. Muscles
3. Functional or Hysterical

1. Due to Upper Motor Neuron Lesions

A. Intracranial

1. Tumour of falx cerebri : Meningioma
2. Thrombosis of unpaired Anterior Cerebral Artery
3. Thrombosis of Superior Saggital Sinus
4. Space Occupying Lesion (SOL) over Motor Area (Vertex) : Gliomas.

B. Spinal (Myelopathy)

1. Non - compressive Myelopathy

A. *Infections :*
   1. Bacterial : Tuberculosis, Syphillis
   2. Viral : Ebstein Barr Virus (EBV), Cytomegalovirus (CMV), HIV, HTLV-1 (Tropical Spastic Paraplegia)

B. *Vascular*
   1. Thrombosis of Anterior Spinary Artery
   2. Embolism : Leriche's syndrome (Saddle shaped thrombus at the bifurcation of the aorta)
   3. Caisson's Disease/Decompression Sickness : (fast ascent after deep sea diving)
   4. Iatrogenic : After surgery for Aorta (Co-arctation or Aneurysm) with prolonged cross clamping time.
   5. Vasculitis : Anti Phospholipid Antibody Syndrome (APLA), Sarcoidosis

C. *Demyelinating Disorders:*
   1. Multiple Sclerosis
   2. Post Infectious Demyelination
   3. Post Vaccine Demyelination

D. *Toxic*
   i. External
      1. Lathyrism
      2. Metals (Arsenic, Bismuth, Lead)
      3. Fluorosis
   ii. Internal
      1. Uremia
      2. Cholemia
      3. Toxemia of Pregnancy

E. *Nutritional*
   i. Pellagra (Niacin deficiency)
   ii. Sub-acute combined degeneration of the spinal cord (SACD)
   iii. Nutritional myelopathy

F. *Traumatic*
   i. Electric : Electric shock, lightening
   ii. Radiation
   iii. Chemical : Intrathecal Methotrexate, Penicillin or Myodil

G. *Degenerative* : Motor Neuron Disease

H. *Hereditary*
   i. Hereditary spino cerebellar ataxia
   ii. Hereditary spastic paraplegia
   iii. Freidrich's ataxia

I. **Neoplasms** : Paraneoplastic syndrome

2. Compressive Myelopathy

A. *Extramedullary Extradural*
   1. Trauma : Fracture dislocation of vertebral column.

2. Infection
   i. Epidural abcess
   ii. Tuberculosis : Cold Abcess, Collapse of Vertebral Column
3. Tumours
   i. Lipomas, Neurofibromas, Meningomas, Leukemia
   ii. Metastasis causing fracture dislocation of vertebral column.
4. Others : Aortic aneurysms compressing the vertebral column, fluorosis.

B. *Extramedullary Intradural*
1. Arachnoiditis : Tuberculosis, Syphillis, Pyogenic, Cryptococcus, Toxoplasmosis, Fungal, Chemical
2. Tumours: Lipoma, Neurofibroma, Meningoma

C. *Intramedullary*
1. Syringomyelia
2. Infection: Tuberculoma, Syphillis (gumma)
3. Tumour : Glioma, Lipoma
4. Trauma : Hematomyelia
5. Others : Hemangioma, A-V Malformation

II. Due to Lower Motor Neuron Lesions

A. *Anterior Horn Cells*
1. Infections : Poliovirus, HIV, HTLV-1
2. Motor Neuron Disease

B. *Roots*
1. Gullian Barre Syndrome
2. Infection :
   i. Tabes Dorsalis
   ii. Viral Infection : Herpez Zoster, EBV, CMV (Radiculitis)
3. Cauda Equina Syndrome
4. Prolapsed Intervertebal Disc
5. Diabetic Amyotrophy

C. *Peripheral Nerve* : Peripheral Neuritis

Table 6.17 : Differences between Functional and Organic Paraplegia

	Functional	*Organic*
1. Tone	Hysterical rigidity may be present, but never hypotonia or clasp knife rigidity	Hypotonia or clasp knife rigidity
2. Power	Astasia abasia: Inability to stand though the motor power is normal in recumbent position	Varies from grade 0 to grade IV
3. Involuntary movements	Usually none	Flexor spasms/ fasciculations
4. Wasting	Usually absent	May be present
5. Sensations; correlation between sensory loss & known anatomical distribution	None. Patient does not burn or cut the anesthetic skin.	Present. Sensory level usually present with a zone of hyperesthesia above.
6. Deep reflexes	Normal or brisk	Absent or brisk
7. Plantar response	Never extensor	Extensor
8. Sphincter disturbances	Absent	Maybe present

Table 6.18 : Differences between Upper Motor Neurone and Lower Motor Neurone Diseases

	Upper Motor Neurone	*Lower Motor Neurone*
1. Affection	Muscle groups	Individual muscles
2. Tone	Clasp knife rigidity	Flaccidity
3. Nutrition	Slight wasting due to disuse	Marked wasting
4. Involuntary movements	Flexor spasms sometimes	Fasciculations sometimes
5. Reflexes	Deep jerks brisk Plantars extensor	Deep jerks absent, plantars flexor
6. Electrical reaction	Normal	Reaction of degeneration

D. *Myoneural Junction* :
   1. Myasthenia Gravis
   2. Eaton Lambert Syndrome
   3. Periodic Paralysis

E. *Muscles*
   1. Polymositis
   2. Myopathy, Myositis
   3. Muscular Dystrophy

Acute Paraplegia

Causes

1. **Due to Upper Motor Neuron Lesions**
   A. *Intracranial*
      i. Thrombosis of unpaired Anterior Cerebral Artery
      ii. Thrombosis of Superior Sagittal Sinus
   B. *Spinal*
      i. Non Compressive Melopathy
         - Acute Transverse Myelitis
         - Infections
         - Vascular
         - Demyelinating Diseases : Multiple Sclerosis, Post Infections, Vaccine
         - Traumatic
      ii. Compressive Myelopathy
         - Extramedullary Intradural : Arachnoiditis
         - Extramedullary Extradural : Fracture Dislocation of vertebral column, Epidural Abcess.
         - Intramedullary : Hematomyelia
2. **Due to Lower Motor Neuron Lesions :**
   A. *Roots* :
      i. Gullian Barre Syndrome
      ii. Viral Radiculitis
      iii. Prolapsed Intervertebral Disc
   B. *Myoneural Junction* : Periodic Paralysis

Gradual Onset Paraplegia

Causes

1. Due to upper Motor Neuron Lesions
   A. *Intracranial*
      i. Tumour of falx cerebri (Meningioma)
      ii. SOL over motor area
   B. *Spinal*
      i. Non-compressive myelopathy
         - Toxic : Lathyrism, Fluorosis
         - Nutritional : Pellagra, SACD
         - Motor Neuron Disease
         - Sub-acute Myelostic Neuropathy (SMON)
         - Hereditary Spastic Paraplegia, Heriditary Spinocerebellar Ataxia, Freidrich's Ataxia
         - Paraneoplastic syndromes
      ii. Compressive Myelopathy
         - *Extramedullary Extradural*
            - Infection : TB Cold Abcess / Collapse of Vertebral Bady
            - Tumours
            - Aortic Aneurysm
            - Fluorosis
         - *Extramedullary Intradural*
            - Arachnoiditis
            - Tumours
         - Intramedullary
            - Syringomyelia
            - Infections
            - Tumours
2. Due to Lower Motor Diseases
   A. *Anterior Horn Cells*
      i. Polio
      ii. Motor Neuron Disease
   B. *Roots*
      i. Tabes Dorsalis
      ii. Diabetic Amyotrophy
      iii. Cauda Equina Syndrome
   C. *Peripheral Neuropathy*
   D. *Myo-neural Junction* : Myasthenia Gravis, Eaton Lambert Syndrome

Table 6.19 : Localisation of the Spinal Cord Lesion in Paraplegia

	Sensory system	Motor system	Reflexs
1. Cl-C4	Sensory loss in the neck.	Spastic quadriplegia. Trapezius involved. and sternomastoid may be	Abdominals and Cremasteric lost. Plantars extensors. Deep jerks brisk.
2. C5-T1	Sensory loss above the manubrium sterni and the upper limbs.	Wasting and weakness of the muscles of the upper limbs. Spastic flexous, adduction. Paraplegia.	Abdominals lost, plantars Deep jerks of the upper limbs lost, those of the lower limbs brisk.
3. T2-L1	Upper limb sensation normal. Sensory loss below the level of the lesion over the thorax and abdomen.	Wasting and weakness of the intercostals and/or abdominal muscles and spastic paraplegia.	Abdominal lost, plantars extensors. Deep jerks of upper limbs. Normal, those of lower limbs brisk. ED
4. L2-I5	Upper limb sensation normal Sensory loss below the anterior superior iliac spine.	Wasting and weakness of flexors and abductors of hip, extensors of the knee & dorsiflexors of the ankle. limb jerks normal. K.J.absent. A.J. brisk.	Abdominal and cremasteric present. Plantars-extensor. Upper
5. S1-S2	Sensory loss over the sole and calves and lower posterior aspect of the thigh.	Weakness and wasting of the gluteii, thigh, calf, peroneal and small muscles of the foot.	Abdominals, cremasteric, upper limb jerks & K.J. normal. Plantars lost A.J. lost.
6. S3-S4	Saddle-shaped anesthesia urine and feces. incout	No weakness but incontinence of and bulbocavernous which are lost	All normal, except anal
7. Conus medullaris	Perianal anesthesia	No paralysis, sphincter disturbances common	All normal, except anal and bulbocavernous which are lost.
8. Cauda Equina	Localisation of lesion depends upon the roots (between L2 and S5) involved.		

E. *Muscle*: Polymyositis, Myopathy, Muscular Dystrophy

Paraplegia with Optic Atrophy

Causes

A. *Hereditary ataxias:*
   1. Friedreich's ataxia.
   2. Sanger Brown ataxia

B. *Infections:*
   1. Syphilis
   2. Tuberculosis
   3. Arachnoiditis

C. *Vascular:* Eel's disease

D. *Toxic:*
   1. SMON
   2. Alcohol

E. *Deficiency:*
   1. Subacute combined degeneration
   2. Pellagra

F. *Demyelinating:*
   1. Disseminated sclerosis
   2. Devic's disease

G. *Miscellaneous:*
   1. Paget's disease of bones
   2. Multiple metastasis

Lesions of the Spinal Cord

Transverse Myelopathy: (Complete spinal cord transection): When there is complete transection, all the motor and sensory functions below the level of spinal cord damage are disturbed.

1. **Sensory:** All sensations (touch, pain, temperature, vibration and position) are impaired below the level of the lesion. Root pains or segmental paresthesia may occur at the level of the lesion. Localized vertebral pain (with tumors and infections) may be present and may be of localizing value.
2. **Motor:** Paraplegia (paralysis of both lower limbs)

or quadriplegia (paralysis of all the four limbs) occurs below the level of the lesion. Initially, the weakness is flaccid and areflexic due to spinal shock, later, hypertonic hyperreflexic paralysis occurs.

At the level of the lesion, lower motor neurone signs (wasting, weakness, areflexia and paralysis) occur due to damage to the anterior horn cells or their ventral roots.

3. **Reflexes:** Below the level of the lesion there is loss is superficial reflexes, extensor plantar and brisk deep reflexes.
4. **Autonomic disturbances:** Anhydrosis, trophic skin changes, impaired temperature control, vasomotor instability, impotence and bladder disturbances may occur.

Causes

1. **Traumatic spinal cord injuries:** There is sudden onset of transverse myelopathy following trauma. Recovery is usually uncommon. Electric shock, lightening or radiation expsoure may cause spinal cord transection immediately or after many years.
2. **Viral transverse myelitis:** There is an acute or subacute onset of transverse myelopathy with tingling and numbness to start with. Recovery often occurs.
3. **Tuberculous transverse myelitis:** Refer Tuberculosis of CNS.
4. **Anterior spinal artery thrombosis:** There is an acute onset of transverse myelopathy but the posterior columns are not affected because they are supplied by the posterior spinal artery.
5. **Multiple sclerosis:** This is common in young females between 20-40 years in age. There are characteristically relapses and remissions of primary optic atrophy, paraplegia and Charcot's triad (staccato speech, intention tremors and nystagmus).
6. **Post Infectious demyelination** : This is characterized by paraplegia after viral infections with neurotropic viruses like mumps, measles, rubella, chicken pox, small pox. Complete recovery usually occurs.
7. **Post-vaccinial demyelination:** This is characterized by paraplegia following vaccination. Recovery may occur.
8. **Compression myelitis:** This is characterized by subacute or gradual onset of one or more features of transverse myelopathy. There is usually presence of root pains due to irritation of the nerve roots at the level and sometimes pain, tenderness, rigidity and deformity of the vertebral column.
9. **Neoplasms:** The spinal neoplasms may be intramedullary, extramedullary or extradural. Differences between intramedullary and extramedullary tumors are as follows:

Multiple Transverse Levels

Multiple transverse levels may occur in the following:

1. Arachnoiditis
2. Multiple secondaries
3. Multiple neurofibromatosis
4. Spinal angiomas
5. Disseminated sclerosis

Hemisection of the Spinal Cord

1. **Sensory:** Loss of pain and temperature on the opposite side and loss of position and vibration sense on the same side below the level of lesion. Hyperaesthethic band at level of lesion.
2. **Motor:** Spastic monoplegia of lower limb or hemiplegia may occur below the level of the lesion on the same side. Segmental lower motor neurone signs occur at the level of the lesion.
3. **Reflexes:** Below the level of the lesion on the same side, superficial reflexes are lost, deep reflexes are brisk and plantars are extensor.

Causes: Extramedullary lesion

Lesions Affecting Spinal Cord Centrally

1. **Sensory:** The decussating fibers of the spinothalamic tract conveying pain and temperature sensations are affected initially causing analgesia and thermoanesthesia in a suspended bilateral distribution. Touch, position and vibration sensations are normal (dissociate anesthesia). Affection of the spinothalamic and

Table 6.20 : Differences between Extramedullary and Intramedullary Tumors

		Extramedullary	Intramedullary
		Radiating	Fumicular pain
1.	Root pains	Common	Rare
2.	Dissociate anesthesia	Uncommon	Common
3.	Pyramidal signs	Marked	Not so marked
4.	Wasting	Minimal	Marked
5.	Brown Sequard syndrome	May occur	Does not occur
6.	Sphincter disturbances	Late	Early
7.	Trophic changes	Minimal	Marked
8.	Spinal tenderness	May be present	Usually absent
9.	CSF proteins	Raised	Normal
10.	Spinal deformities	Common	Absent
11.	Distinct sensory level		Diffuse (no levels)
12.		Saddle Anaesthesia	Sacral Spacing

posterior columns may lead to loss of all the sensations below the level of lesion.

2. **Motor:** When the forward extension affects the anterior born cells, segmental atrophic weakness occurs. Dorsomedian and ventromedian motor nuclei causing scoliosis. Pyramidal tract affection causes spastic weakness below the level of the lesion.
3. **Reflexes:** The deep reflexes at the level of the lesion are lost. Below the level, deep reflexes are brisk, superficial reflexes lost and plantar extensor.
4. **Autonomic disturbances:** Affection of the ciliospinal centre of Budge with C3 -T2 lesion may cause Horner's syndrome.

Causes

1. **Syringomyelia:** This is a chronic progressive disorder in which cavitation occurs in the central gray matter of the spinal cord usually cervical, and sometimes extends into the lower brain-stem (syringobulbia). It is common in males between 25-40 years age. There is gradual onset of the above signs. In addition, trophic changes, kyphoscoliosis and pes cavus occur. If syringobulbia occurs, there is affection of ninth, tenth, and eleventh cranial nerves, nystagmus and Horner's syndrome.
2. **Hematomyelia:** This resembles syringomyelia but the onset is acute following injury and there is involvement of all the four limbs.
3. **Intramedullary tumors:** This resembles syringomyelia in presentation and is often difficult to differentiate clinically.

N.B: *In acute central cord syndrome, after hyper extension injury of the neck, the patient becomes quadriplegic due to cervical trauma but within a few hours regains strength in the legs. However severe motor impairment in the arms remains (man in a barrel syndrome) due to damage to the gray matter at the cervical spinal cord enlargement.*

Lesions of Posterior Column

1. **Sensory:** There is loss of touch, position and vibration sense. With demyelination in the cervical region, neck flexion may elicit a sensation of electric discharges that spreads inferiorly throughout the spine and lower limbs (Lhermitte's sign). Other conditions when this sign is positive : Multiple Sclerosis, Cervical Spondylosis, Syrinyx, SACD, Cervical Tumours, Early radiation myelitis.
2. **Motor:** There is hypotonia but normal power. Gait is high stamping and Romberg's sign is positive.
3. **Reflexes:** Deep reflexes especially the ankle jerk may be lost.

Causes: Tabes dorsalis, Diabetic pseudotabes

Lesions of Posterolateral Columns

1. **Sensory:** Loss of touch, position and vibration sense, especially of the lower limbs. If there is associated peripheral neuropathy, in addition, there will be glove and stocking type of anesthesia and calf tenderness.
2. **Motor:** There is spastic paraparesis with Romberg's sign positive.

3. **Reflexes:** Deep reflexes in the lower limbs may be brisk. Ankle jerk may be lost if there is associated peripheral neuropathy. The superficial reflexes are usually lost and plantar reflex is extensor.

Causes:

1. **Subacute combined degeneration of the spinal cord:** This occurs due to deficiency of vitamin B12 usually after the fourth decade. There is usually associated pernicious anemia and histamine-fast achlorhydria. Neurological features are as below:
2. **Sub-acute myelo-optic neuropathy** (SMON): This commonly occurs in the elderly patients who are habituated to take large doses of enteroquinol for long periods. In addition to the above features, there is optic atrophy.
3. **Pellagra:** This is characterized by diarrhea, dementia and dermatitis in addition to the above features.
4. **Taboparesis:** This is common in younger patient with history of exposure. There are always mental changes and often Argyll Robertson pupils present.
5. **Friedreich's ataxia:** This is a heredofamilial autosomal recessive disorder of early onset involving, in addition to the pyramidal tracts and posterior columns, spinocerebellar tracts (which causes truncal ataxia, titubation, nystagmus and slurred speech), optic atrophy, kyphoscoliosis, pes cavus and cardiac abnormalities (cardiac failure, heart block, bundle branch block, T wave changes). This is a steadily progressive disorder ultimately leading to death due to intercurrent infection, cardiac failure and complications of associated diabetes.
6. **Nutritional myelopathy:** This is due to protein calorie malnutrition and resembles subacute combined degeneration of the spinal cord. Skin changes of vitamin deficiencies are usually evident.

Subacute Combined Degeneration (SACD)

Clinical Features

1. Presenting feature is tingling sensation in the feet and ascending up the leg and then involving the trunk.
2. There is difficulty in walking and unsteadiness of gait which is more pronounced in darkness.
3. There is ataxia and spastic weakness of legs with profound distal loss of postural and vibration sense with bilateral extensor plantars.
4. L'Hermitte's sign is positive (due to posterior column involvement)
5. Concurrent peripheral neuropathy is evidenced by loss of ankle jerks impairment of superficial sensations in glove and stocking pattern.
6. Mild impairment of memory called "megaloblastic maddness".
7. Bilateral optic atrophy is seen in 5-10% cases.

Table 6.21 : Neurological Features of Subacute Combined Degeneration (SACD) of Spinal Cord

I.	Motor System
	1. Tone : Increased
	2. Power : Diminished
	3. Wasting : Absent
	4. Coordination : Normal
II.	Sensory System
	1. Vibration, joint sense : Absent
	2. Touch, temperature pain : Glove and Stocking pattern
III.	Reflexes
	1. Deep Jerks / Ankle Jerks : Brisk lost
	2. Plantars : Extensions
	3. Abdominals : Absent
	4. Sphincters : Frequency, Urgency

Anterior Horn Cell Syndromes e.g. Poliomyelitis (AFP)

1. **Sensory:** Normal
2. **Motor:** There is diffuse weakness, atrophy and fasciculations in the muscles of extremities and trunk. Muscle tone may be reduced or normal.
3. **Reflexes:** Deep tendon reflexes are usually lost.

Causes

1. **Progressive muscular atrophy:** (See motor neurone disease below).

2. **Spinomuscular atrophy:** This is characterized by bilateral affection of the proximal group of muscles usually in the first or second decade. The disease has a slow progressive course.
3. **Diabetic amyotrophy:** There is asymmetrical wasting and weakness of proximal muscles in uncontrolled diabetes.
4. **Syphilitic amyotrophy:** There is asymmetrical wasting and weakness of proximal muscles in a patient with history of exposure and positive VDRL tests.

Combined Anterior Horn and Pyramidal Tract Disease

This is seen in motor neurone disease as below:

Motor Neurone Disease

The disease process affects the motor neurones of the CNS, which are the Betz cells, cranial nerve nuclei and anterior horn cells. There is associated involvement of the pyramidal tracts.

Types:

1. Progressive muscular atrophy - affection of the anterior horn cells.
2. Primary lateral sclerosis - predominant affection of the pyramidal tracts in the spinal cord.
3. Amyotrophic lateral sclerosis - affection of both the pyramidal tracts and anterior horn cells.
4. Progressive bulbar paralysis - affection of the cranial nerve nuclei in the medulla.
5. Pseudobulbar palsy - affection of the pyramidal tract in the brain stem.
6. Combination of 4 and 5.

Motor neurone disease has a gradual onset, and although there are 6 varieties, they merge into each other and, in a given patient various combinations may be found. Hence they are grouped under the common name of motor neurone disease.

Progressive muscle atrophy is the most benign of them, survival being over 10 years. However, once bulbar palsy sets in, prognosis is poor. The clinical features are shown in the table above.

Variants of Motor Neurone Disease (MND)

1. *Madras MND* : 10% of MND in South India, age of involvement 10-30 yrs. Male preponderance (2:1), weakness of facial and bulbar muscles, longevity is prolonged.
2. *Monomelic amyotrophy* : Slow progressive weakness usually concerning one limb, usually upper limbs.

Table 6.22 : Clinical Features of Motor Neurone Disease

	Progressive muscular atrophy	*Primary lateral sclerosis*	*Bulbar palsy*	*Pseudobulbar palsy*
1. Motor System				
a. Tone	Diminished	Increased	Normal	Increased
b. Wasting	Marked	Absent	Of tongue	Absent (Small Spastic)
c. Fasciculations	Present	Absent	Over tongue	Absent
d. Power	Diminished	Diminished	Normal	Diminished
2. Sensory system	Normal	Normal	Normal	Normal
3. Reflexes:				
a. Deep	Absent	Brisk	Normal	Jaw jerk brisk
b. Plantars	Flexors	Extensor	Flexor	Extensor
c. Abdominals	Normal	Preserved till late	Normal	Preserved till late
4. Cranial nerves				
a. Palatal palsy	Absent	Absent	Present	Present Absent (good-gag)
b. Slurred voice & Dysphagia	Absent	Absent	Present	Present (spastic and speech)
5. Respiratory infection	Absent	Absent	Common cause of death	Common cause of death

Table 6.23 : Differential Diagnosis of Lower Motor Neurone Lesions

		Anterior Horn cell	*Roots*	*Myoneural Junction*	*Myopathy*	*Neuropathy*
1.	Distribution of weakness	Distal or proximal. May involve neck flexors	Asymmetrical, Distal or along nerve distribution	Proximal. Bulbar Respiratory	Proximal	Distal or along nerve distribution
2.	Fatigue	Mild	Mild	Severe	Mild-Mod	Mild
3.	Wasting	Marked	Present	Absent	May be present	May be present-Moderate
4.	Fasciculation	Marked	Absent	Absent	Absent	May be present (radiculopathy)
5.	Sensory loss	Absent	Present	Absent	Absent	Usually present
6.	Deep reflexes	Decreased (Increased if associated lateral sclerosis)	Absent	Normal	Present	Decreased - lost

3. *Wasted Leg Syndrome*: lower motor neuron signs in lower limb.
4. *Juvelnile MND* : Juveline Onset MND
5. *Guamine ALS* : family history positive, High incidence of Parkinsons Disease associated complex.
6. *Crural ALS*
7. MND with dementia
8. Hemiplegia type (Mill's variant)

Foramen Magnum Syndrome

1. Suboccipital pain and paraesthesia and neck stiffness occur early.
2. Posterior column signs or "syringomyelic type" of sensory dissociation may occur with tingling and numbness in the fingertips.
3. Spastic quadriparesis with sensory loss and bladder dysfunction may occur.
4. Lower cranial nerves (IX-XII) palsy occur.
5. Downbeat nystagmus, cerebellar ataxia and papilledema (secondary to obstruction of CSF)
6. Contralateral upper limb paresis with ipsilateral lower limb paresis (hemiplegia cruciata) may occur due to affection of decussating pyramidal fibers.

Poliomyelitis

Refer Flaccid Quadriplegia (Pg. 339).

Peripheral Neuropathy

Definition: This is the disorder of peripheral nerves, either sensory, motor or mixed, symmetrical and affecting distal parts of the limbs more than the proximal. By convention, isolated cranial nerve palsies and isolated and multiple peripheral nerve lesions are excluded.

Clinical Features

A. Bilaterally symmetrical
B. Tingling and numbness at the onset
C. Glove and stocking type of anesthesia
D. Calf tenderness
E. Flaccid weakness especially in the lower limbs with foot drop
F. Vasomotor and trophic changes like edema, dryness, desquamation, etc.
G. High steppage gait

Mononeuritis Multiplex: This is a disorder affecting two or more peripheral nerves at one time producing symptoms of numbness, paraesthesia and sometimes pain in their sensory distribution with associated muscle wasting and weakness.

The lower limbs are more commonly affected and the neuropathy is usually asymmetrical.

It occurs in diabetes mellitus, polyarteritis nodosa and uncommonly in other collagen disorders.

Peroneal Muscular Atrophy

A. Common in young adults

Table 6.24 : Diseases Affecting Myoneural Junction

	Myasthenia gravis	*Carcinomatous myopathy (Eaton Lambert Syndrome)*	*Botulism*
1. Etiology	Auto-immune	Unknown.	Cl. botulinum toxin
2. Age and Sex	Young females	Older males.	No predilection
3. Distribution of weakness	Bulbar muscles Respiratory Muscles Proximal muscles	Mainly limb muscles with aching	Bulbar muscles Respiratory muscles
4. Repeated exercises	Progressive weakness	Improves	No effect
5. Deep reflexes	Normal	Decreased	Normal
6. Associated disease	Pernicious anemia, Thymoma, SLE	Oat-cell carcinoma of lung	Gastrointestinal symptoms
7. Tensilon Test	Marked improvement	Mild improvement	No effect
8. EMG	Progressive fatigue Decremental Response	Improves with rapid, repeated stimulation Incremental Response	Slight improvement with repeated stimulation.
9. Treatment	Neostigmine, Steroids, Thymectomy	Guanidine	Guanidine, Polyvalent botulism antitoxin.

Table 6.25 : Differential Diagnosis of Muscular Dystrophy

	Duchenne	*Becker*	*Fascio-scapulo humeral*	*Limb girdle*
1. Inheritance	Sex-linked recessive	Sex-linked recessive	Autosomal dominant	Autosomal recessive
2. Onset	3 years	15-25 yrs.	7-25 yrs.	20-30 yrs.
3. Distribution of Weakness	Proximal > Distal Pelvic > Shoulder	Same as Duchenne	Face, scapula and arms	Pelvic and shoulder gridle
4. Cardiac Involvement	Common	Absent	Absent	Common
5. Progress	Rapid	Slow	Slow	Varies
6. Prognosis	2nd decade-bed bound 3rd decade-death Wheel-chair at 8-14 yrs.	Normal life span	Normal life span	Varies

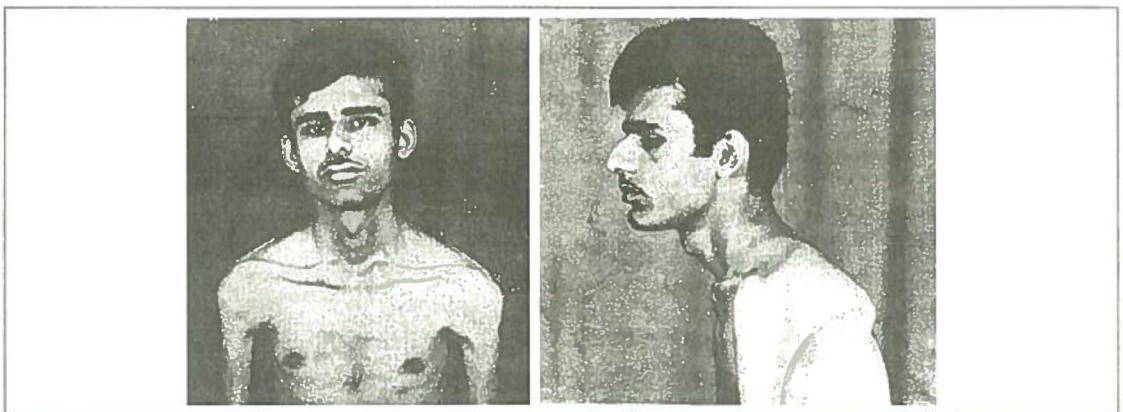


Fig. 6.100: A Case of facioscapulohumeral muscular dystrophy

B. Muscle wasting occurs in the lower limbs. It may also occur in the upper limbs but stops short midway at the leg or the forearm giving a typical inverted champagne bottle appearance
C. High steppage gait
D. Spinal cord deformities: Kyphoscoliosis, pes cavus
E. Distal sensory loss with calf tenderness

Acute Infective Polyneuritis

Refer Flaccid Quadriplegia (Pg. 339)

Myopathies

A. Congenital and familial
B. Gradual onset and slow progress
C. Bilaterally symmetrical
D. Selective groups of muscles may be wasted or hypertrophied
E. Associated spinal anomalies (e.g. kyphoscoliosis) may be present
F. No sensory loss or sphincter disturbances

Table 6.26 : Differences between Conus Medullaris and Cauda Equina Lesions

		Conus medullaris	*Cauda equina*
1.	Root pains	Absent	Present
2.	Sensory changes	Saddle-shaped distribution with perianal anesthesia. Usually symmetrical	May invoke any part of the lower limbs asymmetrically
3.	Motor changes	Absent	Marked motor changes with wasting - asymmetrical
4.	Sphincters	Always involved (yearly)	May be involved (late)
5.	Reflexes	Knee jerk normal Ankle jerk lost Plantar extensor	Knee and ankle jerks may be lost
6.	Impotence	Frequent	Less frequent

7 › Quadriplegia

Definition: Quadriplegia is paralysis of all the four limbs. Quadriplegia may be spastic or flaccid.

Spastic Quadriplegia

Causes

I. Cortical Lesion
A. Cerebral palsy
B. Decerebrate state due to anoxia, hydrocephalous, diffuse sclerosis, pineal tumors, etc.
C. Congenital disorders e.g. microcephaly

II. Brain Stem Lesion:
A. Vertebrobasilar insufficiency
B. Brainstem space occupying lesions
C. Infections e.g. bulbar poliomyelitis
D. Degeneration conditions: syringobulbia, motor neurone disease, etc.
E. Demyelinating disease e.g. disseminated sclerosis

III. High Cervical Cord Lesion:
A. Fracture dislocation of cervical spine
B. Craniovertebral anomaly
C. Cervical spondylosis
D. Hematomyelia
E. Cervical cord tumors

Differential Diagnosis

Cerebral Palsy

A. It is usually present from birth. It may subsequently remain stationary or improve.
B. There is weakness and spasticity in all the four limbs (equal or more in lower limbs) with expressionless face.
C. Mental retardation is predominant and may occur in the absence of weakness.
D. Involuntary movements: Choreoathetosis may be present. It may disappear if hypertonia is predominant.
E. Ataxia, nystagmus and hypotonia may be present if cerebellum is also involved.
F. Epilepsy
G. Skeletal infantilism
H. Optic atrophy and visual field defects
I. Delayed puberty

Decerebrate State

A. Prolonged state of hypertonia
B. Opisthotonos and rigid extension of all the four limbs
C. Upper limbs: Internally rotated at the shoulder, extended at the elbow and hyper pronated. The fingers are extended at the metacarpophalangeal joints and flexed at the interphalangeal joints
D. Lower limbs: They are extended at the hip and knee while the ankles and toes are plantar flexed.

Brain Stem Space Occupying Lesions

A. More common in the younger age group
B. Usually gradual in onset with increased intracranial tension
C. Brainstem signs like diplopia, drop attacks

Fracture Dislocation of the Cervical Spine

Sudden onset of spastic quadriplegia with poor prognosis and no involvement of the cranial nerves.

Craniovertebral Anomalies

A. Short neck, low hairline and restriction of the neck movements (Field's triad)
B. Gradual onset of spastic quadriparesis: hypertonia and brisk jerks in all 4 limbs with extensor plantars
C. Wasting of the small muscles of the upper limbs
D. Sensory loss if spinothalamic tract involved
E. Cerebellar signs e.g. nystagmus, intention tremors

Various Craniovertebral anomalies:

A. Platybasia
B. Basilar invagination
C. Occipitalization of the atlas
D. Atlantoaxial dislocation
E. Separate odontoid process
F. Klippel-Feil syndrome: Fusion of the cervical vertebrae
G. Arnold Chiari malformation (Medulla and cerebellum are elongated and extended downward through the foramen magnum. This may be associated with syringomyelia).
H. Cerebella ectasia

Cervical Spondylosis

A. Pain in neck with muscular spasm and rigidity of the neck muscles. Restriction of neck movements.
B. Headache in the occipital region in the morning.
C. Radicular symptoms: pain radiating down the upper limbs with burning and tingling sensations. There may be associated sensory deficit and loss of tendon jerks depending upon the segments involved.
D. Spastic paraplegia due to compression of pyramidal tract in the cervical region.
E. Vertebrobasilar ischemia: Giddiness or drop attacks precipitated by neck movements, which presses the vertebral arteries with consequent impairment of the blood supply of the brainstem.

Flaccid Quadriplegia

Flaccid quadriplegia includes :

1. Weakness with or without wasting of all the four limbs
2. Hypotonia
3. Loss of deep reflexes, often with preservation of the abdominal reflex and flexor or absent plantar response

Causes

1. **Polyneuropathy**
   A. Acute infective polyneuritis
   B. Porphyria
   C. Diphtheria
   D. Botulism
   E. Triorthocresyl phosphate (TOCP)
   F. Infectious mononucleosis
   G. Infective hepatitis
   H. Organophosphorous poisoning
2. **Muscle diseases**
   A. Acute myasthenia gravis

B. Periodic paralysis

C. Polymyositis

3. **Anterior horn cell disease:** Poliomyelitis

4. **Brain stem lesions with neuronal shock**

Differential Diagnosis

Acute Infective Polyneuritis

(Guillain Barre Syndrome, acute demyelinating polyneuropathy (AIDP))

Acute, frequently severe, fuminant polyradiculoneuropathy involving spinal roots, peripheral nerves and occasionaly cranial nerves (most commonly 7th cranial nerve). Autoimmune in nature.

A. Incidence : 1 in 1 lakh, Age : 20-50 yrs, both sexes

B. Aetiology :

a. Viral (CMV, HIV, EBV, Herpes, Mycoplasma pneumonia), Bacterial (yersinia, campylobacter, salmonella), Post vaccinal, Rabies, Influenza.

b. SLE

c. Hogdkin's disease

C. Clinical features

a. *Onset:* Acute or subacute with fever, backache and pain in the limbs.

b. *Sensory:* Pain and paraesthesia over the affected limbs with or without sensory loss. Muscle tenderness may be present.

c. *Motor: LMN type* weakness of all the four limbs simultaneously or first in the lower limbs and then spreading to the upper limbs. Proximal weakness more than distal. Later respiratory, pharyngeal and laryngeal involvement may require ventillatory support.

d. *Cranial nerves:* Unilateral or bilateral facial palsy, dysphagia (from pharyngeal palsy) and external ophthalmoplegia.

Palate always Escapes

e. Urinary Bladder, if involved, is always late.

f. Autonomic imbalance can also be seen.

D. Clinical variants: Miller Fisher Syndrome : Ophthalmoplegia, ataxia, arreflexia with little weakness in 5% of cases. Presence of anti GQ1b antibodies.

AMAN : Acute Motor Axonal Neuropathy (presence of anti GD1 a antibodies)

AMSAN : Acute Motor Sensory Axonal Neuropathy

Investigations

1. Antibodies:
   - GBS : anti GM_1 antibodies (20-50%)
   - MFS : anti GQ_1 antibodies IgG-(90%)
   - AMAN : anti GD_1 (<50%)
2. CSF : Protein (100-1000 mg/dl) (At the end of Albuminocytological dissociation first week). Xanthochnomia.
3. Abnormal electrophysiological findings on EMG + NCV.

Diagnostic criteria for GBS

Required: 1. Progressive weakness of two or more limbs due to neuropathy; 2. Arreflexia; 3. Disease course <4 weeks; 4. Exclusion of other conditions e.g. vasculitis, SLE, lead toxicity, botulism, diphtheria.

Supportive : Relatively symmetrical weakness; 2. Mild sensory involvement; 3. Facial nerve or other cranial nerve involvement; 4. Absence of fever; 5. Typical CSF; 6. Demylination on electrophysiology.

Treatment

1. IV Immunoglobulin
2. Plasmapheresis

Porphyria

A. *Onset* in the adult life often precipitated by barbiturates, sulfonamides or alcohol.

B. *Polyneuropathy:* Proximal muscle weakness with sensory symptoms, but NO SENSORY LOSS. There may be bulbar and respiratory paralysis.

C. *Mental changes:* Restlessness, mood changes, emotional instability, confusion, convulsions, coma.

D. *Abdominal crises:* Acute abdominal pain which may mimic intestinal obstruction, with or without nausea, vomiting and constipation.

E. *Hypertension*

F. *Urine:* Port wine color on exposure to light.

Diphtheria

A. *Palatal palsy, unilateral or bilateral* by second or third week (no palatal palsy seen in Guillain Barre syndrome).

B. Paralysis of accommodation, usually bilateral, rarely unilateral, by the third or fourth week. There is diminished vision for near objects (therefore unnoticed in myopics). Pupillary response to light and accommodation is sluggish. External ocular movements are usually normal, rarely sixth nerve weakness may be present.

C. *Generalized polyneuropathy* by sixth or seventh week.
   1. Weakness of the lower limbs more than upper limbs
   2. Glove and stocking anesthesia
   3. Loss of postural sense and sensory ataxia
   4. Paralysis of diaphragm, larynx and pharynx
   5. Sphincters are normal and there may or may not be impotency

D. *Cardiac involvement due to vagal palsy* - tachycardia, atrial fibrillation, premature beats and bundle branch block

Botulism

A. *Onset:* Symptoms usually develop within 18-30 hours after ingestion of tinned food.

B. *Gastrointestinal symptoms* like nausea and vomiting occur. In most cases there is severe constipation due to paralysis of the intestinal muscles

C. *Neurological symptoms*
   1. Paralysis of accommodation and sometimes also of the light reflex
   2. Paralysis of the external ocular muscles, ptosis, diplopia and nystagmus
   3. Weakness of the jaw muscles, respiratory muscles and muscles of the trunk and limbs
   4. Tendon reflexes are always normal. Plantars are flexors. There is no sensory disturbance and consciousness is preserved up to the end.

D. There is usually no fever, unless associated respiratory tract infection.

Triorthocresyl Phosphate Neuropathy

A. *Onset:* 10-20 days after ingestion of ginger adulterated with triorthocresyl phosphate

B. Pain in the limbs with inconsistent sensory loss. Wasting and weakness of the distal muscles with BILATERAL WRIST DROP AND FOOT DROP.

C. Retrobulbar neuritis

Acute Myasthenia Gravis

(Refer to Pg. 340)

Polymyositis

A. Subacute, symmetrical weakness of the proximal and trunk muscles. Sometimes only the quadriceps and neck muscles are involved.

B. Pharyngeal and laryngeal muscles may be involved leading to dysphagia and dysphonia.

C. OCULAR and FACIAL MUSCLES are usually SPARED and in 75% distal muscle are spared.

D. Fever, muscle pain and tenderness may be present.

E. Reflexes are usually depressed, but sometimes brisk. (If markedly reduced think of carcinomatous polymyositis).

F. Cardiac involvement: Arrhythmias, myocardial infarction and minor ECG changes.

G. It is precipitated by sunlight, sulphonamides and minor systemic infections.

Poliomyelitis

A. Younger age group. Below 25 years.

B. Pre-paralytic stage - Fever, malaise, headache, drowsiness, insomnia, sweating, flushing, facial congestion, anorexia, vomiting and diarrhea for a day or two.

C. Severe pain in the back and limbs and muscle tenderness.

D. There is flaccid paralysis and wasting of one limb in asymmetrical fashion. Sometimes paralysis occurs in all the four limbs and trunk muscles. The lower limbs are more affected than the upper, and the quadriceps, peronei and tibial groups are most affected. The affection is maximum within the first 24 hours.

E. Bulbar muscles may or may not be involved and ocular muscles are only very rarely involved.

Periodic Paralysis

Table 6.27 : Differential Diagnosis of Periodic Paralysis

	Hypokalemic	*Hyperkalemic*
Inheritance	AD	AD
Onset	Adolescence	Early childhood
Frequency of attacks	Daily yearly	2-3 / day
Duration of attacks	2-12 hrs	1-2 hrs -> 1 day
Precipitating factors	Anxiety, heavy meal and rest after exercise	Cold, emotion infection, rest after exercise and KCl
K level	K decreased	Increased or Normal
Type of channel	Ca channelopathy	Na channelopathy
Treatment	KCl	Acetazolemine Mexinifline

Infectious Mononucleosis

A. Ascending sensory-motor paralysis.

B Fever, sore throat, skin and rash, splenomegaly and lymphadenopathy are usually associated.

C. High levels of Epstein-Barr virus antibody titre and increased IgM and IgG levels.

Infective Hepatitis

Jaundice with peripheral neuropathy.

This may also occur in alcoholism, nutritional deficiency and amyloidosis.

Brain-stem Lesions with Neuronal Shock

A. Usually sudden in onset

B. Cranial nerves always involved along with flaccid weakness of all four limbs, which may become spastic later

C. Vertigo and vomiting due to vestibular involvement

8 › Myasthenia Gravis

Is a neuromuscular disorder characterised by weakness and fatiguability of skeletal muscles due to decrease in number of Acetylcholine receptors at the neuromuscular junction due to antibodies. It is an autoimmune disorder.

A. *Incidence :* Common in men in 50s and 60s; women 20s and 30s; women more frequently affected than men.

B. *Clinical features*

1. *Onset* is insidious or subacute, rarely acute
2. *External ocular movements* are weak. There may be unilateral or bilateral ptosis.

   Pupils are always Spared
3. *Facial:* Weakness of orbicularis oculi is quite constant. Retractors of the angles of the mouth suffer more than elevators resulting in snarling smile.
4. *Other cranial nerves:* There is palatal palsy. Involvement of the masseters prevents closure of mouth (hanging jaw sign). There may be nasal speech and ultimately respiratory paralysis.
5. *Limbs:* Proximal weakness initially in the shoulder girdle, later on may be generalized
6. The weakness is more in the evening and disappears after a night's rest. Usually there is no wasting or loss of deep reflexes.
7. Muscle groups commonly involved in decreasing order are bulbar, neck, limb girdle, distal limb and trunk.
8. If respiratory muscles are affected, mechanical ventillation may be required and patient is said to be in a "Myasthenia crisis".

C. *Diagnosis*

1. *Clinically :*
   a. Breath Holding Time : Breath counting are done to assess vital capacity,
   b. Forward arm abduction (> 5 mins),
   c. On sustained upward gaze increased ptosis may occur,
   d. Single breath count
2. *ACH receptor Antibodies* : Generalised : 90% positive. Ocular : 50% positive

3. *Anti MUSK Antibodies* (muscle specific kinase) positive is 40% of negative cases.
4. *Tensilon test* : Edrophonium 2 mg is given IV. If muscle power is improved within 30 seconds and sustained improvement for 2-3 mintues test is positive. It can be repeated with 8 mg if required.
5. *CT scan* (To look for thymoma) Thymus is enlarged in 70% of MG cases.
6. *Electrophysiological study.*
   a. Repetitive nerve stimulation - decremental pattern.
   b. Single fibre EMG - Increased variability of interpotential interval.

D. *Treatment*

1. Pyridostigmine Orally 30 - 120 mg every 4-8 hours, titrated individually for each patient.
2. Corticosteroids : IV or oral
3. Plasma Exchange : Removes antibodies, used in crisis.
4. Immunomodulators : Azathioprine, cyclophosphamide, mycophendlate mofetil, tacrolimus
5. Thymectomy : In patients under 60 years, improves symptoms.

E. *Drugs contraindicated in MG* :

Antibiotics : Aminoglycosides, Quinolones, Muscle relaxants: pancuronium, D Tubocuan, Betablockers, local anaesthetics, quinine, as these worsen the muscle weakness.

9 Cerebellum

Cerebellum is an infratentorial structure in the posterior cranial fossa, attached to the brain stem by the superior, middle and inferior peduncles through which nerve fibers enter and leave. It has two lateral lobes and a central vermis.

There are four nuclei in the cerebellum:

Dentiform, Emboliformis, Fastigious and Globosus.

Functionally it can be classified as :

1. Archicerebellum: This is connected to the vestibular nuclei for maintaining equilibrium.
2. Paleocerebellum: This is connected to the spinal cord, for maintaining posture.
3. Neocerebellum: This is connected to the cerebral cortex by pontine and olivary connections for voluntary movements.

Connections

Through the superior peduncle (connects cerebellum and midbrain):

A. *Afferent:* Ventral Spinocerebellar tract — It arises from the nuclei on the medial side of the Clark's column, crosses on the opposite side, ascends up to the midbrain and then again crosses, entering the anterior lobe of the cerebellum on the same side. It receives impulses from the Golgi tendon type IB. It sends inhibitory impulses to the motor neurones.

B. *Efferent:* Cortico-pontocerebellar tract — It arises from the lateral lobes and via the superior peduncle crosses to the opposite red nucleus. From the red nucleus it goes to the ventrolateral nucleus of the thalamus from where it goes to the cerebral cortex.

Through the middle peduncle (connects cerebellum and pons):

Efferent: Cortico-pontocerebellar tract - Fibers from the cerebral cortex along the corticospinal tract pass to the cerebellum with a relay in the nuclei of the pons.

Through the inferior peduncle (connects cerebellum and medulla):

A. *Afferent:*

1. *Dorsal-spinocerebellar tract:* From the Clark's column situated deep in the posterior horn, it enters the anterior lobe of the cerebellum via the inferior peduncle. It receives afferents from the muscle spindle type IA.
2. *Olivocerebellar tract:* From the extrapyramidal system to the lateral lobes of the opposite cerebellum.
3. *Vestibulocerebellar tract:* From the vestibular nucleus to the flocculonodular lobe.
4. *Cuneocerebellar tract.*

B. *Efferent:*

1. *Fastigiobulbar tract:* To the reticular area for the control of tone

2. *Fastigiovestibular tract:* To the vestibular nucleus for maintenance of equilibrium

Etiology of Cerebellar Ataxias

Acute Onset

A. *Trauma:* (gives rise to small capillary bleeding).

B. *Infections:*
   1. Encephalitis esp. varicella
   2. Cerebellar abscess

C. Vascular:
   1. Posterior inferior cerebellar artery thrombosis
   2. Anterior inferior cerebellar artery thrombosis
   3. Superior cerebellar artery thrombosis
   4. Vertebrobasilar insufficiency

D. *Demyelinating:* Disseminated sclerosis

E. *Drugs:*
   1. Phenytoin sodium
   2. Barbiturates
   3. Alcohol
   4. Piperazine citrate
   5. Streptomycin, gentamicin, kanamycin

F. *Hyperpyrexia*

Gradual Onset

A. *Congenital:* Craniovertebral anomaly

B. *Hereditary ataxias*
   1. Friedreich's ataxia
   2. Marie's ataxia
   3. Sanger Brown's ataxia
   4. Ataxia telengiectacia
   5. Spinocerebellar Ataxias (Autosomal Dominant)

C. *Familial:*
   1. Refsum's disease
   2. Lipidosis
   3. Leukodystrophies
   4. A-alpha lipoproteinemia
   5. A-beta lipoproteinemia

D. *Degenerative:*
   1. Holmes' primary cerebellar degeneration.
   2. Dejerine Thomas' olivopontocerebellar degeneration
   3. Lhermitte Lejomme's olivorubrocerebellar degeneration
   4. Delayed cerebellar degeneration

E. *Neoplastic:*
   1. Cerebellopontine angle tumors
   2. Cerebellar tumors
   3. Pontine tumors

F. *Alcohol*

G. *Nutrition* : Vit. E deficiency

Clinical Features of Cerebellar Lesions

I. Of Localizing Value

A. *Disorders of postural fixation* (Paleocerebellum)
   1. Hypotonia
   2. Weakness
   3. Pendular Knee Jerk: If the patellar tendon is stimulated while the feet are hanging free, there is a series of jerky to and fro movements of the leg 2½ times back & fourth before the leg finally comes to rest. This response is normally prevented by the 'after-shortening' of the quadriceps femoris.

      Pendular knee-jerk is caused by the hypotonicity of flexor and extensor muscles of the knee and the lack of restraining effect which they normally exert upon each other.
   4. Past pointing.
   5. Barany's test: Slow fall of the outstretched arm on the side of the lesion, when the patient, with his eyes closed and one arm outstretched, is asked to move the limb and bring it back to its original position.

B. *Disorders of movements* (Neocerebellum)
   1. Intention tremors: Increased irregularity of the movements as the

finger approaches the nose in the finger nose test. This results from the involvement of the cerebellar afferent pathways in their connection with the red nucleus and thalamus.

2. Dysmetria: Inability to arrest the movements at desired points due to loss of ability to gauge the distance, speed and power of movement.
3. Dyssynergy: Defective coordination of various muscles and muscle groups participating in a movement. Therefore there is decomposition of movements and the act is broken down into its component parts.
4. Dysdiadochokinesia: There is disturbance of reciprocal innervation of agonists and antagonists. Hence, there is loss of ability to stop one act and follow it immediately by a diametrically opposite act. This is seen when the patient attempts alternate successive pronation and supination of the hand, rapid tapping of the fingers or alternate opening and closing of fists.
5. Rebound phenomenon: Failure of antagonist to counter overshoot movements totally.

C. *Disorders of Gait*

1. Broad base
2. Reeling gait
3. Deviation to the side of the lesion
4. Truncal ataxia
5. Titubation

II. Of No Localizing Value

1. *Static tremors:* Tremors at rest due to hypotonia.
2. *Skew deviation:* Homolateral eye turns downward and inward and contralateral eye turns upwards and outwards.
3. *Nystagmus:* With the hemisphere lesion, the eyes at rest are deviated towards the unaffected side. When the patient attempts to focus his vision elsewhere, the eyes move towards the point of fixation with quick jerks and there are slow return movements to the resting point. The movements are more marked and of greater amplitude when the patient looks towards the affected side.
4. *Vertigo:* Objects move away from the side of the lesion. Sense of rotation of the body in same direction with intra cerebellar lesion and in opposite direction with extra cerebellar lesion.
5. *Speech disturbance:* Staccato, scanning or explosive speech. Sometimes dysarthria.

Differential Diagnosis

Trauma: History of trauma prior to the onset of cerebellar disorders.

Encephalitis: Usually causes acute cerebellar signs. Disturbance of external ocular movements including nystagmus, are more prominent.

Cerebellar Abscess:

A. Symptoms and signs of cerebellar ataxia
B. Symptoms and signs of septicemia
C. Symptoms and signs of raised intracranial tension

Posterior Inferior Cerebellar Artery Thrombosis:

Wallenberg's syndrome (Lateral medullary syndrome). It is characterized by a sudden onset of—

A. Vertigo, vomiting (vestibular nucleus involvement)
B. Dysphagia (nucleus ambiguous)
C. Ataxia (inferior cerebellar peduncle)
D. Ipsilateral anesthesia of the face (descending tract of the V nerve)
E. Contralateral anesthesia of the limbs and trunk (spinothalamic tract)
F. Nasal twang, nasal regurgitation (ipsilateral 9th, 10th and 11th cranial nerves)
G. Ipsilateral Horner's syndrome (Descending sympathetic fibers)
H. Nystagmus and intention tremors (vestibular nerve and cerebellar fibers)

Disseminated Sclerosis: Refer paraplegia

Drugs: Cerebellar ataxia follows ingestion of certain drugs as mentioned above.

Craniovertebral Anomalies:

Refer Quadriplegia

Friedreich's Ataxia: Refer Paraplegia

Sanger Brown's Ataxia

1. Family history
2. Cerebellar signs
3. Optic atrophy
4. Ophthalmoplegia

Marie's Ataxia

1. Family history
2. Cerebellar signs
3. Pyramidal signs

Roussy Levy Syndrome

1. Family history
2. Cerebellar signs
3. Polyneuropathy

Refsum's Disease

(Familial disease of phytanic acid metabolism)

1. Family history
2. Cerebellar ataxia
3. Atypical retinitis pigmentosa
4. Peripheral neuropathy with thickened nerves
5. Deafness
6. Anosmia

A-beta Lipoproteinemia

1. Cerebellar ataxia
2. Pyramidal signs with absent deep reflexes
3. Acanthocytosis on peripheral smear

A-alpha Lipoproteinemia (Tangier's Disease)

1. Cerebellar ataxia
2. Orange or yellowish gray discoloration of tonsils
3. Polyneuropathy

Holmes' Cerebellar Degeneration

1. Starts in middle life (35-40 years)
2. Cerebellar signs
3. Pyramidal signs

Dejerine Thomas Olivopon To Cerebellar Atrophy

1. Usually starts about 50-60 years of age
2. Cerebellar signs
3. Mental changes
4. Parkinsonian features
5. Deep reflexes brisk or depressed

Lhermitte Lejomme's Olivorubrocerebellar Atrophy

Clinically resembles Olivopontocerebellar atrophy. Only distinguished on autopsy.

Delayed Cerebellar Degeneration

Resembles Holmes' but starts at about 60 years.

Cerebellar Neoplasms

1. Cerebellar signs of gradual onset.
2. Signs of raised intracranial tension.

Cerebellopontine Angle Tumor (E.g. Acoustic Neuroma)

1. Cerebellar signs on the same side
2. 5th, 7th and 8th nerve affection on the same side or on both sides. Corneal reflexes are often the earliest to be affected
3. Pyramidal signs on the same or on both sides
4. Signs of raised intracranial tension

Alcoholic Cerebellar Degeneration: Acute or gradual onset of cerebellar signs in an alcoholic. It has to be differentiated from the above conditions.

10 › Tuberculosis of Nervous System

Tuberculosis can affect the nervous system in the following ways:

I. Meningitis
II. Tuberculoma
III. Vasculitis causing infarcts
IV. Tuberculosis of the spine causing Pott's paraplegia
V. Intraspinal granulomas
VI. Arachnoiditis

I. Tuberculous Meningitis (TBM)

A. Pathology

1. *Meninges:* At the base of the

brain, a mass of gelatinous exudate obliterates the cisterna pontis and cisterna interpeduncularis and extends anteriorly along the floor of the third ventricle to cover the optic chiasma and distal ends of the internal carotid arteries. The meninges over the convexity of hemispheres are less involved.

2. *Brain:* Diffuse brain involvement commonly occurs due to:
   a) *Edema* in the absence of infarction
   b) *Infarction* more common in the middle carotid territory
   c) *Tuberculoma*

B. Relation of pathological lesions to signs and symptoms

1. *Meningeal exudate:*
   a) Hydrocephalous.
   b) Cranial nerve palsy.
   c) Meningeal sign.
2. *Infection of brain substance:*
   a) Clouding of consciousness.
   b) Convulsions.
   c) Hypothalamic and brain stem signs.
3. *Arteritis* and vascular obstruction: Focal neurological deficit.
4. *Allergic or hypersensitive:* Massive brain edema and raised intracranial tension in absence of hydrocephalous.

C. Clinical features

1. *Prodromal:*
   a) Listlessness, apathy, irritability, headache
   b) Anorexia, nausea, vomiting, and abdominal pain
   c) Low grade fever
2. Raised Intra-cranial pressure — Headache, vomiting, papilledema
3. *Focal deficit:*
   a) Convulsions
   b) Hemiplegia and monoplegia
   c) Painful ophthalmoplegia
4. *Signs of meningeal irritation:* Neck stiffness, Kernig's sign. etc.
5. *In children:* Progressive spasticity, decerebrate state, convulsions, coma. There is a greater incidence of hydrocephalous, convulsions and brainstem signs with decerebration in children.
6. *Of complications*

D. Clinical Stages

1. Meningeal signs only, without neurological involvement or impaired sensorium.
2. Meningeal signs with neurological involvement but without impaired sensorium.
3. Meningeal signs with neurological involvement and impaired sensorium.

E. Effect of Treatment

Antituberculous treatment modify the course of the illness. If the treatment is started early, prompt and complete remission occurs. If it is started late is not of much avail. Although the patient may recover, he may be left with sequelae.

F. Sequelae

1. *Due to basal exudates:*
   a) Hydrocephalous
   b) Cranial nerve palsy: Deafness, blindness and ophthalmoplegia
2. *Due to spinal block:* Paraplegia, quadriplegia
3. *Due to arteritis:* Hemiplegia
4. *Miscellaneous:*
   a) Mental disturbances
   b) Convulsions
   c) Endocrine disturbances
   d) Ectopic ossification of the hip joint

G. Treatment

1. *Antituberculous Drugs:*

   Those that diffuse freely through

the blood-brain barrier are INH, rifampicin, pyrazinamide, cycloserine and ethionamide. Drugs that diffuse only in the presence of meningeal inflammation are streptomycin and ethambutol. A combination therapy is given for at least 1-1/2 years total of 18 months with two or three of the following: Streptomycin, Isonex, Ethambutol, Rifampicin, Cycloserine, Pyrazinamide and Ethionamide.

2. Steroids:
   a) Toreducepia-arachnoidadhesions
   b) To reduce toxicity and give a feeling of well being
3. *Hydrocephalus:*
   a) Ventriculo-atrial shunt
   b) Anterior third ventriculostomy
   c) Deroofing the fourth ventricle
4. *Spinal Block:*
   a) Oral steroids.
   b) Intrathecal 50 mg hydrocortisone.
   c) Intrathecal streptodornase and streptokinase.
   d) Surgical decompression arachnoiditis.

II. Tuberculoma

A. *Definition*: Single or multiple lesions or tumor-like masses of characteristic granulation tissue which produces symptoms of a space-occupying lesion.

B. *Pathogenesis*: Tuberculomas result from hematogenous spread of infection from lungs, lymph nodes, peritoneum, kidney, bone, skin, etc. The early lesion appears in the cortex or the subcortical region and consists of a central area of incipient or frank necrosis surrounded by epithelioid or giant cells. In some, polymorphs may be seen.

Initially microscopic foci are multiple and around the perivascular area. The lesion enlarges through expansion of the individual foci and later by means of their conglomeration. Thus, tuberculomas are formed which remain isolated or merge together to form a solid mass.

The ultimate evolution depends on hypersensitivity and immune responses. Healing occurs by fibrosis and calcification which impairs the oxygen supply to the organisms by obliterating their vascular channels. There is little participation of fibroblasts till the lesion reaches the surface meninges.

C. *Site*
   1. Posterior fossa and brainstem
   2. Supratentorial: Parietofrontal
   3. Intraventricular
   4. Extradural intracranial: Rare

D. *Clinical Features*
   1. Signs of raised intracranial tension
   2. False localizing signs which may not be false localizing but due to multiple lesions, predominant signs due to a large mass and false localizing signs due to a smaller lesion elsewhere
   3. Focal signs

E. *Investigations*
   1. *X-ray skull:*
      a) Irregular, broken, calcareous shell
      b) Raised intracranial tension
      c) Lobulated calcification, radiolucent in the centre but dense at the periphery
      d) Nodular calcification: Multiple calcareous concretions grouped together
   2. *Angiogram:*
      a) Tumor blush
      b) Reduction in the caliber of the blood vessels traversing the tumor



Fig. 6.101 : Ring enhancing lesions

3. *CT Scan or MRI*: Ring-enhancing lesion on contrast pictures (see below)

F. *Treatment*

Medical:

a) Antituberculous drugs

b) Measures to reduce ICT

Surgical: Excision of tuberculoma

G. *Prognosis*

With antituberculous drugs mortality is reduced to less than 10%. Causes of postoperative deaths are basal meningitis and raised ICT. Morbidity is still high. Blindness, convulsions, hemiplegia and ataxia account for 10% of the cases, 60-70% return to normal life.

III. Tuberculosis of The Spine: Pott's Paraplegia

A. Mechanisms of Paraplegia

1. Fluid abscess in the spinal canal
2. Paraspinal abscess invading the spinal cord
3. Granulation tissue encircling the dura
4. Sequestrated bone
5. Dislocation of the vertebra
6. Thick transverse ridge of the fibrous tissue pressing on the spinal cord and causing ischemia
7. Thrombosis of the radicular artery
8. Tuberculous arteritis of the radicular artery
9. Artery compressed in the intervertebral foramen
10. Pachymeningitis
11. Combination

B. Clinical Picture

1. **Paraplegia in a known case of spinal tuberculosis:** It may begin at any time and during any phase or stage of the vertebral disease, even after apparently sound healing. It is the commonest mode of presentation and easy to diagnose.
2. **Paraplegia as a presenting symptom**
   a) Pain and tenderness in the affected part
   b) Muscle spasm
   c) Restricted spinal movements
   d) Deformity — Gibbus
   e) Palpable cold abscess

   X-ray
   a) Deformity
   b) Diminished joint space
   c) Calcification
   d) Cold abscess
3. **Spinal tumor syndrome**

   There is evidence of spinal cord compression without any clinical or radiological evidence of the disease of the spine. An X-ray usually reveals abnormality in majority of the cases but usually it is detected retrospectively.
4. **Paraplegia due to TB of the posterior neural arch**
   a) Lesion of the pedicles and/or the lamina
   b) Clinically there may be local pain with progressive paraplegia
   c) **X-ray**
      i) Paravertebral shadow of soft tissue
      ii) Destruction of the affected part

C. Treatment

1. **Medical:** Refer TB meningitis
2. **Surgical**
   a) *Indications:*
      i) Paraplegia whilst patient is under adequate conservative treatment for spinal tuberculosis.
      ii) Paraplegia is deteriorating despite conservative treatment
      iii) Paraplegia is of rapid onset
      iv) Paraplegia is complete or severe
      v) Paraplegia is recurrent

vi) Paraplegia is due to disease of the posterior neural arch

vii) Spinal tumor syndrome

viii) When conservative treatment is usually hazardous or impossible e.g. Bed sores, spasms spasticity make immobilization hazardous or in old age, where immobilization is dangerous.

b) *Methods*

i) *Anterolateral decompression:* The spinal canal is exposed through the lateral extrapleural approach and intraspinal abscess, granulation tissues or debris anterior to the spinal cord are removed.

ii) *Costo-transverse section:* This is useful in a poor risk patient. It is not useful for intraspinal tumors as the abscess is evacuated without exposing the spinal canal.

iii) *Anterior approach:* Full visualization of the lesion is allowed by a wider anterior exposure, to facilitate complete excision of all the diseased and devitalized tissues and to provide for immediate fusion by strut graft when there is compression between two adjacent healthy vertebral bodies.

iv) *Laminectomy:* It is contra-indicated in TB of the vertebral body. However, it is the only correct approach in spinal tumor syndrome and posterior neural arch involvement.

IV. Intraspinal Granulomas

Intraspinal granulomas resemble intraspinal SOL

They may be:

A. Extradural

B. Intradural but extramedullary

C Intramedullary

V. Radiculomyelopathy with Spinal Meningitis (Arachnoditis)

A. Infective

1. Tuberculous:
   a) Primary spinal
   b) Secondary to tuberculous basal meningitis.
   c) Secondary to tuberculous vertebral caries.
2. Syphilis
3. Pyogenic
4. Cryptococcus neoformans

B. Non-infective

1. Prolapsed intervertebral disc
2. Trauma
3. Cervical spondylosis
4. Rheumatoid arthritis
5. Postoperative
6. Chemical: Penicillin, streptomycin, anesthesia
7. Intraspinal tumors, spinal angiomas or disseminated sclerosis

C. Idiopathic

Clinical Features

A. Subacute

Onset:

1. Root pains and tingling and numbness with a level of sensory loss and posterior column affection
2. Pain and stiffness of the spine
3. Limb paralysis: Upper motor neurone or lower motor neurone type
4. Bladder: Urinary retention

Presentations:

1. Single level of neurological lesions resembling transverse myelitis

2. Multifocal radiculomyelopathy (multiple levels)
3. Ascending variety (resembling Guillain Barre syndrome)

B. Chronic

1. Slowly progressive over months or years, resembles spinal tumors
2. Root pains — scattered, persistent or severe
3. Lower motor neurone signs in the lower limbs with sensory level higher up

C. Myelogram

1. Dye moves slowly with multiple filling defects and fragmentation.
2. Total block with ragged or concave edge or a pitch fork appearance.
3. Multiple filling defects.
4. Large area of candle glittering.
5. In cauda equina region rat-tail or bundle of faggot stick appearance.
6. Multiple, small, rounded, clear areas of cyst formation.

Prognosis

1. In early cases the prognosis is good with treatment.
2. If there is a delay in the diagnosis irreparable damage may occur.

Treatment

A. Medical

1. Antituberculous drugs
2. Steroids: Prednisolone 60 mg for 1 month followed by lower doses for 3 months
3. Intrathecal hydrocortisone 50 mg. twice weekly
4. If Cryptococcal: Amphotericin B

B. Surgical

1. Decompression with laminectomy
2. Removal of the inflamed meninges

11 Cerebrovascular Diseases

Blood Supply of Cerebral Hemispheres

Cerebral hemispheres receive blood supply from Carotids and Vertebral arteries. Right carotid arises from the arch of the aorta and left carotid arises from brachiocephalic which arises from the aortic arch. Vertebrals arise from the subclavian arteries and the two vertebrals join to form the basilar artery which then bifurcates into two terminal branches-right and left posterior cerebral arteries. The carotid and vertebral artery system join at the base of the brain to form the circle of Willis.

The Anterior Cerebral Artery (ACA)

ACA runs anteriomedially to the interhemispheric fissure, where it joins the opposite ACA by anterior

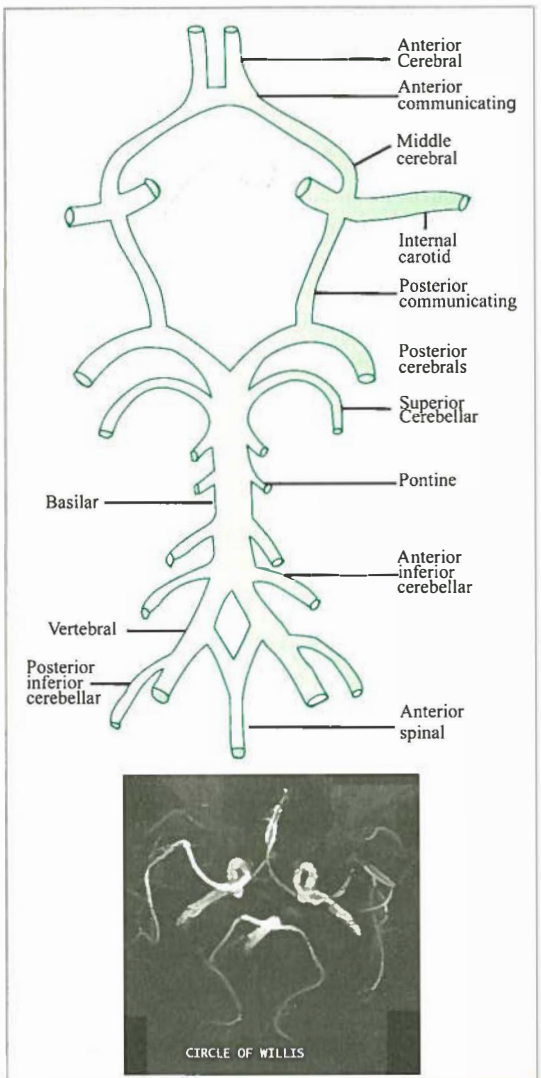


Fig. 6.102: Circle of Willis

communicating artery (anterior portion of Circle of Willis - Fig. 6.71). ACA gives origin to -

1. Medial lenticular branches which supply dorsal aspect of the optic chiasma and hypothalamus, and the medial striate artery (Heubner's artery) which supplies blood to the anteroinferior limb of the internal capsule and anterior aspects of putamen and caudate nuclei.
2. Callosal branches which supply the septum pellucidum and the fornix.
3. Hemispheric branches which supply the medial surface of the hemisphere and upper border of frontal and parietal lobes.

The Middle Cerebral Artery (MCA)

MCA supplies most of the lateral surface of the cerebral hemisphere and deep structures of the frontal and parietal lobes. It gives lenticulostriate arteries, which nourishes the adjacent corona radiata, external capsule, claustrum, putamen, part of globus pallidus, body of the caudate nucleus and superior portion of the anterior and posterior limbs of the internal capsule. Other branches are orbitofrontal and anterior temporal arteries. The main trunk then divides into proximal and distal group of arteries.

The Posterior Cerebral Artery (PCA)

PCA are the terminal branches of the Basilar artery and supplies the occipital lobes, the inferomedial portions of the temporal lobes, medial ventral, lateral ventral, posterior and superior thalamus, hippocampus fornices and psalterium.

Cerebrovascular Syndromes

Stroke: It is a relatively abrupt onset of focal neurological deficit resulting from diseases of arteries or veins that serve the central nervous system.

Types

1. *Completed stroke:* It is the term applied to the temporal profile of the stroke syndrome in which the deficit is prolonged and often permanent. Most of them reach the maximum of neurological dysfunction within an hour of onset.
2. *Stroke in Evolution:* It is the term applied to the temporal profile in which the neurological deficit occurs in a step wise or progressive fashion, culminating in a major deficit in the absent of treatment. In carotid territory if the progression has stopped for 24 hours, it is not likely to progress. However in vertebro-basilar territory the deficit may progress for up to 72 hours.

Transient Ischemic Attacks (TIA)

TIAs are sudden episodes of focal non-convulsive neurologic dysfunction that completely resolves within 24 hours but mostly by 1 hr. They are vascular in etiology and commonly last 2-15 mins and are followed by complete recovery.

1. TIA in Carotid system: This is characterized by one or more of:
   a) Ipsilateral amaurosis fugax
   b) Contralateral hemiplegia
   c) Contralateral hemianesthesia
   d) Contralateral homonymous hemianopia
   e) Aphasia
2. TIA in Vertebrobasilar system: This is characterized by one or more of the following:
   a) Bilateral or shifting motor or sensory dysfunction
   b) Bilateral homonymous hemianopia
   c) Diplopia, dysphagia or dysarthria by itself are not considered TIAs, however in combination with (a) or (b) should be considered as vertebrobasilar TIAs.

Causes

I. **Cerebral Infarction (85%):** This may be due to
   a) *Thrombosis:* Due to atherosclerosis, syphilis or TB
   b) *Embolism:* This involves predominantly MCA and PCA. ACA and Basilar arteries are not commonly involved. Embolus may arise from
      1. Heart: Myocardial infarction, mural thrombus arrhythmias, valvular heart diseases, mitral valve prolapse, prosthetic valves, infective endocarditis, marantic endocarditis, congenital heart disease, cardiac tumors.
      2. Extracranial Vasculature

c) *Lacunar infarction* is related to hypertension and affects small penetrating vessels of basal ganglia or brainstem.

II. **Hemorrhage (15%):** This could be subarachnoid intra-cerebral or intraventricular, and may be due to:

1. Hypertension
2. Saccular aneurysms
3. Arteriovenous Malformations
4. Vasculitis
5. Blood dyscrasias
6. Drugs
7. Trauma
8. Neoplasms

Table 6.29 : Risk Stratification Score (ABCD Score)

Risk Stratification Score ABCD² Score	
Age > 60	1
Blood Pressure	
SBP > 140 or DBP > 90	1
Clinical Symptoms	
Unilateral weakness	2
Speech disturbance only without weakness	1
Duration	
> 60 minutes	2
10-59 minutes	1
Diabetes	
(oral medications / Insulin)	1

Score	Risk (3 month rate of stroke)
0	0
1	2
2	3
3	3
4	8
5	12
6	17
7	22

Risk of stroke after a TIA is 10-15% in first 3 months

Arterial Syndromes

I. **Carotid Artery Syndrome**

Occlusion of the ICA in the neck may be asymptomatic in the presence of adequate collateral circulation especially if the occlusion develops slowly. If the collateral circulation is inadequate, infarction of the homolateral hemisphere may occur.

It is characterized by:

1. Headache- localized or generalized with focal seizures
2. Contralateral hemiplegia
3. Contralateral hemianesthesia
4. Contralateral homonymous hemianopia
5. Aphasia (if dominant hemisphere is involved) or Apractagnosia (if non-dominant hemisphere is involved)
6. Amaurosis fugax or sudden transient monocular blindness either as a "Curtain" or "Shade" effect that progresses from the top to the bottom or the sides of the visual fields, or as an iris diaphragm.
7. Transient, partial, ipsilateral Horner's syndrome may occur due to compromise of the sympathetic fibers.
8. Mid-cervical bruit extending throughout systole (50% stenosis) or even extending to diastole (90% stenosis). If stenosis is greater than 90% it may disappear.
9. Lowered retinal artery pressure in the ipsilateral eye on ophthalmo-dynamometry.

II. **Anterior Cerebral Artery Syndrome**

It depends upon the site of occlusion and patency of the collaterals.

A. **Hemisphere branch occlusion**

1. Contralateral hemiplegia affecting the legs more than the arms.
2. Contralateral hemianesthesia affecting the legs more than the arms
3. Sphincter disturbances
4. Transcortical motor aphasia (Unilateral left sided lesions)
5. Gait and postural disorders
6. Paratonia and abnormal reflexes (grasp, snout, sucking and rooting)

7. Loss of initiative and spontaneity
8. Memory and emotional disturbances
9. Akinetic mutism (Bilateral mesiofrontal involvement)

B. Medial striate or Heubner's artery occlusion

Leads to contralateral monoparesis with involvement of face and arm without sensory loss.

C. Basal branches occlusion: Leads to transient memory disorders, anxiety and agitation.

D. Pericallosal artery occlusion: Causes Apraxia, agraphia and tactile anomia of the left hand.

III. Middle Cerebral Artery (MCA) Syndrome

The clinical picture depends on the site of occlusion and availability of collaterals. It is characterized by:

1. Contralateral hemiplegia affecting the face and arm more than the leg.
2. Contralateral hemianesthesia affecting the face and arm more then leg. There is also loss of cortical sense like stereognosis, discrimination and tactile extinction.
3. Contralateral homonymous hemianopia or inferior quadrantanopia.
4. Aphasia when dominant lobe is involved
5. Inattention, neglect, denial of illness and apractic syndromes mainly with nondominant hemispheric lesions.
6. Paresis and apraxia of conjugate gaze to the opposite side.
7. Alexia and agraphia (Left angular gyrus lesion)
8. Gerstmann's syndrome (Finger agnosia, acalculia Agraphia and right-left disorientation).

IV. Posterior Cerebral Artery (PCA) Syndrome :

The clinical picture varies with the site of occlusion and availability of collaterals. Partial syndromes are usually present.

A Hemisphere branch occlusion :

1. Contralateral homonymous hemianopia with occasional macular sparing
2. Visual and Color agnosia

B. Bilateral hemisphere branches occlusion:

1. Bilateral homonymous hemianopia
2. Cerebral blindness - bilateral visual loss with normal pupillary reflexes and fundus
3. Apraxia for ocular movements
4. Agnosia for familiar faces (Prosopagnosia)
5. Agitated delirium (mesio-temporo-occipital lesion)
6. Anton syndrome or denial of blindness (parietal lobes involved)
7. Balint syndrome- optic ataxia, psychic paralysis of fixation, inability to look to the peripheral field and disturbance of visual attention.

C. Callosal branch occlusion

This affects the left occipital region and splenium of corpus callosus and causes Alexia without agraphia (agnostic alexia)

D. Penetrating branch to thalamus occlusion

1. *Dejerine and Roussy's Syndrome :*
   a) Contralateral hemianesthesia.
   b) Transient contralateral hemiparesis.
   c) Dysesthesia on the affected side (Thalamic Pain)
   d) Involuntary movements - Choreoathetosis, hemiballismus, etc. (Ventral posteromedial and postero - lateral nuclei are affected).
2. Aphasia (Left pulvinar nuclei affected).
3. Amnesia (Mesial Thalamoperforators affected)
4. Akinetic mutism

E. Penetrating branch to midbrain occlusion

1. Ipsilateral oculomotor palsy with

contralateral hemiplegia *(Weber's Syndrome)*

2. Ipsilateral oculomotor palsy with contralateral cerebellar ataxia *(Nothnagel Syndrome)*
3. Ipsilateral oculomotor palsy with contralateral rubral tremor / ataxia and contralateral hemiplegia (Benediect's syndrome).
4. Combination of Nothnagel and Benedikts syndrome is Claude's Syndrome - Ipsilateral oculomotor palsy with contralateral ataxia and tremor. No hemiplegia.
5. *Parinaud's syndrome*
   a) Supranuclearparalysisofelevation
   b) Defective convergence
   c) Convergence retraction nystagmus
   d) Lid retraction (Collier's sign)
   e) Skew deviation (Setting sun sign)
   f) Light near dissociation
6. Unilateral or Bilateral Internuclear ophthalmoplegia
7. Pseudoabducent palsy
8. Peduncular hallucinations - often silent, mobile and colorful and frequently pleasurable
9. Decerebrate rigidity, Locked-in syndrome and disturbances in consciousness.

Lacunar Infarctions

Lacunae are small ischemic infarcts that range in diameter from 30 - 300 μm and result from occlusion of the penetrating arteries, chiefly from anterior choroidal, middle cerebral, posterior cerebral or basilar arteries. The most frequent sites are putamen, bases pontis, thalamus, posterior limb of internal capsule and caudate nucleus. The primary pathology is lipohyalinosis of the arteries.

Long-standing hypertension and atherosclerosis are common predisposing factors. TIAs shortly before the onset of a lacunar stroke is frequent, but headache is infrequent. Although they usually carry good prognosis, multiple lacunae may cause pseudobulbar palsy and dementia.

Clinical Syndromes

1. **Pure motor hemiparesis:** Lacunae in internal capsule or basis pontis causes opposite face and arm weakness more than leg. There is no aphasia, apractagnosia, sensory, cortical or visual disturbances.
2. **Pure Sensory stroke:** Lacunae in ventral lateral nucleus of thalamus causes paresthesias and hemi-sensory loss on opposite side. Subjective symptoms are much more than objective sensory loss.
3. **Ataxic Hemiparesis:** Lacunae in posterior limb of internal capsule or basis pontis cause weakness predominantly in the legs and incoordination of the arm and legs without dysarthria and facial involvement.
4. **Dysarthria - Clumsy hand syndrome:** Lacunae deep in basis pontis causes supranuclear facial palsy, dysarthria, deviation of the tongue and loss of fine motor control of the hand.

Treatment of Acute Ischemic Stroke and Transient Ischemic Attack (TIA)

1. *Anti-hypertensive drugs:* BP should not be lowered precipitously. BP must be lowered only in severe cases (systolic BP > 200 mmHg). Usually Calcium antagonists are preferred. Nimodipine, a cerebroselective calcium channel blocker, can be used.
2. *Intravascular volume must be maintained*
3. *Osmotic therapy* with mannitol may be given to control edema of large infarcts, but isotonic volume must be replaced to avoid hypovolemia.
4. *Anticoagulants*: Initially with heparin, including low molecular weight heparins.

Thrombolysis

Recombinant Tissue Plasminogen Activator (rtPA) is approved for thrombolysis in acute stroke.

Dosage : 0.9 mg/kg - (10% as bolus, remaining over 60 minutes) maximum of 90 mg.

Indications

1. Diagnosis of stroke (Nonreversible symptoms)
2. Duration of symptoms < 3 hrs. (max - 4.5 hrs). Maximum time duration in a stroke during which thrombolysis can be attempted (WINDOW PERIOD) is 4.5 hours.
3. CT scan showing no hemorrhage or edema of > one-third MCA territory
4. Age > 18 yrs.
5. **Thrombolysis** (see below)
6. **Other medical therapy** :
   a. Antiplatelets : Asprin, Clopidogrel
   b. Cholesterollowering agents: Statin therapy
   c. Prevention of DVT, bedsores, aspiration pneumonias, urinary tract infections.

Contraindications

1. BP> 185/110 despite treatment
2. Platelets <1 lac, HCT <25%
3. Glucose <50 or >400 mg/dl
4. Use of heparin within 48 hrs
5. Prolonged PTT or INR
6. Rapidly improving symptoms
7. Prior stroke or head injury within 3 months.
8. Prior IC bleed
9. GI bleed in last 21 days
10. Recent MI
11. Coma / stupor

Intracerebral Hemorrhage

Causes

1. Arterial hypertension
2. Berry aneurysm
3. Arteriovenous malformations
4. Bleeding diathesis
5. Primary or metastatic brain tumors
6. Vasculitis
7. Cortical vein or dural sinus thrombosis

Clinical features

I. General features

A. Sudden onset without any prodromal symptoms

B. Headache and vomiting

C. Various level of alertness or unconsciousness

D. Convulsions are rare and previous history of hypertension may be present in 80 - 90%

E. Retinal hemorrhages may be present on ophthalmoscopy.

II. Specific signs of location

A. *Putaminal hemorrhage* (55% of cases)

1. Flaccid hemiplegia
2. Hemianesthesia
3. Homonymous hemianopia
4. Transient global aphasia (dominant hemi-sphere) or apractagnosia (nondormant hemisphere) with impaired ability to perform tasks like striking a match or dressing etc.
5. Contralateral gaze palsy - patient looks to the side of lesion.
6. Coma if it ruptures into the ventricles.

B. *Thalamic hemorrhage* (20-30% of cases)

1. Hemianesthesia affecting all modalities of sensations
2. Hemiparesis
3. Conjugate gaze palsy (as putaminal hemorrhage)
4. Nonfluent, anomic aphasia with intact repetition and comprehension with lesions of the dominant thalamus.
5. Disorders of movements if extension to sub thalamic regions - supranuclear vertical gaze palsy, convergence retraction nystagmus, skew deviation, etc.

C. *Cerebellar hemorrhage:* (10% of cases)

1. Headache usually occipital and of sudden onset
2. Nausea and vomiting especially with head motion
3. Vertigo, dizziness and drowsiness
4. Ipsilateral facial palsy
5. Ipsilateral gaze palsy

6. Trunk ataxia more than ipsilateral limb ataxia
7. Horizontal nystagmus with fast component towards the side of lesion
8. Small reactive pupils
9. Neck rigidity, slurred speech & bilateral hyper-reflexia and Babinski signs may be present.

D. *Pontine hemorrhage* (5-7% of cases)

1. Coma present at the onset
2. Hyper pyrexia
3. Pin-point reactive pupils
4. Bilateral pyramidal signs
5. Gaze palsy
6. Ocular bobbing - rapid conjugate downward movement of the eyes followed by a slow drift upward to the primary position.

E. *Subcortical white mater* (10-15% of cases)

The first four hemorrhages described above are commonly due to hypertension. However, subcortical white mater or lobar hemorrhages are due to other causes. The clinical syndrome produced by lobar hemorrhage resembles occlusive cerebrovascular diseases.

Mechanism of Neurological deficits in Hemorrhage

The blood that escapes from the blood vessels into the cerebral tissue directly injures the axons, cell bodies, glia and arterioles and venules, which may contribute to continued bleeding.

Hemorrhage in the periventricular brain is likely to rupture through the ependyma into the ventricular system with immediate impairment of consciousness and potential for delayed development of obstructive hydrocephalus.

As the escaped blood clots, vasogenic brain edema develops because blood brain barrier is disrupted. The zone of vasogenic edema surrounds the clot. Breakdown of constituents within the clot may create an osmotically active region that draws water into the clot from surrounding edematous brain. The combined effects of blood clot and vasogenic edema acts as a supratentorial mass lesion that produces herniation syndromes.

Table 6.30 : Differences between Hypertensive and Lobar Hemorrhages

	Hypertensive hemorrhage	*Lobar hemorrhage*
1. Etiology	Hypertension	Vascular anomaly, Blood dyscrasias, Tumors, Angiopathy, etc.
2. Site	Putamen, thalamus, cerebellum and pons	Parieto-temporal area occipital lobes (subcortical white matter)
3. Convulsions	Rare	More common
4. Coma	Common	Uncommon even with massive hemorrhage because it does not rupture in the ventricles
5. Functional Recovery	Poor	Good. Full recovery in 50% of cases

Cerebral Berry Aneurysms

Cerebral aneurysms are more common in females and increase with age. Aneurysms under 1 cm diameter are not likely to rupture.

They are characterized by absence of one layer of the vascular wall (muscular media) and absence or fragmentation of elastic lamina. Anterior circulation has 85% and posterior circulation 15% of aneurysms. Fifteen to twenty percent have multiple aneurysms. Congenital factors are responsible for the defects of the vessel wall, but since it increases with age, degenerative processes also may be responsible.

The three common sites of aneurysm are:

1. Junction of anterior communicating with anterior cerebral artery
2. Junction of internal carotid and posterior communicating artery
3. Main division of middle cerebral artery.

Syndromes

I. *Intracavernous Aneurysm of Internal Carotid Artery*

A. *Unruptured*

1. Ocular pain

2. Sixth, third or fourth nerve palsies with small pupils due to occulosympathetic dysfunction.
3. Pain and numbness in the distribution of ophathlmic division of fifth nerve.
4. Rarely bilateral ophthalmoplegia

B. *Ruptured (Carotid-cavernous fistula)*

1. Ocular Pain
2. Pulsating exophthalmos
3. Cephalic or ocular bruit (it diminishes on digital compression of carotid in the neck)
4. Chemosis and redness of conjunctiva
5. Diplopia due to sixth, third or fourth cranial nerve palsy.
6. Decreased visual acuity due to pressure on the optic nerve, glaucoma or retinal and optic nerve hypoxia.

II. Posterior Communicating Artery Aneurysm

1. Headache and ocular pain
2. Oculomotor paralysis with pupillary involvement

III. Middle Cerebral artery aneurysm

1. Headache
2. Convulsions: partial or generalized tonic-clonic
3. Aphasia
4. Transient sensorimotor deficits

IV. Basilar Artery Aneurysm

Unruptured basilar aneurysms may present with

1. Vertebrobasilar TIA
2. Alternating hemiplegia with cranial nerve palsy
3. Ataxia
4. Cerebello - pontine angle syndrome
5. Atypical facial pains
6. Sixth seventh or third nerve palsy
7. Non-hemorrhagic thalamic infarction

Subarachnoid Hemorrhage

Subarachnoid hemorrhage is bleeding into the cranial subarachnoid space

Causes

I. Primary

1. Saccular aneurysm
2. Arteriovenous malformation
3. Vasculitis
4. Cortical thrombophlebitis
5. Blood dyscrasias
6. Spontaneous

II. Secondary: Intracerebral hemorrhage leaking into the ventricular system.

Clinical Features

I. Symptoms of raised intracranial pressure: There is a sudden onset of severe, excruciating headache which radiates to the neck and is increased by neck flexion, Valsalva's maneuver and head movements. It is associated with vomiting papilledema and altered consciousness. Rarely syncope, convulsions, confusion and low back-pain may occur.

II. Signs of Meningeal irritation: Once blood has leaked into subarachnoid space there is usually neck stiffness, positive Kernig's sign and positive Brudzinski's sign.

III. Associated Signs of aneurysm: Ocular pain due to mass effect or paralysis of oculomotor cranial nerve may be present.

IV. Focal Signs: Focal signs are usually absent. However they may occur due to spasm of the surrounding artery, intracerebral extension, cerebral edema or mass effect from extra-parenchymal hematoma. The focal signs may be sudden visual loss, hemiparesis, aphasia and sensory loss.

Clinical Grades (Hunt 1967)

Complications

I. Neurological

1. *Rebleeding:* Bleeding may recur within 3 days and peaks at 7-10 days after the initial bleed. It declines after 30 days and long- term recurrence of bleeding occurs in 3.5%
2. *Vasospasm:* This may occur in 30% of cases

due to release of vasoactive substances from blood into the subarachnoid space. Spasm induced ischemia may lead to hemiparesis, cortical sensory loss, hemianopia, altered consciousness and urinary incontinence.

3. *Others:* Hydrocephalus, cerebral edema and convulsions, hyponatremia cerebral salt wating syndrome.

II. Medical

1. *Pulmonary:* Neurogenic pulmonary edema pneumonia, atelectasis, etc.
2. *Cardiac:* Cardiac arrhythmias like premature beats, ventricular tachycardia, ventricular fibrillation, etc. These are due to stimulation of autonomic nervous system by subarachnoid blood.
3. *Others:* Urinary tract infection, vaginitis, gastrointestinal hemorrhage, thrombophlebitis and SIADH

Management

I. *Medical*

1. *Measures to reduce the raised intracranial tension:* Mannitol 350 mg. intravenously daily for 3-4 days, furosemide 40 mg orally or glycerol 50-200 ml. orally daily are useful. Dexamethasone 4 mg 6 hourly parenterally also helps to lower the intracranial tension.
2. *General Measures:* Bed-rest (for atleast 3 weeks and about 6 weeks if surgery is not contemplated), analgesics, stool softeners.
3. *Antihypertensive drugs*: If BP is high, it should be lowered with appropriate drugs. BP should be lowered very gradually and not abruptly, as it will disrupt cerebral autoregulatory reflexes.
4. *Nifedipine* 10 mg sublingual is useful to immediately lower the blood pressure, it could be repeated after 10 to 15 minutes up to 40-60 mg. Diazoxide and Sodium nitroprusside are other useful drugs. However they have to be given IV and are hence not used nowadays.
5. *Nimodipine* 30 mg, tds, is the drug of choice as it is a specific cerebrovascular Calcium channel antagonist. It is available IV also.
6. *Antiplatelet agents:* Low dose Aspirin (75 to 325 mg) and Ticlopidine have been used.
7. *Anticoagulants:* Warfarin when indicated.
8. *Epsilon amino caproic acid* (EACA) 24-48 gm/day protects against recurrence of hemorrhage by preserving the clot that ultimately seals the bleeding point.
9. *Management of unconscious patient*: See Coma
10. *Symptomatic treatment:* Analgesics like dextro propoxyphene or paracetamol are useful for severe headache.

II. Surgical

1. Aneurysmectomy: If the berry aneurysm is on the surface of the brain, it must be removed or ligated because there is a high incidence of recurrence of the bleeding in the second and third week.
2. Hydrocephalus: VP shunt
3. Newer Endovascular techniques - coiling or clipping of aneurysms.
4. Angioplasty of cerebral vessels in case of severe vasospasm when ischemic symptoms appear despite of maximum medical therapy.
5. Internal carotid artery ligation: This is done gradually over several weeks if the aneurysm is not surgically accessible.

12 Parkinsonism

Parkinsonism is a disorder of the extrapyramidal system, characterized by tremor, rigidity, bradykinesia and postural disturbances.

Parkinson's Disease (Paralysis Agitans)

Parkinson's disease (PD) most commonly affects persons over the age of 55 years, and is characterized by : bradykinesia, rest tremor, rigidity and postural instability. (Atleast two of these and a response to levodopa should be usually present to make the diagnosis). The substantia nigra has two parts, the pars reticulata (made up of nonpigmented cells) and the pars compacta (made of pigmented neurons).

Pathophysiology: The disease is uncommon before the

age of 40 years and there is a slight male preponderance. The Parsi community in Bombay had an age-adjusted prevalence ratio of 192/100,000, which is higher than that in most other studies. The incidence of PD is less in smokers but the cause of this is not known.

The corpus striatum has a rich concentration of acetylcholine (Ach). Ach is synthesized and released by small striatal neurons, upon which it has an excitatory effect. Dopamine is synthesized by the pigmented neurons (pars compacta) of the substantia nigra and is transported via the nigrostriatal pathway to the corpus striatum, where it has an inhibitory effect on striatal neurons. It is thought that a functional equilibrium exists in the striatum between acetylcholine (which is excitatory) and dopamine (which is inhibitory).

In PD, there is a loss of pigmented neurons in the substantia nigra in the midbrain and locus ceruleus in the pons, with characteristic intracytoplasmic, eosino-philic inclusion bodies (Lewy bodies) in the surviving neurons. As a result, the dopamine content in the corpus striatum is markedly decreased. At least 80% of the pigmented neurons in other parts of the CNS and also of certain nonpigmented neurons, especially in the nucleus basalis of Meynert (in the substantia innominata).

There may also be a decrease in other neurotransmitters like noradrenaline, 5 hydroxy-tryptamine (5 HT), gamma-aminobutyric acid (GABA), enkephalins and substance P.

The concentration of acetylcholine in the striatum is preserved but in those with dementia, acetylcholine content in the cerebral cortex is decreased, probably as a result of loss of neurons in the substantia innominata. Moreover, demented patients with PD, like those with Alzheimer's disease, also have a loss of somatostatin neurons in the cortex. Low 5 HT concentrations in the brain, may contribute to the depression commonly seen in patients with PD.

Etiology

I. **Idiopathic:** Primary or Paralysis Agitans.

II. **Secondary:**

- A. *Drugs:* Reserpine, Phenothiazines, butyrophenones, Metoclopramide etc.
- B. *Infection:* Encephalitis lethargica, AIDS, dementia complex, cysticercosis and Creutzfeldt - Jakob disease.
- C. *Vascular:* Atherosclerosis and Hypertension.
- D. *Toxic:* N-methyl-4-phenyl-tetradropyridine, (MTPT), Manganese carbon monoxide, carbon disulphide, cyanide and methanol.
- E. *Head-injury:*
- G. *Degenerative:* Alzheimer's disease, Pick's disease, Communicating hydrocephalous.

III. **Parkinsonism Plus Syndrome:**

- A. *Sporadic:*
  1. Progressive supranuclear palsy
  2. Shy-Drager syndrome
  3. Striatonigral degeneration
  4. Parkinson's disease - amyotrophic lateral sclerosis
  5. Cortical - basal ganglionic degeneration
  6. Olivopontocerebellar atrophy
- B. *Inherited:*
  1. Huntington's disease
  2. Olivopontocerebellar atrophy
  3. Hallervorden - Spatz disease
  4. Neuroacanthocytosis

Clinical Features

The progression of the disease is usually gradual over many years but occasionally it may be more rapid over a few months.

1. The initial symptom is usually tremor involving one hand, which then spreads to involve the leg on the same side before becoming bilateral. It may also involve the head and jaw. The tremor is present at rest at a rate of 4-6 per second. It is absent during sleep. It is partially relieved by complete relaxation, when the patient is in a relaxed state of mind and during action. It is aggravated by anxiety. In some patients, there is also a faster, postural tremor at a rate of 7-8 per second. Other characteristics of parkinsonian tremor are supination - pronation of the forearm, adduction-abduction of the thumb and flexion-extension of the fingers (which gives rise to the 'pill rolling' tremor commonly seen).



Fig. 6.103: Mask like face in Parkinsonism

2. Rigidity manifests symptomatically as stiffness of the muscles and mainly involves the neck, trunk and proximal parts of the limbs. It is described as 'lead pipe' rigidity because the increase in muscle tone is present throughout the range of movement. When tremor is super-imposed on the rigidity, there is a 'cog wheel' effect, which is most easily elicited at the wrist and elbow.
3. *Bradykinesia* implies a difficulty in initiating voluntary movement (such as getting up from a chair) and a slowness of movement which results in a progressive increase in the time taken to perform daily activities. This is probably the most disabling feature of Parkinson's disease. Moreover, spontaneous movements like arm swing while walking are absent.
4. *Postural abnormalities* manifest as a flexed posture of the trunk and limbs together with a difficulty in maintaining one's balance when that posture is disturbed by an external force.
5. *Face:* The combination of these four cardinal features gives rise to characteristic signs and symptoms. The face has a mask like appearance with few spontaneous movements of expression and a staring appearance because of decreased blinking of the eyes. On tapping the glabella, the patient continues to blink with each tap (unlike in normal individuals where the blinking stops after a few taps).
6. *Eye movements* are usually normal except for difficulty in convergence. There may be some limitation of upward gaze and minimal disturbances of saccadic and pursuit eye movements.
7. The *voice* is slow, monotonous and of low volume.
8. *Increased sweating and seborrhea* is often noted on the face. There is difficulty in swallowing, especially later in the disease course, with consequent dribbling of saliva.
9. The *handwriting* becomes small (micrographia) and untidy.
10. *Movements:* Because of bradykinesia the patient often sits still in one posture with little movement for a long time. He may have difficulty in getting up from the chair or bed and in the later stages even rolling over in the bed may not be possible. Voluntary movements become slow and the patient takes a progressively longer time to perform everyday activities like dressing and bathing. Repetitive movements like supination - pronation of the forearm or tapping the floor with the feet are slow and of low amplitude. But sometimes, when the patient is agitated or startled, he is capable of rapid movement but this is only temporary.
11. Constipation is very common and urinary frequency and incontinence may also be present.
12. *Gait:* One of the earliest signs of Parkinson's disease is loss of arm swing while walking. The gait has other characteristic features. 'Freezing' implies a difficulty in starting to walk (start hesitation) and also an inability to maneuver through narrow passages such as through a doorway or around an obstacle (gait hesitation). The gait is usually shuffling and slow. Some patients have a festinant gait in that progressive steps become faster, as though the patient is chasing his centre of gravity. This may end in a fall.

    The posture is stooped with flexion of the neck, trunk and limbs. The arms are adducted, flexed at the elbow and wrist; there is ulnar deviation of the hand and flexion of the metacarpophalangeal joints with extension at the interphalangeal joints. When the patient is standing, a slight push forwards or backwards may make the

patient take a few steps in that direction to keep his balance propulsion and retropulsion respectively) and the patient may even fall. This is because the patient is unable to make the slight postural adjustments normally required to keep one's balance. Spontaneous falls are not frequent early in the disease. Postural hypotension may be present in a few patients.

There are no objective sensory impairments (other than an impairment of olfactory sensation in some patients). Both the deep and superficial reflexes are normal and there is no significant decrease in muscle power.

13. *Cognitive and psychiatric complaints* are common. Some of them may be side effects of drugs (e.g., confusional states, hallucinations and psychosis). About 40% of patients suffer from depression even early in the disease. The patient may also have difficulty in making decisions and may become dependent on others. There is thought to be a premorbid personality type in PD (introspective, rigid, diffident). The intellect is usually well preserved but late in the disease course about 15% of patient will develop frank dementia (when dementia is defined by DSM-III criteria).

Progress and Mode of Death

In most patients the disease progresses gradually over about 10 years until they become wheelchair-bound or bed ridden because of severe bradykinesia, rigidity and postural instability. Death may occur from aspiration pneumonia, septicemia from urinary tract infection, decubitus ulcers or from secondary causes like vascular disease or neoplasia.

Diagnosis

The diagnosis of Parkinson's disease is based on the clinical symptoms and signs and by excluding other causes of Parkinsonism (secondary Parkinsonism and Parkinsonism - plus syndromes).

Conditions which may initially be confused with PD are essential tremor and depression, which are far commoner conditions.

Essential tremor is often inherited as an autosomal dominant trait. It may appear at any age. It is mainly a postural tremor at a frequency of 5-8 per second, there usually being no tremor at rest. Other signs and symptoms of Parkinson's diseases are absent. Characteristically, alcohol reduces or abolishes the tremor and beta blockers and primidone are also useful.

Patients with *depression* often have an expressionless face, stooped posture and relative immobility and these may be confused with PD. Moreover, depression is a common accompaniment of Parkinson's disease and some who ultimately develop PD have depression as their presenting symptom. But in such cases, other features of PD will become manifest within a period of one year.

Other causes of psychomotor retardation should be considered and these include the normal aging process, drug intoxication, systemic illness, frontal lobe syndromes, akinetic mutism, catatonia, subcortical dementia, normal pressure hydrocephalus and other movement disorders.

Blood and CSF examination and cerebral imaging studies such as CT and MRI scans are non contributory in making the diagnosis of PD but may be of use when there is a suspicion of other causes of Parkinsonism. Positron emission tomography (PET) scans, when available, will show a decreased uptake in the striatum in patients with PD.

Staging

The ***Hoehn and Yahr Scale*** can be of use in assessing the severity of the disease and to decide the line of management.

Table 6.31 : Staging : Hoehn and Yahr Scale

Stage I	:	Unilateral involvement
Stage II	:	Bilateral involvement but no postural abnormalities.
Stage III	:	Bilateral involvement with mild postural imbalance; the patient leads an independent life.
Stage IV	:	Bilateral involvement with postural instability; the patient requires substantial help
Stage V	:	Severe, fully developed disease; the patient is restricted to bed and chair.

I. Anti-Parkinsonism Drugs

Drugs used in the treatment of PD (with the possible exception of deprenyl), do not alter the progression of the disease but they do enable the patient to remain independent and functional for a longer period.

The decision as to when to start treatment and with what drugs depends on the predominant symptoms at that time, the functional capacity of the patient and whether the patient is able to carry out his occupation and activities of daily life with reasonable efficiency. The staging system of Hoehn and Yahr can be of use in making this decision but the decision should be individualized for each patient.

Drug treatment should be delayed as long as possible, and when started, the dose of the drug should be gradually increased until the required benefit is achieved. The goal should be to relieve the symptoms to manageable levels and not necessarily to give complete relief from symptoms. This is because all the drugs have got side effects, both short term and long term, which are minimized by using smaller doses of the drugs.

A. *Patients in stages I and II of the Hoehn and Yahr scale* either require no treatment or may be treated with anticholinergics, amantadine or deprenyl.

   1. The *anticholinergics* are mainly useful in decreasing the rest tremor. These drugs attempt to maintain the ratio between dopamine and acetylcholine in the striatum. Commonly used drugs are trihexyphenidyl (1 to 2 mg qid), benztropine (0.5 to 1.0 mg tid), benzhexol hydrochloride (2 to 5 mg qid) and orphenadrine (50 mg qid), starting with a small dose. Frequent side effects are dryness of the mouth, constipation and slight blurring of vision which are not harmful in themselves. They should be used with caution in the elderly, as they can cause acute urinary retention and confusion. They are contraindicated in patients with glaucoma as they may precipitate an acute rise in the intra ocular tension.

   2. *Amantadine* is more effective than anticholinergics and is also useful in decreasing the tremor. It is an antiviral drug but in addition it releases stored dopamine from presynaptic terminals. Therefore it is only useful in the early stages of the disease. The usual dose is 100 mg bid. Side effects include ankle edema and livido reticularis (a reddish mottling of the skin of the lower extremities), both of which are not harmful) but in higher doses it may cause an acute confusional state.

   3. *Deprenyl (selegiline)* is a monoamine oxidase B inhibitor which inhibits the catabolism of dopamine in the brain (unlike MAO-A inhibitors which inhibit the catabolism of dopamine in the peripheral tissues). It could retard the progression of PD as judged by the duration of disease after which it becomes necessary to start levodopa. When used in conjunction with levodopa, it decreases the amount of levodopa required. Moreover, it is also useful in the management of the long term side effects of levodopa. Because of these properties, there is a trend to use deprenyl early in the course of PD. The average dose is 5 to 15 mg/day given in divided doses twice a day.

B. *Patients in stage III, IV and V of the Hoehn and Yahr scale* usually require levodopa. Anti-cholinergics or amantadine may be used in conjunction with levodopa to increase its efficacy or relieve specific symptoms like rest tremor.

   1. *Levodopa* is the cornerstone of drug therapy for Parkinson's disease. A good response to the drug is seen in at least 75% of patients. The most beneficial effect is on bradykinesia and postural instability.

      Dopamine does not cross the blood brain barrier but its precursor levodopa does. In the brain, levodopa is converted to dopamine by dopa-decarboxylase, thereby replenishing

the dopamine loss in the striatum. When given alone, it is converted to dopamine by dopa-decarboxylase present in peripheral tissues and only about 5% of the dose enters the brain. To prevent this, a peripheral decarboxylase present in peripheral tissues and only about 5% of the dose enters the brain. To prevent this, a peripheral decarboxylase present in peripheral tissues and only about 5% of the dose enters the brain. To prevent this, a peripheral decarboxylase inhibitor (either carbidopa or benserazide) is used in combination with levodopa. Such a combination markedly decreases (by about 80%) the amount of levodopa required.

Plain levodopa tablets are available but most patients receive levodopa-carbidopa combinations (L-C). These combination tablets are available as L-C 275 (250 mg levodopa; 25 mg carbidopa), L-C 110 (100 mg levodopa; 10 mg carbidopa and L-C Plus (100 mg levodopa; 25 mg carbidopa). The combination of levodopa and benserazide (in a ratio of 4:1) is not widely available.

L-C is started in small dose (e.g. half a tablet of L-C Plus tid or qid) and gradually increased every few days to achieve the required benefit. Even though the maximum dose of L-C 275 is about 6 to 8 tablets/day, there is a strong indication to use dopamine agonists or deprenyl in patients whose symptoms are not adequately controlled by smaller doses of levodopa. If a patient who is on plain levodopa is to be started on L-C, there should be at least a 12-hour gap between the discontinuation of levodopa and the starting of L-C.

Early side effects of levodopa are nausea, vomiting, cardiac arrhythmias and orthostatic hypotension. These are due to peripheral conversion to dopamine and are usually relieved by the addition of carbidopa. In addition, domperidone and taking the drug after meals are also effective in relieving the gastrointestinal side effects. An overdosage of levodopa can result in psychiatric and cognitive symptoms (such as delirium, hallucination and psychoses) and dyskinesias.

MAO-A inhibitors (used as antidepressants) are contraindicated and sympathomimetics should be used with caution as these can cause an acute rise in the blood pressure. Levodopa is contra-indicated in patients with malignant melanoma since levodopa is a precursor of melanin and may thus induce a recurrence of melanoma.

At least 65% receiving plain levodopa or L-C (without dopamine agonists or deprenyl) develop long term side effects in varying severity after 2-5 years:

a. Some patients, especially those with dementia, show a decreased response to the drug. Increasing the drug dose often results in an acute confusional state.
b. In the 'wearing-off' effect, the duration during which the drug is effective becomes progressively less. In such cases, the total daily dose should be given at more frequent intervals (sometimes every 1 to 2 hours) with a concomitant decrease in the amount of each dose.
c. In the 'on-off' effect, the patient fluctuates between 'on' periods with activity (and often also dyskinesias) and 'off' periods with akinesia and rigidity. These fluctuations are unpredictable, sudden and not related to the timing of drug intake.

Both the 'wearing-off' and 'on-off' effects are often associated with dyskinesias which take the form of choreoathetotic movements. These side effects may be due to defective absorption of levodopa because IV administration of the drug often results in a more stable clinical state.

These late onset side effects of levodopa are difficult to treat. The addition of deprenyl or dopamine agonists together with a decrease in the dose of levodopa may be of help and, the early introduction of either of these drugs may delay and minimize these side effects. Omitting levodopa completely has not been found to be useful and may even be harmful because of severe akinesia postural disturbances and rigidity which may result. Experimentally, sustained-release forms of L-C and subcutaneous administration of a dopamine receptors agonist (e.g. lisuride) via an infusion pump, are being tried to minimize these long term side effects.

2. *The dopamine receptor agonists are bromocriptine, pergolide and lisuride.* There are two known dopamine receptors in the brain-D_1 and D_2. Stimulation of D_1 receptors increase intracellular cyclic AMP but the same is not true on stimulation of D_2 receptors. D_2 receptors are more important in alleviating the motor symptoms of Parkinsonism but stimulation of D_1 receptors may produce additional benefit. Bromocriptine acts only on D_2 receptors. The usual dose is 15 to 30 mg/day given in divided doses (tid or qid), starting with a small dose (2.5 mg HS). Pergolide (1 to 4 mg/day) given tid or qid acts both on D_1 and D_2 receptors and therefore may be more powerful with a longer duration of action than bromocriptine. The side effects are similar to those of levodopa except that abnormal involuntary movements are less prominent and neuropsychiatric side effects may be more marked.

II. Other drugs:

1. Since depression is a common accompaniment, it should be identified and treated with tricyclic antidepressants and/or ECT when required. MAO-A inhibitors are contraindicated in patients receiving levodopa as they may cause an acute rise in the blood pressure.

   Psychiatric and cognitive symptoms such as confusional states, hallucinations and psychoses are more common in elderly patients who may also be demented. These symptoms are often caused or aggravated by the antiparkinsonian medication. In such cases, decreasing the dosage of the drug can be of use and, if necessary, psychosis can be treated with clozapine (which does not have significant extrapyramidal side effects).

2. Patients in whom a faster postural tremor predominates will benefit from beta blockers (propranolol - 40 to 80 mg tid; metoprolol) or primidone (50 mg HS, increased gradually to a maximum of 250 mg/day).

III. Regular exercise Program

Parkinson's disease is usually a slowly progressive disease and this should be impressed upon the patient and his relatives so that the patient is encouraged to live an independent life for as long as possible. A regular exercise program and accessory aids, when necessary, will help in achieving this objective. In the later stages, the help of a physiotherapist will be of value.

IV. Prevention of precipitating factors

Patients with PD have an aggravation of

symptoms if there is any super added illness and therefore infections should be promptly treated and surgery avoided unless absolutely necessary.

V. Surgery

Small surgical lesions of the globus pallidus or ventrolateral nucleus of the thalamus using steriotaxic techniques reduces or abolishes the tremor and rigidity in the contralateral limbs but does not benefit the bradykinesia and postural instability. At present it is rarely resorted to because of more effective drugs and the morbidity associated with the procedure. But it may be used in exceptional cases where the patient is young and has incapacitating tremor and rigidity on one side of the body which are resistant to drugs. Adrenal medullary transplant to the corpus striatum was initially thought to be helpful but its value has not been substantiated. At present, trials are on to the assess the usefulness of transplantation of fetal substantia nigra neurons.

Secondary Parkinsonism

1. **Drugs:** Reserpine (especially in large doses) depletes dopamine from the nerve terminals in the striatum while the neuroleptics and metoclopramide block the dopamine receptors) but anticholinergics are effective. The parkinsonian symptoms usually subside within a few months after discontinuation of the drug.
2. **Infections:** The patients with post encephalitic Parkinsonism tend to be of a younger age group than those with idiopathic PD and the Parkinsonism symptoms are usually milder and progression is slow. Moreover, other features such as oculogyric crisis, dyskinesias, tics, diplopia or other focal neurological deficits are frequently present. Response to levodopa is usually good.
3. **Vascular:** Parkinsonism resulting from multiple small infarcts have long standing, poorly controlled hypertension and also other features of multi-infarct dementia such as pseudobulbar palsy, exaggerated tendon reflexes, extensor plantars and a short stepped gait, apart from impairment of cognition. Response to levodopa is poor.
4. **Toxins:** MPTP is converted in the glial cells of the brain to MPP+ by the action of monoamine oxidase B. MPP+ is then taken up into dopaminergic neurons via the dopamine

Table 6.32 : Parkinsonism - Plus Syndromes

	Pathology	*Clinical*
1. Multiple system atrophy	Alpha synucleinopathies	Age of onset : 50 years Median survival 6-9 years Rigidity and akinesia predominate & tremor is less **Autoimmune involvement** - postural hypotension, sweating, pedal edema, syncope **Urinary involvement** - urgency, retention, incontinence, impotence in men **2 types of MSA** (p) Parkinsonian symptoms predominant (c) cerebellar symptoms predominant **Primary autonomic failure** : Shy-Drager syndrome
2. Progressive supranvellar palsy (Steele Richardsons syndrome)	Tau gene mutations	Age of onset : 6 -7 decade Survival : 5-10 years akinetic parkinsonism, unsteadiness, slowness, **Falls occur early in disease.** No tremor **Eye** : Supranuclear gaze palsy affecting down gaze first & then upward gaze. Some develop dementia
3. Corticobasal degeneration	Tau gene mutations	**Alien limb** - involuntary purposeless movements of a hand, rigidity, involuntary movements, myoclonic jerks, higher mental function involvements

re-uptake system. Once in the dopaminergic neurons, MPP+ combines with neuromelanin, releases toxic free radicals and thus destroys the dopaminergic neurons. Experimentally, it has been found that MPTP toxicity can be prevented by deprenyl (a monoamine oxidase B inhibitor), mazindol (a dopamine re-uptake blocker) and vitamins C and E (which are antioxidants and free radical scavengers).

MPTP induced Parkinsonism is very similar to idiopathic PD both clinically and pathologically and also in its response to levodopa.

5. **Metabolic:** Post anoxic Parkinsonism is often accompanied by dystonic postures and athetoid movements. Levodopa may be helpful.

This term includes other neurodegenerative conditions of unknown etiology, which have other characteristic features in addition to Parkinsonism.

The following features should suggest that the patient may not have Parkinson's disease but rather one of the other causes of Parkinsonism:-

a. Early onset of Parkinsonism
b. Early loss of postural reflexes with frequent falls
c. Dementia appearing early in the disease course
d. Ocular palsies, especially downward and horizontal
e. Cerebellar signs
f. Postural hypotension
g. Exaggerated tendon reflexes and extensor plantar responses
h. Signs of anterior horn cell damage (fasciculations, muscle wasting, absent reflexes)
i. Poor response to levodopa therapy

13 › Coma

Definition: "Coma" is derived from the Greek "Koma" meaning deep sleep. Coma has been defined as absence of any psychologically understandable response to external stimuli or inner need.

Signs of Coma

The signs in a comatose patient may be due to:

I. Altered physiological function
II. Raised intracranial tension
III. Herniations syndromes.

I. Altered physiological function

In a comatose patient five parameters may be altered which are assessed.

1. **State of consciousness:** This is the level of the individual awareness and the responsiveness of his mind to himself, the environment and the impressions made by his senses. Various terms used in the past to define different degrees of coma are:

   a. *Coma:* There is a complete loss of consciousness from which the patient cannot be aroused by painful stimuli, all reflexes are lost including corneal, light cough, swallowing, etc.

   b. *Stupor:* This is a state of partial loss of response to the environment. The patient is difficult to arouse and though he can be briefly aroused, it is slow and inadequate. The patient is otherwise not aware of his environment and falls back into the stuporous state.

   c. *Lethargy or hypersomnia:* This is morbid drowsiness or prolonged sleep from which the patient can be aroused or awakened. He appears to be in complete possession of his senses but goes back to sleep as soon as the stimulation is removed.

   d. *Syncope:* This is transient, partial or complete suspension of consciousness with impaired circulation and respiration, pallor, perspiration and cold skin.

   e. *Fugue state:* This is a disturbance of consciousness, lasting hours or days, in which the patient performs purposeful acts, but later, consciously fails to remember actions carried out during that period.

   f. *Confusion:* This is a mild lowering of the level of consciousness. There is impaired, capacity to think clearly and with customary rapidity, and to perceive, respond to and remember questions or directions.

   g. *Delirium:* This is characterized by confusion, disordered perception and loss

of attention. There is marked disorientation in time, excitement and hyperkinesia.

These terminologies are best avoided and it is more valuable to give a detailed description of patient's level of consciousness.

Table 6.33 : Evaluation of Severity of Coma (Edinburgh Classification)

Grade 0:	Fully conscious
Grade 1:	Drowsy, but responds to verbal commands
Grade 2:	Unconscious, but responds to minimal pain stimulus
Grade 3:	Unconscious, but responds to strong pain stimulus
Grade 4:	Unconscious with no response to pain

Glasgow Coma Scale (GCS)

The scale gives an assessment of the state of consciousness and predicts the outcome. The scale comprises three tests: eye, verbal and motor responses. The sum of the three values is calculated. The minimum GCS is 3 (deep coma or death), while the maximum is 15 (fully awake person). GCS 11-15 has a good prognosis, 5-10 intermediate and 3-4 poor prognosis.

2. **Respiratory patterns:** Comatose patients often have characteristic respiratory pattern depending upon the site of lesion and its etiology.

Table 6.34 : Glasgow Coma Scale

	Score
Eye opening response (E)	
No response	1
In response to pain	2
To loud noise/voice	3
Spontaneously	4
Motor response (M)	
No verbal response	1
Extension posturing (decerebrate)	2
Flexion posturing (decorticate)	3
Flexion/withdrawal to pain	4
Localizes pain	5
Obeys commands	6
Verbal response (V)	
No response	1
Incomprehensible words	2
Inappropriate words	3
Confused/Disoriented	4
Oriented	5

a. *Hyperventilation:* This is present with hypoxia, acidosis, salicylate poisoning, severe infections, brain compression and psychogenic causes.

b. *Hypoventilation:* This is present with respiratory failure, sedative-narcotic overdosage and brain-stem compression.

c. *Cheyne- Stokes respiration:* This is characterized by alternate periods of hyperpnea and apnea. It is present with bilateral cerebral hemisphere dysfunction as in hypertensive or metabolic diseases. It also occurs with impending transtentorial herniation.

d. *Central Neurogenic Hyperventilation (CNH):* This is characterized by a sustained, rapid, regular and deep hyperpnea. It is seen in lesions of Ascending Reticular Activating System (ARAS) and often suggests transtentorial herniation with mid-brain compression.

e. *Apneustic breathing:* This is characterized by a pause at full inspiration indicating lesion of lower pons.

f. *Ataxic or cluster breathing:* This is characterized by irregularly irregular breathing pattern and is seen with compression of medulla oblongata.

It must be noted that CNH, apneustic and ataxic breathings are common in patients with structural lesion in brain. Hence if they are present in a patient with metabolic coma, it suggests herniation.

3. **Pupils:** Equal and normally reactive pupils suggest that the oculomotor nerve and the upper brain-stem are intact. Full and conjugate eye movements suggest that midbrain and pontine tegmentum are intact.

a. *Pupillary reaction* helps to differentiate structural from metabolic causes of coma. Pupillary pathways are relatively resistant to metabolic insult and hence in metabolic disorders, pupils are reactive to light. Absence of light reflex suggests structural lesion, asphyxia, hypothermia and drugs like barbiturates, atropine and glutethimide.

b. *Fixed and dilated pupils* suggest instillation of

mydriatic drops or direct trauma to the orbit or oculomotor nerve.

c. *Hippus:* This is spontaneous, rhythmic constriction and dilatation of pupils which suggest mid-brain damage.

e. *Irregular pupils:* 1-2 mm irregularity may be normally present or may occur with early oculomotor nerve palsy, trauma or mydriatic eye drops.

4. **Eye movements and Ocular reflexes:**
   a. Conjugate gaze to one side suggests ipsilateral frontal lobe lesion or contralateral pontine lesion.
   b. Sundown deviation is seen with mid-brain compression.
   c. Ocular bobbing occurs with primary pontine hemorrhage.
   d. Horizontal eye roving is seen with mild metabolic coma.
   e. *Doll's eye movements or oculocephalic reflex:* On vertical or horizontal rotation of the head, conjugate deviation of the eyeballs occur on the opposite side if brainstem is intact. If brainstem is damaged the eyes follow the direction of the head rotation. In hypoglycemia and hepatic encephalopathy this response is brisk. However, as the metabolic coma progresses, the abnormal response eventually ensues. This reflex must not be attempted if there is doubt about trauma to the cervical spine.
   f. *Caloric response or oculovestibular reflex:* After the external auditory canal is cleared of wax, the patient is put in supine position with head elevated to 30° and the external canal is then irrigated with cold water (7°F below body temperature). This will result in horizontal nystagmus with fast component to the opposite side if vetibulo-oculomotor brainstem pathways are intact. In metabolic or structural brain-stem lesion, there is dysconjugate ocular movement. In sedative-hypnotic overdose, a forced asymmetrical downward deflection may be present.
   g. *Cilio-spinal reflex:* A noxious stimulus over the skin of neck, face or upper trunk causes bilateral pupillary dilatation if the sympathetic pathways are intact.
   h. *Corneal reflex:* On touching the cornea with a wisp of cotton, there is blinking of both the eyelids if fifth and seventh cranial nerves are intact. This reflex is absent early in posterior fossa or brainstem lesion.
5. **Motor response:** Distinct motor response can occur in various levels and types of coma. Application of noxious stimuli leads to various postures:
   a. *Decorticate posture:* Flexion of any or all the limbs suggests lesion in the descending motor pathways above rostral mid-brain.
   b. *Decerebrate posture:* Extension of the limbs suggests lesion in the midbrain and upper pons due to herniation or toxic or metabolic disorder.
   c. *Triple flexion:* Decerebrate upper extremities with lower limb flexion is triple flexion response which results from the spinal reflex secondary to damaged descending motor tracts.
   d. *Cortical response:* When there is lesion of the cerebral hemispheres, several motor and behavioral patterns, similar to those of a normal infant functioning at the thalamic level appear. They are bilateral symmetrical such as sucking, snorting, grasping, motor perseveration and gegenhalten (increased muscle tone to passive movements).

II. Raised Intracranial Pressure (ICP)

The normal ICP is 2-15 mm of Hg. It is raised with any space-occupying lesion in the brain. The symptoms and signs of raised ICP are headache, vomiting, papilledema, bradycardia, hypertension, Cheynes-Stokes respiration, yawning and hiccuping.

III. Herniation Syndromes

There are two herniation syndromes-uncal and transtentorial-which can rapidly cause irreversible brain-stem damage if untreated at an early stage. A third type infratentorial herniation is not common.

1. *Uncal herniation:* This results from an expanding intracranial lesion in the temporal lobe or lateral cranial vault. Uncus and the hippocampal gyrus compresses the adjacent midbrain the oculomotor nerve and the posterior cerebral artery. Initially

Table 6.35 : Clinical Features of Herniation Syndromes

	Uncal	*Transtentorial*
1. Pupils:	Initially ipsilateral dilated but Reacting later fixed and dilated.	Small reactive or fixed.
2. Respiration:	Normal, Cheyne-Stokes or CNH	Normal, Cheyne-Stokes or CNH or ataxia.
3. Eye movements:	Initially normal, later III N palsy	Initially full, later poor response to doll's eye movement or calorictest
4. Motor signs:	Normal, hemiparesis, decorticate or decerebrate	Decerebrate or flaccid, with unilateral or bilateral hemiplegia.

there is ipsilateral pupillary dilatation with contralateral hemiplegia. Later, there is decorticate and decerebrate posturing and loss of ocular reflexes. As the pons is compressed, the corneal reflex is lost and when medulla is involved there may be apnea, hypotension and cardiac arrest.

2. *Transtentorial or central herniation:* This is associated with lesions in frontal, parietal or temporal lobes. Diencephalon or midbrain is displaced. The signs are given in the table.
3. *Infratentorial:* The signs and symptoms are due to herniation of the cerebellum and mesencephalon upward through the transtentorial notch, obstructing CSF and venous return or a downward herniation through the foramen magnum causing fatal cardio-respiratory failure.

Causes of Coma

I. Coma is a late development of diseases, the nature of which is suggested by other symptoms:

1. *Severe systemic infections:* Septicemia, typhoid, cholera, pneumonia, malaria, Weil's disease
2. *Infections of nervous system:* Meningitis, encephalitis, cerebral abscess, GPI, trypanosomiasis
3. *Cerebral tumors*
4. *Metabolic:* Diabetes, hypoglycemia, uremia, hepatic encephalopathy, electrolyte disturbances, Addison's disease, hypothyroidism, hypothermia.
5. *Toxic:* Arsenic, lead, milk alkali syndrome, drugs.
6. *Cerebral anemia:* Cardiac failure, hypotension, hypoxia, etc.

II. Coma comes early and is the most prominent feature of the illness:

A. *Supratentorial*
   1. Extracerebral:
      a. Head injury: Concussion, confusion, epidural or subdural hematoma
      b. Subarachnoid hemorrhage
      c. Meningitis
   2. Intracerebral
      a. Cerebro-vascular accidents: thrombosis, embolism, hemorrhage, venous thrombophlebitis
      b. Encephalitis
      c. SOL: Neoplasm, abscess
      d. Pituitary apoplexy

B. *Subtentorial*
   1. Pontine, midbrain or cerebellar hemorrhage.
   2. Basilar artery occlusion

C. *Cardiac:* Stokes-Adams syndrome, hypertensive encephalopathy.

D. *Post-epileptic*

E. *Metabolic:* As above

F. *Toxic:* Barbiturates, alcohol, opium, heroin, kerosene etc.

G. *Miscellaneous:* Heat stroke, Caisson's disease, extreme cold

Mechanism

1. **Supratentorial lesions:** These produce alteration in consciousness through the herniation syndromes. In intracerebral lesions local or generalized hemispheric deficits occur before the onset of coma.

In extracerebral lesions altered consciousness may be the earliest manifestation.

2. **Subtentorial lesions:** Coma can occur with intrinsic brainstem lesions like cerebrovascular accident by destruction of ARAS. Extrinsic lesions cause compression either by the neuronal tissue damage or through herniation syndrome leading to asymmetrical motor signs, cranial nerve palsies, and vomiting.
3. **Extra-cranial disorders:** Normal brain requires oxygen and glucose for its metabolism. Only 2 gm of glucose exists as reserve in brain. Cerebral cortex and hippocampus are most sensitive to glucose depletion. Thiamine and pyridoxine are required for glucose metabolism 3.3 cc of oxygen per 100 gm brain tissue per min is required for normal metabolism in brain. Mental changes occur when less than 2.5 cc of oxygen per 100 gm. brain tissue per minute is available and coma occurs when it falls to 0.2 cc.

   The characteristic features of endogenous disorders leading to coma are:

   a. Decreasing level of consciousness precedes motor signs.
   b. Motor abnormalities: There are three types of motor abnormalities.
      i. Tremors - Coarse and irregular.
      ii. Asterixis - sudden asynchronous palmar flapping at the wrist which are absent at rest and maximum with sustained posture. These occur probably because of the electrical lapses in the controlling muscles.
      iii. Multifocal myoclonus - Unpatterned movements of the facial and proximal muscles of the limbs.

Treatment

I. **Management of the unconscious patient:**

1. *Respiration:* A clear airway must be maintained so that oxygenation of blood and brain do not suffer. This is done by pulling the tongue forward and doing throat suction as often as required. Humidified oxygen may be administered if hypoxia is suspected. If there is respiratory depression, stimulants like nikethamide (Coramine) may be given round the clock. Endotracheal intubation may be required if secretions cannot be adequately removed and if this is required for more than 48-72 hours, tracheostomy may be required.
2. *Circulation:* Patients with raised intracranial tension are usually hypertensives. Sometimes, the patient may be unconscious and in shock. He must be adequately hydrated with intravenous fluids. If hypotension persists after adequate hydration, venous cutdown and a CVP (central venous pressure) line must be maintained. If it is normal or high in presence of hypotension, vasopressors like mephentermine or dopamine hydrochloride may be given.
3. *Nutrition:* An unconscious patient can be adequately nourished orally through the Ryle's tube. Whilst feeding, the patient must be propped up, either by raising the head end of the bed or using 2-3 pillows, to prevent aspiration. Daily 2000-2500 ml of fluids and about 1500-2000 calories are given with combination of milk, fruit juices, vegetable soups, rice kanji, aerated waters and sugar. In uremia, fruit juices and coconut which contain large amounts of potassium are restricted unless urine output is adequate and serum electrolytes do not show hyperkalemia. Similarly milk is also restricted in uremia.
4. *Oral cavity:* The mouth must be regularly cleaned especially with glycerine borax preferably 2-3 times a day. Oral infections and parotitis are very common if this care is neglected. Secretions, if any, must be regularly sucked with the help of suction machine.
5. *Urinary care:* The patient usually passes urine in bed which would require repeated changing of bedsheets. If this is not done, bedsores and infections occur. Hence, in a male patient a condom catheter is passed which would prevent bed soiling. However,

this is not possible in females. Again in some unconscious patients there is retention of urine. In such cases, a self retaining Foley's catheter is put. Once a patient is put on a self retaining catheter, various measures to prevent and treat urinary tract infection are undertaken as follows:

a. Catheter dressing must be done daily.
b. Bladder washes may be given if there is pyuria.
c. Bladder exercises must be given after a few days to prevent loss of tone of bladder muscles by periodically clamping the catheter for few hours.
d. Urine must be sent regularly for routine and culture examination. If urinary infection is present, urinary antibiotic syrup like co-trimoxazole, nitrofurantoin, chloram-phenicol or ampicillin may be given through the Ryle's tube. Injectable gentamicin may be required for Pseudomonas infection.

6. *Bowel:* Comatose patients are often constipated. This can be prevented or treated by regular simple or saline enemas on alternate days. If the patient has diarrhea, it must be promptly controlled with binding mixtures, metronidazole, antibiotics or antimotility agents like loperamide. Bedsores develop rapidly if patient remains dirty in fecal matter. Nursing care to keep perianal and genital region clean is of utmost importance.

7. *Skin:* The bed must be regularly made. Bedsheets must be dry and whilst preparing the bed, creases should be avoided. If the bed is wet, skin may become sodden and later bedsores develop. To prevent this, the patient must be regularly turned and kept on each side alternately and sometime prone. Special care must be taken of the pressure points. Alcohol and spirit must be used to clean the skin. This is followed by liberal powdering.

   In spite of good care of skin, however, if the bedsore does develop, it must be dressed regularly with hydrogen peroxide and antibiotic dressings must be applied. The affected part must be kept free from pressure.

8. *Eyes:* If the eyes of the comatose patient remains open, exposure keratitis and ulcerations may occur which can be prevented by putting antibiotic eyedrops in the daytime and ointment at night. The eyes must be closed and if required padded and bandaged.

   If the eyes remain closed, the chance of exposure keratitis is not present but even then the eyes must be cleaned 3-4 times with plain clean water.

9. *Passive physiotherapy:* An immobile patient often develops stiff joints. To prevent this, the limbs must be regularly moved at all joints for a few times through its complete range. This may be repeated 2-3 times a day.

II. **Removal of the cause:** Removal of the cause is most important in therapeutics. They may not be often obvious. However, if it is obvious and treatable it must be treated. A few examples are as follows:

1. Gastric lavage, analeptics and naloxone for narcotic poisons.
2. Atropine and oximes for organo-phosphorous poisoning.
3. Forced alkaline diuresis for barbiturate poisoning.
4. Ice-baths in heat stroke.
5. Removal of the patient from the contaminated atmosphere and administration of oxygen and carbon dioxide in carbon monoxide poisoning.

14 › Syphilis of Nervous System

Syphilis usually affects the nervous system in the tertiary stage. However, it may show affection even in the secondary stage.

Neurosyphilis usually occurs 10-30 years after the primary infection, hence it is more common between the age of 30 and 60 years.

Males are affected more than females.

Neurosyphillis is rare but with the epidemic of HIV, its incidence is increasing.

Classification

A. **Parenchymatous:** Direct affection of nervous system by spirochetes.
   1. GPI (General paralysis of insane)
   2. Tabes dorsalis
   3. Primary optic atrophy

B. **Meningovascular:** Neurological involvement secondary to vascular affection
   1. *Cerebral form*
      a) Cerebral thrombosis
      b) Vertical meningitis
      c) Gummatous basal meningitis
      d) Encephalomalacia
      e) Gumma
   2. *Spinal form*
      a) Acute transverse myelitis
      b) Meningomyelitis
      c) Hypertrophic, cervical, pachymeningitis
      d) Erb's spinal paralysis
      e) Amyotrophy
      f) Radiculitis
      g) Gumma
      h) Caries of the spine

General Paralysis of Insane (GPI)

Site of Lesion: Diffuse involvement of the cerebral cortex

Clinical Features

I. *Mental Changes:* These are the earliest symptoms and the earliest change is usually impairment of intellectual efficiency. There is loss of power to concentrate, impairment of judgment, memory defects lability of mood leading to imbecility. This is the simply dementic form.

In the grandiose type there is a sense of euphoria and delusions of grandeur.

The other emotional states commonly seen are mania, depression, paranoid and schizophrenia.

In the terminal stages there may be incontinence of urine and stools and the patient may become bedridden.

II. *Disturbance of Speech and Writing:* Usually the patient has slurred speech. Grammar is affected due to mental changes. Words and sentences may be wrongly used or omitted. There may be nominal aphasia and echolalia. Patient may be unable to write in a straight line and there may be micrographia. The writing often depicts the mental state of the person. Spasticity and tremors also affect the writing.

III. *Progressive Spastic Paraplegia:* There is gradual onset of weakness of both lower limbs due to involvement of the motor cortex.

IV. *Disturbance in Reflexes:* Due to spastic paraplegia, there is loss of abdominal reflex, brisk ankle and knee jerks and extensor plantar reflex.

V. *Disturbance in Pupils:* The patient may have small, unequal or irregular pupils. There may be Argyll Robertson or reverse Argyll Robertson pupils.

VI. *Tremors:* Tremors in GPI are conspicuous on voluntary movements. They are coarse tremors best seen in the facial muscles, especially lips and tongue, and in the outstretched hand.

VII. *Congestive Attacks of GPI:* Also called apoplectiform episodes, these are characterized by sudden focal neurological deficit. Hemiplegia is the commonest. There may be hemianopia, aphasia, apraxia, monoplegia, paraplegia or quadriplegia. There may also be transient loss of consciousness.

Recovery is usually complete within a week.

CSF Picture: Increased proteins with moderate pleocytosis: 15-100 cells. Colloidal gold curve is paretic. CSF VDRL is positive.

Treatment

I. Penicillin: Benzathine penicillin 2.4 mega units intramuscular, per week for 4 weeks. It may be repeated after 4 to 6 months.

II. Convulsive shock therapy for psychiatric symptoms.

III. Fever or malarial therapy used commonly in the past, and for some resistant cases in the recent past is no longer advocated.

Tabes Dorsalis

Site of Lesion: Nerve root distal to the posterior root ganglion which may be followed by ascending degeneration of the posterior columns.

Clinical Features

I. *Subjective Sensory Disturbances:* The patient may complain of one or more of the following:
   - A. Lightening pains: These are pains which come suddenly and go suddenly, like lightening, and at different sites during each episode. These occur classically in tabes dorsalis.
   - B. Fixed pains: These pains are dull aching and constant at a particular site.
   - C. Root pains: These are root pains in the lower thoracic i.e. in the girdle area.
   - D. Girdle pains: These are root pains in the lower thoracic i.e. in the girdle area.
   - E. Pains of tabetic crisis: Paroxysmal painful disorder of the function of various viscera e.g. gastric, rectal, nasal, laryngeal, renal, urethral, etc.
   - F. Patient may have the feeling of walking on cotton wool due to affection of the posterior columns.

II. *Objective Sensory Loss:*
   - A. There is loss of position and vibration sense almost always involving the lower limbs and sometimes involving the upper limbs due to affection of posterior column.
   - B. Pain, temperature and touch are affected late. The common area of affection are — butterfly area of the face, inner side of the arms, saddle shaped area around the anus and over tendo Achillis (Abadie's sign).
   - C. Loss of testicular sense.

III. *Hypotonia:* Being a lower motor neurone disease due to affection of the nerve root distal to the posterior root ganglion, there is hypotonia.

IV. *Ataxia:* Due to the posterior column affection there is loss of position and vibration sense which leads to sensory ataxia. Hence the Romberg's sign is positive.

V. *Disturbance In Reflexes:* The deep reflexes are lost especially the ankle and knee jerks which must always be lost in a case of tabes dorsalis. Plantar response is flexor, unless there is associated GPI (Taboparesis) when it may be extensor.

VI. *Disturbance In Pupils:* Same as in GPI

VII. *Attitude and GAIT:*
   - A. The patient stands on a wide base with eyes fixed to the ground.
   - B. When he wishes to walk, due to hypotonia the limb is lifted to a greater extent than normal and because the position sense is affected, it is brought down with a stamp (high stamping gait).

VIII. *Sphincter Disturbances:*
   - A. Impotence is sometimes an early symptom.
   - B. There may be incontinence of urine and feces.
   - C. The classical disturbance is a loss of bladder sense. Hence the bladder accumulates urine with the patient unaware. This gives a false impression of retention of urine. However, in tabes dorsalis the patient can voluntarily evacuate his bladder.

IX. *Trophic Changes:*
   - A. Perforating ulcers occur usually on the pad of the great toe.
   - B. Charcot's joints: Painless swelling of the knee joints.

X. *Crisis:* As described in sensory disturbances above.

CSF Picture: The proteins may be raised, especially gamma globulins. There may be mononuclear cells, usually not more than 100/c.c. Colloidal gold curve is tabetic or luetic.

Table 6.36 : Difference between Peripheral Neuropathy and Tabes Dorsalis

	Peripheral Neuropathy	*Tabes Dorsalis*
1. Power	Always affected	Never affected
2. Calves	Tenderness marked	Anesthetic
3. Gait	High steppage	High stamping
4. Pupils	Normal	Argyll Robertson type
5. Romberg's sign	Absent	Present

Treatment

I. **Specific:** Same as for GPI

II. **Symptomatic**

1. *Lightening pains:* Analgesics and carbamazepine
2. *Tabetic crisis:* Carbamazepine
3. *Ataxia:* Physiotherapy and use of walking sticks
4. *Bladder disturbances:* Training the patient to evacuate his bladder at regular intervals irrespective of the sense of fullness. If there is dribbling, the patient must be advised to carry a portable receptacle.
5. *Charcot's joints:* Rest, physiotherapy and arthrodesis

Primary Optic Atrophy

Primary optic atrophy is characterized by:

I. Chalky white disc

II. Clear cut margins

III. Normal arteries and veins

IV. No exudates or hemorrhages

The patient may come with blindness and his fundus may show the above changes and therefore syphilis has to be considered in the differential diagnosis.

Meningovascular Syphilis

Due to the affection of meninges and vessels, various parts of the CNS can be affected. Hence meningovascular syphilis is classified as cerebral and spinal.

I. Cerebral Syndromes

A. **Cerebral thrombosis:** Patient presents like a typical cerebrovascular accident and his CSF and blood VDRL is positive.

B. **Vertical meningitis:** There is involvement of the part of the cerebrum over the vertex. Hence there is:

1. Pain and tenderness over the vertex.
2. Focal neurological deficits e.g. hemiplegia, aphasia, etc.

C. **Gummatous basal meningitis:** There is affection at the base of the skull where there are cranial nerves and hence the patient presents with multiple cranial nerve palsies.

D. **Encephalomalacia:** This resembles GPI

Table 6.37 : Differences between Parenchymatous and Meningovascular Syphilis

	Parenchymatous syphilis	*Meningovascular syphilis*
1.	Direct affection of the nervous system	Neurological affection secondary to vascular involvement
2.	Onset after primary lesion is later	Onset after primary lesion is earlier
3.	CSF is normal or shows raised proteins.	CSF shows picture of chronic meningitis
4.	CSF colloidal gold curve is paretic or luetic	CSF colloidal gold curve is meningitic
5.	Fever therapy is useful in GPI	Fever therapy is useless
6.	Prognosis is poorer	Prognosis is better

E. **Gumma:** This resembles a space occupying lesion and hence brain tumour. However it is so rare that it should never be diagnosed clinically.

II. Spinal Syndromes

A. **Transverse Myelitis:** There is an acute onset of paraplegia resembling acute viral transverse myelitis.

B. **Meningomyelitis:** There is a subacute paraplegia resembling compression myelitis.

C. **Erb's spinal paraplegia:** There is a very gradual onset of paraplegia resembling lathyrism.

D. **Cervical pachymeningitis:** There is upper motor neurone type of paralysis in the lower limbs and lower motor neurone type of paralysis in the upper limbs. This remains a differential diagnosis of syringomyelia.

E. **Amyotrophy:** This resembles progressive muscular atrophy.

F. **Caries of spine:** This resembles TB spine.

G. **Radiculitis:** This resembles neuralgic amyotrophy.

H. **Gumma in spinal cord:** This resembles intra-medullary tumor, but being very rare, like cerebral gumma, must never be clinically diagnosed.

Treatment

A. Penicillin: As for GPI

B. Physiotherapy

Medical Emergencies

7

1 › Cardiac Arrest

Cardiac arrest is a sudden stoppage of the heart resulting in an inadequate cerebral circulation which leads to coma within one minute, but recovery would be complete if hypoxia is relieved within 3 minutes. If hypoxia exceeds 4-5 minutes severe and permanent brain damage occurs. Immediately call for help.

Management

I. **Basic Life Support/ Basic Cardiac Life Support (BCLS)**

The airway, breathing and circulation are maintained simultaneously as rapidly as possible as follows:

A. ***Airway:*** The airway must be patent. If foreign body is suspected, the patient must be rolled on one side and 4-5 forceful blows must be delivered rapidly between the shoulder blades with the heel of the hand. The patient is then put in supine position and abdominal thrusts in an upward direction are given to the patient just below the xiphisternum. Presence of foreign body can be checked in the pharynx by sweeping deeply across the posterior pharynx with the index finger.

After the foreign body is excluded, the patient should be kept in supine position as he may require external cardiac massage and artificial respiration. The patient's head must be lifted with one hand under the neck and the other hand pressing the forehead so that the head is tilted backwards to keep the upper airway patent.

B. ***Breathing:*** Once the airway patency is maintained and if the breathing is inadequate, artificial ventilation must be given. With the above position, the patient's nostrils must be sealed with thumb and index finger and mouth-to-mouth respiration must be given to the patient. This is done by taking a deep inspiration and exhaling in the patient's mouth and then the patient is allowed to exhale passively. This procedure is continued at the rate of 16-18/min. In hospitals, an Ambu bag is used.

C. ***Circulation:*** With the patient in supine position, neck extended and legs elevated, a sudden sharp thrust is given on the chest wall. This may restore the effective beating of the heart especially if the cardiac arrest is due to cardiac standstill. In absence of response, external cardiac massage is given.

External cardiac massage: The heel of both the hands, one above the other, the arms straight and extended and in the kneeling position, the lower sternum of the patient is compressed firmly to depress it for at least 4-5 cm. for about half a second. This is carried out with a rocking movement, regularly and rhythmically at the rate of about 60/min. This aids cardiac emptying and perfusion of the vital organs.

II. **Advanced Cardiac Life Support (ACLS)**

Once the basic life support is maintained an ECG must be taken to determine whether the cause of cardiac arrest is ventricular asystole or ventricular fibrillation.

A. If it is **ventricular asystole,** while electrical methods of treatment like external

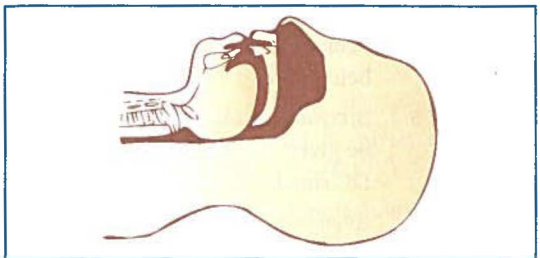


Fig. 7.1 : Patient in supine position with head flexed shows the tongue obstructing the airway

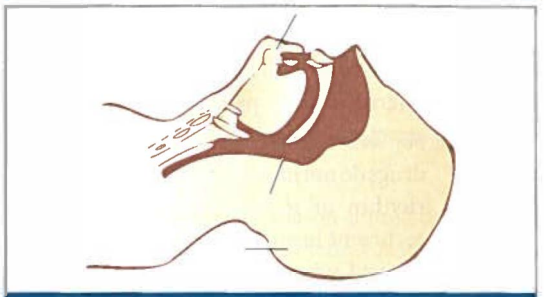


Fig. 7.2 : Patient in supine position with head tilted backwards showing the tongue being lifted up and the airway patent

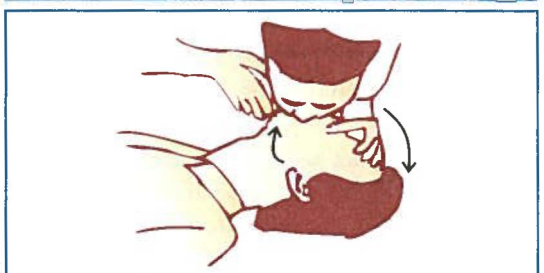


Fig. 7.3 : Mouth-to-mouth respiration

cardiac pacemaker are made available, the following drugs are given:

1. *Epinephrine (Adrenaline):* 1 ml of 1:1000 epinephrine is given intravenous followed by a bolus of dextrose. Epinephrine may restart the heart if cardiac arrest is due to ventricular asystole. In case of ventricular fibrillation epinephrine makes the heart more amenable to electrical therapy. It makes the myocardium more responsive and crude ventricular fibrillation is converted to fine ventricular fibrillation.



Fig. 7.4 : External Cardiac Massage

2. *Calcium:* 10 ml calcium gluconate 10% is injected I.V. or sometimes intra-cardiac. It improves the contractility of the heart and hence is given to patients requiring repeated epinephrine injection. It is rarely used.
3. *Sodium bicarbonate:* 10 ml of 7.5% sodium bicarbonate is infused slowly intravenously to correct metabolic acidosis. Calcium should not be mixed with sodium bicarbonate in the drip as a precipitate of calcium carbonate occurs. This is also rarely used.
4. *Vasopressors: Nor-epinephrine* 1:1000 is initially given in the dose of 2 ml and later repeated if hypotension persists. Dopamine may be given in the dose of 100 mcg/ml (by adding 50 mg of dopamine in 500 ml of saline) intravenously slowly. The rate of the drip is adjusted according to the response. *Low dose dopamine or dobutamine* is the drug of choice.

B. If it is **ventricular fibrillation** the following drugs are used in addition:

1. *Lignocaine:* 50-100 mg is injected intravenously as a bolus and may be repeated after 15-20 min. It raises the fibrillation threshold and prevents the recurrence of ventricular fibrillation.
2. *Propranolol* 5-10 mg may be given intravenously as an antiarrhythmic

Ventricular fibrillation

MANAGEMENT

Precordial thump

↓ No reversion

DC shock - 200 J.

↓ No reversion

DC shock - 200 J

↓ No reversion

DC shock - 300 J

↓ No reversion

1. Endotracheal Intubation
2. Adrenaline 1mg IV

↓ No reversion

Cardiopulmonary resuscitation in the ratio 5 : 1 cardiac massage: ventilation.

DC shock 360 J

↓

DC shock 360 J

↓

DC Shock 360 J

Ventricular Asystole

Precordial thump

↓

Exclude Ventricular fibrillation

↓ NEA

Endotracheal intubation

↓ NEA

Epinephrine 1 mg IV

↓ NEA

10 CPR in the ratio 5 : 1

↓ NEA

Atropine 3 mg IV once only

↓ NEA

Pacemakers

NEA = No Electrical Activity

agent. Newer ultrashort-acting betablockers like esmolol are now being used.

3. *Bretylium tosylate* 5-10 mg/kg I.V. may be given. It increases the efficacy of DC shock.
4. *Adenosine* is used for SVT.

III. Specific measures

A. *For ventricular asystole:* If cardiac arrest persists in spite of the above measures, external cardiac pacing is done. If this is negative or required for a long period, internal cardiac pacemaker is inserted.

B. *For ventricular fibrillation:* If the above drugs do not immediately revert the cardiac rhythm or if ventricular fibrillation is recurrent inspite of the above measures a Direct Current (DC) shock is given to the heart with 200 joules. It should be repeated if required after a few minutes with 300 Joules and then up to 400 Joules.

Recurrent ventricular fibrillation can be prevented by the use of IV *Lignocaine* in a drip of 500 ml of glucose. Alternatively, *Bretylium, Quinine* or *Procainamide* can be given IM.

Resistant ventricular fibrillation may be due to hyperkalemia and hypomagnesemia. Hence these electrolyte abnormalities should be corrected with *glucose-insulin* drip and 10-20 ml of KCl or 10-15 ml of 20% *magnesium sulfate* IV respectively. If these measures also fail, open-chest cardiac resuscitation should be done.

IV. Management After Successful Resuscitation but Unconscious Patient

1. Endotracheal Intubation with controlled ventilation should be continued with the help of a ventilator to keep the pO2 at 100 mm Hg and pCO_2 at 30-40 mm Hg.
2. Blood pressure must be maintained at 100 mm Hg systolic, if required with the help of vasopressors like *dopamine*.
3. Acid-base and fluid electrolyte balance should be maintained.

4. *Mannitol* 350-500 ml I.V. or dexamethasone 4 mg 6-8 hourly I.V. should be given if there is cerebral edema.
5. *Phenytoin sodium, diazepam* or *phenobarbitone* should be given if there are convulsions.
6. Aspiration pneumonia should be prevented by appropriate antibiotics.

If the patient recovers consciousness within 12 hours, there is a good chance for complete neurological recovery. If after 12 hours, pupils are fixed, corneal reflexes absent and deep tendon reflexes also absent, prognosis is poor.

Termination of Cardiopulmonary Resuscitation

Cardiopulmonary resuscitation should be continued till there is cerebral death. Cerebral death is presumed if deep coma, absent spontaneous respiration and heart beat and fixed dilated pupils persists for more than 20 mins. EEG would be flat in case of cerebral death.

2 › Cardiac Failure *(Refer Chapter 5)*

3 › Ischemic Heart Disease

Acute Coronary Syndrome / Acute Myocardial Infarction / Unstable Angina *(Refer Ch. 5)*

4 › Stokes Adams Syndrome

Stokes Adams syndrome is a transient syncope or unconsciousness due to cerebral ischemia because of poor or absent ventricular output.

Management

1. **Immediate measures:** Immediate measures must be taken to resuscitate the heart. A sharp blow over the precordium may be enough to start it. External cardiac massage with mouth-to-mouth respiration may be required.
2. If the ECG shows ventricular fibrillation, **external electric shock** with a **DC defibrillator** may start the heartbeat.
3. **Temporary pacemaker** should be introduced and external pacing should be done till a permanent pacemaker is inserted.
4. **Drugs:** Till the pacemaker is inserted, in case of ventricular asystole the following can be given:
   a. *Isoprenaline:* 0.1-0.4 mg injected intravenously directly or 1 mg in a drip of 200 ml of 5% glucose.
   b. *Ephedrine or epinephrine:* 0.2-0.5 ml of 1:1000 solution can be given intracardiac, intra-venously or intramuscularly.
   c. *Sodium bicarbonate:* 100 ml of 7.5% solution may be given intravenously to combat acidosis.
   d. *Steroids:* Injection hydrocortisone 100 mg intravenously may be given to relieve edema, if any, around the AV node.
   e. *Hydrochlorothiazide, sodium lactate, atropine and aminophylline* can be used.

5 › Hypertensive Crisis

Refer to JNC VII criteria for hypertensive urgency and emergency (Refer Pg. 48).

Management

I. The patient must be preferably **hospitalized** and given complete **bed rest** and **tranquilizers** like diazepam 5-10 mg or alprazolam 0.25 mg three times a day.

II. **Anti-hypertensive drugs**
   1. *Nifedipine:* In a hypertensive crisis, nifedipine (5-10 mg) capsule can be cut to allow the liquid to come out. It is absorbed sublingually and lowers the BP in 15-20 min. The effect lasts for 3-6 hours. It can be repeated every 5-10 min up to 60 mg/day. Sudden lowering of BP may precipitate stroke and therefore must be avoided.
   2. *Sodium nitroprusside:* It causes vascular smooth muscle relaxation equally affecting both the arterioles and venules resulting in decreased peripheral resistance and venous

tone. Thus, it reduces both the preload and afterload resulting in reduced myocardial oxygen consumption. It is given as 50 mg dissolved in 500 ml of dextrose (100 mcg/ml) and given in the dose of 20 mcg/min. It has to be protected from light as it can decompose to toxic thiocyanate on exposure to light. The anti-hypertensive effect appears in 30 sec and lasts for only 2 minutes after stopping the drip. It thus produces a smooth lowering of blood pressure and is thus useful in acute myocardial infarction and low cardiac output states.

3. *Nitroglycerine:* It is given in the dose of 5-10 mg/min IV It is a venodilator which acts within 2-5 min.
4. *Esmolol:* It is a short-acting beta-blocker. It is given in the dose of 500 mg/kg/min for 4 min and then 150-300 mg/kg/min.
5. *Nicardipine:* Causes vasodilation in the dose of 5-10 mg/hr IV after about 10 min.
6. *Labetalol:* It is an alpha as well as beta-blocker given as 20-80 mg IV every 10 min.
7. *Enalapril:* It is given in the dose of 2.5 -5 mg IV 6 hourly. It acts in about 10-15 min.
8. *Diazoxide:* It directly acts on the arterioles and dilates them. It is given in the dose of 5 mg (250-300 mg) over 1-5 minutes slowly intravenously. There is a rapid lowering of blood pressure over 1-3 mins and the effect lasts for about 24 hours. It causes sodium retention. Hence it has to be combined with 40 mg furosemide. Since there is a precipitous fall in BP, it is contra-indicated in coronary and cerebral vascular diseases. It also causes hyperglycemia and hence is also contraindicated in diabetes mellitus.
9. *Hydralazine:* It is given in the dose of 30-40 mg intramuscularly every 8 hourly. It is a peripheral vasodilator.
10. *Phentolamine:* It is very useful in hypertensive crisis due to pheochromocytoma. It is given in the dose of 5-15 mg IV. It acts within 1-2 min.

III. **Treatment of the cause** whenever possible: e.g. surgical removal of tumor in pheochromocytoma.

6 › Hypertensive Encephalopathy

Hypertensive encephalopathy is acute transient cerebral dysfunction associated with a rapid rise of diastolic blood pressure due to constriction of the central arterioles leading to cerebral edema and clinically characterized by headache, vomiting, convulsions, unconsciousness and focal neurological deficits like hemiplegia, blindness, aphasia, etc, in an hypertensive patient.

Management

I. **Anticonvulsants:**
   1. *Diazepam:* Diazepam 10 mg should be given intravenously. It can be repeated after 10 min. till convulsions stop.
   2. *Phenytoin:* Loading dose of phenytoin sodium is given, followed by maintenance dose.
   3. *Barbiturates:* Phenobarbitone 100-200 mg. intramuscularly or diluted in 50 ml of saline, intravenously over 10 mins. Now rarely used.
   4. *Diazepam* and *barbiturates* may cause serious hypo-tension and respiratory failure if given intravenously. *Paraldehyde* 5 ml intra-muscular is another useful drug to control convulsions.

II. **Antihypertensive drugs:**
   1. *Nifedipine:* See hypertensive crisis.
   2. *Diazoxide:* See hypertensive crisis.
   3. *Sodium nitroprusside:* See hypertensive crisis.
   4. *Chlorpromazine:* It has antihypertensive, anti-emetic and tranquilizing effects. It is useful in toxemia of pregnancy. It is given as 50-100 mg intramuscularly or slowly intravenously 2.5 mg every 2-5 mins till the blood pressure falls.

5. *Magnesium sulphate* IV is also useful in toxemia of pregnancy and is drug of choice.

III. Measures to reduce raised intracranial tension: Mannitol 350 ml and furosemide 40 mg intravenously with glycerol orally is helpful.

IV. Management of unconscious patient.

V. Treatment of the cause.

7 Shock

Shock is a state of inadequate tissue perfusion of the vital organs like brain, liver, kidneys etc. due to a reduction in the cardiac output.

Management

I. Emergency Management: The following measures should be carried out in all patients with shock because if promptly treated, shock is initially reversible.

1. *Head-low position:* The patient must be given head low position to increase the filling pressure of the right ventricle and raise the cardiac output.
2. *Respiration:* A clear airway must be ensured either by pulling the tongue out or by keeping a metal airway. If required endotracheal intubation may be carried out to ensure adequate ventilation. High concentration of oxygen should be given.
3. *Fluids:* An intravenous drip should be started using a large bore needle. The IV fluid used depends upon the type of shock. In hemorrhagic shock- blood transfusions, in burns- plasma or saline and in cardiogenic shock- dextran is given. Transfusion of fluids should be slowed down when central venous pressure is about 5 cm above the sternal angle.
4. *Acid-base balance:* Metabolic acidosis which accompanies shock should be treated with 50-100 cc. of 7.5% sodium bicarbonate. The dose of sodium bicarbonate may have to be repeated till acidosis is corrected because acidosis may depress the myocardial contractibility and cause resistance to the action of catecholamines.

II. Specific treatment

1. *Vasopressors and inotropes* are useful because they have a positive inotropic effect (increase in contractility of the myocardium) and peripheral vasoconstricting action. They are useful in cardiogenic shock due to myocardial infarction or arrhythmias. Usually there is hypotension and raised CVP. However, it is important to ensure adequate blood volume (central venous pressure more than 5 cm) before using these drugs, otherwise the peripheral vasoconstrictive effect may further reduce the circulation to the vital organs. The commonly used drugs are:-
   a. *Dopamine:* 500 mcg in 500 ml of dextrose is given slowly through a microdrip to ensure 5-15 µg/kg/min. The dose has to be adjusted depending upon blood pressure. This is especially useful in cardiogenic shock.

      It affects both β_1 and α - receptors with a predominance of beta effect. It therefore causes an increase in cardiac output and in blood pressure.
   b. *Dobutamine:* It is given in the dose of 2-30 µg/kg/min IV. It acts on beta-receptors and improves cardiac output. However, blood-pressure may not rise and in fact may fall. The combined use of dobutamine and dopamine produces greater increases in arterial pressure and cardiac output than either agent alone.
   c. *Nor-epinephrine:* 2-4 mg in 500 ml. of dextrose, adjusted to administer 20-30 drops/min. Usually 1-25 µg/min is required. Now rarely used.
   d. *Mephentermine:* 30-60 mg given IM or in a 5% glucose drip till the blood pressure is maintained. Now rarely used.
   e. *Epinephrine* (for anaphylactic shock), *dopexamine, amrinone and milrinone* can also be used.
2. *Corticosteroids:* 100-500 mg. of hydrocortisone hemisuccinate is often given

immediately intravenously. It is especially useful in anaphylactic, cardiogenic, septic shock, neurogenic shock and adrenal crisis.

3. *Antibiotics:* Antibiotics like gentamicin, 1-1.5 mg/kg IV as loading dose plus third generation cephalosporins like ceftazidime 1 gm 4-6 hourly and metronidazole 500 mg 8 hourly are used in gram negative septicemia. Cloxacillin, nafcillin or oxacillin are useful if staphylococcal infection is present. If the source of sepsis is not identified or the patient is neutropenic, broad-spectrum coverage with an aminoglycoside (loading IV dose of gentamycin 1.0-1.5 mg/kg or tobramycin) and a semisynthetic penicillin or cephalo-sporin can be used.
4. Miscellaneous:
   a. *Chlorpromazine:* 25-30 mg has been found useful in septic shock. It acts by alpha-adrenergic action on the arterioles resulting in diminished pooling of the blood in the periphery.
   b. *Heparin:* This may prevent intravascular clotting in septic shock. Heparin 2000-5000 units are given every 6 hourly.
   c. *Intra Aortic Balloon Counterpulsation (IABP)* is useful in cardiogenic shock. It reduces left ventricular diastolic volume by reduction of aortic impedance in end-diastole and it increases systemic, cerebral and coronary perfusion pressures in early diastole. Pulmonary congestion is reduced and myocardial pump performance and oxygenation improves.

8 › Anaphylactic Shock

Anaphylactic shock is a relatively uncommon emergency which requires prompt and vigorous treatment.

Management

1. **Epinephrine:** 0.5-1.0 ml of 1:1000 epinephrine is given SC or IV and repeated every 15 min. until improvement. Its alpha adrenoceptor agonist activity causes peripheral vaso-constriction whereas its beta-adrenoceptor agonist activity is useful as a bronchodilator. It also imparts further release of chemical mediators concerned in the pathogenesis of the reaction.
2. **Histamine (H1) antagonists:** 10-20 mg chlorpheniramine may be given slowly intravenously and repeated if required for 24 hours. It counteracts the effects of histamine, which is one of the most important mediators concerned in anaphylaxis and correlates well with the degree of hypotension. It is particularly effective in the management of angioedema, pruritus and urticaria.
3. **Corticosteroids:** 200 mg of hydrocortisone hemisuccinate may be given intravenously but it has little place in the immediate management of anaphylaxis since its beneficial effects are delayed for several hours. However, early administration may help prevent deterioration after the primary treatment has been given.
4. **Volume replacement:** It is required in patients with circulatory collapse. Intravenous fluids should be given and monitored by central venous pressure line. Large volumes of electrolyte solutions may be necessary because plasma loss may be very high in severe anaphylaxis. Colloid solutions like plasma protein fraction or dextran are preferable.
5. **Miscellaneous:**
   a. *Bronchodilators:* Aminophylline, salbutamol or terbutaline may be given for bronchospasm.
   b. Oxygen with assisted ventilation.
   c. *Emergency tracheostomy* for laryngeal edema or respiratory obstruction.

9 › Pulmonary Embolism & Deep Vein Thrombosis

Pulmonary embolism (PE) is blockage of the pulmonary vasculature by blood clots, venous thrombi, fat, air, foreign bodies or fragments of malignant tumors. The majority of PEs arise from deep vein thrombosis (DVT) of the iliofemoral system.

Investigations

1. *Baseline CBC and coagulation studies* and for hypercoagulable state - factor V Leiden and lupus anticoagulant/anticardiolipin antibody are carried out immediately. Protein C, S and antithrombin III should be tested 4-6 weeks after discontinuation of oral anticoagulants.
2. *Guaiac test* for stool occult blood should be negative and there should be no other risks for bleeding (tumor, bleeding diathesis, etc).
3. *Ventilation-perfusion (V/Q) lung scan and pulmonary angiography* are useful for PE.
4. *LE duplex doppler study* is important. *ECHO and venogram* can be done.

Management

I. **Medical**

1. *Relief of pain:* Severe pain can be relieved by opiates like injection pethidine 100 mg IV or morphine 15 mg IV.
2. *Heparins*: Bolus 80-150 units/kg heparin (unless contra-indications) is followed by IV 15-18 units/kg//hr titrated individually so that aPTT is two times therapeutic range (aim for 60-90 secs). The patients' previous trends and clinical history should be considered while adjusting dosage. Heparin is continued for 5-10 days.

Table 7.1 : Suggestions to Adjust Drip

aPTT (sec)	Bolus (units)	Hold For	Rate Change (ml/hr)	When to Recheck
< 50	2500-5000	10 mins	+ 200	6 hrs
50-60	0	0 min	+ 100	6 hrs
60-85	0	0 min	0	next AM
86-95	0	0 min	- 100	next AM
96-120	0	30 mins	- 100	6 hrs
> 120	0	60 mins	- 200	6 hrs

Low molecular weight heparins have equal or greater antithrombotic effect and should be considered in certain clinical situations.

Platelet count should be done at least QOD while on heparin since there is a risk of heparin-associated-thrombocytopenia or thrombosis.

3. *Warfarin:*

Heparin is simultaneously given with warfarin until PT/INR (International Normalised Ratio) is therapeutic for 48 hrs and then heparin is discontinued. Warfarin is started at 10 mg po QHS for 2 days, then 5 mg po for 1 day and adjusted according to therapeutic goals given below:

Table 7.2 : Therapeutic Goals

Indication	INR
First DVT	2-3
Second DVT	3-4
PE	3-4
Atrial Fibrillation	2-3
Prosthetic Valve-Tissue	2-3
Prosthetic Valve-Mechanical	2.5-3.5
Antiphospholipid Antibody	3-4

It is continued for 3 months or indefinitely if risk factors are still present or there is recurrent thromboembolism.

4. *Thrombolytic agents:* Streptokinase or urokinase or recombinant tissue plasminogen activator (rt-PA). ***Streptokinase:*** IV bolus 2,50,000 units over 30 mins is followed by 1,00,000 units/hr IV for 24 hours. The clot usually lyses in 3-5 days. A venepuncture or venesection is done prior to the therapy, because if venous puncture is required after the administration of streptokinase, uncontrollable bleeding may occur.
5. *Digitalis:* Usually digoxin 0.5 mg is rapidly given IV to increase the output of failing right ventricle.
6. *Vasopressors like Isoprenaline:* This is given in the dose of 0.5-1.0 mg IV and repeated if required. It increases the cardiac output and heart rate in case they are low.
7. *Antibiotics:* Ampicillin 500 mg 6 hourly should be given to control infection in case of pulmonary infarction.
8. *Oxygen:* This should be given through the Wolfe's bottle.

II. **Surgery:** Emergency pulmonary embolectomy can be done before the clots become fragmented, disseminated or organized in selective cases.

III. **Preventive:** Pulmonary embolism or DVT is often precipitated by various factors, which should be controlled.

1. Prolonged immobilization in bed should be avoided especially in the elderly.
2. The posture should be frequently changed.
3. Active and passive movements of the lower limbs should be carried out.
4. Respiratory exercises should be taught.
5. Dehydration should be prevented and anemia, obesity and infections treated.
6. Low dose heparin: In critically ill patients & those in whom it is likely to occur, heparin 5000 units 12 hourly or LMW heparin can be given. In this small dose, heparin reduces the rate of combination of antithrombin III with activated factor X and thrombin. This enhances the body's anti-thrombotic processes and prevents thrombus formation.
7. *IVC Filters* can be used to prevent PE in patients with DVT who cannot be anti-coagulated or in those with persistent PE inspite of anticoagulation.

10 › Hemoptysis

Hemoptysis is expectoration of blood.

TYPES: There are two types of hemoptysis.

1. *True hemoptysis:* Hemorrhage from the lungs, the bronchial tree and trachea.
2. *Pseudo hemoptysis:* Hemorrhage from the nose, mouth, pharynx and larynx.

Causes

I. **True hemoptysis:**

A. *Cardiac:* Mitral stenosis, aneurysm of aorta, left ventricular failure and primary pulmonary hypertension.

B. *Respiratory:* Pneumonia, tuberculosis, bronchogenic carcinoma and adenoma, pulmonary embolism, lung abscess, bronchiectasis and other infections of lung and bronchi, trauma to the airways and lung and A-V malformations.

C. *Immunological:* Goodpasture's syndrome Wegener's granulomatosis and Polyarteritis nodosa.

D. *Bleeding disorders:* Thrombocytopenic purpura, agranulocytosis, leukemia, hemophilia and anticoagulant therapy.

E. *Iatrogenic:* Following bronchoscopy, lung biopsy, endotracheal intubation and anticoagulant therapy.

II. **Pseudo hemoptysis:**

1. Trauma of mouth, pharynx and larynx.
2. Tuberculosis, syphilis or pyogenic infection of mouth, pharynx and larynx.
3. Malignancy of mouth, pharynx and larynx.
4. Bleeding spongy gums in scurvy.

III. **Functional and Malingerer**

Table 7.3 : Differences Between Hemoptysis and Hematemesis

		Hemoptysis	*Hematemesis*
1.	Appearance of blood	Bright red and frothy	Coffee ground mixed with food
2.	Preceding symptom	Coughing and tickling sensation in throat	Vomiting
3.	Associated symptoms	Cough, expectoration, fever	Abdominal pain, vomiting, indigestion, giddiness
4.	Following day	Rusty sputum	Tarry stools
5.	Reaction of blood	Alkaline	Acid

Management

Usually hemoptysis is scanty and stops spontaneously. However, since it is an alarming symptom, physicians tend to over-treat it. If hemoptysis is massive, the following treatment should be given.

I. **Reassurance:** Patient must be reassured.

II. **Treatment of shock:** If there is massive

hemoptysis and patient is likely to have bled profusely, management for shock must be carried out in the following way:

1. Blood must be collected for the estimation of hemoglobin (Hb), packed cell volume (PCV) and grouping and cross matching.
2. Intravenous normal saline must be started.
3. Blood transfusion may be required if Hb and PCV are falling and tachycardia and hypotension occur.
4. Head-low position and intermittent oxygen may be given.

III. **To Stop Bleeding:**

1. *Fogarty Catheter:* Massive hemoptysis is treated with tamponade technique. A balloon tipped Fogarty catheter is passed through the bronchoscope and it is inflated proximal to the bleeding site. The pressure is maintained for a few hours or even days, especially if the patient is a poor surgical risk.
2. *Bronchial artery embolisation:* Bronchial artery angiogram is done and the affected bronchial artery is embolised with sclerosing liquid. This would stop bleeding.
3. *Surgery:* The affected bronchial artery can be tied by a surgical operation or the affected lung can be removed.
4. *Antitussives:* Linctus codeine must be given to suppress cough because coughing prevents normal clotting after hemorrhage.
5. *Posture:* The patient should be given bed rest in a semi-reclining position and leaning on the elbow of the affected side to minimize aspiration of blood and spread to the unaffected bronchi.

IV. **Treatment of the cause:** The cause of hemoptysis - Tuberculosis, aspergillosis, pneumonia or pulmonary edema should be appropriately treated.

1. *Percutaneous intracavitary infusion of amphotericin* can be given in cases of massive hemoptysis due to pulmonary aspergillosis.
2. *Radiotherapy* can be utilized to stop massive uncontrolled hemoptysis from bronchial carcinoma.

V. **Prevent Aspiration:**

1. *Bronchial aspiration* may be required frequently to prevent atelectasis of the unaffected lung.
2. *Endotracheal tube:* The functional airway can be protected by insertion of a special endotracheal tube with an inflatable cuff through the main stem bronchus into the non-bleeding lung.
3. *Rigid bronchoscopy:* This may be needed in massive hemoptysis to remove blood clots.
4. *Avoid sedatives.*

11 〉 Bronchial Asthma

Bronchial asthma consists of increased responsiveness of bronchial tree, which is characterized by frequent attacks of dyspnea due to generalized bronchial constriction.

Management

I. **Acute Bronchial Asthma:** Acute attack of bronchial asthma requires urgent medical treatment. Following measures should be taken:

1. *Oxygen:* Hypoxia should be corrected by oxygen inhalation. Oxygen should be given intermittently and humidified. Usually high concentration of oxygen (6-8L/min) is required as there is no danger of CO_2 retention.
2. *Bronchodilation:* Bronchospasm can be treated with one or more of following:
   a. Inhaled nebulised beta agonists : High dose of inhaled beta agonist like Salbutamol 2.5-5 mg or terbutaline 5-10 mg nebulized through oxygen or 20-50 puffs into a large space devise should be given and repeated every 4 hours.
   b. Intravenous Beta agonists: Salbutamol 200 mg or Terbutaline 200 mg should be given over 10 min or infusion of 3-20 mg/min or Aminophylline 0.25-

0.5 mg. diluted up to 20 ml. with 5% glucose intravenously.

c. Injection Epinephrine 0.5 ml (1:1000) can be given subcutaneously.

3. *Steroids* if the attack is severe, intravenous glucose saline infusion along with 100 mg of soluble hydrocortisone should be administered. IV methyl prednisolone is used now as an agent of choice. It should not be given rapidly as it can cause arrythmias.

4. *Hydration:* If dehydration is present, 5% glucose saline should be given till dehydration is corrected.

5. *Antibiotics:* Penicillin or cephalosporins or ciprofloxacin or tetracycline may be given to check respiratory infection.

6. *Ipratropium bromide* 2.5 mg nebulized and given 8 hourly may be useful, especially for smokers.

7. *Mechanical Ventilator:* This may be needed if the patient develops hypoxia, hypercapnea, unconsciousness, drowsiness or respiratory arrest.

8. *Bronchoalveolar Lavage:* This is useful to wash act mucus plugs.

9. *Follow-up:* After acute attack subsides, steroids must be continued for 6 weeks. Future management depends on the type of asthma. Sedatives and vigorous chest physiotherapy should not be given.

II. Chronic Bronchial Asthma:

After an acute attack subsides, the patient may require long term treatment to prevent relapse.

1. *Bronchodilators:* These drugs may be required to treat bronchospasm. Often long term treatment is required.

   a. *Beta-2 stimulants:* Salbutamol 2-4 mg three times a day or terbutaline 2.5-5 mg three times orally are the other available bronchodilators. The action is physiological and hence these are commonly used nowadays.

   b. *Aminophylline:* This drug is a very popular oral bronchodilator. However, it is erratically absorbed orally and hence its effect on oral administration is variable. However, it is effective rectally.

   c. *Ephedrine* 30 mg in divided doses three times a day is the oldest and yet the most effective bronchodilator. However, it is contraindicated in cardiac patients.

   d. *Isoprenaline* 20 mg sub-lingual or by inhalation helps to relieve bronchospasm. It should be avoided in presence of cardiac diseases. Rarely used now.

2. *Corticosteroids:* In few cases when the above drugs fail to get effective response, oral prednisolone should be considered. It should be given in the dose of 5-15 mg daily for 4-6 weeks and then gradually tapered off.

3. *Atropine compounds:* Ipratropium bromide an atropine derivative decreases the amount of cyclic guanosine monophosphate (cGMP) in respiratory muscles and mast cells by blocking cholinergic input. Increased levels of cGMP cause mast cell degranulation and bronchial smooth muscle contraction.

4. *Antibiotics:* Doxycycline or tetracycline with or without macrolides like roxithromycin or azithromycin are used if infection is present.

5. *Allergy:* If the responsible allergen is detected the patient should be put into an environment free of the allergen. If skin tests show hypersensitivity to certain allergens, desensitization should be carried out by serum administration.

6. *Ketotifen:* This drug acts by stabilizing the mast cell membrane and preventing the release of intracellular mediators like histamine, SRS etc. It is given in the dose of 1 mg three times a day orally for at least 1 month. It is useful in young patients with extrinsic asthma.

12 Respiratory Failure

Respiratory failure is said to exist when partial pressure of oxygen in blood at rest is below 60 mm of Hg or that of CO_2 is above 45 mm of Hg.

Management

I. **Maintenance of clear airways:** This is one of the most important points to be borne in mind while treating the patient with respiratory failure.

1. *Supervised coughing* in a conscious patient and changing the patient's position frequently from side to side may help clear up the airway. Cough may be limited by exhaustion, muscular weakness, air trapping or pain due to rib fracture or pleurisy.
2. *Oral cavity* should be cleared of thick secretions by a rolled gauze piece held in an artery forceps. Secretions at the back of the throat or in the trachea should be removed by frequent suction.
3. *Mucolytic agents:* Mucolytic agents like bromhexine orally are helpful to liquefy secretion. Acetylcysteine 1-2 ml of 20% solution may be instilled through the tracheostomy tube (if tracheostomy is done). This should be immediately followed by mechanical suction.
4. *Bronchoscopic aspiration:* If the cough is ineffective and the airway needs to be cleared, bronchoscopic aspiration may have to be repeated once or even twice over the first few hours.
5. *Endotracheal intubation:* If the secretions are reaccumulating rapidly or if aspiration from the esophagus or upper respiratory tract seems likely, a cuffed endotracheal tube may be passed and repeated aspirations may be carried out.
6. *Tracheostomy:* Tracheostomy may be a life saving procedure for some patients but it has got its own limitations, which must be considered. It is especially helpful if the open airway has to be maintained for over 72 hours and when there is profound respiratory insufficiency because it reduces the physiological dead space.

II. **Bronchodilators:** Respiratory failure is often associated with obstructive airway disease and obstructive airways worsen an existing respiratory failure. Bronchodilators help to oxygenate the airways and subsequently blood. Various bronchodilators used are as follows:

1. *Aminophylline:* This is a very potent bronchodilator. It acts by inhibiting the phosphodiesterase and thus preventing the breakdown of cyclic AMP. It is given in the dose of 0.25 gm intravenously diluted in 10 ml of 10-25% dextrose and injected slowly. Alternately it may be given in 500 ml of 5% glucose with 0.5-1.0 gm of aminophylline in a drip. It also has a central respiratory stimulant action.
2. *Beta-2 (sympathomimetic) drugs:* Orciprena-line, salbutamol or terbutaline act synergistically with aminophylline and achieve maximum bronchodilatation. They stimulate adenyl cyclase which converts ATP to 3-5' cyclic AMP. The average dose required for salbutamol is 8-24 mg and terbutaline is 10-30 mg in divided doses orally, IM or IV in a drip. Nebulized solutions of Salbutamol 2.5-5 mg 4 hourly or Terbutaline 5-10 mg may also be given.
3. *Corticosteroids:* If there is marked bronchospasm not responding to the above drugs prednisolone 20-40 mg orally or dexamethasone 4-16 mg/day parenterally may be given.

III. **Oxygen therapy:** Oxygen is a double-eged sword and should be used with great caution. Oxygen therapy is useful because it corrects hypoxia— one of the major consequences of respiratory failure. However, in a patient of chronic obstructive lung disease, hypoxia is the only stimulus to the respiratory centre because prolonged hypercapnia decreases the ventilatory response to carbon dioxide and acidosis. Administration of oxygen would theoretically decrease the respiratory stimulus and aggravate hypercapnia. However, in practice, if continuous

oxygen is given at low flow rates these problems are not so common and on the contrary depriving a patient in hypoxia of oxygen causes more problems. Oxygen must be well humidified and administered through nasal catheter or mask.

IV. **Respiratory stimulants** may be used when the patient has impaired consciousness. Usually Nikethamide (2-4 ml. of a 25% solution IV) is used but its effect is transient. Vanillic acid diethylamide (3-24 gm. in 540 ml.) by IV drip gives a more prolonged respiratory stimulation.

V. **Mechanical Ventilation:** If adequate respiratory effort cannot be maintained by endotracheal intubation and alveolar hypoventilation becomes a critical factor for survival, the use of assisted ventilation becomes necessary. Initially this may be given via a cuffed endotracheal tube even when the patient is conscious but sedated. Endotracheal tubes can be tolerated for 48 hours and sometimes even up to a week. Later tracheostomy may be needed.

VI. **Treatment of cause**

1. Precipitating factors like smoking or allergens must be avoided.
2. Patients with industrial disease of lung causing respiratory failure may benefit by change of occupation or residence.
3. Diuretics and digitalis are helpful in pulmonary edema and cor pulmonale.
4. Anticoagulants may be required for pulmonary embolism.
5. ACTH and corticosteroids are useful in respiratory centre paralysis in certain disorders like acute infective polyneuritis and may have to be given in large doses.
6. Antibiotics may be required if respiratory infection is the cause or an aggravating factor.
7. Long-term bronchodilators, salbutamol, aminophylline, ephedrine or epinephrine may be required in bronchial asthma.
8. Massive pleural effusion or pneumothorax may require drainage.

13 > Tension Pneumothorax

Tension pneumothorax is a medical emergency which may result in death if left untreated. The air leaks from the lungs into the pleural cavity, but a ball valve leak prevents this air from leaving the pleural cavity. This results in a marked rise in intrapleural pressure which completely collapses the lung, markedly shifts the mediastinum to opposite side, prevents cardiac filling and results in a fall in cardiac output.

Management

1. **Emergency insertion of needle:** A large bore needle (17-18 gauge BD needle) first passed through a sterilized flat piece of rubber or cork (to form a hilt), is inserted into the second right intercostal space (if right sided) in the midclavicular line or fifth left intercostal space (if left sided) in the axillary line, preferably after local infiltration with 2% procaine hydrochloride.

   As soon as the needle enters the pleural space, air escapes, intrapleural pressure falls and the patient feels comfortable. As soon as possible the needle should be connected via a sterilized rubber tube to an underwater seal, which should be connected to an electric suction pump that would provide a negative pressure of 20-30 cm of water.
2. **Oxygen:** Proper administration of humidified oxygen at a high flow rate of 8-10 liters/min helps to relieve anoxemia and cyanosis.
3. **Treatment of shock:** Lowering of intrapleural pressure itself relieves shock because ventilation improves, anoxemia is corrected, venous return increases and so does cardiac output. However, if the medullary centres have been affected by anoxemia, it may take some time to recover. These patients may require intravenous fluids, vasopressors like mephentermine and respiratory stimulants like nikethamide.
4. **For associated hemothorax or pyothorax:** Removal of the respective fluid must be done through an incision in the lower intercostal spaces.
5. **Treatment of cause:** Tuberculosis if present must be appropriately treated.

14 Hematemesis

Hematemesis is vomiting of blood.

Causes

I. Common

1. Peptic ulcer
2. Chronic gastritis
3. Hiatus hernia
4. Carcinoma stomach
5. Ruptured esophageal varices
6. Drugs: Aspirin, steroids, anticoagulants

II. Uncommon

7. Mallory-Weiss syndrome
8. Blood dyscrasias
9. Malignant hypertension
10. Uremia
11. Cerebrovascular accidents
12. Collagen disorders
13. Neoplasia of GI tract
14. Spurious

Management

I. Conservative Treatment

1. *Maintenance of adequate blood volume:* A patient with massive bleeding, who is in shock, requires immediate measures to rapidly restore blood volume, even before a proper history is taken or examination is done. An intravenous drip of dextran, saline, plasma or glucose is started whilst waiting for blood. Many blood transfusions may be required and should be given.
2. *Gastric Lavage:* Distension of the stomach by blood clots prevents an atonic stomach from arresting bleeding by contraction of the stomach wall. Hence, a Ryle's tube must be passed and the stomach must be lavaged with ice-cold water or saline until the returning fluid is clear and free of blood clots. This not only helps to control bleeding but also minimizes vomiting and helps to monitor the activity of bleeding.
3. *H2-receptor antagonist:* IV Ranitidine 50 mg 12 hourly may be helpful in arresting bleeding as it inhibits the secretion of acid. Once bleeding has stopped and oral feeds are started, ranitidine 150 mg or famotidine 20 mg may be given twice a day orally.
4. *Antacids:* When peptic ulcer is the cause of bleeding, aluminium hydroxide or magnesium trisilicate are useful and may be given. If pains are severe, ice-cold milk and antacids may be given as an intragastric drip.
5. *Sucralfate:* Sucralfate 1 gm 6 hourly is useful in peptic ulcer disease. It coats the ulcer and prevents the action of acid on the ulcer, thus aiding in healing.
6. *Proton pump inhibitors:* IV Pentaprazole or omaprazol can be given. Unlike H2 blockers, they have no drug interactions.
7. *Vasoconstrictor drugs:* When bleeding is due to esophageal varices, pitressin 20 units diluted in 500 ml. of isotonic saline or dextrose is given over 4-6 hours and repeated till bleeding stops. The dose is gradually tapered over the next 12-24 hours. It causes abdominal cramps and should be used with ECG control.
8. *Esophageal tamponade* with Sengstaken Blakemore tube may be tried in a case of variceal bleeding if pitressin drip fails to stop bleeding. This stops bleeding by mechanical compression of bleeding varices. Complications are esophageal erosions or rupture, aspiration and asphyxia from tracheal obstruction by the balloon.
9. *Diet:* While there is bleeding, nothing is given orally except ice pieces. Once bleeding has stopped, bland diet may be given. The food given must be of low residue and the patient must be encouraged to chew it well. Gastric irritants like tea, coffee, alcohol, smoking, aerated water, chillies are avoided.
10. *Vitamins and Hematinics:* Vitamin C and A are often given in a bleeding patient usefulness is doubtful. Once bleeding stops, if iron deficiency anemia is detected, iron may be given.

II. **Surgical**

1. *Endoscopic intervention* is treatment of choice.
2. *For peptic ulcer:* If there is massive, continuous and uncontrolled bleeding, the following surgical procedures may be tried: Under-running of bleeder, excision of ulcer, partial gastrectomy, pyloroplasty and vagotomy. Now rarely done.
3. *For portal hypertension:* Emergency sclerotherapy, Varix ligation or porto-caval anasto-mosis can be done, but mortality and morbidity are high. Hence, patient must be carefully selected with the following criteria: serum albumin above 3 mg%, bilirubin < 3 gm%, prothrombin time not more than 4 sec. above control, absence of ascites and encephalopathy.

15 › Acute Gastroenteritis / Food Poisoning

Acute gastroenteritis is characterized by vomiting, diarrhea and abdominal cramps following ingestion of some irritant or infected food. It is caused by ingestion of Salmonella organisms or toxin of Staphylococci, E. coli, Cl. welchii and even normal intestinal flora. Fungi like Candida albicans and enteroviruses may also cause gastroenteritis.

Management

1. **Diet:** The patient should be given a bland diet with added salt and sour lime. If there is no vomiting, over 2000 ml of fluid should be given in the form of soup, coconut water, fruit juices, kanji, dal water or barley water. Milk and milk products should be avoided. Soft foods like bananas, mashed potatoes, soft rice, toast and biscuits are given if the patient tolerates them.
2. **Fluids and electrolytes:** The patient is encouraged to take oral fluids. If vomiting prevents oral intake or if there is severe dehydration, intravenous fluids should be given. The amount of fluids given should be such that the patient has a urine output of 1-1.5 liters/day. Sodium loss can be corrected by 500 ml of isotonic saline, in addition to the normal saline equaling the volume of vomits and stools. With severe diarrhea potassium too is lost. It is best given orally as fruit juices, coconut water and vegetable soups. If necessary, oral potassium citrate 2-3 gm 6 hourly is given. Intravenous potassium is given, if required, in a drip of 500 cc 5% glucose containing 20-40 mEq of it.
3. **Acid-base:** Patients with diarrhea lose bicarbonate and may frequently develop metabolic acidosis. Ketoacids due to starvation may aggravate it. Sodium bicarbonate 2-4 gm orally 3-4 times may be given. It can also be given intravenously as 100 cc of 7.5% sodium bicarbonate.
4. **Antibacterials:** In case of bacterial infection, oral streptomycin 1 gm tds or chloramphenicol 250 mg four times a day was given in the past. Oral quinolone, ciprofloxacin or ofloxacin and tinidazole or metronidazole are often combined. Oral sulfonamides are also useful.
5. **Symptomatic**
   a. Abdominal cramps could be relieved by propantheline tablets.
   b. Binding of stools is achieved by pectin kaolin 1 tablespoon three times a day, codeine sulfate 15 mg three times a day or diphenoxylate 5 mg three times a day.
   c. Vomiting can be controlled by metoclopramide or domperidone 10 mg tds
6. **Prophylaxis:** All uncooked and cold, stored, outside food should be avoided.

16 › Acute Pancreatitis

Acute pancreatitis is an acute abdominal medical emergency. Obstruction of the pancreatic duct or regurgitation of bile into the pancreas damages the pancreatic acini and releases, initially, minute amounts of trypsin which activates phospholipase to produce fat necrosis, elastase to produce hemorrhagic pancreatitis and kallikrein to produce shock.

Management

1. **Analgesics:** The severe abdominal pain requires

high doses of analgesics. Injection pethidine 100 mg IM 8 hourly or meperidine may be required. Morphine is avoided as it causes spasm of sphincter of Oddi.

2. **Fluids and electrolytes:** Hypovolemic shock is common and requires adequate fluids intravenously. About 2-3 liters of fluids should be given to ensure a daily urine output of 1.5-2 liters. Glucose, potassium and calcium supplements should also be given as required.
3. **Nil by Mouth:** Patient must not be given anything by mouth.
4. **Blood transfusion:** This is helpful if blood hemoglobin level has fallen as happens with hemorrhagic pancreatitis.
5. **Antibiotics:** Gentamicin 60 mg or ampicillin 500 mg 8 hourly helps to eradicate secondary infection.
6. **Trasylol:** 500,000 units as an intravenous bolus has been useful in experimental animals. Its value in human being is not yet proved.
7. **H2-receptor antagonists:** This has not been found useful.
8. **Drugs to inhibit pancreatic secretion:** Food and gastric juice in the duodenum stimulate pancreatic secretion. Hence stomach should be kept empty by passing a nasogastric tube and applying suction. Orally nothing is given except antacids, till abdominal pain subsides.

   Propantheline bromide 15-30 mg IM every 8 hourly or pipenzolate bromide 5 mg IM 8 hourly helps to decrease pancreatic secretion.
9. **Monitoring:** TPR, BP and abdominal girth must be regularly monitored.
10. **Pancreatic abcess and gallstone pancreatitis** will need antimicrobials and SOS surgery.
11. **Pseudocyst** can be aspirated under CT guidance.

17 〉 Hepatic Coma

Hepatic encephalopathy is a potentially reversible disturbance of brain function due to liver disease and/or portal-systemic shunting of the blood.

Precipitating Factors

A. **Trauma:** Ascitic tapping or surgery
B. **Infections:** Pneumonia
C. **Vascular:** GI bleeding and portal vein thrombosis
D. **Miscellaneous:** Electrolyte imbalance, high protein diet and diarrhea

Pathogenesis

The clinical features of hepatic coma are due to the action of nitrogenous toxins on the brain. Many toxins present in the gut, which fail to get metabolized in the liver, reach the brain through blood circulation.

Management

1. **The precipitating factors** as mentioned above must be treated or avoided if possible. E.g. hypokalemia should be treated with potassium and drugs like morphine, pethidine or diuretics should be avoided if possible.
2. **Diet:** Oral proteins are to be discontinued because of the deleterious effects of ammonia that is formed in the gastrointestinal tract. However, parenteral amino acids can be given as they prevent endogenous nitrogen breakdown. Branched chain amino acids leucine, isoleucine and valine are given as 500 ml. of 8% solution and are especially useful. They are contra-indicated if there is associated azotemia.
3. **Measures that affect intestinal bacteria**
   a. *Neomycin 4 gm/day or ampicillin* 2-4 gm/day are used to sterilize the bowel and thus reduce endogenous ammonia production. If there is associated renal insufficiency neomycin is not given, as it is nephrotoxic.
   b. *Lacto-acidophilus bacillus:* This lowers the colonic pH which probably alters the gut flora and perhaps also reduces the intestinal absorption of ammonia.
   c. *Lactulose:* This is a synthetic disaccharide effective in the treatment of hepatic coma. It lowers the pH and causes diarrhea. It can be given orally in the dose of 30-45 ml. 6 hourly or as an enema with 300 ml of lactulose with 700 ml water.

d. *Cleaning enema and bowel washes:* This is usually done at least twice a day using tap water. It can be given with lactose 25% instead of water. The procedure is continued till the returning fluid is free of fecal matter. This is one of the most effective methods of reducing bowel flora and nitrogenous material.

4. **Fluids, electrolytes and calories:** Initially all fluids and calories are administered parenterally. About 1,200 calories per day are given in the form of 10-25% dextrose. Glucose 4 gm/kg/day is usually given round the clock to prevent hypoglycemia.

   Hypokalemia is a common complication and hence 60 mEq/day of potassium should be given slowly intravenously in three divided doses. Potassium is usually given orally once oral feeds are started. Lactic acidosis, which is also common, is treated with parenteral sodium bicarbonate.

5. **Infection:** Infections should be controlled with antibiotics. Prophylactic use of antibiotics to prevent infection is controversial because their use may encourage the growth of Candida group of organisms.

6. **Artificial hemoperfusion:** The aim of hemoperfusion is to clear the amino acids from the blood in view of severe hyperaminoaciduria in fulminant hepatic failure. With hemoperfusion the amino acid clearance is rapid (50 gm in 4 hours). Clinically improvement is significant, but ultimate survival rate is not affected.

7. **Mannitol:** Intravenous 350-500 ml of mannitol helps the raised intracranial tension.

Table 7.4 : Antibiotics for Infections in Hepatic Coma

Organism	Drug
N. meningitidis/ S.pneumoniae	Penicillin G 300,000 units/kg/day (max 24 million units/day) IV q2h or q4h (10-14 days for S.pnemoniae and 5 days after afebrile for N. menigitidis) or ceftriazone or cefotaxime or chloramphenicol
H. influenza	Chloramphenicol 1 gm IV 6-8 hrly or cefotaxime or ceftriaxone
E.coli	Chloramphenicol 1 gm IV 6-8 hrly
Streptococci	Penicillin 1-2 mega units IV 2 hourly
S. aureus	Oxacillin 2 g IV q4h or Vancomycin 1 g IV q12h or Rifampin
S. epidermidis	Vancomycin 1g IV q12h
P. aeruginosa	Ceftazidime 2g IV q8h with IV aminoglycoside therapy
Listeria monocytogens	Ampicillin 2 g IV q4h or Penicillin G 2 million units IV q2h and aminoglycoside for 3-4 wks
Aseptic meningitis	Supportive care (enteroviruses) High dose acyclovir (herpesvirus)

18 › Coma

(Refer Pg. 365)

19 › Meningitis

Meningitis is the inflammation of leptomeninges. It is commonly due to pyogenic bacteria and tubercle bacillus and less commonly due to any virus, spirochete or fungus.

Pyogenic Meningitis

The common organisms causing pyogenic meningitis are meningococci, pneumococci, H. influenza, streptococci, staphylococci, E. coli and Pseudomonas.

Management

I. **Specific treatment:** The specific treatment of pyogenic meningitis is high doses of appropriate antibiotics, preferably two drugs.

   A. *When the causative organism is not known*: Usually two or three drugs are given initially to cover a wide range of organisms. Dexamethasone 0.4 mg/kg q12h for days is benificial for bacterial meningitis due to Hemophilus type b:

      1. Infants aged 1-3 months: Ampicillin *plus* Cefotaxime or Ceftriaxone *plus* Dexamethasone.
      2. Infants above 3 montha, children and young adults: Cefotaxime or ceftriaxone *plus* Dexamethasone.

3. Older adults (above 50 yrs): Cefotaxime or ceftriaxone *plus* Ampicillin *plus* Dexamethasone.

   These are continued till the patient is better and CSF improves. Thereafter, the dose is reduced. However, once the causative organism is identified, the drug effective against that is given and the others discontinued.

B. *When the causative organism is known:* The drugs given depend upon the type of organism and antibiotic sensitivity tests.

II. **Management of unconscious patient:** If the patient has altered consciousness, nursing care for unconscious patients should be given.

III. **Management of raised intracranial pressure:** As given above.

IV. **Symptomatic treatment:**

1. *High fever* can be reduced by tepid sponging over the body and oral or intramuscular paracetamol 500 mg every 6-8 hours. Acetyl salicylic acid can also be used orally or rectally.
2. *Convulsions* can be controlled with phenobarbitone 30-60 mg 8 hourly or phenytoin sodium 100 mg 8 hourly. For uncontrolled convulsions, diazepam 5-10 mg can be used intravenously.
3. *Hypotension and shock* may occur with meningococcal meningitis. Hydrocortisone hemisuccinate 100 mg IV 6 hrly or dexamethasone 6 mg IV 6 hourly may be used.

V. **Treatment of complications:** If brain abscess develops in surgically accessible area, it should be drained. For symptomatic hydrocephalus not responding to dehydrating measures, ventriculo-atrial shunt should be done.

Tuberculous Meningitis

Management

I. **Specific treatment:** The above drugs should be given as soon as the diagnosis is made:

1. *Rifampicin* 450-600 mg orally half an hour before breakfast.
2. *Isonicotinic acid hydrazide* (INH) 300-400 mg orally.
3. *Pyrazinamide* 1.5-2 gm orally.

   These drugs should be continued for 9-18 months.

If drugs cannot be given orally the following drugs may be given.

1. *Injection Streptomycin* 1 gm IM.
2. *Injection* INH 400 mg IM.

Once oral intake is started the above three drugs are started.

II. **Steroids:** Initially dexamethasone 4 mg 12 hourly is given and later oral prednisolone 30-40 mg with antacids is given for 3-6 months and gradually tapered. Steroids are supposed to help reduce complications.

III. **Management of unconscious patient**

IV. **Management of raised intracranial tension**

V. **Treatment of complications:** Refer pyogenic meningitis for III, IV and V.

20 Cerebrovascular Diseases

(Refer Pg. 349)

21 Subarachnoid Hemorrhage

(Refer Pg. 356)

22 Epilepsy

Epilepsy is a brief recurrent disorder of cerebral function due to sudden electrical discharge of cerebral neurones and is usually associated with disturbance of consciousness.

Management

I. **Immediate treatment of an attack of fit:**

1. The patient should be protected from injury. He should be moved away from fire and sharp or hard objects.

2. Padded mouth gag should be inserted between the teeth to avoid tongue injury.
3. Tight clothing should be untied and adequate clear airway should be maintained.
4. Diazepam 5-10 mg should be given slowly intravenously till the fits subside. It can be repeated if required. However, care should be taken as it may cause sudden respiratory arrest.

II. Long term drug therapy

Principles:

1. The drugs should be given in adequate doses for an adequate period such that there is cessation of convulsions. It should be continued for at least 3 years after the last fit.
2. Abrupt discontinuation of the drugs must be avoided as it may precipitate status epilepticus. Drugs must be increased or decreased gradually.
3. Preferably convulsions must be controlled with a single drug. However, if required, combination of drugs may be given.
   A. *Grand-mal* epilepsy can be controlled by one or more of the following drugs:
      1. Phenytoin sodium 200-400 mg. daily.
      2. Carbamazepine 600-1800 mg daily in divided doses.
      3. Sodium valproate 0.25-1.0 gm daily.
      4. Phenobarbitone 60-180 daily.
      5. Primidone 750-1500 mg daily in divided doses.
   B. *Focal epilepsy* can be controlled by one or more of phenobarbitone, phenytoin sodium, primidone and carbamazepine. Sodium valproate is not very useful for focal epilepsy.
   C. *Petit mal* epilepsy can be controlled by:
      1. Ethosuximide 750-1500 mg daily.
      2. Sodium valproate 250-1000 mg daily.

III. Social and Psychological aspects:

1. The patient and the relatives should be educated about the nature of the illness, its precipitating factors and its consequences.
2. Restrictions should be minimum especially in children as they are in danger of being over protected. Cycling, driving and swimming alone at sea should be avoided.
3. The patient should be advised to take occupation in which neither he, nor the community is put at risk by propensity of fits. Exposure to moving machinery and work at height should be avoided.

Status Epilepticus

Status epilepticus is alternate period of convulsions and unconsciousness without any intervening normal period. It is a medical emergency because it may be fatal if not rapidly controlled.

Management

I. Maintenance of airway: The airway should be clear to prevent asphyxia. Hence
   A. Throat suction must be done frequently
   B. Oral airway may be inserted.
   C. The head must be turned to one side to prevent aspiration.

II. Protection from injuries: During an epileptic fit, the patient is prone to develop injuries. Hence
   A. Side railings should be applied to the bed to prevent a fall.
   B. Padding should be applied around the joints.
   C. Mouth gag should be applied to prevent tongue bite.

III. Anti-convulsants:
   A. Diazepam 10 mg IV to be repeated after 10 minutes if required.
   B. Diphenylhydantoin 25-50 mg/min IV in a drip up to 1000 mg totally or till the seizures stop.
   C. Phenobarbitone 200 mg. I.M. or I.V. diluted in 50 ml normal saline over 10 minutes. (Serious hypotension and respiratory failure may occur when these two are given).

D. Paraldehyde 5 ml. I.M. on either buttock.

E. General anesthesia: If the above measures fail.

IV. **Management of unconscious patient:** As above.

V. **Subsequent treatment:**

A. The dose of anti-convulsant drugs must be adjusted.

B. Infections if present must be treated with appropriate antibiotics as they may precipitate status epilepticus.

23 › Sickle Cell Crisis

Patients of sickle cell anemia may be asymptomatic but under certain circumstances like exposure to cold, anoxia, acidosis or infection, increased sickling may occur resulting in sickle cell crisis.

Management

1. **The precipitating cause** should be removed. The patient must be taken to a warm area and infection must be treated with antibiotics.
2. **Oxygen** inhalation may also be helpful.
3. **Hydration:** Adequate hydration must be maintained with oral or intravenous fluids with monitoring of urine output.
4. **For painful sickle crisis:** Analgesics
5. **Exchange transfusion:** To reduce HbS <30%
6. **For priapism:** Priapism is due to thrombosis of the cavernous sinus of the penis by sickled cells. Cold application of ice letting out blood from the sinus, spinal anesthesia or local infiltration with procaine are all useful but following relief of priapism, the patient is often left impotent.
7. **Other drugs:** The other drugs useful for sickle cell crisis are plasma volume expanders like dextran, anticoagulants and papaverine. Antibiotics may be required.
8. **Folic acid:** Folic acid long daily must be given to aid in hemopoeisis.
9. **For aplastic crisis:** Red cell transfusions.
10. **For leg and ankle ulcers:** Rest, limb elevation, antimicrobials, zinc sulfate dressing.
11. **Anti-sickling agents:** Hydroxyurea, Butyrate compounds.
12. **Pneumococcal vaccine**
13. **Bone marrow transplantation**

24 › Acute Hemolytic Crisis

Acute hemolytic crisis may occur with any hemolytic anemia but is commonly seen following mismatched blood transfusion, autoimmune hemolytic anemia and following administration of certain drugs (like primaquine, chloroquine, quinine, chloramphenicol, sulfa, etc.), especially in patients whose red cells have glucose-6-phosphate dehydrogenase deficiency.

Management

1. **The precipitating factor** like blood transfusion or drug must be immediately stopped.
2. **For anemia:** If there is a rapidly developing anemia due to massive hemolysis, blood transfusions or packed cell transfusions should be given preferably with fresh blood and washed red cells. Till the blood is available intravenous fluids should be started.
3. **Corticosteroids:** Hydrocortisone hemi-succinate 100 mg 6-8 hourly should be given especially if hemolysis has occurred following mismatched blood transfusion or autoimmune hemolytic anemia.
4. **For renal failure:** Rapid hemolysis may lead to acute renal shutdown, which can be prevented by maintaining the circulation with intravenous fluids. Other measures which are useful are:
   a. *Mannitol:* 350 ml of 20% solution intravenously.
   b. *Alkali:* Sodium bicarbonate 7.5% 50-100 ml intravenously followed by oral sodium bi-carbonate 1 gm 6 hourly to alkalinize the urine.
   c. *Furosemide:* 100-500 mg intravenously may be given as required if urine output is below 500 ml in spite of adequate circulating blood volume. This may sometimes open up the kidneys.
   d. *Dialysis:* If there is acute renal shutdown,

which is not relieved by the above measures, hemodialysis may be needed.

25 › Aplastic Anemia

Aplastic anemia is a severe anemia due to depression of the bone marrow which results in red cell aplasia, leukopenia and thrombocytopenia.

Management

1. **Removal of cause:** The causative agent should be searched and if found should be immediately stopped e.g. chloramphenicol or industrial toxin.
2. **Barrier Nursing:** Barrier nursing should be carried out to prevent infection to the patient.
3. **Antibiotics:** High doses of potent antibiotics may be required to counter infection. Gentamicin or amikacin with anti-pseudomonal antibiotics like cephalosporins or piperacillin are usually given.
4. **Blood transfusions:** Packed red cell transfusion should be given to maintain the hemoglobin at 8-10 gm%. Platelet transfusion is given to treat bleeding.
5. **Androgens:** Oxymetholone 3-4 mg/kg/day is given for 3-6 months. Alternatively methyl-testosterone 1-2 mg/kg/day is given. These agents and steroids may stimulate the bone marrow. They are contraindicated with liver disease.
6. **Immunosuppressive agents:** Some of the cases of aplastic anemia have an immunological abnormality. Anti-lymphocytic globulin (ALG) with cyclosporin 5 mg/kg/day can be given.
7. **Folic acid:** 10 mg daily acid hemopoeisis.
8. **Granulocyte Colony Stimulating factors** (G-CSF and GM-CSF) may be required.
9. **Allogeneic bone marrow transplantation** can be tried.
10. **Corticosteroids** used only for treatment failures.

26 › Hemophilia

Hemophilia A and B are X-linked recessive disorders which primarily affect the males, are transmitted by females and is characterized by deficiency of coagulation factor VIII and IX respectively.

Management

1. **Local measures:** When bleeding is in muscles or joints, the affected part should be lightly padded and immobilized in a position of maximum utility. Anterior and posterior nasal ice packs should be given for epistaxis. Firm local pressure may stop bleeding from superficial cuts and wounds. Local hemostasis can be achieved by applying fibrin glue or thrombin.
2. **Replacement therapy in Hemophilia A:** If bleeding is mild, factor VIII can be replaced by fresh frozen plasma. However, if bleeding is severe, cryoprecipitate (16-17 times richer than plasma) or factor VIII concentrates (200-250 times richer than plasma) should be given. Factor VIII levels should be raised to at least 25% of normal by injecting 10-15 units of factor VIII/kg body weight. **Hemophilia B** is treated with fresh frozen plasma or factor IX.
3. **Epsilon amino caproic acid (EACA):** EACA is given in a dose of 100 mg/kg 6 hrly orally especially if minor surgery like tooth extraction is planned.
4. **Tranexamic Acid** is an anti-fibrinolytic agent which is also used.
5. **Miscellaneous:**
   a. *Analgesics:* Paracetamol or dextropropoxyphene are useful to relieve pain. Aspirin should be avoided.
   b. *Antibiotics:* Ampicillin 1-15 gm/day may be required to treat infections.
   c. *Intramuscular injections* and cuts and wounds should be avoided. The former may produce deep-seated hematomas.
   d. *Hematinics* like iron and vitamin B complex may be required if blood loss is severe.

27 › Renal Colic

Renal colic is a sudden severe pain in the loin that may radiate into the lumbar region, down the groin and into the testicle on the same side. It may last from minutes to several hours and leaves the patient rolling in bed and writhing in agony. Nausea, vomiting, sweating and abdominal distension may also be present.

Management

1. **Bed rest** and **warmth** over the affected area helps to relieve pain.
2. **Analgesics:** Severe colic may require morphine 15 mg or pethidine 100 mg IM. Dextropropoxyphene or pentazocine orally are also useful.
3. **Antispasmodic:** Atropine 0.6 - 1.2 mg IM often helps to relieve the pain.
4. **Urinary antiseptic:** In presence of infection, urinary antiseptics like norfloxacin 400 mg twice daily ciprofloxacin 200 mg twice daily may be given.
5. **Fluids:** A high fluid intake is advised to achieve a good urine output. If urine output falls, immediate investigations like plain x-ray urinary tract, pyelography and cystoscopy with urethral catheterization must be required.
6. **Surgery:** If the urinary obstruction is present due to a treatable cause like stone, it must be removed surgically. Only medical treatment is unlikely to cure it.

28 Acute Retention of Urine

Acute retention of urine is inability to pass urine which has collected in the urinary bladder.

Management

1. **Reassurance:** The patient who is unable to pass urine is often anxious and strains to pass urine, the failure of which increases the anxiety. The patient should be reassured and asked to relax.
2. **Local measures:** Hot water bag may be applied to the hypogastrium. This is however, avoided in neurogenic bladder with loss of sensations as the patient might burn the skin. Alternatively he may be put in a water bath. These maneuvers may relieve retention.
3. **Cholinergic agents:** Injection carbachol 0.25-0.75 mg may be given intramuscularly. This stimulates bladder wall contraction. However, this is avoided if surgical obstruction is definitely known. It may aggravate bronchial asthma and ischemic heart disease.
4. **Catheterization:** If retention persists, a simple urinary catheter should be passed under strict aseptic precautions, urine evacuated and catheter removed. If repeated catheterization is needed, a self-retaining Foley's catheter should be used. Once catheterization is done, adequate fluids should be administered to achieve a good urine output. Urinary antiseptics should also be given and if required bladder washes.
5. **Supra-pubic aspiration:** If per urethral catheterization is not possible due to impassable obstruction, urine can be evacuated from a full urinary bladder by per abdominal needle aspiration just above pubic symphysis. Strict aseptic precautions should be maintained.
6. **Supra-pubic catheterization:** When repeated catheterization is required, suprapubic cystostomy should be done and catheter inserted into the urinary bladder.
7. **Treatment of cause:** Obstruction to the flow of urine should be removed surgically if possible e.g. prostatic enlargement or bladder neck obstruction.

29 Acute Renal Failure (ARF)

Acute Renal Failure (ARF) is sudden decrease in glomerular filtration rate (GFR) resulting in oliguria (urine output less than 400 ml/day) and elevated blood urea nitrogen (BUN) and serum creatinine.

In hypercatabolic state of acute renal failure there may not be reduction in GFR but BUN production far exceeds the ability of the kidneys to excrete it.

Management

I. **Oliguric phase:** Acute tubular necrosis (ATN) is usually a self-limiting disorder and at present there is no specific therapy. Hence the treatment consists of:
   a. Treatment of the cause when treatable.
   b. Avoiding nephrotoxic agents.
   c. Minimizing the complications of uremia.

1. *Fluids:* In an oliguric patient the daily fluid intake should not be more than previous day's urine output and extrarenal losses (insensible sweating, nasogastric drainage, diarrhea etc.). The fluid balance can be determined by weighing the patient daily. Dehydration as well as over hydration is to be prevented.
2. *Diet:* 40 gm of protein of high biological value (first class proteins) should be given with high carbohydrate content to provide 30 calories/kg/day to prevent endogenous protein breakdown. 50-75 mEq of sodium may be given if there is no hypertension, but potassium should be restricted.

   If the patient is unable to tolerate oral feeding, aseptic hyperalimentation should be given providing essential amino acids and hypertonic glucose. This helps to lower the mortality and slows the rise of blood urea.
3. *Electrolyte and acid-base balance:* Hyperkalemia is common in renal failure. It can be prevented by avoiding potassium rich foods, potassium supplements and potassium sparing diuretics. Hyperkalemia is treated with intravenous 50 ml 50% glucose with 5-10 units of insulin, 100 mEq of sodium bicarbonate and 10-30 ml of calcium lactate or gluconate. Sodium bicarbonate is also useful to treat metabolic acidosis.
4. *Infection:* Infection is prevented especially in acute renal failure because the body's response to infection in uremia is blunted. Indwelling catheter use is prevented, if possible. Adequate pulmonary toilet should be given and antiseptic care of the infusion sites should be taken.
5. *Hypertension:* Renal hypertension requires high doses of potent antihypertensive agents like propranolol and drugs like hydralazine and nifedipine which increase the renal blood flow.
6. *Dialysis:* When the conservative line of treatment fails to maintain optimum clinical status, dialysis should be instituted. It is also considered when there are multiple complications like hyperkalemia, hypo-natremia, acidosis, hypertension, over-hydration, pericarditis etc. Usually alternate day peritoneal or hemodialysis is given, but in hypercatabolic states daily dialysis may be required.

II. Diuretic phase:

During this stage, the aim is to maintain adequate fluid and electrolyte balance. During this stage, excess fluid retained during oliguric phase is excreted and the patient may be dehydrated if fluids are restricted.

30 › Diabetic Ketoacidosis

Diabetic ketoacidosis is the exaggeration or deranged energy metabolism due to deficiency of insulin which results in accumulation of acid metabolites and ketone bodies.

Management

I. Immediate care: In a suspected case of diabetic ketoacidosis, immediately on admission, tests for blood glucose, electrolytes, BUN, creatinine, blood gases and urine acetone must be done. Blood must be collected for sugar, acetone, electrolytes, bicarbonates and urea. Whilst awaiting the reports, fluid loss must be replaced with saline. If doubt exists, 50 cc. of 5% glucose I.V. would help to clarify that the patient is not in hypoglycemic coma.

II. Fluid and Electrolyte balance:

Fluid: Circulating insulin present is ineffective because of poor tissue perfusion. Hence, tissue perfusion must be improved. For volume replacement normal saline(NS) is given to treat hypovolemia, followed with NS or ½ NS at 150-200 cc/hr. (Watch for CHF). One litre of fluid can be given in the first half hour and subsequently 1 litre per hour till dehydration is corrected. Fluid replacement can be done with isotonic saline which prevents too rapid a fall in extracellular osmolality.

Electrolytes: Initially due to tissue catabolism, potassium enters the circulation resulting in

"false" hyperkalemia. However, once insulin therapy is started, along with glucose, potassium too enters the cells leading to a fall in serum potassium levels. Hence, serum potassium must be monitored and hypokalemia must be prevented with potassium supplements. Replacement with potassium is started after K is 4-4.5. Sodium bicarbonate is only given if serum bicarbonates are less than 10 mM/l and pH less than 7.0 Bicarbonates can cause hypokalemia, a paradoxical fall in the pH of CSF and impaired oxyhemoglobin dissociation. Hence, its use is not advocated in milder cases.

III. **Insulin:** Insulin therapy forms the main stay of treatment of diabetic ketoacidosis. It not only lowers the blood sugar but also prevents further lipolysis thereby preventing accumulation of ketones and hydrogen ions. A variety of regimes differing in dose, frequency and routes of administration have been advocated. There is no simple formula to calculate the requirement of insulin and it is more often an intellectual guess.

A. *Conventional therapy:* Consider loading *insulin* dose (0.15 U/kg) and start drip at 3 – 10 units/hour. Usually 1 unit/10 kg/hr and goal of dropping glucose by 75-100 mg/dl/hour. Once glucose is 200-300, bicarb 17-20, anion gap resolved and trace/no ketones in urine, consider change to SQ insulin and starting D5W. Make sure to overlap drip with SQ for at least 20-30 minutes.

B. *Low dose therapy:* The unphysiological nature of the conventional therapy results in marked fluctuations in plasma insulin levels and the risk of hypoglycemia and hypokalemia. The low dose therapy, which is more physiological, reduces these problems.

The circulating insulin levels ranging from 100-200 units/ml can be obtained by a constant intravenous infusion of insulin at a rate of 2-12 units/hr. This produces a rapid and steady fall of blood glucose.

Procedure: Insulin is given in 500 ml of isotonic saline or glucose saline depending upon body weight (0.1 units/kg/hr). The rate of flow is adjusted to deliver 1 ml or 15 drops a minute (approximately 6-8 units/hr.) This also includes the insulin lost by adsorption on to the glass surface and rubber tubes. To minimize the adsorption, human albumin or a plasma substitute containing gelatin (haemaccel) may be used. A pediatric drip set can be used in place of the infusion pump. Patient should be in ICU unit until stable and off insulin drip. The precipitating cause must be treated e.g. *i*nfection *i*nfarction, no *i*nsulin, *i*ncisions (surgery), *i*ntoxication.

Advantages:

1. Frequent estimations of biochemical parameters are not essential.
2. The fall of blood glucose starts immediately without any lag period and is steady and predictable.
3. There is virtually no risk of hypoglycemia or hypokalemia.

IV. **Phosphate:** Phosphate depletion parallels potassium loss and since phosphates are required for the synthesis of 2-3 D.P.G., decreased synthesis of the latter would shift the oxygen dissociation curve to the left leading to cellular hypoxia. This could thus be replaced as potassium phosphate. For phosphate < 0.5 mg/dl, 15 mg/kg (0.5 M/Kg) is given over 4 hours. For phosphate 0.5-1.0 mg/dl, 7.7 mg/kg (0.25 mM/Kg) is given over 4-6 hours.

V. **Magnesium:** Supplemented to keep normal or high end of normal in cardiac patients (exception – renal patients). Oral preparations include Mg Gluconate (500 mg tablet = 2.5 meq) and Mg Oxide (140 mg tab = 7 meq). Mg Sulfate for IV comes in amps: 1 amp = 1 gram (8 meq). Usually repleted with 1-2 grams and rechecked before giving more.

31 〉 Hypoglycemi a

Hypoglycemia is an abnormal depletion of the blood glucose concentration, which is manifested by a characteristic symptom complex, initiated when the nervous system is deprived of glucose. Symptomatic hypoglycemia occurs when blood levels are less than 40 mg%.

Treatment of Hypoglycemic Attack

I. **Glucose:** Early in the attack in a conscious patient, glucose or sugar containing liquids may be given. If he is unable to take it orally, 50 cc of 50% glucose given IV often has a dramatic response. Subsequently the patient is encouraged to take frequent small feeds and glucose.

II. **Drugs**

1. *Epinephrine:* 0.5 cc of 1:1000 epinephrine is given subcutaneously. It stimulates hepatic gluconeogenesis and counteracts hypoglycemia.
2. *Glucocorticoid:* 100 mg of hydrocortisone hemisuccinate or 4 mg of dexamethasone may be given I.V.
3. *Glucagon:* 1-2 mg. I.M. raises blood sugar. It is expensive for routine use.
4. *Mannitol and furosemide* are used to reduce cerebral edema.

Prevention of Hypoglycemia

I. **Reactive hypoglycemia**

A. *Diet:* Reactive hypoglycemia can be managed by simple dietary manipulations. A high protein diet has been advocated as amino acids stimulate insulin release to a lesser extent than glucose. Hence, decreased intake of sugar containing foods, frequent high protein meals and caloric restriction are useful.

B. *Drugs:*

1. *Anticholinergic drugs* are used to inhibit vagal action and delay gastric emptying in patients with accelerated glucose absorption.
2. In the anxious, hyperkinetic patient avoidance of caffeine and cigarettes and the use of mild tranquilizers like meprobamate or diazepam may be beneficial.
3. *Phenformin hydrochloride* has been reported to alleviate hypoglycemia in these patients by inhibiting intestinal glucose absorption thereby inhibiting insulin release.
4. *Insulin inhibitors:* Certain substances like diazoxide, propranolol and diphenyl-hydantoin sodium have been used for treatment of hypoglycemia. However, they have not been thoroughly evaluated as yet.
5. In patients with hypoglycemia associated with early onset of diabetes, beneficial effect has been reported with Sulfonylureas probably because they restore the sensitivity of beta cells to physiological stimuli.

II. **Fasting hypoglycemia:**

A. *Surgery:* In insulinomas, surgical resection of the functioning islet cell tumor has been advocated.

B. *Streptozotocin:* In non-resectable tumors of the pancreas, this drug is useful as it selectively destroys pancreatic tissue. However, following this, the patient may require life-long insulin therapy.

32 › Respiratory Acidosis

Respiratory acidosis is characterized by an increase in pCO_2 and decrease in pH. Bicarbonate is normal until renal compensation sets in and increased it. This is done by excreting chlorides in preference to bicarbonates, thus lowering serum chlorides.

Management

1. **The underlying disease** causing respiratory acidosis must be treated.
2. **Oxygen:** This is required for acute hypoxia but must be given with extreme caution because there is progressive decreased sensitivity of the respiratory centre to prolonged exposure to acidosis and hypercapnia. Hence, hypoxia is the only ventilatory stimulus and administration of oxygen removes it and worsens the patient. If required, oxygen should be given in the concentration of 24-55% with Venturi mask.
3. **Sodium bicarbonate:** If there is uncontrollable hypercapnia and very low pH, sodium bicarbonate is given in small doses. In asthma, it would raise the pH and cause bronchodilatation.

The risks are pulmonary congestion and late metabolic alkalosis. Usually 50-100 cc of 7.5% sodium bicarbonate is used.

4. **Ventilation:** The patient should be put on assisted ventilation till such time that he recovers from his basic disease.
5. **Bronchodilators, postural drainage and antibiotics** should be used as required.

33 〉 Metabolic Acidosis

Metabolic acidosis is characterized by decrease in pH and reduction in bicarbonate concentration. It is compensated by a reduction in pCO_2.

Management

1. **Alkalis:** The primary aim of treatment is to raise the systemic pH to a level where cardiac performance and response to catecholamines is restored and dysrhythmias are less likely to occur.

   Sodium bicarbonate should be given intravenously. Rapid replacement, however, may result in paradoxical rise in pH of CSF and impaired oxygen delivery, hypocalcemia and hypokalemia. Hence, only partial correction of acidosis to a pH of 7.2 should be aimed at and no alkalies should be given if pH is above 7.3.
2. **Specific treatment:** The underlying metabolic derangement should be treated e.g. withdrawal of toxic substances, hyperglycemia, fluid and electrolyte imbalance.
   a. *Diabetic ketoacidosis:* In diabetic ketoacidosis, insulin therapy would enhance ketoacid utilization with bicarbonate regeneration and spontaneous correction of acidosis. Hence alkalies are given only if pH is less than 7.1 or bicarbonates are less than 6 mEq/l.
   b. *Alcoholic ketoacidosis:* This also responds to glucose and saline infusions and alkalies are given only if pH is less than 7.1
   c. *Proximal tubular acidosis:* Here the threshold for bicarbonate is set below the normal value of 26 mEq/L. Hence, bicarbonate wasting occurs when the plasma bicarbonate is raised above the apparent renal threshold. Hence correction of acidosis with bicarbonates increases bicarbonaturia. A new approach is to decrease the effective circulatory volume by sodium restriction. Contraction of the extracellular fluid would reset the glomerulotubular balance upwards and raise the fractional rate of sodium and consequently bicarbonate reabsorption by the proximal tubule.
   d. Methyl alcohol: Administration of ethyl alcohol may be useful Acidosis is corrected by dialysis.
3. **Dialysis:** Whenever the acidosis is severe and uncorrected by large doses of alkalies, hemodialysis or peritoneal dialysis must be done.

34 〉 Respiratory Alkalosis

Respiratory alkalosis is characterized by an increase in pH and decrease in pCO_2. Renal compensation would reduce the plasma bicarbonate concentration.

Management

1. The treatment of the underlying cause usually corrects respiratory alkalosis.
2. **Rebreathing bag:** If there is syncope or tetany due to psychogenic hyperventilation, a rebreathing paper bag would allow carbon dioxide retention and correction of acid-base abnormality. This should be used cautiously and only if serious cerebrovascular disorder has been excluded.
3. **Sedative:** If rebreathing in a bag is not possible, sedatives like diazepam 5-10 parenterally may be helpful.

35 〉 Metabolic Alkalosis

Metabolic alkalosis is characterized by an increase in pH and an increase in bicarbonates. The respiratory response is not usually fully compensated and hence there is only a slight elevation of pCO_2.

Management

I. **Saline-responsive:** In this group of patients the urinary chloride is less than 10 mEq/L.
   1. Intravenous or oral sodium chloride and potassium chloride are given which suppresses acid excretion and promotes bicarbonate excretion.
   2. In severe cases, mineral acids like arginine monohydrochloride is given to titrate the excessive bicarbonate stores. Ammonium chloride too, can be used, but has CNS toxicity.

II. **Saline resistant:**
   1. *Potassium:* This is useful in hyperldosteronism as potassium reverses the intracellular shift of hydrogen ions and enhances bicarbonate excretion.
   2. *Spironolactone:* In hyperaldosteronism, this drug acts as a physiological antagonist.
   3. *Acetazolamide:* In edematous states where saline therapy is contraindicated, acetazolamide is useful as it increases the excretion of bicarbonates and reduces edema.

36 › Dehydration

Dehydration is a deficit in total body water. Almost all forms of dehydration are associated with loss of electrolytes as well.

Management

1. **Fluids:** The patient with dehydration requires fluids. The amount and type of fluid required depends upon the nature of the fluid lost e.g. plasma or blood should be given for burns, dextrose in a comatose patient and saline in vomiting. The amount of fluid varies. It depends upon the amount lost. Adequate hydration can be judged from physical signs, urinary output and specific gravity and hematocrit.
2. **Electrolyte and Acid-base:** The associated electrolyte or acid-base disturbance must be simultaneously corrected e.g. in diarrhea, potassium should be supplemented, in diabetic acidosis, sodium bicarbonate may be required.
3. **Treatment of cause:** The primary cause must be treated. Insulin for diabetes mellitus, corticosteroids for Addison's disease, pituitary extract for diabetes insipidus, etc.

37 › Hypernatremia

Hypernatremia is increase in serum sodium.

Management

The treatment depends upon the underlying cause.

1. When water loss is accompanied by little or no sodium loss as in diabetes insipidus, oral replacement with water or intravenous dextrose is adequate. To treat diabetes insipidus, desmopressin or vasopressin may be necessary.
2. When water loss is also accompanied by loss of electrolytes, Ringer's lactate solution may be used.
3. If there is increased body sodium, in addition to water replacement a diuretic like furosemide 40 mg may be given.

38 › Hyponatremia

Hyponatremia is diminished serum sodium.

Management

1. **Fluid restriction:** The intake of fluid is restricted below the urinary and insensible fluid losses.
2. **Saline infusion:** When neurological manifestations occur due to hyponatremia, the electrolyte imbalance must be corrected with normal or hypertonic (3%) saline intravenously. The amount of sodium required can be calculated by the following formula:

   Sodium (Na) deficit (mEq) =

   0.6 X (Normal Na - Patient's sodium) (Wt in Kg)

   Saline infusions should be avoided in dilutional hyponatremia.
3. **Treatment of cause:** The treatment of cause should be instituted. In SIADH, demeclocycline or lithium salts may be given, whereas in dilutional hyponatremia, along with water restriction, judicious use of diuretics is useful.

39 Hyperkalemia

Hyperkalemia is a rise in serum potassium level. It is a potentially life threatening complication most often occuring with uremia.

Management

I. To counteract the action of potassium and cause its intercellular shift.

1. *Calcium gluconate* 10-30 ml of 10% solution is injected intravenously slowly. It antagonizes the toxic effects of potassium but does not reduce serum potassium level.
2. *Glucose insulin drip:* 500 cc. of 5-10% glucose is given in a drip with about 20-30 units of insulin. Potassium ions enter the cell along with glucose with the help of insulin.
3. *Sodium bicarbonate:* 100-200 ml of 7.5% sodium bicarbonate cause a change in pH temporarily. Hence, potassium ions migrate from plasma to the cells.
4. *Hemodialysis:* In a case of chronic renal failure, hemodialysis itself can reduce the potassium levels.

II. To remove potassium from the body.

Cation exchange resin: Sodium resin (Kayexalate) 20 gm mixed with 30 ml of 50% sorbitol (to prevent constipation) is used. It can also be given rectally as a retention enema for 30 minutes.

III. Treatment of the cause:

The treatment of the primary disease e.g. Addison's disease with steroids, hypoaldosteronism with 9 alpha fluorohydro-cortisone etc. helps to correct the serum potassium levels.

40 Hypokalemia

Hypokalemia is reduced serum potassium level.

Management

The treatment consists of replacement therapy with potassium. Usually oral route is preferred. Potassium chloride 1 gm three or four times a day is given. If serum potassium is 3 mEq/L, the potassium deficit is usually 300 mEq and at 2-2.5 mEq/L, the deficit is usually 500 mEq. Such large deficits usually require intravenous potassium in 500 ml 5% glucose drip, each drip containing 40 mEq of potassium and lasting 6-8 hours.

41 Acute Hypercalcemia

Acute hypercalcemia is increase in serum calcium.

Management

Correct dehydration, increase renal calcium excretion, decrease bone resorption, and treat the underlying disorder.

1. IV hydration 2.5-4 liters NS per day; watch for CHF.
2. IV furosemide 10-20 mg IV BID after volume replete; keep I=O.
3. Specific treatments in approximate desirability of use:
   a. Calcitonin 4 U/Kg SQ BID to 8 U/Kg SQ QID – rapid acting, short acting, often see rebound.
   b. Etidronate 7.5 mg/kg over 4 hours QD x 3-7 days. Slower acting, more effective.
   c. Pamidronate 15-45 mg IV slowly QD x 6 days or as single IV infusion of 90 mg over 24 hours. Also very effective.
   d. Plicamycin (mithramycin-chemotherapy agent) 25 mcg/kg over 4-6 hours Q 1-2 days. Be careful in renal or hepatic failure.
   e. Gallium nitrate 200 mg/m^2 body surface area in 1 liter IV fluid per day x 5 days.

      Nephrotoxin, but also very effective.
   f. Glucocorticoids 200-300 mg hydrocortisone IV QD x 3-5 days.

42 Amebic Dysentery

Amebic dysentery is the disease due to invasion of the intestine by Entameba histolytica.

Management

I. Symptomatic:

1. Diarrhea must be treated with binding mixtures.

2. Fluid and electrolyte imbalance must be corrected with appropriate intravenous infusions.
3. General debility and anemia should be treated with iron, vitamin B complex therapy and high protein diet.

II. **Definitive Treatment:**

1. *Metronidazole:* 800 mg three times a day is given for 8-10 days. It is useful for both intestinal as well as extraintestinal amebiasis. It causes nausea, vomiting and metallic taste in the mouth. It can also be given intravenously 500 mg/100 ml 8 hourly.
2. *Tinidazole:* This has similar pharmacological effects as metronidazole but the toxic effects are less marked. It is given in the doses of 600 mg. thrice daily for five days.
3. *Emetine:* In severe amebic dysentery associated with liver involvement, emetine hydrochloride 65 mg for 3 to 10 days is given along with metronidazole or tinidazole.
4. *Diloxanide furoate* is given in the dose of 0.5 g. three times a day for 10 days especially in luminal cases.
5. *Iodochlorhydroxyquinoline* and *Diiodohydroxyquinoline* given for 8-10 days are also useful in intestinal amebiasis.
6. *Tetracycline:* In acute amebic dysentery Tetracycline 250 mg four times a day helps to eradicate luminal amebae.

III. **Prevention**

Amebiasis can be prevented by avoiding contact with food contaminated with human feces. The drinking water should be boiled and vegetables should be washed in a strong detergent and rinsed in dilute acids like vinegar.

43 › Bacillary Dysentery

Bacillary dysentery is caused by acute infection due to Shigella group of organisms.

Management

I. **Correction of water and electrolyte imbalance:** Most patients can be managed at home. Fluid intake should be adequate, oral electrolyte solutions are given to correct the water and electrolyte losses. Potassium 3-4 gm thrice daily orally may be required as it is lost in diarrhea fluid.

II. **Specific treatment:** Shigella organisms are sensitive to sulphonamide drugs. Phthalyl sulphathiazole is given in the dose of 1.5-2 gm. 8 hourly. Succinylsulphathiazole is the other drug of choice. Once the diarrhea is under control, the dosage can be reduced. If sulphonamide resistance is present, ampicillin 250 mg 6 hourly or tetracycline 250 mg 6 hourly can be given.

III. **Prevention:**

Prophylaxis can be achieved by the following measures:

1. Isolation of proved cases
2. Disinfection of excreta, clothing and bed linen of the patient
3. Protection and treatment of carriers
4. Prevention of fecal contamination of food and water

44 › Cholera

Cholera caused by V. cholerae was one of the most common gastrointestinal emergencies in tropical countries. It is characterized by acute onset of diarrhea, vomiting, fluid and electrolyte depletion, dehydration and acidosis. V. cholerae produces an exotoxin which stimulates the adenyl cyclase in the intestinal epithelial cell and resultant increase in the 3.5 cyclic AMP leads to secretion of isotonic fluid by all segments of the secretion into the intestinal lumen. This occurs in absence of any demonstrable histological lesion in the intestinal cells, or capillary endothelial cells of lamina propria.

Management

1. **Isolation:** The patient should be isolated and all the excreta of the patient measured and properly disposed off.
2. **Fluid, electrolyte and alkali** Intravenous fluids should be immediately started with 500 cc of normal saline at the rate of 50-100 ml/min.

initially till the pulse volume improves. Later, the rate of saline, injection can be reduced. Along with saline 200-500 cc of 7.5% soda bicarbonate or 1/6 normal lactate can be given. The amount of fluid to be given daily should be more than the volume of stools passed. Once vomiting subsides and pulse volume improves, fluid should be given orally. **Dacca solution** is commonly used. It consists of:

1. Sodium chloride 5 gm.
2. Sodium bicarbonate 4 gm.
3. Potassium chloride 1 gm.
4. Distilled water up to 1 litre.

Sodium absorption through the intestine is enhanced when it is administered simultaneously with glucose and amino acids. Glucose, in addition, combats acidosis. Hence, these substances are also added to the oral solution.

Composition of oral fluid:

1. Sodium chloride 4.2 gm/L (72 mEq/L)
2. Sodium bicarbonate 4.0 gm/L (46 mEq/L)
3. Potassium citrate 5.75 gm/L (25 mEq/L)
4. Glucose 20.0 gm/L (110 mEq/L)
5. Glycine 8.25 gm/L (110 mEq/L)
6. Boiled water up to 1000 ml.

At home, **oral rehydration solution** can be prepared as follows:

1. Table salt	1 teaspoon
2. Soda bicarb	1 teaspoon
3. Potassium citrate	1 teaspoon
4. Glucose	1 tablespoon
5. Boiled water	1 litre

Sour lime or any other flavoring agent may be added. Fluid should be given till diarrhea stops. Usually it occurs in 1-2 days.

3. **Antibiotics:** Although adequate fluids alone result in rapid recovery, a dramatic reduction in the duration and volume of diarrhea occurs with antibiotics. Tetracycline 500 mg 6 hourly should be given for 5 days. Chloramphenicol and furazolidone are other drugs, also effective, but less than tetracycline.
4. **Prevention:** Immunization by standard commercial vaccine containing 10 billion killed organisms per ml. gives limited protection for 4-6 months. Hence, it is only useful for travelers who visit the endemic areas for a short period.

45 〉 Typhoid

(Refer Pg. 98)

46 〉 Dengue

Dengue is caused by four distinct subgroups of dengue viruses, which occurs through mosquito (*Aedes aegypti*) bites. Dengue viral infection can present in three clinical patterns.

I. Classic Dengue Fever

Clinical Features

1. *Conjunctivitis:* Prodromal symptoms following incubation period of 5-8 days. Conjunctival congestion and tenderness upon pressure on eyeballs are seen.
2. *Fever, coryza and headache:* Abrupt onset with splitting headache, retro-orbital pain, backache, leg and joint pains. Headache is aggravated by head movements. *Saddle back fever* may be present- fever disappears after a few days of onset and returns after few days.
3. *Insomnia, anorexia* (with loss of taste or bitter taste), *weakness, lymphadenopathy, skin rashes*

Diagnosis

Leukopenia (with neutropenia) with isolation of virus from blood and rising viral antibody titre. Mostly it is a serological diagnosis.

Treatment

Symptomatic treatment with analgesics and antipyretics.

II. Dengue Hemorrhagic Fever (DHF)

WHO Criteria for Diagnosis of DHF

1. *Fever:* Acute onset, high continuous fever lasting for 2 - 7 days.

2. *Hemorrhagic manifestation* including atleast a positive tourniquet test and any one of the following: petechiae, purpura, ecchymosis, epistaxis, bleeding gums, hematemesis, melena.
3. *Liver enlargement*
4. *Thrombocytopenia:* Platelet count < 1,00,000/mm^3
5. *Hemoconcentration:* Hematocrit increased by > 20%

Table 7.5 : WHO Clinical Classification of Drugs

Grade	Clinical Features
I	Fever, Constitutional symptoms, positive tourniquet test
II	Grade I plus spontaneous bleeding
III	Grade II plus circulatory failure, agitation
IV	Grade II plus profound shock (DSS) Undetectable Blood Pressure

All four grades are associated with hemoconcentration and thrombocytopenia

III. **Dengue Shock Syndrome (DSS)**

WHO Criteria for Diagnosis of DSS

Weak pulse with narrowing of pulse pressure (< 20 mm Hg) or hypotension with cold, clammy skin and restlessness

Management of DHF and DSS

Both DHF and DSS are treated entirely symptomatically with fluid replacement, blood transfusions and corticosteroids. Patients often need ICU care with hemodynamic monitoring, antimicrobials, hematological and nutritional support.

47 › Leptospirosis

Leptospirosis is a zoonotic infection which is caused by *Leptospira interrogans*, a tightly coiled spirochete with one axial filament.

Reservoirs of infection include rodents, skunks, foxes, domestic livestock and dogs. Human infection can occur either by direct contact with urine or tissue of infected animals or indirectly through contaminated water, soil or vegetation. Transmission may occur through cuts, mucous membrane and possibly unbroken skin. Tissue damage results from direct toxic action of leptospira or immune response to leptospiral antigens.

1. Most infections appear 7-14 days after exposure and last for 5 -10 days & *resolve spontaneously.*
2. *Biphasic illness*

   Initial first phase (leptospiremic phase) lasts for 4 -9 days and leptospira are present in the blood and CSF.

   Second phase (immune phase) follows after a period of apparent recovery. The symptoms worsen for another 2-4 days. Meningitis and iridocyclitis are more common. Leptospiral antibodies are present in the blood, leptospira disappear from the blood and urine cultures are positive for the organism.

Clinical Features

1. *Fever:* High grade with chills and rigors
2. *Headache*: Severe and retro-orbital or occipital
3. *Conjunctival suffusion:* Pericorneal reddening or hyperemia.
4. *Myalgia:* Severe and affect muscles of thigh and lumbar areas. Severe muscle tenderness and cutaneous hyperesthesia present
5. *Asceptic meningitis:* Combination of fever, headache, neck stiffness or pain due to myalgias suggests meningitis. CSF is usually acellular for first 7 days. Aseptic meningitis occurs in 90% of patients with abnormal CSF.
6. *Cough, pharyngitis, lymphadenopathy, skin rash, uveitis.*
7. *Gastrointestinal:* Nausea, vomiting, abdominal pain, hemorrhage, splenomegaly, acute dilatation of gall bladder with cholecystitis, diarrhea, hepatomegaly, jaundice.
8. *CNS:* Drowsiness, encephalitis, cranial nerve palsies.

Management

1. *Penicillin* 1.5 million units IV 6 hrly for 7 days or any beta-lactam antibiotic.

2. *Doxycycline* 100 mg orally twice daily for 7 days started within 4 days of onset of symptoms
3. *Fluid and electrolyte therapy*: Especially for renal failure and jaundice.
4. *Dialysis* for renal failure
5. *Exchange transfusions* in severe hyperbilirubinemia.
6. *Blood transfusion* may be required if anemia and thrombocytopenia present.

48 › Diphtheria

Diphtheria is an acute infectious disease caused by Corynebacterium diphtheriae and characterized by local exudates on the mucous membranes of nose, throat and larynx and systemic toxemia.

Management

1. **Bed-rest:** This is required as the toxins can affect the heart. Usually bed-rest is required for 3-6 weeks.
2. **Antitoxin:** Anti-diphtheria serum, prepared from horses which have been immunized by injection of diphtheria toxin, is given subcutaneously or intramuscularly in the dose of 10,000 - 1,00,000 units depending on the severity of the disease. It may be repeated after 12 hours, if required. A test dose is usually given before giving the injection to exclude hypersensitivity.
3. **Antibiotics:** A course of ampicillin or erythromycin 500 mg 6 hourly should be given to eradicate the diphtheria bacillus. Antibiotics do not have any effect on the existing toxemia, which can be neutralized only by the antitoxin.
4. **General Management:**
   a. *Diet:* In mild cases, normal diet may be allowed. In moderate to severe cases, initially, fluids are given orally. Gradually semi-solid diet is added and by 2-4 weeks, solid diet is given. If there is palatal palsy semi-solid food is preferred to liquids because liquids may be regurgitated from the nose. If swallowing is affected, feeding should be with Ryle's tube.
   b. *Care of mouth:* The mouth should be cleaned by wiping with damp wool swabs, which are burnt after use. Similarly, nasal discharge should be removed. Syringing the throat and gargling are best avoided.
5. **Treatment of Complications:**
   a. *Cardiac failure:* Diuretics and digitalis may have to be given. Digitalis is not very helpful in diphtherial myocarditis.
   b. *Palatal palsy:* Head-low position may be given to drain the secretions of the mouth.
   c. *Laryngeal obstruction:* Tracheostomy may be required if there is laryngeal obstruction.
6. **Prophylaxis:** Active immunization is given to children at age fourth, fifth and sixth month along with tetanus and pertussis.

49 › Tetanus

Tetanus is the disease caused by the toxin of Clostridium tetani and is characterized by muscular rigidity, spasms and autonomic disturbances.

Management

1. The patient must be kept in isolation in a separate ward and dark room with minimal noise.
2. **ATS** (anti-tetanus serum) 10,000 units is given intravenously on admission to neutralize circulating toxin. Anti-tetanus immunoglobulin is also available, but is costly.
3. **Penicillin:** Injection procaine penicillin 8 lakhs units should be given daily intramuscularly for 8-10 days or one dose of benzathine penicillin 2.4 mega units should be given to kill the clostridial organisms in the wound.
4. **Local wound and ear infection** should be adequately treated with dressing or antibiotic drops. The wound should be kept open as the bacteria grow rapidly in anaerobic conditions.
5. **Muscle relaxants:** High doses of diazepam may be required repeatedly if there are spasms. Usually it is given 4-6 hourly up to 300-400 mg daily. Other drugs like chlorpromazine 25-50 mg IV 6 hourly and Methocarbamol (Robinex) reduces muscle spasm.
6. **Tracheostomy:** If there are repeated spasms or

laryngeal spasms, tracheostomy is done to bypass the upper airway.

7. **Mechanical ventilation:** May be given in severe cases after paralyzing the respiratory muscles.
8. **Antibiotics:** Higher antibiotics may be required for secondary bacterial infection.
9. **Prophylaxis:** Tetanus toxoid is given at sixth, seventh and eighth months as one of the three components of triple vaccine. A booster dose is given at 2 yrs and subsequently every five yrs.

50 › Rabies

Rabies is a fatal viral disease of the central nervous system following infected dog bite. It can also occur due to bite of other animals like cat, fox, wolf, etc.

Management

1. **Isolation:** The suspected patient of rabies should be isolated in a quiet room with facilities for intensive care. Strict barrier nursing should be carried out to protect the nursing staff.
2. **For anxiety:** The patient with rabies is conscious and aware of the impending death. He should be reassured and high doses of potent tranquilizers should be given. Usually diazepam 5-10 gm 6 hourly is given.
3. **Nutrition:** Hydrophobia prevents oral intake. Hence, on admission, even if the patient can swallow well, a Ryle's tube should be passed because, as the disease advances, spasms become more painful and passage of Ryle's tube becomes difficult. Through the Ryle's tube about 2000 ml of fluids with about 2000 calories should be given in the form of fruit juices, rice kanji, milk, coconut water, soups, etc.
4. **Anti-rabies serum** should be given if available.
5. **Prevention:**
   a. Immunization of persons bitten by an animal with anti-rabies vaccine may be helpful even after the bite because of long incubation period.
   b. Animals must also be immunized and strict quarantine of stray animals must be observed.
   c. Human diploid cell culture rabies vaccine should be given to the medical and nursing staff in contact with the patient.

51 › Cerebral Malaria

(Refer Pg. 91)

52 › Acute Poisonings

Management

I. Removal of unabsorbed poison:

A. *Ingested poison* can be removed by:
   1. *Inducing vomiting* with hypertonic saline (if the patient is conscious and cooperative).
   2. *Gastric lavage* in unconscious and uncooperative patients.
   3. *Cathartics* if the patient is seen after 4 hours.
   4. *Bowel washes.*

B. *Inhaled:* If the poison is inhaled:
   1. The patient should be removed from the contaminated atmosphere.
   2. Fresh air or oxygen must be given.

C. *Injected:* For injected poison:
   1. A tourniquet should be applied above the site of injection.
   2. The poison should be sucked by breast pump.

II. Removal of absorbed poison:

In cases of poison excreted by the kidneys:

A. *Increasing urinary output and changing the pH* to that which is optimal for excretion of the poison.

B. *Peritoneal and hemodialysis:* Common poisons which can be eliminated by this mechanism are barbiturates, salicylates, amphetamines, lithium, Mysoline, carbamates, etc.

III. Antidotes:

A. ***Universal antidotes***

Table 7.6 : Universal Antidotes

	Chemical substance	Action	Household equivalent
1.	Activated charcoal	Absorbant	Burnt toast
2.	Magnesium oxide	Neutralizes acid	Milk of magnesia
3.	Tannic acid	Neutralizes alkalis	Strong tea

B. ***Specific antidote:*** These could be given for certain poisons e.g.
   1. Nalorphine for morphine
   2. Oximes and atropine for organo phosphorous compounds.

IV. Maintenance of vital functions:

A. *Airway:* Patent, functioning airway must be maintained as follows:
   1. Suction of throat and nasopharynx.
   2. Insertion of oral airway.
   3. Tracheostomy, if required.
   4. Mechanical respirator, if there is respiratory palsy.

B. *Blood Pressure:* If there is hypotension I.V. fluids, plasma expanders, vasopressors and corticosteroids may be given.

C. *Acidosis* must be corrected by 100 ml 7.5% soda bicarb, intravenously.

D. *Hydration, Nutrition* and *Electrolytes:*
   1. 2000-2500 ml/day or fluids must be given if urine output is about 1000-2000 ml. It may be given as 5% glucose or 5% glucose-saline.
   2. 40-60 mEq of potassium should also be given.

E. *Temperature:* Hypothermia often occurs in barbiturate poisoning. It can be treated by:
   1. Warm blankets
   2. Air-conditioned room and warming of the inspired air

F. *Urine:*
   1. *Condom catheter in males* to prevent soiling of the bed
   2. *Self-retaining catheter* if there is urinary retention. Urinary infection, which commonly follows, must be treated

G. *Bowels:* Enema should be given on alternate days.

H. *Skin:*
   1. Position should be changed often.
   2. Daily sponging should be done and spirit and talcum powder should be used to harden the skin at pressure points.

V. Symptomatic:

A. *Fever:* It should be treated by anti-pyretic agents like paracetamol and tepid sponging.

B. *Pain:* Analgesics like aspirin may be used.

C. *Abdominal colic:* Belladonna compounds may be used.

VI. Management of complications:

A. *Due to poison.*

B. *Due to coma:* Urinary tract infections, respiratory infection, bedsores.

C. *Due to therapy:* Thrombophlebitis.

VII. Medical responsibilities.

A. The samples of body fluid should be saved for chemical analysis.

B. The police should be informed.

C. In case of death due to poisoning, an autopsy must be asked for and the organs must be sent for chemical analysis.

53 › Organophosphorous Compound Poisoning

Management

I. Removal of unabsorbed poison by inducing vomiting, hypertonic saline or gastric lavage.

II. Antidotes:

A. *Atropine:* Atropine counters the muscarinic effects. It is available as 0.6 mg/ml (dilute) and 6 mg/ml (concentrated) solutions. Initially 5 cc of concentrated atropine is taken in a syringe and slowly injected I.V. till signs of atropinization appear e.g. dry

warm skin, dilated pupils, tachycardia, etc. Further I.V. dosage may then be abandoned and dilute atropine can be used for maintenance for the next 2 to 3 days. If signs of atropiniza-tion do not appear, concentrated atropine may be used. Signs of over-atropinization are restlessness, disorientation, delirium, irrelevant talk and hyperpyrexia.

B. *Oximes:* Oximes counter the nicotinic effects of organophosphorous poisoning and should be used early when nicotinic effects like fasciculations or paralysis are present. They are of little value if given after 24 hours. Pyridine-2-Aldoxime Methiodine (PAM) the most commonly available oxime is given in the dose of 1 gm I.V. slowly and repeated after 30 minutes if required.

III. **Management of complications:**

A. *Pulmonary edema:* This is common complications and must be treated by throat suction, oxygen, intravenous furosemide 80-100 mg. atropine till signs of atropinization and hydrocortisone 100-200 mg.

B. *Respiratory paralysis:* Mechanical respirator.

C. *Bronchopneumonia:* Chloramphenicol or ampicillin or 3rd generation cephalosporin should be given 1 gm 8 hourly for 8-10 days..

54 › Acute Alcoholic Intoxication

Management

I. **Gastric lavage** should be done to remove unabsorbed alcohol.

II. **Hypoglycemia** should be corrected with 50 ml of 50% glucose I.V. along with vitamin B complex especially thiamine. (Blood should be collected for blood sugar estimation) prior to the administration of I.V. glucose).

III. **Mannitol** 350 ml of 20% solution can be given IV if the patient fails to improve consciousness.

IV. **If alcohol is contaminated with methyl alcohol:** The patient will have marked metabolic acidosis which is treated by soda bicarb I.V. Hemodialysis may be helpful.

V. **If the patient develops delirium tremens:** I.V. glucose with vitamin B complex and sedatives e.g. diazepam are helpful.

VI. **Treatment of associated complications**

A. Antibiotics should be given for bronchopneumonia.

B. Antacids and bland diet may be required for gastritis.

N.B.: *If an alcoholic continues to be comatose, in spite of treatment, think of mixed poisoning, head injury or hepatic coma.*

55 › Barbiturate Poisoning

Management

I. **Assessment:** The patient must be assessed whether in mild, moderate or severe intoxication. If mild or moderate no vigorous treatment is necessary. The patient must be observed for deepening coma and analeptics; coffee and caffeine may be given.

II. **Airway** must be kept patent as follows:

A. The tongue must be pulled forward.

B. Oxygen 30% is given as higher levels cause hypercapnia.

C. The airway must be cleared of all secretions by suction.

D. Endotracheal intubation (E.T.) may be done to maintain the patient's airway patent.

E. Tracheostomy and bronchoscopic suction may be required if atelectasis is present or if ET is required for more than 48 hours.

F. Intermittent positive pressure respiration is required, if severe respiratory depression with cyanosis and dilated pupils occur.

III. **Shock** is treated by head low position, IV fluids, blood and norepinephrine or mephentermine.

IV. **Gastric lavage:** It is to be given only if recent ingestion, because barbiturates are rapidly absorbed from the gastrointestinal

tract. Laryngospasm may complicate this procedure, which may be avoided by preliminary endotracheal intubation.

V. **Forced alkaline diuresis:**

(To promote renal excretion of barbiturates)

A. 6-10 liters of 5% glucose-saline are given.

B. Mannitol 150-200 ml 2-3 times/day.

C. Furosemide 40-80 mg if urine output is less than fluid intake.

D. Soda bicarb 100 mEq 4-5 times I.V. to alkalinize the blood, which mobilizes barbiturates and facilitates their excretion.

E. Electrolytes are to be given depending on their serum levels.

F. Proper intake and output chart must be maintained.

VI. **General nursing care:**

A. The bladder must be catheterized or a condom catheter may be applied to have an accurate measure of the urine.

B. The patient must be turned every 2 hours and kept on his sides.

C. Care of the mouth, skin and eyes must be taken.

VII. **Dialysis:** It is reserved for profound intoxication especially if anuria or uremia develops.

56 › Acute Salicylate Poisoning

Management

I. **Gastric Lavage:** This should be done immediately to remove as much salicylates as possible from stomach.

II. **Antacids:** Aluminium hydroxide or milk 2 hourly drip through a nasogastric drip, slowly helps to reduce gastric irritation.

III. **Correction of metabolic disturbances:**

A. *Respiratory alkalosis:* This could be treated by I.V. 5% glucose-saline with 60-80 mEq of KCl to correct hypokalemia.

B. *Metabolic acidosis:* This could be treated by I.V. sodium bicarbonate 7.5% 100-150 ml depending upon the arterial pH.

IV. **Symptomatic:**

A. Tepid cold sponging should be done for hyperpyrexia.

B. Anticonvulsants like diazepam, paraldehyde, etc. are given if there are convulsions.

C. Calcium gluconate 20 ml I.V. is given if tetany is present.

V. **Hemodialysis:** To eliminate salicylates or if acid-base imbalance cannot be corrected.

57 › Carbon Monoxide Poisoning

Carbon monoxide (CO) poisoning results from accidental or suicidal inhalation of CO. The toxic effects of CO are due to its high affinity for hemoglobin, which is 200 times more than that of oxygen.

Management

1. **First aid:** The patient should be removed from his environment immediately, the rescuer entering the room in crouching position, holding his breath in deep inspiration. The patient should be immediately given mouth-to-mouth respiration.

2. **Oxygen:** As soon as it is available, 100% oxygen should be given through the oronasal mask. Hyperbaric oxygen (at 2 atmosphere pressure) helps quicker dissociation of carboxyhemoglobin.

3. **Respiration:** Endotracheal intubation should be done if required and the patient may be put on a respirator.

4. **Measures to reduce intracranial tension:** Initial hypoxia damages capillary endothelium and causes cerebral edema. Mannitol, furosemide and glycerol should be given (See raised intracranial tension).

5. **Miscellaneous:** All clothing should be loosened. Hypothermia may be used. Fluid and electrolyte balance must be maintained.

58 Carbon Dioxide Narcosis

Hypercapnia is defined as a $PaCO_2$ in excess of 45 mm Hg at rest. Carbon dioxide narcosis occurs when $PaCO_2$ exceeds 90 mm Hg.

Causes

1. **Central**: Brain stem lesions, central sleep apnea, neuromuscular (peripheral neuropathy, myasthenia gravis, myopathies)
2. **Chest wall:** Kyphoscoliosis, ankylosisspondylitis, trauma, pulmonary (chronic bronchitis, emphysema)

Management

1. Forced ventilation **with intermittent positive** pressure respirator
2. **Correction of acidosis and electrolyte imbalance**
3. **Treatment of underlying disorder**
4. **Oxygen**: This should be administered in a controlled manner (about 2 litres/min) for patients with chronic hypercapnia (e.g. COPD)
5. **Drugs like morphine and sedatives should be avoided in chronic hypercapnia.**

59 Snake Bite

There are about 400 species of Indian land snakes and 30 species of Indian sea snakes. Of the land snakes, 40 are poisonous and of the sea snakes 29 are poisonous. The common poisonous land snakes are the cobra, Russell's viper, saw scaled viper, green pit viper, Echis and krait. The first two are responsible for most of the deaths.

Management

I. First aid

1. *Reassurance:* The patient must be reassured that every snakebite is not poisonous and even if poisonous can be successfully treated.
2. *Immobilization of the part:* The affected part must be immobilized in a functional position (by a splint and application of a crepe bandage) to reduce the rate of spread of the venom. **NO** incision or suction is recommended now.
3. *Tourniquet (only in cases of krait bite):* The site of bite should be lightly wiped by a clean cloth and a band of clean cloth like handkerchief 2-4 cm. wide should be firmly tied 5 cm. above the bite. The tourniquet should be tight enough to occlude the lymphatics but not the arterial or venous circulation. It should be released every 15-20 minutes for 1-2 minutes and reapplied just proximal to the advancing edematous area.
4. *Transport:* The patient must be transported to the nearest medical centre. The snake must be identified and preserved. If it is dead it should be carried to the hospital along with the patient.

II. Medical

1. *On admission in hospital:* An IV line should be established, tetanus toxoid administered, nursing in a lateral position continued, and an anxiolytic drug given if required.
2. *Mandatory observation of the patient for 24 hours* for signs of systemic envenoming is required since krait bite victims sometimes show delayed onset of signs.
3. *Anti-venom therapy:* This is a life-saving passive immunotherapy which would be effective only if the venom is circulating in the body and has not fixed to the tissues resulting in specific toxic effects. Polyvalent antivenom should be given intravenously for its maximum effect, within 24 hours of the bite. It is most effective within 4 hours, of less value after 8 hours and of questionable value after 24 hours. The dose of the anti-venom depends on the amount of envenomation. It is given intravenously:
   a. For local swelling but no systemic symptoms: 20-50 ml.
   b. For systemic symptoms or hemorrhagic abnormalities: 50-90 ml.
   c. For severe systemic manifestation: 100-150 ml.

d. Larger doses are given to children and underweight persons to neutralize relatively higher venom concentration. 1 ml of polyvalent antivenom neutralizes 0.6 mg. of cobra, 0.6 mg of viper and 0.45 mg of krait and saw scaled viper venoms. Monovalent sera are more specific and more potent and should be used if the snake has been identified.

Before administering the antivenom, skin sensitivity test should always be performed to avoid severe anaphylaxis.

4. *Antibiotics:* Broad-spectrum antibiotics like ampicillin, chloramphenicol or tetracycline 250 mg four times a day may be given to check infection of the devitalized part especially in viper bites.
5. *Fluids, electrolytes, diuretics, pressor amines* are used judiciously for management of hypovolemia, fluid overload and cardiac complications.
6. *Analgesics:* This may be required for pain. Aspirin 300 mg. three times a day with antacids or dextropropoxyphene may reduce the pain.
7. *Blood constituents:* In hypovolemia, plasma, its substitutes or albumin may be given to expand plasma volume. Red cells lost due to lysis or bleeding may require packed cells or whole blood.
8. *Antihistaminics, Adrenaline* and *Steroids:* They have to be available to manage anaphylaxis or allergic reaction occurring due to the administration of antivenom.

III. Specific Treatment:

1. *Neostigmine:* In cobra-bite, 95% of the offending toxins produce neuromuscular block by acting on post junctional membrane of motor end plate, similar to curare, resulting in paralysis, which is reversed by neostigmine. It is not effective if the neuro-muscular block is complete. Neostigmine should be given as soon as the neurological signs appear and should be continued till complete neurological recovery. Premature discontinuation may lead to a relapse. Neostigmine 0.5 mg IV is given every half hour for six injections, and then if the symptoms have reduced, every hourly for three injections followed by one injection every 2-3 hours till all the signs of paralysis have disappeared. Each dose of neostigmine is preceded by 0.6 mg of atropine IV.

   This treatment is not only highly effective, but also completely safe as there are no side effects.
2. *Heparin and coagulation factors* are not recommended now.
3. *Human fibrinogen:* 300-600 gm is given intravenously within the first 24 hours of treatment after effective control of clotting.

IV. Treatment of Complications

1. *Shock:* Hypovolemic shock is best treated with 5% albumin, which is superior to glucose or saline solutions. Dopamine and corticosteroids are used if necessary and electrolyte disturbances, if present, are corrected.
2. *Acute renal failure:* Oliguria and hematuria are the earliest signs. It is treated by restoration of fluid and electrolyte balance, and administration of 300 cc of 20% mannitol or 200-500 mg. of furosemide. If renal shut down occurs, hemodialysis may be required.
3. *Respiratory failure:* Respiratory muscle paralysis leads to respiratory failure with resultant hypoxia and hypercapnia. This requires ventilation with a respirator or Ambu bag and proper control of blood gases.

60 Scorpion Bite

There are nearly 1000 species of scorpions and 86 of them are found in India. The Indian red scorpion produces neurotoxic venom that is toxic to man. *Palamnaeus gravimanus*, also found in India, inflicts painful sting without systemic envenoming.

Management

I. First Aid:

1. *Cuts at sting site and tourniquet* are **not** advisable.
2. *Local Pain* can be relieved by application of cold or ice over the site of sting.

II. Medical:

1. *For Pain:* If the pain is intolerable, local anesthesia can be given using 2% lignocaine without adrenaline. Oral or sublingual non-steroid anti-inflammatory agents (NSAID) can also be given. In the past, inj. dihydroemetine 60 mg/ampoule was injected in the local site of the bite.
2. Oral diazepam is useful in *relieving anxiety.*
3. *Correction of Dehydration:* Dehydration due to vomiting, salivation and sweating should be corrected by continuous vigorous oral rehydration solution. This helps to correct initial hypotension and shock. IV crystalloid solution or hydration by nasal tube may be necessary in a confused, agitated child.
4. *Fluid replacement* must be done since hypovolemia is one of the proposed mechanisms of shock syndrome in scorpion sting.
5. *Electrolyte imbalance* should be corrected.

III. Scorpion Antivenin

This is available in India. It does not prevent or protect the victim from development of severe cardiovascular manifestations and it may give anaphylaxis. The half life of antivenin is 11-102 times longer than venom and takes 45 minutes to reach peak tissue concentration. It does not prevent the autonomic storm. Recently it has been reported that scorpion antivenin is no better than a placebo.

IV. Specific Treatment:

1. *Prazosin* is a selective alpha-1 adrenergic receptor blocker. Its pharmacological properties can antagonize the hemodynamic, hormonal and metabolic toxic effects of scorpion venom.

   Dose: 125-250 μg in children and 500 μg in adults; repeated 3 hourly until there are signs of clinical improvement in tissue perfusion i.e. warming of extremities, increase in urine out put, appearance of severe local pain at sting site which was absent or tolerable on arrival, disappearance of paresthesias, reduction or improvement in heart rate, pulmonary edema and reduction in raised blood pressure, and rise of blood pressure in hypotensives without hypovolemia. The dose should be repeated six hourly till extremities became dry and warm. If the initial dose has been vomited, prazosin dose should be repeated.

   In confused, agitated, non-cooperative children, prazosin should be administered by nasal tube after giving IV diazepam. First dose phenomenon is rare with this dose. However due care should be taken to avoid postural fall in blood pressure. Children should not be allowed to be lifted. Postural hypotension should be treated by giving head low position and IV fluids.

V. Treatment of Complications:

1. *Pulmonary Edema:* In addition to prazosin, patients should be given *IV aminophylline* 5 mg/kg diluted in dextrose as a slow bolus to counteract the associated bronchospasm. If available, isosorbide buccal spray is useful or powder of nitroglycerine should be rubbed on the gum. *IV frusemide* (10-20 mg) should be given to reduce the preload and pulmonary congestion.

   IV sodium nitroprusside drip (SNP) 3-5 μg/kg/min can be started and dose should be raised continuously according to patient's response. Blood pressure should be closely monitored and maintained at the level of systolic 80-90 mm Hg. SNP has to be prepared from fresh powder every 4 hours, the bottle and IV line should be protected from light. At times a severe case may require 15-36 hours of SNP drip to clear pulmonary edema. Oral or injectable cyanocobalamin can be given to avoid cyanide toxicity whenever SNP is given for

long time. *IV nitroglycerine* can be used if SNP is not available.

2. *Shock/hypotension*: Early administration of IV dobutamine 5-15 µg/kg/minute with simultaneous SNP drip may be life saving.
3. *DIC, subdural haematoma and hemiplegia* are known to occur and should be treated with fresh blood transfusion.
4. *Delirious or comatose patients* may benefit from hyperbaric oxygen.
5. *Non-cardiac pulmonary or secretory pulmonary edema or adult respiratory distress syndrome* are rarely seen due to red scorpion envenomation but may necessitate tracheal intubation and hyperventilation.

61 〉 Hyperpyrexia

Hyperpyrexia is extremely high body temperature, which left untreated may damage various organs and results in death. Usually the rectal temperature is higher than 105°F and may be associated with sweating, headache, dizziness, restlessness, confusion, convulsions and coma.

Management

I. **Measures to reduce body temperature:**

1. The patient should be transferred to an *air-conditioned room* if available, and the temperature of the room kept as low as possible.
2. *Tepid sponging* with sheets soaked in cold water should be started. Alternately, the patient should be dipped in a bath of cold water. Alcohol can be added to the cold water bath as it helps to increase heat loss from the body.
3. *Ice water enema* can be given to lower the temperature.
4. *Ice-cap* should be placed on the head and forehead should be frequently compressed with ice.
5. *Oxygen* should be given at 6-8 liters/min. with the help of nasal catheter.
6. *Lytic cocktail* consisting of pethidine 100 mg, phenergan 50 mg and chlorpromazine 50 mg is used to lower the body temperature.
7. *Aspirin* capsule can be used per rectally.

II. **Sedation:** Phenobarbitone 30-60 mg three times a day helps to relieve restlessness, convulsions and reduce metabolic heat production.

III. **Fluid and electrolyte balance** should be maintained. If there is **dehydration,** isotonic saline should be given.

IV. **Management of unconscious patient:** If the patient is unconscious. (Refer Coma Pg. 365).

62 〉 Drowning

Drowning is asphyxiation from submersion in water. If drowning is in fresh water, the aspirated water enters the circulation producing hemodilution, severe hemolysis and hyperkalemia. If it occurs in salt water, the aspirated fluid is hypertonic and hence causes diffusion of the blood into the alveoli resulting in pulmonary edema.

Management

I. **Immediate treatment:** Immediately after the patient is rescued, respiratory support should be given by clearing the airway and giving mouth-to-mouth respiration. If the Ambo bag is available it should be used. If available, oxygen should also be administered.

If the carotid pulse is not palpable, an external cardiac massage should be given.

The patient should be transferred to the hospital and basic life support continued in the ambulance. Even if respiration and circulation are adequate, the patient must be hospitalized for at least 48 hours for observation.

II. **In the hospital**

1. *Respiration:* The airway should be cleared and a cuffed endotracheal tube should be passed. Suction of throat and lung should be done as required. If spontaneous ventilation is absent or inadequate, intermittent positive pressure respiration should be given.
2. *Circulation:* In sea-water drowning,

hypovolemia commonly occurs and hence theyshouldbetreatedwithplasmaexpanders like dextran. If hypotension persists in spite of adequate fluid replacement, vasopressors like mephentermine 60 mg intravenously or dopamine 0.2 mg in a drip of 500 ml should be given.

3. *Blood transfusion:* Thisis required if there is massive hemolysis and hemoglobin level falls.
4. *Alkali:* Acidosis, which is usually present should be corrected by 7.5% sodium bicarbonate intravenously.
5. *Diuretics:* Furosemide 40-80 mg IV is useful in pulmonary edema.
6. *Steroids:* Hydrocortisone 100 mg IV 8 hourly has been used in very ill patients but is of doubtful value.
7. *Antibiotics:* Usually a broad spectrum antibiotic like ampicillin or tetracycline 1-1.5 gm daily may be used to prevent or treat aspiration pneumonitis.

Electrocardiography

8

1 Introduction

An electrocardiogram (ECG) is a graphic record of the electrical activity of the heart.

The ECG paper is a specially prepared paper with small and large squares. The ECG paper moves at a rate such that in one minute 300 large square or 1,500 small squares are covered. Thus 1 small square equals 0.04 sec. and one large square equals 0.20 sec. To calculate the heart rate, one must divide 1,500 by the number of small squares between two heartbeats. The vertical axis represents the voltage. One small square equals 0.1 mV.

The normal ECG consists of P, Q, R, S, T and U waves.

The P wave signifies atrial activity and it is normally an upright wave. It precedes the QRS complex. The QRS complex signifies ventricular depolarization. The Q wave is the negative deflection that precedes the R wave, whereas the S wave is the first negative deflection that follows the R wave. The R wave signifies ventricular repolarization and normally it is upright. The U wave is the positive deflection that follows the T wave. It probably represents re-polarisation of Purkinje's fibres, ventricular septum or slow ventricular repolarisation.

The PR interval is the time taken for the impulse to go from the S.A. node to the ventricles. The QT interval is the time taken for the ventricular events-depolarization and repolarization.

The ECG is reported as follows:

1. Standardization: Full/Normal
2. Voltage
3. Rate
4. Rhythm
5. Axis
6. Position
7. P Wave
8. PR Interval
9. QRS Complex
10. QRS Duration
11. ST Segment
12. T Wave
13. QT Interval
14. U Wave
15. Conclusion

2 Normal ECG

Interpretation

Voltage: There is no exact definition of normal voltage. Usually the R and/or S wave in each lead varies from one to four or five big squares.

Rate: Varies from 60-120/min.

Rhythm: Regular

Axis: The normal mean frontal plane QRS axis lies between - 30° and + 100°.

Position: The normal position is intermediate i.e. there is an R wave in both leads aVL and aVF.

Rotation: Normally there is no clockwise or counterclockwise rotation i.e. transition from S to R wave occurs between lead V_2 and V_4

P wave: The normal P wave is not more than 0.25 mV in amplitude and not more than 0.12 sec duration.

PR interval: The normal PR interval is between 0.12 and 0.20 sec.

QRS complex: In standard leads there is a dominant R wave. In lead V_1 there is a small r wave and big S wave. Gradually the R wave increases and the S wave decreases in amplitude from V_1 to V_6

QRS duration: The normal QRS duration is from 0.04 to 0.12 sec.

ST segment: The normal ST segment is isoelectric.

T wave: The T wave is normally inscribed in the same direction as the QRS complex. It is usually upright except in lead aVR and V_1.

QT-c interval: Normal QT-c interval is from 0.35 to 0.43 sec.

U wave: Normally the U wave is absent or it may be just present. Its amplitude and duration are less than that of the T wave.

3 › Waves and Complexes

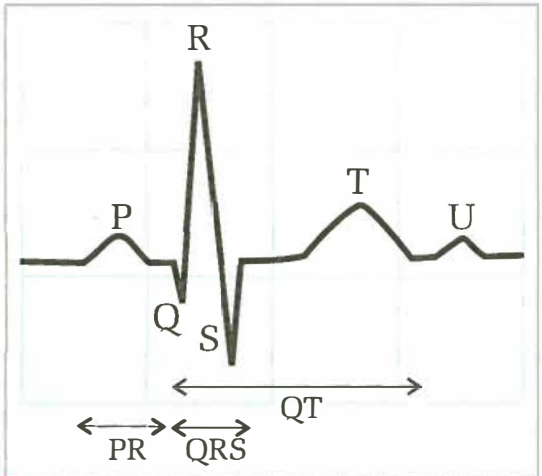


Fig. 8.1 : Normal ECG tracing showing the components of an ECG complex

P Wave

The P wave is produced by atrial depolarization. This wave is best visualized in lead II and normally does not exceed 3 mm. in height (0.3 mV) or 3 mm horizontally (0.12 sec.). The P wave is upright in all leads except aVR.

Abnormalities: The P wave is

1. *Absent* in atrial fibrillation, nodal rhythm, sinoatrial block and hyperkalemia.

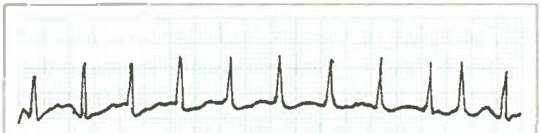


Fig. 8.2 : Absent P waves

2. *Wide and notched (**P-mitrale**)* in left atrial enlargement.
3. *Tall and peaked (**P-pulmonale**)* in right atrial enlargement.

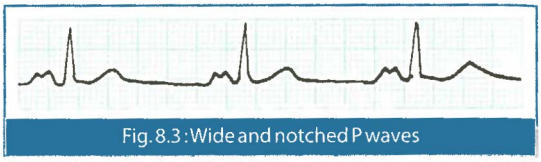


Fig. 8.3 : Wide and notched P waves

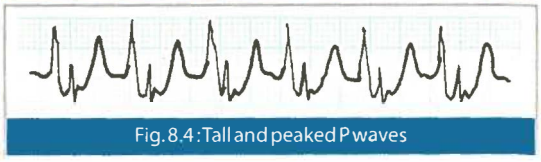


Fig. 8.4 : Tall and peaked P waves

Causes of atrial enlargement:

a. Mitral or Tricuspid stenosis.
b. Secondary to pulmonary hypertension.
c. Secondary to cor-pulmonale.
d. Secondary to ventricular hypertrophy.
e. Lutembacher's syndrome (MS with ASD)
f. Left atrial myxoma.
g. Cor triatrium

4. *Inverted in Lead* I in dextrocardia, incorrect electrode placement and retrograde atrial activation.

QRS Complex

The QRS complex is produced by ventricular depolarization. It is a complex comprising of Q, R and S waves.

1. **Q wave:** The Q wave is the negative deflection that precedes the R wave. It denotes depolarization of the ventricular septum from left to right.
2. **R wave:** The R wave is the first positive deflection of the QRS complex. It denotes depolarization of the ventricles, at first the anteroseptal portion, followed by the major ventricular muscle mass.
3. **S wave:** The S wave is the first negative deflection of the QRS complex that follows the R wave. It occurs due to depolarization of the posterobasal part of the left ventricle, pulmonary conus and the uppermost part of the interventricular septum.
4. **R' wave and S' waves:** The R' wave is the second positive wave of the QRS complex and the S' wave is the second negative deflection of the QRS complex after the R wave.

The relative heights of the QRS complex vary with the leads examined, the position of the heart and the degree of abnormality present.

Voltage of QRS Complex

Low Voltage: The QRS complex is the less than 5 small squares in most of the leads. This occurs in *pericardial effusion, myxedema, emphysema,* and in some individuals with a *thick chest wall.* An erroneous low voltage may be recorded if the machine is placed on half standardization.

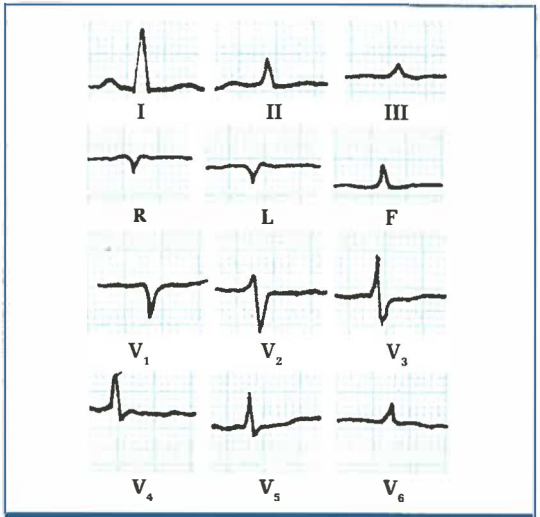


Fig. 8.5: Low voltage

High Voltage: This signifies ventricular hypertrophy.

1. **Left:** The sum of the S wave in lead V_1 and R wave in lead V_6 would be more than 35 small squares.
2. **Right:** There would be a tall R wave more than 7 small squares in lead V_1.

Axis

The axis is determined by noting the QRS complex in leads I and III.

Left Axis Deviation is said to occur when the axis lies between -30° and -90°

If there is a prominent R wave in lead I and a prominent S wave in lead III, it is left axis deviation.

Causes

1. Left ventricular hypertrophy
2. Left anterior hemi-block
3. During expiration
4. High diaphragm - ascites, obesity, pregnancy, and abdominal tumors.
5. Emphysema
6. Hyperkalemia
7. Endocardial cushion defect, Primum ASD, tricuspid atresia
8. Cardiomyopathies

Right Axis Deviation is said to occur when the axis lies between +90° and +180°

If there is a prominent S wave in lead I and a prominent R wave in lead III, it is right axis deviation.

Causes

1. Right ventricular hypertrophy, acute RV strain, pulmonary embolism
2. Right bundle branch block
3. Left posterior hemiblock
4. Normal variation, infancy
5. During inspiration
6. Dextrocardia
7. Emphysema, cor pulmonale
8. Congenital Heart Diseases: Secundum ASD, Fallot, severe PA, TAPVD

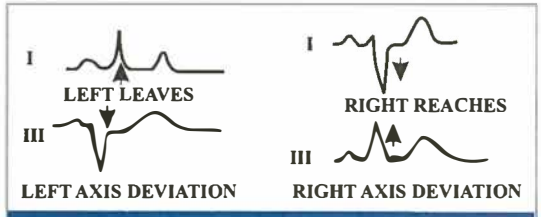


Fig. 8.6: Left and right axis deviation. Leave each other = Left axis deviation (LAD). Reach for each other = Right axis deviation (RAD)

T Wave

The T wave is produced by ventricular repolarization. It is a smooth dome-shaped wave with two limbs asymmetrical, the peak being nearer the end than the beginning. It is normally upright, except in leads III, aVF, V_1 and V_2.



Fig. 8.7: Inverted T waves

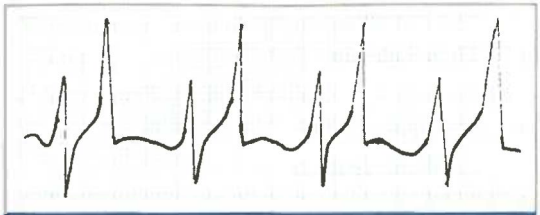


Fig. 8.8: Tall T waves

Abnormalities: The T wave is

1. *Inverted* in myocardial ischemia. The two limbs of the T wave become symmetrical with myocardial infarction.
2. Flat in thick chest-walled individuals, emphysema, pericardial effusion, myxedema, myocarditis, myocardial ischemia, non-penetrating chest injuries, hypokalemia, hypocalcemia, hyperventilation and anxiety state.

U Wave

The U wave represents the slow repolarization of the Purkinje's fibers, the papillary muscles or the ventricular septum. It follows the T wave and precedes the P wave of the next cycle. It has the same polarity as the T wave and hence it is upright in most of the leads.

U waves tend to be inverted in II, III, V_1 and V_2. It is transiently inverted during *angina, acute pulmonary embolism, left ventricular overload and digitalis effect* and sometimes in *myocardial infarction*. In myocardial infarction most of the changes may revert to normal and yet inverted U waves may persist.

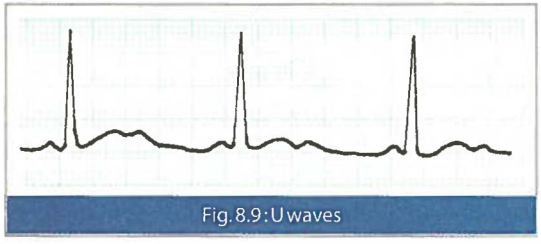


Fig. 8.9: U waves

P-P and R-R Interval

When there is sinus rhythm, the P-P and R-R intervals are equal. They are used to calculate the heart rate. The P-P interval denotes the atrial rate and the R-R interval denotes the ventricular rate.

Calculation of heart rate: In 1 minute, with the normal speed, 1500 small squares are covered. Hence if the P-P or R-R intervals is X and the heart rate/minute is Y then if X squares cover 1 beat, 1500 squares cover Y beat (heart rate/min).

$$Y = \frac{1500}{X} \text{ beats/min.}$$

Thus the heart rate can be calculated by dividing 1500 by the number of small squares between two consecutive P or R waves. The R-R interval in the ECG below is 25. Thus the heart rate is 1500/25=60 beats/min.



Fig. 8.10: Heart rate 60/min

PR Interval

The PR interval is measured from the beginning of the P wave to the beginning of the QRS complex and hence the term PQ interval is more accurate. It represents the time interval between atrial and ventricular depolarization and hence includes the time taken for atrial depolarization, atrial repolarization and the delay of excitation in the AV node.

The **normal PR interval** ranges from 0.12-0.20 seconds.

Abnormalities: The PR interval is

1. *Increased* in *Rheumatic fever (Minor Jones criteria), ischemic heart disease,* following *digitalis or quinidine therapy,* with *ASD* and *mumps.*

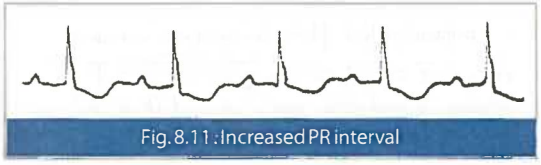


Fig. 8.11: Increased PR interval

2. *Decreased* in *WPW and LGL syndromes* and AV *nodal rhythm.*

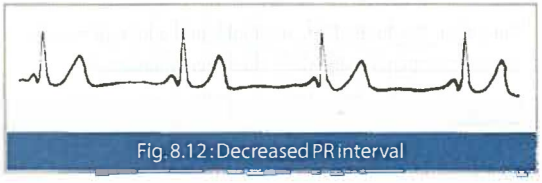


Fig. 8.12: Decreased PR interval

QRS Interval

The QRS interval is the time taken for ventricular depolarization. It is measured from the beginning f the Q wave to the end of the S wave.

The upper limit of a **normal QRS interval** is 0.1 sec.

Abnormalities: The *QRS interval greater than 0.12* seconds indicates bundle branch block or intraventricular conduction defect.

Bundle Branch Block (BBB)

Definition : BBB is a delay or block in conduction to the right or left main branch of the bundle of His.

Diagnosis : BBB is diagnosed on an ECG by

1. An abnormally prolonged QRS interval of 0.12 sec. or more due to a delay in and an abnormal spread of excitation through the ventricles.
2. The VAT is prolonged.
3. The ST segment is depressed and T waves are inverted.

Classification

1. Unilateral BBB
   a. Right BBB (RBBB).
   b. Left BBB (LBBB).
2. Peripheral left ventricular conduction defects
   a. Left anterior fascicular block (LAHB).
   b. Left posterior fascicular block (LPHB).
3. Bilateral BBB
   a. RBBB with LAHB.
   b. RBBB with LPHB.
   c. Alternating RBBB and LBBB.
   d. RBBB/LBBB with prolonged AV conduction.
4. Trifascicular block

Right Bundle Branch Block (RBBB)

In RBBB there is right axis deviation and rsR^1 pattern of QRS complex in leads V_1 and V_2.

Causes

1. In a normal person young people without any cardiac lesion
2. Coronary heart disease
3. Myocarditis
4. Right ventricular strain e.g. acute pulmonary embolism
5. Congenital e.g. ASD (ostium primum type)

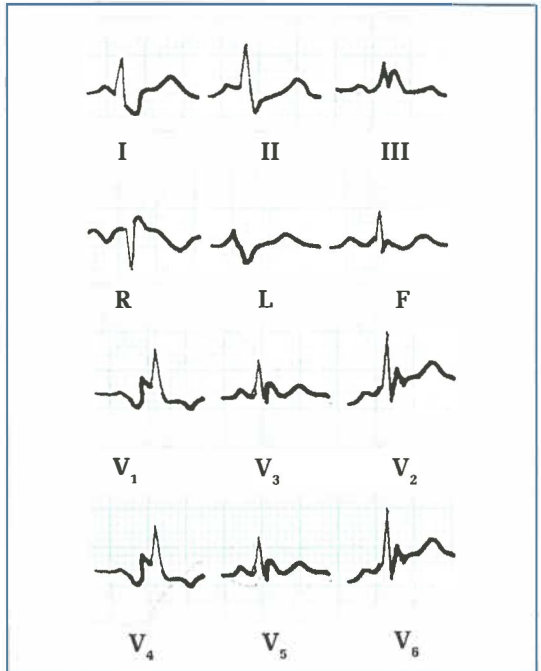


Fig. 8.13 : Right bundle branch block

6. Any condition that produces right ventricular hypertrophy
7. Hypertension

Differences between RBBB and RVH

		RBBB	RVH
1.	QRS interval	More than 0.12 sec.	Less than 0.12 sec.
2.	Rt. ventricular leads	rsR' complex	QR complex
3.	VAT	More than 0.06 sec.	0.03 - 0.05 sec.

Left Bundle Branch Block (LBBB)

In LBBB there is usually left axis deviation and rsR^1 pattern of QRS complex in leads V_5 and V_6

Causes

1. Coronary heart disease
2. Cardiomyopathy and myocarditis
3. Heart failure
4. Aortic valve disease
5. Hypertension
6. Drugs: Quinidine

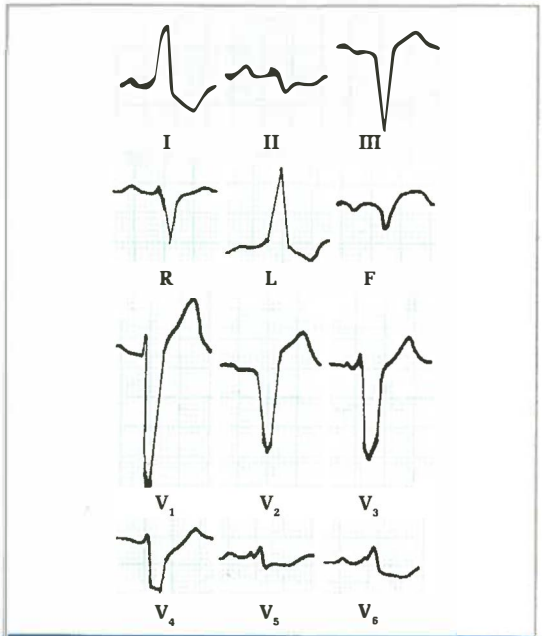


Fig 8.14 : Left Bundle Branch Block

N.B.: Voltage criteria for the diagnosis of LVH are not valid in the presence of LBBB.

QT Interval

The QT interval represents the duration of ventricular systole and is measured from the beginning of the Q wave to the end of the T wave. It varies with the heart rate. QT interval corrected for the heart rate is called QT-c interval.

Normally QTc interval does not exceed 0.44 sec.

$$QTc = \frac{\text{QT interval}}{\text{R-R interval}}$$

Abnormalities: The QT interval is

1. *Increased* in acute rheumatic carditis, myocarditis, hypokalemia, hypocalcemia, following quinidine, prenylamine lactate and procainamide therapy, cerebrovascular accidents and cardiac syncope.

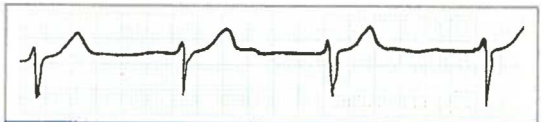


Fig. 8.15 : Increased QT interval

2. *Decreased* in hypercalcemia and following digitalis and phenytoin sodium therapy.

ST Segment

The ST segment is measured from the ST junction to the beginning of the T wave. It is usually iso-electric but may be slightly depressed (0.5 mm) or elevated (0.2 mm) in precordial leads. The depression or elevation of the ST segment should be evaluated in relation to the TP segment (i.e. the part between the end of the T wave and beginning of the P wave of the following cardiac cycle). It represents the time between ventricular depolarization and repolarization.

ST segment must not deviate more than 1 mm above or below isoelectric line in any lead.

Abnormalities: The ST segment is

1. *Sagging* in coronary artery disease.
2. *Mirror image of correction mark* in digitalis effect.
3. *Depressed and convex upwards* in strain pattern.
4. *Raised with convexity upwards* in myocardial injury.
5. *Raised with concavity upwards in pericarditis.*

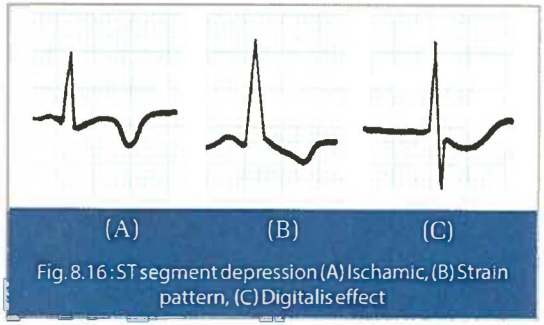


Fig. 8.16 : ST segment depression (A) Ischamic, (B) Strain pattern, (C) Digitalis effect

Causes of Raised ST segment

1. Acute Myocardial infarction
2. Prinzmetal vasospastic angina
3. Ventricular aneurysm
4. Pericarditis
5. Early repolarization

Causes of Depressed ST segment

1. Acute subendocardial ischaemia/infarction
2. Digitalis effect and toxicity
3. L.V. hypertrophy and strain

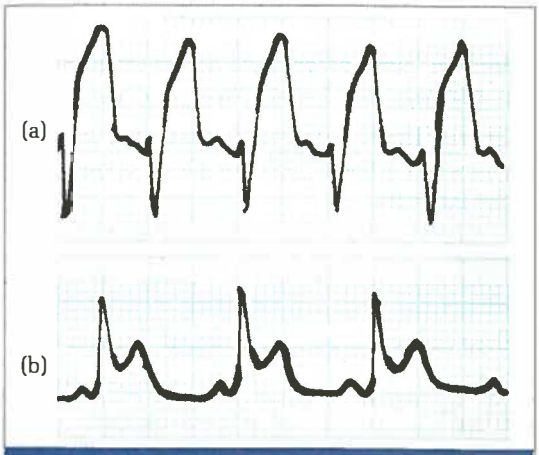


Fig. 8.17: Raised ST segment: a) convexity upwards (myocardial injury), b) concavity upwards (pericarditis)

4 Myocardial Infarction

(Refer Pg. 214)

Myocardial infarction (MI) is a sum total of:

1. Myocardial injury (Raised ST segment convex upwards).
2. Myocardial ischemia (Inverted T-waves peaked and symmetrical).
3. Myocardial necrosis or completed infarction (Deep and wide Q wave).

ECG criteria are essential criteria for diagnosis of MI

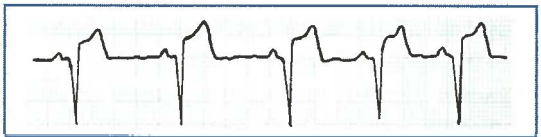


Fig. 8.18: Acute myocardial infarction - Q waves, ST elevation and T wave inversion.

5 Ventricular Enlargement

The ECG changes in ventricular hypertrophy are:

1. **Increased voltage**: In ventricular hypertrophy the muscle cells are not increased in number. The action potential of a hypertrophied muscle cell is not increased. However, the height of the QRS complex is increased due to altered geometric projection of the electrical forces.
2. **Wide QRS**: The QRS interval increases upto 0.12 sec. due to a delay and alteration of conduction. The VAT also increases.
3. **ST depression**: ST depression occurs due to endocardial ischaemia and fibrosis.
4. **T wave inversion**: T wave inversion is asymmetrical due to changes in repolarization.

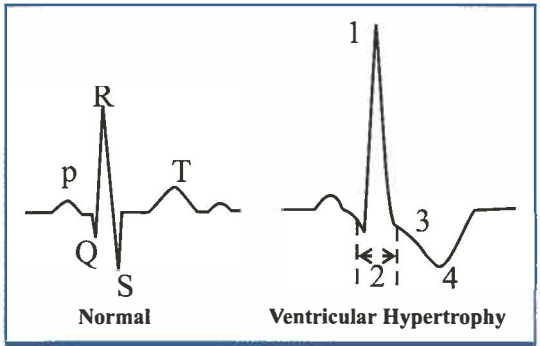


Fig. 8.19: ECG changes in ventricular hypertrophy. 1. Increased voltage. 2. Wide QRS complex. 3. ST depression and 4. T wave inversion

Right Ventricular Hypertrophy

Causes

1. *Congenital Heart Diseases*: Fallot's tetrad, Reversal of shunts (Eisenmenger's syndrome), etc.
2. *Acquired Heart Diseases:* Mitral stenosis, ASD, etc.
3. *Pulmonary Diseases:* COPD, Cor pulmonale, etc.

Criteria for RVH

1. Right axis deviation > 90^0
2. **R in V_1 + S in V_6 > 11 mm**
3. R in V_1 or S in V_6 > 7 mm
4. R/S ratio in V_1 > 1
5. R/S ratio in V_6 < 1
6. T wave inversion in V_1-V_4
7. ST depression
8. P Pulmonale
9. Delay in Intrinsicoid deflection

Left Ventricular Hypertrophy

Causes

1. Hypertension
2. Coronary artery disease
3. Mitral insufficiency
4. Aortic valvular disease

5. Congenital heart disease: Patent ductus arteriosus, co-arctation of aorta, tricuspid atresia.
6. Cardiomyopathies.

Criteria for LVH

1. Left axis deviation > -30^0
2. **R in V_1 or V_2 + S in V_5 or V_6 > 35-40 mm**
3. R in V_5 or V_6 > 25 mm
4. R in I + S in III > 25 mm
5. R in I or aVL > 14 mm
6. T wave inversion in I, aVL
7. ST depression in V_4-V_6
8. P mitrale
9. Delay in Intrinsicoid deflection

Biventricular Hypertrophy

Causes of Biventricular hypertrophy

1. Ventricular septal defect
2. Cardiomyopathy
3. LV hypertrophy due to any cause with pulmonary hypertension and right ventricular strain as with:
   a) Hypertension
   b) Coronary artery disease
   c) Aortic valve disease and mitral regurgitation
   d) Patent ductus arteriosus

Criteria for Biventricular Hypertrophy

1. LV Hypertrophy + Right axis deviation
2. RV Hypertrophy + Left axis deviation
3. LV Hypertrophy + dominant R in V_1 & aVR and deep S in V_5
4. RV Hypertrophy + large Q & R in V_5 and V_6

6 › Rhythm Disturbances

Sinus Rhythm

The normal heart has sinus rhythm. The SA node is under the influence of the vagus nerve. Increased vagal tone decreases and decreased vagal tone increases the heart rate.

Sinus Bradycardia

Definition: Sinus bradycardia occurs when the SA node discharges less than 60 times per minute.

Diagnosis: The R-R interval is more than 25 small squares with normal PQRST complexes occurring at regular intervals.

Causes

Physiological	*Pathological*
1. Sleep and rest	1. Acute MI (Inferior & Posterior infarction)
2. Cold	2. Hypothyroidism
3. Fright	3. Raised intracranial pressure
4. Starvation	4. Obstructive jaundice
5. Athletes	5. Glaucoma
6. Convalescence from infectious diseases	6. Drugs: Propranolol amiodarone, digitalis, quinidine

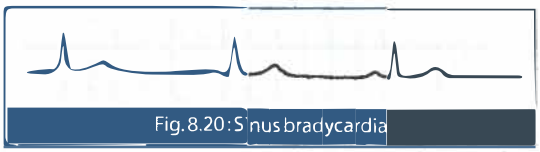


Fig. 8.20: Sinus bradycardia

Sinus Tachycardia

Definition: Sinus tachycardia occurs when the SA node discharges more than 100 times per minute.

Diagnosis: The R-R interval is less than 15 small squares with normal PQRST complexes occurring at regular intervals.

Causes

Physiological	*Pathological*
1. High altitude	1. Thyrotoxicosis
2. Exercise	2. Anxiety state
3. Excitement	3. Fever and infections
4. Pregnancy	4. Excessive tea, coffee, tobacco and alcohol consumption
5. Pain	5. Cardiac failure
6. Postprandial	6. Drugs: Atropine, adrenaline, hydralazine

7. Hemorrhage & shock
8. Pulmonary embolism
9. Vagal Palsy-diphtheria
10. Others: Burns, cirrhosis, Addison's disease

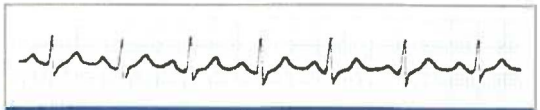


Fig. 8.21 : Sinus tachycardia

Sinus Arrhythmia

Definition: Sinus arrhythmia is alternate periods of tachycardia and bradycardia which occurs due to an irregular discharge of the SA node associated with phases of respiration. Tachycardia occurs towards the end of inspiration and bradycardia occurs towards the end of expiration.

Mechanism: Reflex stimulation of the vagus nerve from the receptors in the lungs causes sinus arrhythmia.

Diagnosis: PQRST complexes are normal but occur irregularly in relation to phases of respiration, so that the R-R interval varies.

Significance: It is a normal physiological phenomenon, more marked in young persons. It is accentuated by vagotonic procedures like digitalis, carotid sinus or eyeball compression and abolished by vagolytic procedures like exercise, atropine and amyl nitrate.

Supraventricular Premature Beats (SVPB) or Extrasystoles

Definition: SVPB occurs due to a premature discharge of an ectopic focus, situated above the ventricles, either in the atrium or the AV node.

Characteristics

1. An atrial beat occurs prematurely so that P' wave is recorded earlier than the anticipated P wave.
2. Premature atrial excitation leads to an alteration in the P wave and the PR interval as the impulse travels along unusual pathways. The P wave may be upright, inverted or diphasic.
3. The premature beat usually initiates a ventricular complex which resembles the normal beat; hence the QRST complex of the premature beat resembles the QRST complex of the normal beat.
4. The compensatory pause is incomplete i.e. the sum total of the R-R intervals of the normal beat preceding and following a premature beat is not the normal R-R interval.



Fig. 8.23 : Supraventricular premature beats. The first 4 beats are normal whereas the fifth beath is premature. The P wave is altered, the QRST complex is same as that of the normal beat and the compensatory pause is incomplete

Causes

1. Idiopathic
2. Heart diseases: Coronary, rheumatic, thyrotoxicosis, diphtheria, hypertension
3. Excessive use of tea, coffee, tobacco and alcohol
4. Drugs: Digitalis, amphetamine, adrenaline, thyroxine and emetine
5. Hypoxia/Anoxemia: Anemia, shock
6. Reflex: Peptic ulcer, kidney and gallstones.
7. Manipulation of intrathoracic organs during surgery on the heart or thoracic organs.

Treatment: Most of the extrasystoles are benign and require no treatment except reassurance. If the cause is found, removal of the cause (e.g. alcohol, smoking, thyrotoxicosis, etc.) would abolish extrasystoles. However, in heart diseases like mitral stenosis they may presage

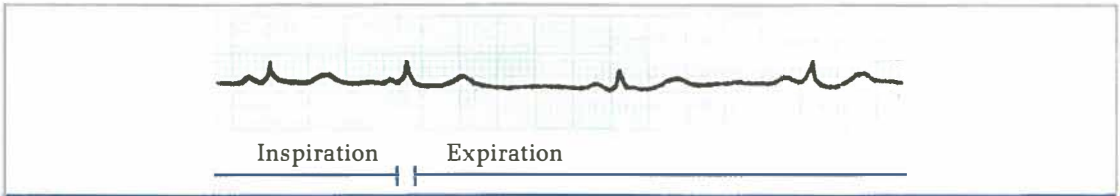


Fig. 8.22 : Sinus arrhythmia; RR internal varies: = RR interval between the first two beats is 18 small squares, whereas RR interval between third and fourth beat is 25 small squares. There is no change in the PQRST complex.

atrial fibrillation or supraventricular tachycardia and should be treated by the following drugs:

1. *Digitalis:* 0.25 mg digoxin thrice daily initially and later to a maintenance dose of 0.25 mg once a day.
2. *Quinidine:* 0.2 gm three to four times daily orally.
3. *Potassium salts, propranolol* (40-120 mg daily) or *Diphenylhydantoin sodium* (300 mg daily) if the extrasystoles are induced by digitalis.

Paroxysmal Supraventricular Tachycardia (SVT)

Definition: SVT is a series of three or more SVPBs which may occur for a few beats or continuously for several hours or days. The last beat of the series is followed by a compensatory pause that is incomplete. Usually the rhythm is regular and at a rate of 150-250/min.

SVT is a narrow QRS complex tachycardia at rates between 150-250/min with sudden onset and sudden termination.



Fig. 8.24: Paroxymal supraventricular tachycardia with rate 187 min. The P waves have merged with the T waves of the preceding heat (P' wave).

Mechanisms: There are 5 different mechanisms.

1. A-V nodal re-entry
2. A-V nodal re-entry using a concealed extranodal pathway
3. S.A. nodal re-entry
4. Intra-atrial re-entry
5. Automatic atrial tachycardia

The first two account for 90% of cases. The P wave occurs simultaneously with QRS and is hence not visible in A-V nodal re-entry. However, in A-V nodal re-entry with a concealed extranodal pathway, the P wave follows QRS complex. In SA nodal re-entry and intra-atrial re-entry, the P wave precedes QRS complex. In the former, its morphology is same as sinus P wave, whereas in the latter it is different. In automatic atrial tachycardia, there is a characteristic warm up phenomenon i.e. there is gradual acceleration at the onset of tachycardia and gradual slowing before termination of the tachycardia. A common example is PAT with block of digoxin toxicity.

Diagnosis: SVT is continuous run of SVPBs, so that each P' wave is followed by a QRS complex.

N.B.: *The spread of the impulse through the atrial muscle occurs more slowly than a normal sinus beat or SVPB. Hence, the P-R interval is prolonged and the P' wave may be obscured by the preceding QRS complex simulating junctional tachycardia.*

Causes: Same as SVPB.

Significance: SVT may last for a few seconds to several days. It is usually benign and if without an underlying cause does not reduce life expectancy. Persistence of SVT in a patient with organic heart disease may lead to cardiac failure and coronary insufficiency. Persistence for a very long period, even in a normal individual, may cause cardiac failure.

Treatment Principles

1. A-V nodal re-entry, A-V nodal re-entry using a concealed bypass tract or S-A re-entry usually responds to *mechanical measures to increase vagal tone and drugs that slow ventricular rate* like verapamil, propranolol and digoxin.
2. *Intra-atrial re-entry and automatic atrial tachycardia* are not usually terminated by the above measures. The treatment of choice is control of ventricular rate by verapamil, propranolol or digoxin followed by either quinidine or procainamide.
3. In PAT with block, digitalis must be withdrawn.

Treatment

1. *Mechanical measures to increase the vagal tone:*
   a) Carotid sinus massage, first on the right side and then on the left side, for 3-5 seconds at a time, may stimulate the vagus nerve and abolish the tachycardia.
   b) Self-induced gagging
   c) Valsalva maneuver or Muller maneuver terminates this tachycardia by stimulating the vagus nerve, slowing conduction and prolonging refractory period of A-V node.

d) The 'duck-diving reflex': Ice water splashed on the face or ice cubes in polythene bags placed on the face.

2. *Drugs:* If mechanical measures fail, the following drugs may be useful:
   a) *Verapamil* 5 cc intravenously slowly often dramatically abolished SVT. Once sinus rhythm is established oral verapamil 40-120 mg three times a day may be given to maintain the sinus rhythm.
   b) *Adenosine* purine nucleoside IV 3 mg with saline (Refer Ch. 15)
   c) *Esmolol,* an ultrashort acting beta-blocker.
   d) *Digitalis, quinidine, propranolol, diphenylhydantoin sodium and potassium salts* as mentioned for SVPB are also useful. *Amiodarone or Disopyramide* orally have recently been found useful.
3. *D.C. Shock:* If mechanical methods and drugs fail or if the patient is hemodynamically unstable, cardioversion is achieved by selectively synchronized direct current countershock. Energies of 100-500 J. are usually successful.

Atrial Flutter and Fibrillation

Definition: Atrial flutter is rapid and regular contraction of the heart at a rate about 220-350/min. Varying degrees of AV block lead to a much slower ventricular rate. The P waves of the atrial flutter have a saw-tooth appearance and are called flutter waves.

Atrial fibrillation is a chaotic rhythm of the atria which causes small twitches of the atrial myocardium instead of an active atrial contraction which normally aids ventricular filling in the second rapid filling phase of the ventricular diastole.

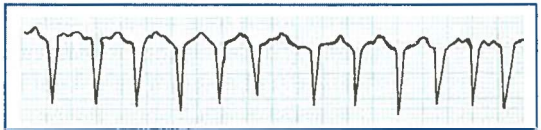


Fig. 8.25: Atrial fibrillation

Hemodynamic consequences:

This depends on the patients underlying cardiac status and the ventricular rate. There is loss of atrial contribution to left ventricular filling which can reduce cardiac output especially in a person with diminished left ventricular compliance.

A rapid ventricular response would reduce the diastolic filling which again can reduce cardiac output and cause hypotension, dizziness, and unconsciousness. Coronary insufficiency may occur together with increased oxygen demand due to rapid rate. This may precipitate angina. Rapid rate can also precipitate cardiac failure and acute pulmonary edema.

Causes

Common

1. Rheumatic heart disease
2. Coronary heart disease
3. Thyrotoxicosis
4. Diphtheria
5. Drugs: Digitalis, adrenaline, emetine.
6. Excessive use of tea, coffee, tobacco and alcohol
7. Mitral valve prolapse
8. Sick sinus syndrome
9. Hypoxemia of any cause

Uncommon

1. Constructive pericarditis
2. Cor-pulmonale
3. Bronchogenic carcinoma
4. A.S.D.
5. Hypertension
6. Lone atrial fibrillation
7. W.P.W. syndrome
8. Cardiomyopathy

Diagnosis

A. *Atrial flutter*
   1. Fast atrial rate of 220-350/min. with ventricular rate half or one-fourth of the atrial rate
   2. P waves replaced by flutter waves
   3. Ventricular rhythm usually regular, unless there is a changing AV block

B. *Atrial fibrillation*
   1. Irregularly irregular ventricular rhythm

2. P waves replaced by fibrillation waves
3. Normal QRS complexes

At times the rhythm may alternate between flutter and fibrillation and a precise difference cannot be discerned. This is called *"flutter fibrillation."*

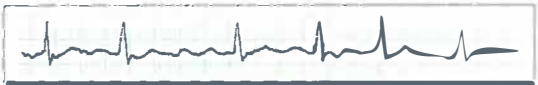


Fig. 8.26: Atrial flutter-fibrillation

Hemodynamic consequences

The hemodynamic consequences of atrial fibrillation or flutter depend upon the patients' underlying cardiac status and the ventricular rate. With atrial fibrillation, the atrial kick of the second rapid filling phase of ventricular filling is absent with reduction of cardiac output especially in patients with reduced left ventricular compliance. A rapid ventricular rate would reduce the diastolic filling and further reduce the cardiac output. This may result in hypotension and reduced cerebral as well as coronary perfusion resulting in dizziness and angina. A rapid ventricular rate can cause cardiac failure or acute pulmonary edema especially in patients with mitral stenosis.

Principles of Treatment

I. To slow the ventricular rate
II. To restore sinus rhythm - Cardioversion
   A) By drugs
   B) By DC shock or pacing.
III. Anticoagulation and atrial fibrillation.
IV. To find out the cause and eliminate it.

Treatment

I. **Drugs to slow the ventricular rate:** There are three types:- Verapamil, Propranolol and digoxin. The onset of action of intravenous verapamil and propranolol is more rapid than that of intravenous digoxin. However, the half-life of digoxin is longer. Again with cardiac failure verapamil and propranolol should not be used.
   1 *Digoxin:* This is given in the dose of 0.25 mg IV followed by repeat doses of 0.25 mg/day.
   2. *Beta-blocker: Propranolol* is given in the dose of 1 mg over 1 minute. The dose can be repeated every 5 minutes to a total dose of 0.15 mg/kg. Even metoprolol, atenolol or esmolol can be used, provided the LV function is good.
   3. *Verapamil:* This is given in the dose of 5-10 mg IV over 1-2 minutes. If there is no response, a repeat dose of 10 mg IV can be given after 20 minutes. If the initial response of ventricular slowing is short lived, a continuous infusion can be used intra-venously in the dose of 5 mcg/kg/min. Orally 40 mg tds up to 120 mg tds can be added to digoxin even if LV function is poor.
   4. *Amidarone*

II. A) **Drug Cardioversion :** *Drugs to convert atrial fibrillation:* Once the ventricular rate is controlled, conversion to sinus rhythm can be attempted. Some patients with atrial flutter may convert to sinus rhythm with verapamil alone. However, oral quinidine or procainamide can be used for chemical conversion. They slow the con-duction and prolong refractory period of the atria. However, if the ventricular rate has not been controlled first, they may increase the heart rate due to a vagolytic effect on the A-V node and slowing of the atrial flutter rate, both of which increase the A-V conduction.
   1. *Quinidine:* This is given orally in the dose of 200 mg every 2 hours for 2-3 doses followed by 200 mg every 6 hourly. In successful cases, usually the conversion occurs by second or third dose. If atrial fibrillation is long standing, over 12 months, or left atrium is markedly dilated, cardioversion should not be attempted because sinus rhythm is usually not maintained.
   2. *Procainamide:* This is given in the dose of 0.25 gm every 2 hours up to 3 doses followed by 0.25 gm 6 hourly. Usually quinidine is preferred to this drug.

3. *Flecainide:* 2 mg/kg IV over 10 mins.
4. *Disopyramide* 50-150 mg IV slowly.
5. *Amiodorone*: 200-400 mg tds.

II. B) **DC Current or Pacing**

1. *Direct current (DC) cardioversion:* If the patient has hypotension, loss of consciousness or pulmonary edema, the treatment of choice is cardioversion with electric shock synchronized to the QRS complex (to avoid inducing ventricular tachycardia or fibrillation). Initially energy of 50-100 J is given and repeated up to 400 J. This usually helps to reset the rhythm to sinus or at least slows down the ventricular rate, which then can be treated with drugs.
2. *Rapid atrial pacing:* This can be done in patients of atrial flutter who are hemodynamically stable. The atrial pacing conversion is attempted with the electrode in the right atrial appendage or high right atrium with rapid pacing at rates faster than the flutter rate. This may result in conversion to the sinus or atrial fibrillation, or increase in flutter rate.

III. *Anticoagulation and AF:*

Patients with mitral stenosis, cardiomyopathy and history of systemic thromboembolism, who are at a high risk for systemic embolism, must be anticoagulated with heparin.

Ventricular Premature Beat or Extrasystole (VPB)

Definition: VPB occurs due to premature discharge of an ectopic focus in the ventricles.

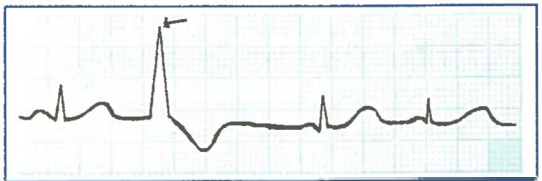


Fig. 8.27: Ventricular premature beats

Characteristics

1. The beat arises prematurely.
2. Since the impulse originates in the ventricles and does not activate the atria, P wave is absent.
3. The QRS complex is wide, bizarre and tall, with T waves in the opposite direction as the major deflection of the QRS complex i.e. if the R wave is prominent, the T wave is inverted and if the S wave is prominent, the T wave is upright.
4. The compensatory pause is complete because VPB does not depolarize the SA node. The impulse from the SA node following a VPB does not active the ventricles as they will be in the refractory period. The ventricles will respond only to the next sinus impulse and hence the interval between the two sinus beats preceding and following the VPB will be exactly twice the normal interval between two sinus beats.

Types

A. VPBs in 24 hour ECG tracing

B. VPBs following myocardial infarction

Significance: An extrasystole can occur in a normal person without any lesion of the heart. Usually it is benign and of no significance. However, it is significant if Lown's criteria are fulfilled:

1. It occurs for the first time after the age of 40.
2. It is associated with a heart lesion.
3. It is multifocal.
4. It occurs more than 5 times per minute.
5. There is R on T phenomenon.
6. It occurs in salvos of 2 or more.
7. It occurs following exercise.

Causes: Same as SVPB.

Treatment: Same as SVPB.

Paroxysmal VentricularTachycardia (VT)

Definition: VT is a series of three or more VPBs which may occur for a few beats or continuously for several hours or days. The last beat of the series is followed by a compensatory pause that is complete. Usually the rhythm is regular at 160-200/min.



Fig. 8.28: Ventricular Tachycardia

Mechanism: Similar to SVT.

Diagnosis: VT is a continuous run or VPBs with the QRS complexes smoothly merging with the ST segment and T waves giving an appearance of large, wide undulations which are irregular.

Causes

1. Ischemic heart disease
2. Cardiomyopathy
3. Primary electrical disease
4. Mitral valve prolapse
5. Valvular heart disease
6. Myocarditis
7. Hypoxemia
8. Acidosis
9. Hypokalemia, hypomagnesemia

Treatment

1. Intravenous *Xylocaine* 100 mg as a bolus and then in a slow drip often reverts the arrhythmia.
2. *Procainamide:* If IV Xylocaine is unsuccessful, IV procainamide 1 gm over 20 min is given repeated up to 2 gm unless there is hypotension. The maintenance infusion rate is 2-6 mg/min.
3. *Bretylium:* This is given IV in the dose of 5-10 mg/kg over 10-20 min. If this is unsuccessful, a repeat dose of 5-10 mg is given after 20 min followed by a drip at the rate of 1-2 mg/min. The full anti-arrhythmic effect of IV bretylium takes 30 minutes.
4. *Quinidine, propranolol, phenytoin or disopyramide* may be used for long-term prophylaxis.
5. Low-current D-C shock with 25-50 J. may be given if immediate restoration is required. If there is no response, the dose is doubled up to 200J.

Table 8.1 : Differences between VT and SVT with Aberrant Conduction

	Ventricular tachycardia	*Supraventricular tachycardia with aberrant conduction*
1. QRS duration more than 0.14 sec.	May be present	Absent
2. rsR' in lead V_6	May be present	Absent
3. Left axis deviation	Usually present	Usually absent
4. Carotid sinus massage	No effect.	Arrhythmia may be reverted to sinus rhythm.

Ventricular Fibrillation and Flutter

Definition: Ventricular fibrillation is a disorganized and chaotic activity of the heart, which results in irregular and deformed deflections of varying height, width and shape. This condition is terminal unless cardioverted.

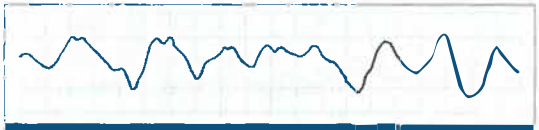


Fig. 8.29: Ventricular fibrillation

Ventricular flutter is a very rapid and regular ectopic ventricular discharge with an abnormal intraventricular conduction resulting in a wide, bizarre and sine-like QRS complex fused with the T wave.

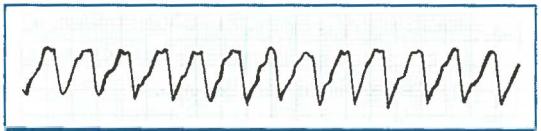


Fig. 8.30: Ventricular flutter

Causes:

1. Coronary heart disease
2. Drugs: Digitalis, adrenaline and anesthesia
3. During cardiac surgery, due to hypoxia
4. Hypothermia
5. Electric shock

Diagnosis: Bizarre ventricular pattern of different shapes and sizes.

Treatment:

1. *D.C. Shock* and cardioversion. This is started with 200 J. If it is unsuccessful, a second shock of 200 J is given immediately. If this is also unsuccessful a maximum of 320-400 J are given.
2. *Intravenous Xylocaine* 100 mg bolus and 200 mg in a drip.
3. Intravenous *propranolol* 5-10 mg.

Torsade de Pointes (Polymorphic VT)

Torsade de Pointes is a ventricular arrhythmia characterized by QRS complexes of changing amplitude with a characteristic twisting around the isoelectric line on ECG. The rate is around 200-250/min. It may revert spontaneously to sinus rhythm or degenerate to ventricular fibrillation. It occurs in the setting of prolonged QT interval.

Causes

1. Congenital QT prolongation
2. *Drugs:* Quinidine, procainamide, disopyramide, prenylamine phenothiazine, tricyclic antidepressants and overdose of lidocaine.
3. *Electrolyte disturbances:* **Hypokalemia, hypocalcemia and hypomagnesemia**
4. *Cardiac lesions:* Myocarditis, Mitral valve prolapse.
5. *Bradyarrhythmias*
6. *CNS:* Subarachnoid hemorrhage
7. *Miscellaneous:* Organophosphorous and arsenic poisoning, liquid protein diet, anorexia nervosa.

Treatment

1. Elimination of *precipitating cause or stop culprit drug.*
2. *Class 1a or III agents contraindicated as they worsen the arrhythmia*
3. *Overdrive pacing:* Either atrial or ventricular overdrive pacing at a rate above 20 beats/min higher than the sinus rate of the patient.
4. *DC cardioversion:* If the episode is prolonged or there is ventricular fibrillation, DC cardioversion is usually required.
5. *Isoproterenol/ Isoprenaline* 2-6 mcg/min may be used until temporary pacemaker can be inserted. In some cases, Bretylium and lidocaine has been successfully used.
6. *IV Magnesium* has been used even when magnesium levels have been normal.

7 Conduction Defects Atrioventricular Block (AV Block)

DEFINITION: AV block is disturbance in the conduction of the atrial impulses through the AV conducting system.

Classification

A. Incomplete
   1. *First degree* AV block: Delay in AV conduction.
   2. *Second degree AV block:* Intermittent interruption of AV conduction.

B. Complete or third degree AV block: Complete interruption of AV conduction.

First Degree AV Block

There is a delay in conduction of every impulse passing through the AV node. This results in prolongation of the PR interval to above 0.2 seconds. The rhythm is regular and no beat is dropped.

Causes

1. Idiopathic in the absence of any heart disease
2. Coronary artery disease
3. Rheumatic fever
4. Drugs: Digitalis, quinidine, propranolol
5. Acute infectious diseases
6. Congenital heart diseases: Atrial septal defect, Ebstein's anomaly.

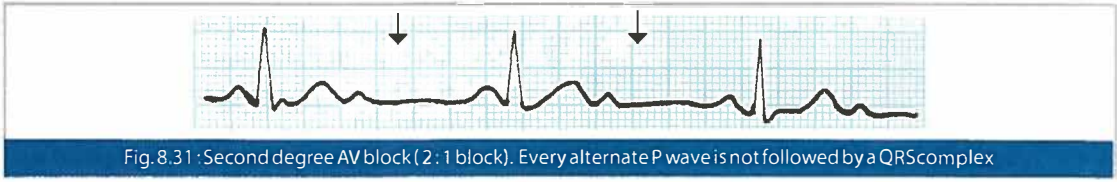


Fig. 8.31: Second degree AV block (2:1 block). Every alternate P wave is not followed by a QRS complex

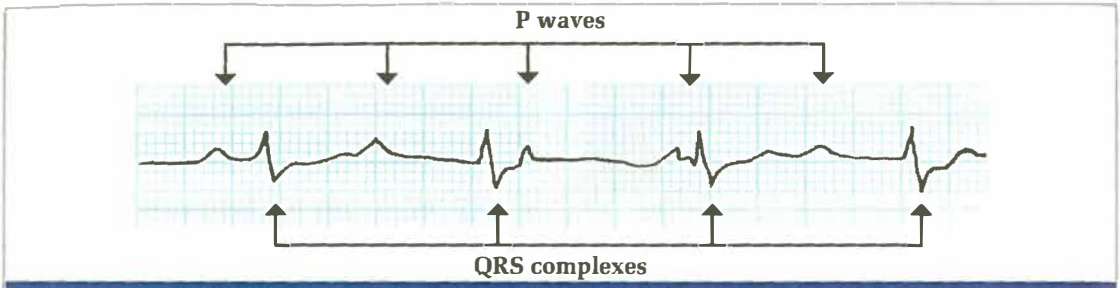


Fig. 8.32: Complete Heart Block (Complete AV dissociation): The atrial rate is 88/min., whereas the ventricular rate is 64/min.

Second Degree AV Block

Second degree AV block is an intermittent interruption of AV conduction so that some of the impulses are conducted to the ventricles and others are blocked. It may be of the following types.

1. **Wenckebach type (Mobitz type I):** Here there is a gradual increase in the PR interval in subsequent beats till one beat is completely blocked and therefore that P wave is not followed by a QRS complex. The pause due to the dropped beat allows the conducting system to recover. A normal PR interval and a gradual increase in the PR interval with every beat follow in a cyclic fashion, till once again a beat is dropped. It may respond to atropine. Temporary pacing is often done.
2. **Mobitz type II:** Here, the ventricle fails to respond to the atrial contraction periodically. This may occur at a regular or irregular interval so that for a particular number of QRS (ventricular) complexes there may be correspondingly more P (atrial) waves e.g. if for 5 QRS complexes there are 6 P waves, it is known as a 6:5 block. It usually needs pacing.
3. **Constant block:** Here there is a fixed AV relationship. Thus for every 2 or more P waves (atrial activity) there is one QRS complex (ventricular activity) e.g. If after every third P wave there is one QRS complex it is a 3:1 block.

Causes

1. Acute rheumatic carditis
2. Coronary heart disease
3. Diphtherial carditis
4. Drugs: Digitalis
5. As a protective mechanism with fast supraventricular rhythms e.g. atrial tachycardia, atrial flutter.

Third Degree AV Block (Complete AV Block)

There is a permanent interruption of AV conduction so that all supraventricular impulses are blocked. Ventricles are activated by a subsidiary ectopic pacemaker and therefore there is no relationship between atrial and ventricular pacemakers. These two rhythms are asynchronous. Hence P waves and QRS complexes occur at a different but constant rate. The rate of the QRS complex is almost half that of the P wave.

Causes

1. Inferior wall myocardial infarction due to Right coronary occlusion.
2. Congenital complete AV block
3. Coronary heart disease
4. Congenital heart diseases: Ostium primum type of ASD, VSD
5. Drugs: Digitalis, quinidine, procainamide
6. Lenegre's idiopathic sclerodegenerative disease
7. Lev's disease
8. Intracardiac surgery
9. SOL: Tubercle, gumma, tumor

8 › Effect of Drugs and Electrolytes

Digitalis

Digitalis Effect

A patient on digitalis may have certain changes in his ECG as adequate digitalization is reached. They do not indicate the need to reduce the dose of digitalis. These changes are:

1. The ST segment is depressed, rounded and

concave (scooped). The T wave is dragged downwards giving an appearance of T wave inversion. These ST-T changes occurring in leads with a prominent R wave suggest a therapeutic effect. However, if these changes occur in leads with mainly a negative QRS complex, it indicates that the drug is causing relative subendocardial coronary insufficiency and therefore the drug must be stopped.

2. The QT interval is shortened due to the shortening of the ventricular systole.



Fig. 8.33 : Digitalis effect (Scooped ST segment)

DIGITALIS TOXICITY: The toxic effects of digitalis may be as follows:

1. Sinus bradycardia
2. Premature beats - unifocal, multifocal or bigeminy
3. Supraventricular arrhythmias - paroxysmal atrial tachycardia, atrial flutter and atrial fibrillation
4. Ventricular arrhythmias - ventricular tachycardia, ventricular flutter and ventricular fibrillation
5. SA block, first, second and third degree AV block, and bundle branch block

Quinidine

QUINIDINE EFFECT: Quinidine produces ST depression and flattening of the T wave like digitalis, but unlike digitalis there is an increased QT interval and the T wave may be notched and widened.

QUINIDINE TOXICITY: The toxic effects of quinidine may be as follows:

1. SA block.
2. First, second or third degree AV block.
3. Bundle branch block: QRS complex gradually widens and blends with the T wave giving a wide, bizarre, biphasic deflection
4. Ventricular arrhythmias - idioventricular rhythm, ventricular premature beats, ventricular tachycardia, ventricular fibrillation and cardiac asystole.
5. AV junctional rhythm.



Fig. 8.34 : Quinidine effect (ST depression with tenting of T waves)

Potassium

Hyperkalemia: (Refer Pg. 401)

ECG changes with gradual rise in potassium are as follows:

1. Peaked, tall and tented T waves (This also occurs in posterior wall myocardial infarction)
2. The amplitude of the P wave decreases and finally disappears completely because though the sinoatrial node fires an impulse, the atrial myocardium is not activated
3. The amplitude of the R wave decreases and the QRS complex gradually widens and blends with the T wave giving a wide, bizarre, biphasic deflection.

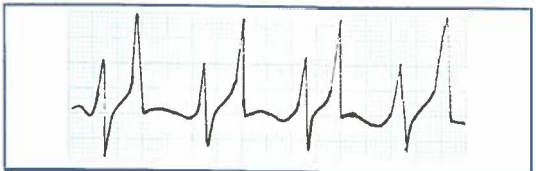


Fig. 8.35 : Hyperkalemia (Tall T waves)

Hypokalemia: (Refer Pg. 401)

ECG changes with gradual fall in potassium are as follows:

1. Depressed ST segment and flattened or inverted T waves
2. Prominent U waves
3. Prolonged QT interval and PR interval
4. SA block rarely.

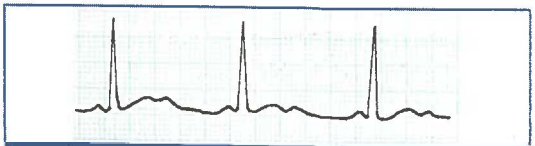


Fig. 8.36 : Hypokalemia (Prolonged QT interval and prominent U waves)

For details refer to P.J. Mehta's "Understanding ECG" (6th Ed) and "Interpreting ECG" (2nd Ed)

Radiology

9

1 › X-ray Chest

An X-ray of the chest is normally taken anteroposteriorly or postero-anteriorly, depending upon the direction of the rays from a source to the plate. The postero-anterior (P.A.) view is the common view in use, because the heart size is less exaggerated and hence more normal than in the anteroposterior (A.P.) view.

Normally the chest X-ray is well centralized so that both the clavicles are at the same level. It they are not at the same level the X-ray is poorly centralized.

If the breast shadows are visualized, the plate is of a female patient.

The right diaphragm is slightly higher than the left with clear costophrenic and cardiophrenic angles.

The rib cage and clavicles are normally well visualized.

The cardiac shadow consists of a smooth right border formed by the superior vena cava, right atrium and inferior vena cava. The left border is formed by aortic knuckles, pulmonary artery, left atrial appendage, right ventricle and left ventricle, from above downwards. The ratio of the chest wall to the cardiac shadow is 2:1; if there is cardiac enlargement this ratio becomes less. It is slightly increased in emphysema.

The aortic knuckle is prominent in aortitis, atherosclerosis or aneurysm. The pulmonary artery is prominent in pulmonary hypertension. The pulmonary artery shadow is absent in pulmonary stenosis or pulmonary atresia.

In right atrial enlargement there is a straightening of the left border and double density of the two atria. In right ventricular enlargement the cardiac shadow enlarges outwards, but in left ventricular enlargement the cardiac shadow enlarges outwards and downwards, having boot-shaped configuration.

The lung shadows are visualized next. Normally they are translucent. It is important to look for radio-opaque shadows or hyper translucency in the lung shadow.

Most of the vascular shadows (white linear) in the lung fields are due to branches of the pulmonary artery. They are usually accompanied by a corresponding branch of the bronchus. The pulmonary arteries form the major bulk of the hilar density. In contrast, pulmonary veins have low density. They may be seen in the upper lobes just lateral to the upper lobe artery. The lymphatics, interstitium, alveoli and pleura cast a very low density and are difficult to identify.

A normal X-ray chest is described in the following manner:

1. View
2. Centralization
3. Exposure
4. Sex
5. Diaphragm
6. Cardiophrenic angle and Costophrenic angle
7. Clavicles
8. Rib Cage
9. Cardiac Shadow
10. Lung Shadow
11. Conclusion

Homogenous Opacity of one Hemithorax



Fig. 9.1 : Homogenous opacity of the left hemithorax

Causes

1. Pleural effusion
2. Consolidation
3. Atelectasis
4. Pulmonary agenesis
5. Destroyed lung (Chronic inflation, fibrosis)
6. Pneumonectomy

Pleural Effusion - Refer Pg. 135

Collapse of the Lung - Refer Pg. 143

Pulmonary Embolism

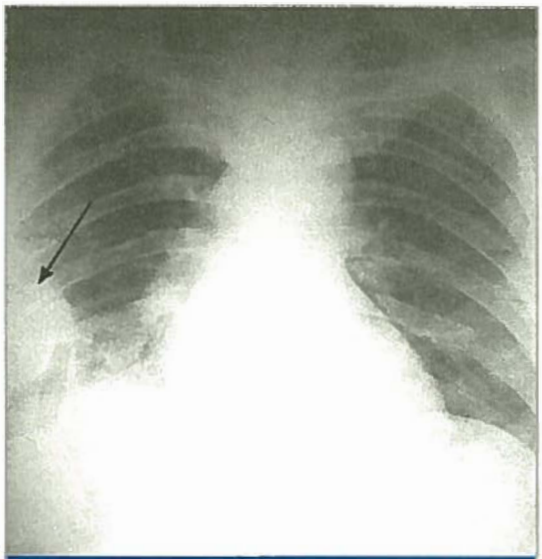


Fig. 9.2: Pulmonary embolism, Radio-opaque wedge-shaped shadow at the right base

1. Wedge shaped opacity above diaphragm (Hampton's Hump)
2. Raised diaphragm, which moves poorly on inspiration.
3. Enlarged right descending pulmonary artery (Palla's sign)

Pulmonary Edema

Features: *"Bats wing appearance"* of confluent shadows extending from the hilum into the mid zone.

Homogenous Rounded Opacity

(Solitary Pulmonary Nodule or Coin Lesion in Lung)

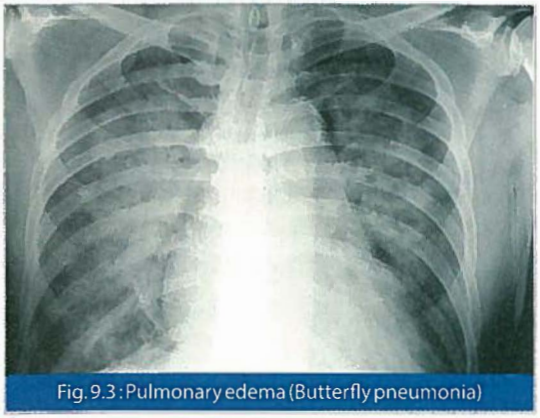


Fig. 9.3: Pulmonary edema (Butterfly pneumonia)

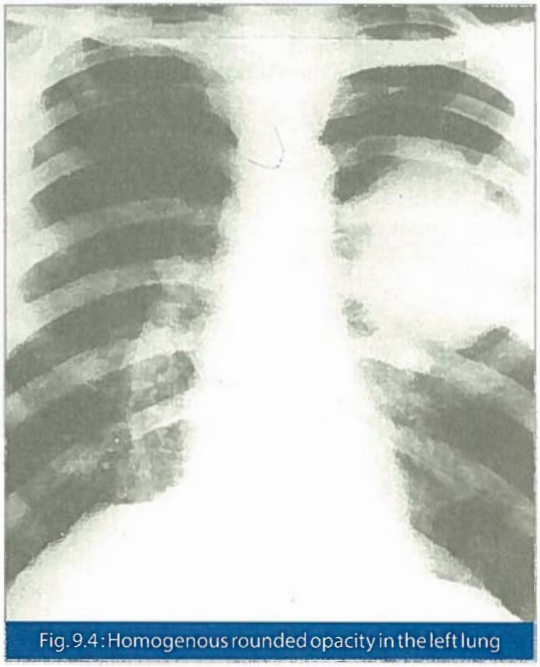


Fig. 9.4: Homogenous rounded opacity in the left lung

Causes

A. *Infectious:* Tuberculosis, Histoplasmosis, Coccidioidomycosis, pneumonia, etc.
B. *Neoplasms:* Bronchogenic carcinoma, adenoma, metastatic nodule, mesothelioma or fibroma of the pleura, hamartoma, etc.
C. *Cysts:* Hydatid and Bronchial
D. *Vascular:* Pulmonary infarction and AV fistula
E. *Occupational diseases:* Silicosis, anthracosis etc.

Bronchiectasis (Refer Pg. 175)

1. Multiple, ring-shaped shadows, especially at the base
2. Areas of fibrosis or haziness

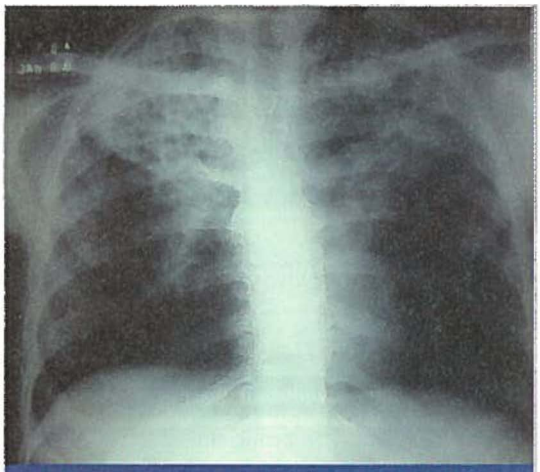


Fig. 9.5: Bilateral upper and mid-zone Bronchiectasis

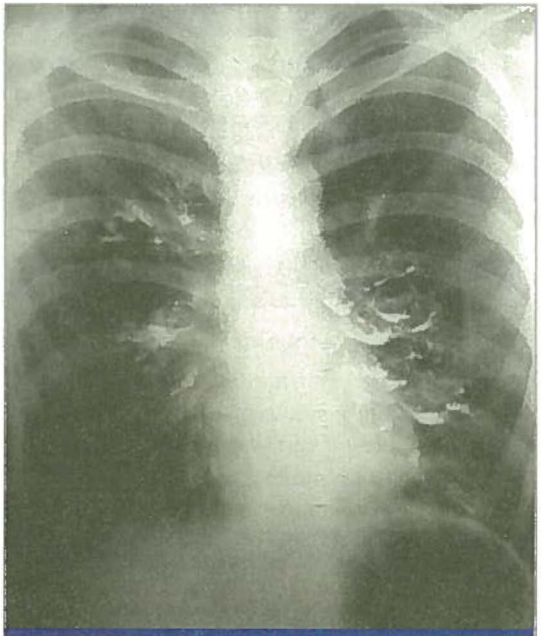


Fig. 9.6: Bronchogram showing cystic bronchiectasis

Miliary Mottling (Refer X-ray Pg. 161)

Causes

A. *Infection:*
   1. Bacterial: Disseminated tuberculosis, broncho-pneumonia, brucellosis, etc.
   2. Fungal: Histoplasmosis, coccidioidomycosis, blastomycosis, etc.

B. *Allergic:* Tropical eosinophilia, Loeffler's syndrome, drug reaction

C. *Neoplastic:* Lymphangitis, carcinomatosis, alveolar cell carcinoma, leukemia, lymphoma, etc.

D. *Pneumoconiosis*

F. *Cardiac:* Multiple pulmonary infarction, pulmonary edema

G. *Miscellaneous:* Rheumatoidarthritis, sarcoidosis, hemosiderosis, interstitial pulmonary fibrosis, hyaline membrane disease

H. *Artifacts:* Skin warts, etc.

Hypertranslucency

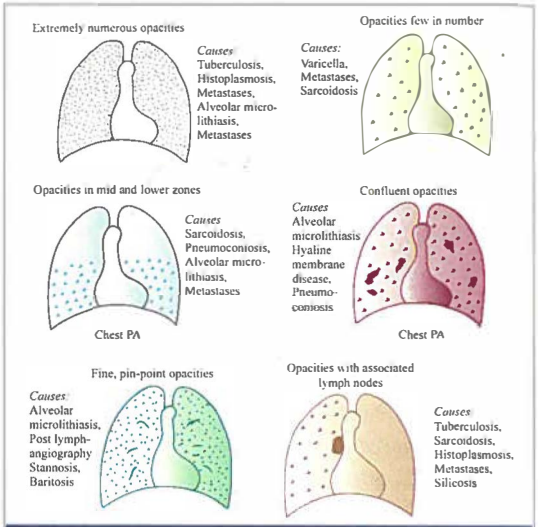


Fig. 9.7: Multiple opacities (different types)

Causes

Unilateral

1. *Pleural:*
   a) Pneumothorax
   b) Contralateral pleural thickening (apparent, hyper-translucency)
2. *Pulmonary:*
   a) Unilateral obstruction
   b) Bullae
   c) Eventration of the left dome of the diaphragm
3. *Chest wall*
   a) Mastectomy
   b) Absent pectoral muscle

Bilateral

1. *Pleural:* Bilateral pneumothorax
2. *Pulmonary:*
   a) Emphysema
   b) Bronchial asthma
   c) Bullae
3. *Cardiac*
   a) Primary pulmonary hypertension
   b) Ebstein's anomaly
   c) Fallot's tetrad with pulmonary atresia

Emphysema - Refer Pg. 168

Pneumothorax - Refer Pg. 149

Elevation of the Diaphragm

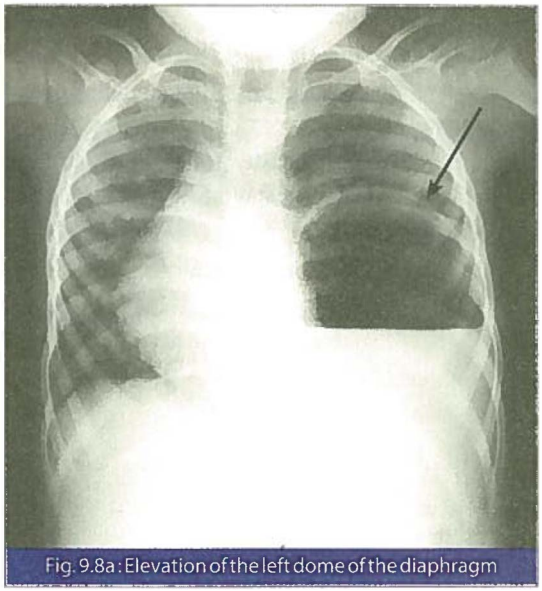


Fig. 9.8a: Elevation of the left dome of the diaphragm

Causes

Unilateral:

1. Amebic abscess
2. Subphrenic infections
3. Subdiaphragmatic tumor
4. Basal pleural or pulmonary infection
5. Basal pulmonary infarction
6. Eventration of diaphragm
7. Phrenic nerve palsy
8. Scoliosis

Bilateral

1. Pregnancy
2. Obesity
3. Ascites
4. Large abdominal mass
5. Abdominal distension
6. Infants

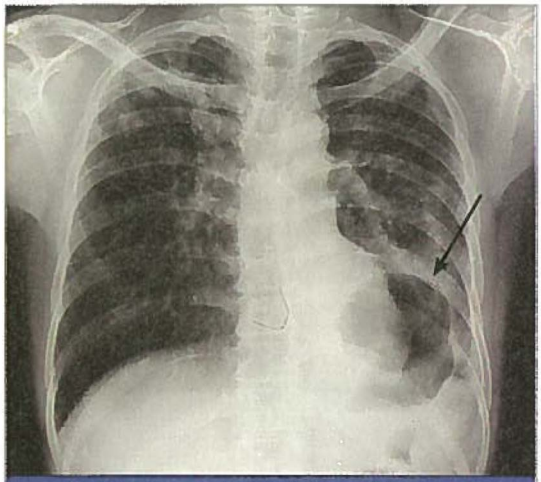


Fig. 9.8b: Eventration of left dome of diaphragm

Bilateral Hilar Lymphadenopathy

(More than 5 mm is pathological)

Causes:

A. *Infection*
   1. Tuberculosis
   2. Histoplasmosis
   3. Recurrent chest infections
   4. AIDS

B. *Neoplasms*
   1. Lymphomas
   2. Metastasis

C. *Occupational diseases & Other*
   1. Silicosis
   2. Berylliosis
   3. Sarcoidosis

Mediastinal Shadow

Causes

A. *Lymphadenopathy*
   1. Tuberculosis

2. Sarcoidosis
3. Lymphomas
4. Leukemias
5. Metastasis

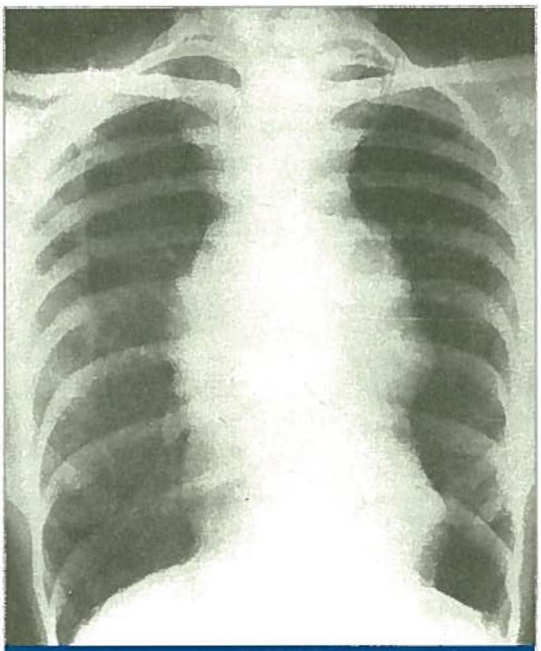


Fig. 9.9: Enlarged mediastinal shadow

B. *Aorta:*
   1. Aneurysm
   2. Unfolding
   3. Anomalous origin of the great vessels

C. *Cysts:*
   1. Dermoid teratoma
   2. Cystic hygroma
   3. Bronchogenic cyst
   4. Pleuro-pericardial cyst
   5. Meningocele

D. *Thymus:*
   1. Enlargement
   2. Tumor

E. *Esophagus:*
   1. Achalasia cardia
   2. Hiatus hernia
   3. Enterogenous cyst

F. *Miscellaneous:*
   1. Lipoma, mesothelioma
   2. Mediastinal abscess
   3. Cardiac aneurysm or tumor

Calcification in Chest (Refer Fig. 4.25)

Causes

A. *Pulmonary / Parenchymal Calcification:*

I. Diffuse:
   1. Infection: Tuberculosis, abscess, histoplasmosis, varicella, pneumonia
   2. Tumor: Hamartoma, pulmonary A-V aneurysm, metastasis from osteogenic sarcoma
   3. Unknown: Broncholiths, alveolar micro-lithiasis
   4. Silicosis
   5. Hemosiderosis (long standing mitral stenosis)
   6. High density (post-lymphography, baritosis, stannosis)

II. Solitary
   1. Infection: Tuberculosis, histoplasmosis
   2. Hamartoma (popcorn calcification)

B. *Cardiac Calcification:*
   1. Aortic arch
   2. Constrictive pericarditis
   3. Valves or valve rings
   4. Thrombi and myxomas
   5. Coronary arteries

C. *Mediastinal Calcification:*
   1. Lymph glands: Tuberculosis, sarcoid, pneumoconiosis
   2. Tumors: Teratoma, dermoid, thyroid adenoma

D. *Pleural Calcification:*

I. Diffuse
   1. Infection: Tuberculosis, pyogenic empyema
   2. Asbestosis

II. *Focal (Subpulmonic plaques)*
   1. Asbestosis
   2. Talcosis

E. *Chest Wall Calcification:*
   1. Ribs (Bone islands, Costal cartilages)
   2. Muscles and soft tissue (Cysticercosis, Guinea worm, Dermatomyositis)
   3. Phleboliths

F. *Egg Shell Calcification:*
   1. Silicosis
   2. Coal workers Pneumoconiosis
   3. Sarcoidosis

2 X-ray Chest - Heart

Pulmonary Oligemia

Lung vessels are of reduced caliber in lung fields.

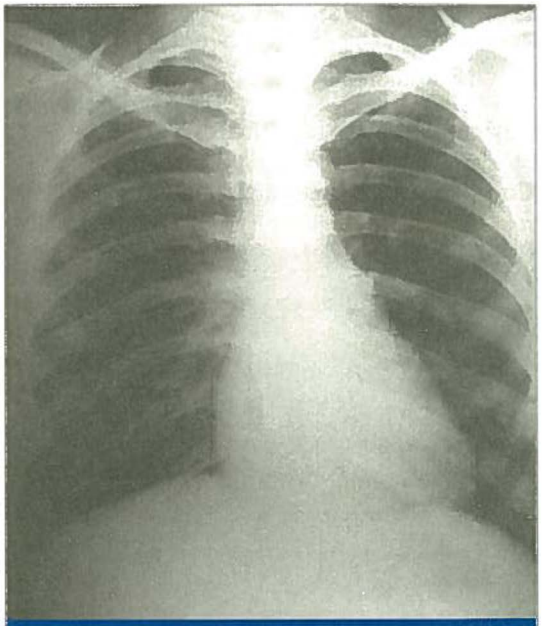


Fig. 9.10: Pulmonary oligemia (Case of Pulmonary stenosis)

Causes:

1. Fallot's tetrad. Fallot's triad, Truncus arteriosus
2. Severe pulmonary stenosis

Pulmonary Plethora

Dilated vessels throughout the lung fields

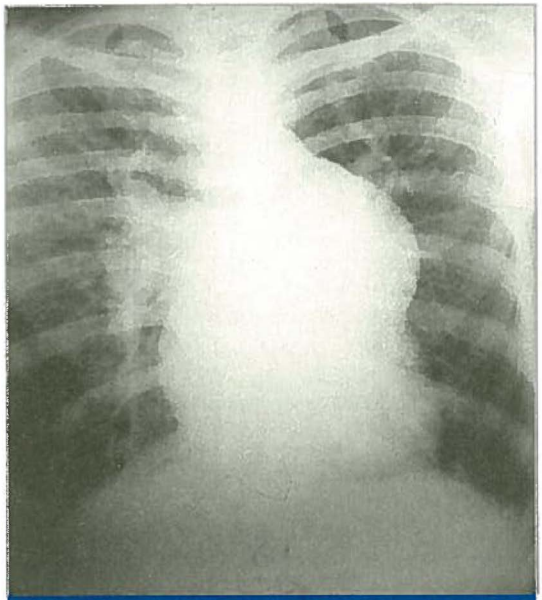


Fig. 9.11: Pulmonary plethora (Case of left to right shunt)

Causes

1. Left ventricular failure
2. Valvular heart diseases: MS, MI, AS, AI

Pulmonary Arterial Hypertension

Bulging central arteries, abruptly tapering to small peripheral branches.

Causes:

1. Recurrent pulmonary emboli
2. Chronic pulmonary disease
3. Long standing left heart disease
4. Left-right shunt

Pulmonary Venous Congestion

Increased vascular markings due to venous congestion in lungs

Causes:

1. Left sided heart failure
2. Cor-pulmonale
3. Pulmonary emboli

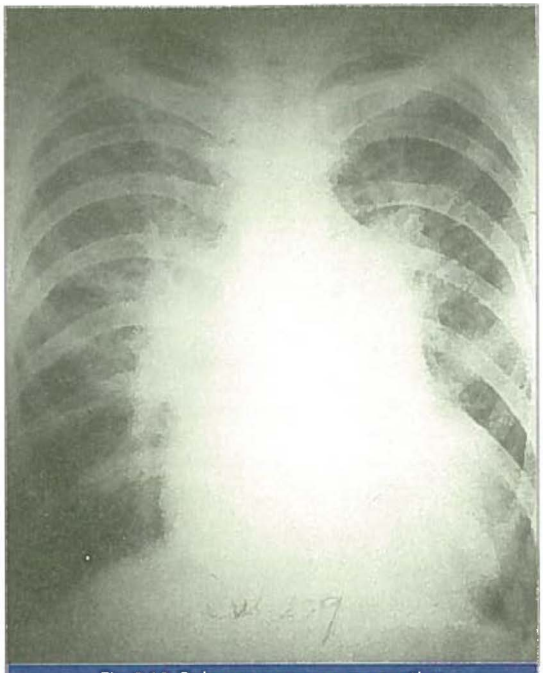


Fig. 9.12 : Pulmonary venous congestion

Table 9.1 : Left to Right Shunt (ASD, VSD and PDA)

	ASD	VSD	PDA
1. Pulmonary plethora	+	+	+
2. Aortic knuckle	Small	Small or normal	Large or normal
3. Chamber enlargement	RVH	LVH RAH	LVH RVH

Mitral Stenosis - Refer Pg. 215

Mitral Incompetence - Refer Pg. 232

Aortic Incompetence - Refer Pg. 237

Aortic Stenosis & Hypertension - Refer Pg. 241

Left Ventricular Aneurysm

Bulging of a part of the wall of the left ventricle which appears as a distinct bulge from the smooth outline of the left border of the heart which may be enlarged. Sometimes calcification may be present.

Cardiac Failure

1. Heart size is enlarged

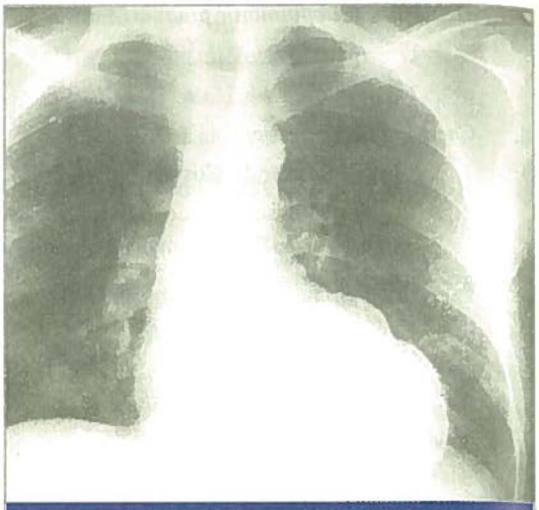


Fig. 9.13 : Left ventricular aneurysm

2. Pulmonary marking are prominent at the apex
3. Kerley B line may be present
4. Evidence of pulmonary edema or phantom tumor opacity (which disappears once failure is treated) may be present (Fig 4.21 Pg. 138)
5. Hydrothorax

Pericardial Effusion - Refer Pg. 259

Constrictive Pericarditis - Refer Pg. 71

Rib Notching - Refer Pg. 256

Causes

1. *Arterial:*
   a) Aortic: Coarctation of aorta
   b) Subclavian: Blalock Taussig operation
   c) Pulmonary oligemia: Fallot's tetrad, pulmonary stenosis, Ebstein's disease
2. Venous: Superior and inferior venae cavae blocks
3. Arterio-venous fistulae
4. Nerves: Neurofibromatosis
5. Idiopathic

3 › Plain X-ray Abdomen

The diagnostic potential of X-ray chest because of

the superb natural contrast of air is less generously available. Plain-X-ray abdomen must be evaluated as follows:

1. Lung bases and diaphragm: For basal pneumonia, pleurisy, gas under the diaphragm
2. Extraabdominal soft tissues: (An incarcerated hernia may be the cause of patient's bowel obstruction)
3. Skeletal structures: Lumbar vertebra, vertebral pedicles, spleen and kidneys may be visualized
4. Fat and muscle plane: Psoas muscle
5. Solid organs: Liver, spleen and kidneys
6. Gas shadow in stomach and colon
7. Calcification
8. Intraperitoneal air and fluid

Paralytic Ileus

Diffuse fluid and gaseous distension of small and large bowels and if the plate is taken in upright position, air and fluid levels may be present at the same level.

Causes: Peritonitis, drug effect, bowel ischemia, trauma

Bowel Obstruction

Proximal to the lesion the gut is distended with gas and fluid, distally the gut is empty. The upright X-ray shows step-ladder distribution.



Fig. 9.14: Intussusception

Causes

In adults:

1. Adhesions
2. Hernia
3. Tumor

In children:

1. Hypertrophic pyloric stenosis
2. Duodenal atresia
3. Meconium ileus
4. Intussusception
5. Volvulus

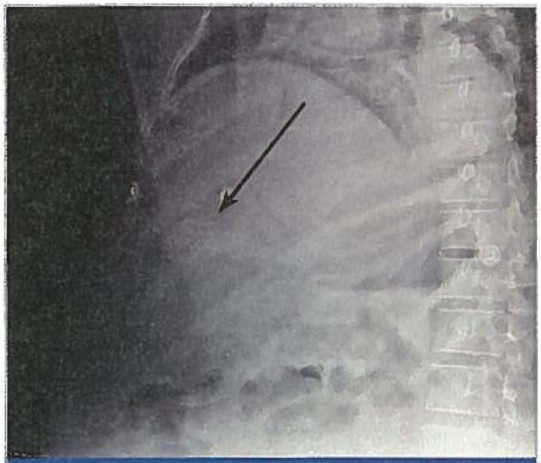


Fig. 9.15: Gall stones

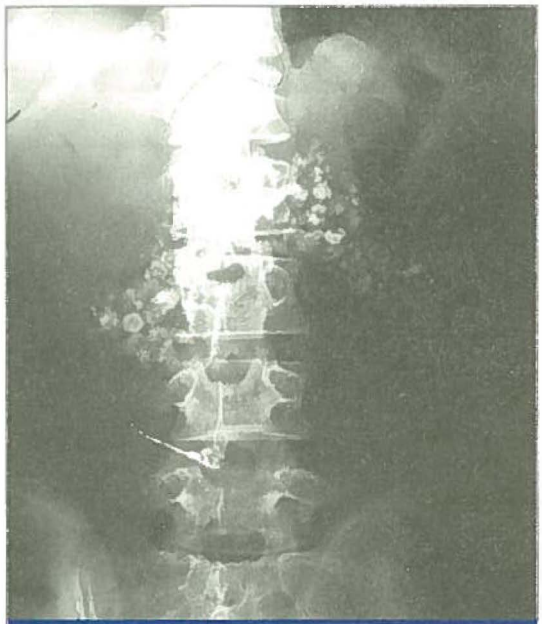


Fig. 9.16: Calcified pancreas

NB: Local vascular accidents like mesenteric artery occlusion may also cause distended loops, but here the loops have thick walls because of the gross edema and the gas transradiancies in adjacent loops may be separated by 1 cm wide areas of opacity.

Air under the Diaphragm

On the right side, normally diaphragm and liver shad-



Fig. 9.17: Renal calculi

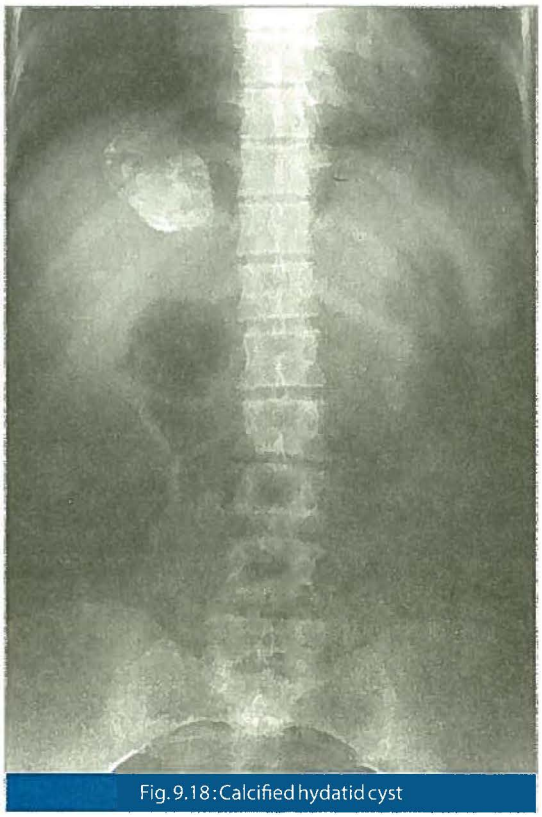


Fig. 9.18: Calcified hydatid cyst

ows merge with each other. If there is free gas in the peritoneal cavity it will ascend in standing position and lie between the diaphragm and the liver density.

Causes

1. Perforation of a viscus
2. Following abdominal surgery
3. Tubal insufflation test
4. Peritoneal dialysis
5. Infection of peritoneum by gas forming organisms

Calcification in Abdomen

Causes:

1. Fecaliths
2. Phleboliths
3. Calcified lymph nodes
4. Calculi: Renal, biliary, pancreatic, splenic
5. Calcified fetus
6. Liver: Amebic abscess, tuberculosis, calcified hydatid cyst, histoplasmosis, brucellosis
7. Calcification of abdominal wall, cysticercosis
8. Pancreas: Chronic pancreatitis
9. Suprarenal: Addison's disease, neuroblastoma
10. Splenic: Splenic cyst

4 › Urogenital System

'KUB': (Radiography for Kidney Ureter and Bladder)

This includes plain X-ray pictures of abdomen and pelvis.

Preparation

Three days preceding the investigation, the patient is put on a low-residue diet. The patient is given deflatulant medication like methyl polysiloxane or activated charcoal and mild purgation e.g. bisacodyl or castoroil on the night previous to the day of procedure. Patient is kept fasting overnight.

TECHNIQUE: AP view of abdomen is taken while the patient is in a state of full inspiration. Another antero-posterior view is taken by centering the tube on pubic symphysis. Alternatively both the areas may be covered in the same film.

INTERPRETATION: In a normal person the psoas shadows are seen running obliquely downwards from

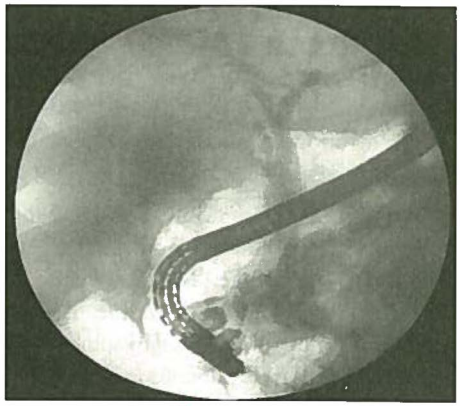




Fig. 9.19 & 9.20 : Endoscopic Retrograde Cholangio Pancreatography (ERCP) showing chronic pancreatitis & sketch of the hepato-biliary tree (area analysed by ERCP)

the vertebral column. The kidneys are situated opposite the second lumbar vertebra lateral to psoas shadow, the right kidney is slightly lower than the left one.

Kidneys are bean shaped structures with the concave hilum facing the vertebral column. Normally they measure 4" X 3" X 1".

The delineation of kidneys is due to the contrast provided by the translucency of perirenal fat. In very thin individuals and old men, the kidneys may not be well visualized. Poor preparation also will obscure kidney shadows.

In case of acute pyelonephritis the psoas and kidney shadows may appear fuzzy.

Large Kidney

1. Hydronephrosis
2. Pyonephrosis, abscess
3. Polycystic kidney (bumpy shadow)
4. Compensatory hypertrophy due to atrophy of the other one
5. Renal tumor
6. Nephrotic syndrome

Small Kidney

1. End stage renal disease
2. Chronic pyelonephritis
3. Hypoplastic kidney
4. Renal artery stenosis

There can be unilateral agenesis of kidney causing absence of renal shadow on that side. Alternatively the kidney may be ectopic (e.g. Pelvic).



Fig. 9.21 : IVP showing small kidney on right side

Calcification

The presence of calcification in the kidney is confirmed by taking lateral X-ray in which the shadow will fall on the vertebral column.

Causes

1. Renal calculi
2. Nephrocalcinosis
3. Renal tubular acidosis
4. Hyperparathyroidism
5. Milk alkali syndrome
6. Prolonged recumbency
7. Chronic abuse of calcium/vitamin D
8. Medullary sponge kidney

9. Renal tuberculosis
10. Artifact (Guinea worm, tablet in intestine)
11. Dermoid cyst
12. Calcification in tumor

'IVP' (Intravenous Pyelography) or Excretory Urography

Principle : Sodium iothalamalate is a radiologic contrast material containing iodine which is selectively excreted by glomerular filtration, which is not reabsorbed.

Preparation is similar as for KUB.

Technique: Before injecting the dye, iodine sensitivity should be checked. Anti-histaminics, adrenaline, hydrocortisone and oxygen should be available along with other resuscitative equipment. The patient should be asked not to take water after the previous evening, to obtain a good contrast. However, patients with diabetes, myeloma, old age and compromised renal function should be well hydrated to avoid nephrotoxicity due to the contrast medium. If the patient is on diuretics they should be omitted for 3 days prior to the procedure, lest the contrast be poor.

'KUB' is done as a pilot procedure to assure that the preparation is adequate.

Abdominal binder is applied tightly enough to compress the ureters. Twenty to 40 ml of contrast medium along with an antihistaminic is injected slowly intravenously. Abdominal radiographs are taken at 1, 3, 5, 10, 15 and 30 minutes, the binder is then released and at 45 minutes, 'prone' and standing films are taken. Bladder is picturized when the patient gets a sensation of fullness and desire to empty it.

A radiogram is taken immediately after evacuation of the bladder.

Interpretation

1. **Promptness of appearance of nephrogram:** Normally a good nephrogram should be seen in one minute film. Nephrogram is delayed and contrast is poor if renal functions are impaired. Late appearance of nephrogram and hyper concentration is seen in the kidney with renal artery stenosis. A congenitally small kidney is small in size. There is no delay in appearance of nephrogram.

   Nephrogram will appear late, persist for longer time and will progressively show hyper concentration in acutely obstructed kidney which previously had good function.

2. **Kidneys:** The kidneys are normally situated on either side of the vertebral column between L1 and L4 vertebrae. They are bean shaped structures and smooth in outline. The surface would show indentations left by some old scar of pyelonephritis. Fetal lobulations would be seen, if present. Polycystic kidney would show bumpy outline and stretched calyces. Cysts would cast a negative shadow.

3. **Pelvocalyceal system:** The corners of the calyces would appear nipped off in renal tuberculosis. There may be pyelotubular reflux especially at the upper and lower-pole calyces. In acute papillary necrosis, sloughed out papilla may cast a negative shadow. The calyces will show progressive blunting and ultimately clubbing in hydronephrosis. Oblique view may be taken for posteriorly situated calyces.

4. **Ureters:** Ureters may be dilated in hydronephrosis. They also may look dilated with the use of anti-spasmodics, oral contraceptives and during pregnancy. They would look spastic with infection. They would look narrow and pulled towards vertebral column in case of retroperitoneal fibrosis. The beaded appearance occurs in renal tuberculosis and ureteritis cystica. Both may present with painless hematuria, however in the latter condition, there is no deformity of calyces.

5. **Bladder:** A thimble bladder is seen with spastic bladder and chronic or tuberculous cystitis. In women, bladder capacity is often large. A paralytic bladder has a large size. The bladder neck would be elevated and with convex indentation due to prostate enlargement. Trabeculations and diverticula are seen with bladder neck obstruction and spastic bladder. Diverticula may be congenital or may develop in flaccid atonic bladder which had been poorly drained. Neoplasms may show filling defects.

5 Barium Studies

Details of the gastrointestinal tract can be studied if the gastrointestinal tract is filled with radio-opaque substance like barium.

For the barium meal, the patient swallows a suspension of radio-opaque barium sulfate, whilst the radiologist observes its passage on the fluorescent screen, or on the TV monitor of an image intensifier. Films are taken to provide a permanent record of any abnormality discovered. The barium enema is used in the diagnosis of diseases of the large intestine and rectum. Barium suspension is introduced into the rectum as an enema and manipulated around the colon to the cecum.

Esophageal Varices

Situation: In the submucous and subepithelial layers by anastomosis of left gastric and short gastric veins with the esophageal veins.

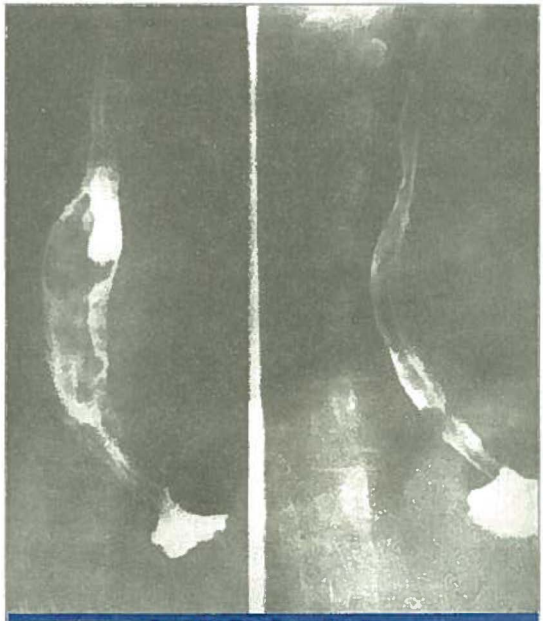


Fig. 9.22: Esophageal varices

Causes:

1. Portal hypertension
2. Cirrhosis of liver
3. Transiently in viral hepatitis
4. Alcoholic

Mechanism: The exact mechanism is not known. With inspiration the portal to esophageal venous pressure falls, hence blood flows from portal to esophageal veins which become varicose because of poor submucosal support.

Appearance

1. On esophagoscopy: Blue rounded projections under the mucosa.
2. On barium swallow: Long thin, evenly spaced lines of normal mucosa disturbed by the varices as filling defects in the regular contour of the esophagus.

Hiatus Hernia

1. On plain X-ray a ring shadow containing a fluid level and superimposed on the cardiac shadow.
2. Barium studies show esophagus and the cardiac end of the stomach protruding up through the normal hiatus.

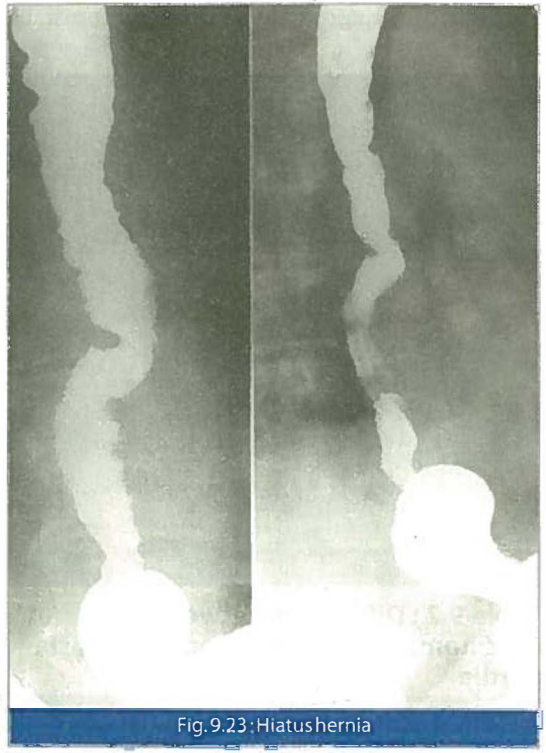


Fig. 9.23: Hiatus hernia

Achalasia Cardia

1. Esophagus is dilated
2. There is an area of smooth narrowing just distal to the dilated segment

3. Gas shadow is absent in stomach on plain X-ray abdomen

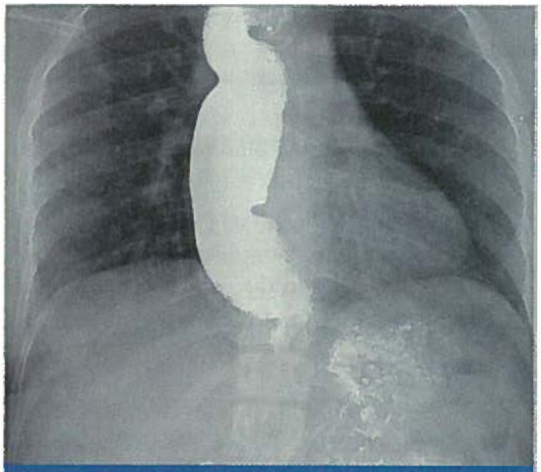


Fig. 9.24 : Achalasia cardia

Carcinoma of Esophagus

Irregular narrowing of the lumen with slight proximal dilation.

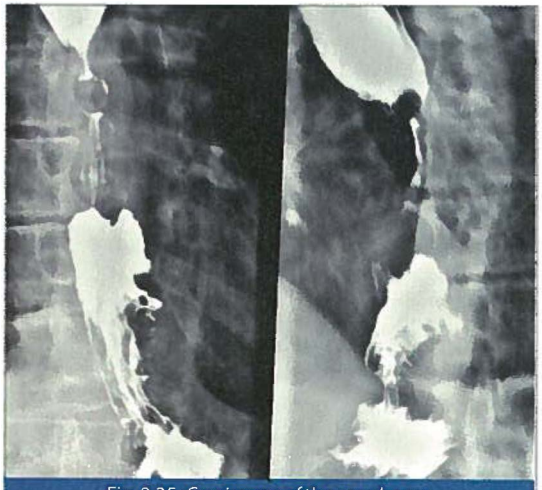


Fig. 9.25 : Carcinoma of the esophagus

Table 9.2 : Difference between Carcinoma of Esophagus and Achalasia Cardia

		Carcinoma esophagus	*Achalasia cardia*
1.	Narrow lumen	Eccentric	Central
2.	Outline	Irregular	Smooth
3.	Affected area	Rigid	Moves freely with heart movement

Gastric Ulcer

1. A constant projection from the main barium shadow in the stomach due to ulcer crater. It is conical with apex pointing outwards from the stomach.
2. Some small craters and those below the incisura ulnaris may be seen as small spherical opacities surrounded by a transradiant zone. There may be some deformity or interruption of rugal pattern nearby due to surrounding edema. The average gastric ulcer crater will be invisible radiologically after about 4 weeks. However, healing takes about 6 weeks. A recurrent ulcer crater on a new site will probably heal with greater ease than one on the old site, where scar tissue and poor blood supply will be factors delaying healing.

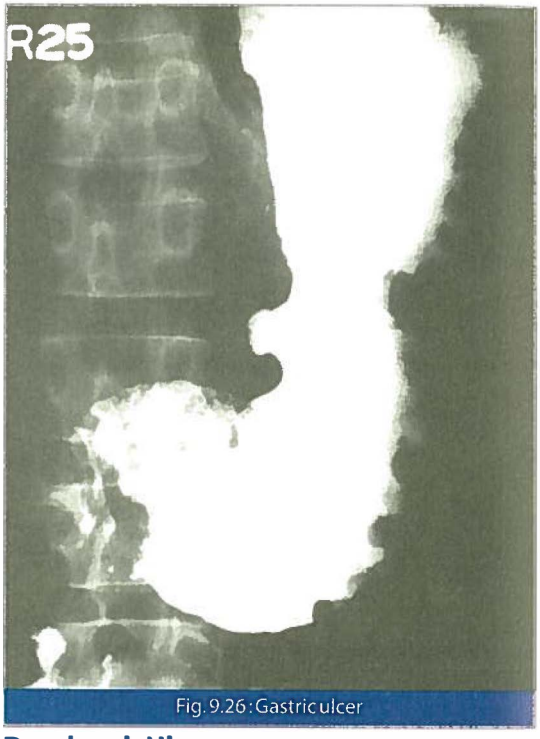


Fig. 9.26 : Gastric ulcer

Duodenal Ulcer

1. Deformity of the duodenal cap may be caused by an ulcer crater, edema, fibrosis, muscular spasm or a combination of these lesions.
2. Barium in the crater may appear as a niche projection from the general contour of the cap, if it is seen tangentially.

3. If it is seen en face after compression, it appears as an isolated spot, the surrounding edema causing a translucent area.
4. If the ulcer is chronic, the rugae may converge towards it giving a stellate appearance.
5. If the ulcer is large, barium may remain in the crater after the rest of the cap has emptied.



Fig. 9.27: Duodenal ulcer

Pyloric Stenosis

1. Large excess of resting gastric fluid, 6 hours after fasting.

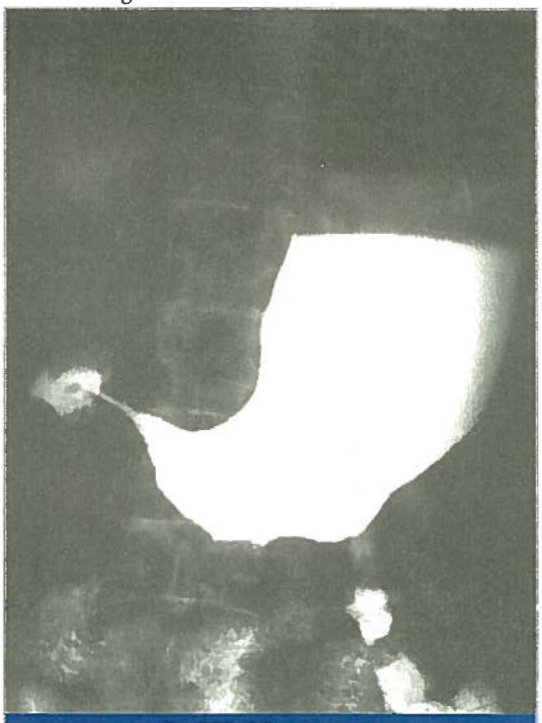


Fig. 9.28: Pyloric stenosis

2. Slow initial emptying of stomach after barium meal, in spite of periods of vigorous peristalsis. Slow final emptying with a large barium residue after 6 hours.
3. In severe cases, stomach is dilated.

Causes of Delayed Gastric Emptying

1. Pyloric stenosis
2. Physiological upset following vomiting caused by distaste for barium
3. Emotional upset due to grief, anxiety or even upsets associated with asthma and migraine

Carcinoma of the Stomach

1. A primary neoplastic ulcer is often indistinguishable from a simple ulcer.
2. Filling defect in the barium shadow or a thumb mark type of defect by a large fungating mass
3. Hour glass stomach due to annular constricting type of growth
4. Narrow irregular gastric outline due to submucous, diffuse, infiltrating neoplasm

Table 9.3 : Differences Between Peptic Ulcer and Malignant Ulcer

	Peptic ulcer	*Malignant ulcer*
1. Rugae	Converge towards ulcer	Interrupted
2. X-ray after 4 weeks	Great shrinkage	Moderate or no shrinkage

Ileocecal Tuberculosis

1. Filling defects or absence of filling of caecum due to spasm
2. Irregular contour, persistent narrowing of the ileum and cecum or shortening of the ascending colon
3. Irregular lumen with contractions and dilatations
4. Multiple fluid levels
5. Calcification of mesenteric lymph nodes may be present.

Crohn's Disease

1. A localized narrowing with irregularity of colon wall. (Absence of concave indentations of the two ends of narrow area).

2. The whole colon may be narrow, ribbon-like as in ulcerative colitis, but the ulcers are deeper and burrow into the submucosa which is disorganized and gives cobblestone appearance.
3. Strictures and fistulas may be present.

Ulcerative Colitis



Fig. 9.29: Ulcerative colitis

1. Slight irregularity of colon margins due to barium outlining areas of ulcerated mucosa
2. Later colon becomes shortened, narrow and ribbon-like with absence of normal haustrations
3. Small spiky projections of ulcer crater may be present
4. Irregular transradiancies of polyposis may be present.

Neoplasm of Colon

1. An area of narrowing of the colonic lumen which may be eccentric or annular.
2. A concave indentation of the lumen just beyond the narrowing.



Fig. 9.30: Malabsorption

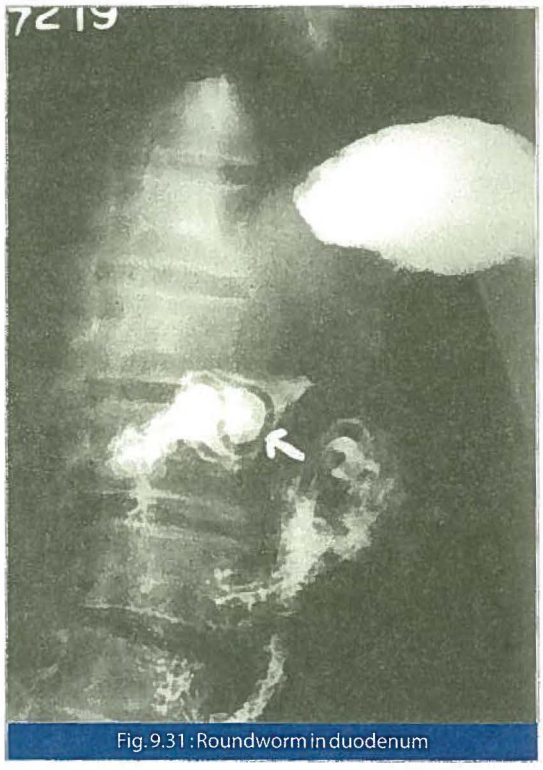


Fig. 9.31: Roundworm in duodenum

6 X-ray of Bones

X-ray of the bone must be viewed as follows:

A. *Soft Tissues*: Swelling or muscle wasting.

B. *Bony Surfaces*

1. Periosteal new-bone formation: This is seen as a linear density, parallel to the cortex. It is seen in healing scurvy, hypervitaminosis A and D and infantile cortical hyperostosis.
2. Juxta-articular erosions
3. Diffuse cortical resorption: This is the typical loss of diaphyseal cortex seen in hyper- parathyroidism

C. *Shape and Size of the Bone*: Fractures, dislocation and congenital anomalies.

D. *Internal Structure of the Bone*: Mineralization, localized destruction, etc.

Osteomyelitis

A. **Acute Osteomyelitis:**

1. Slight focal decalcification
2. Soft-tissue swelling
3. Faint periosteal new-bone formation

B. **Chronic Osteomyelitis:**

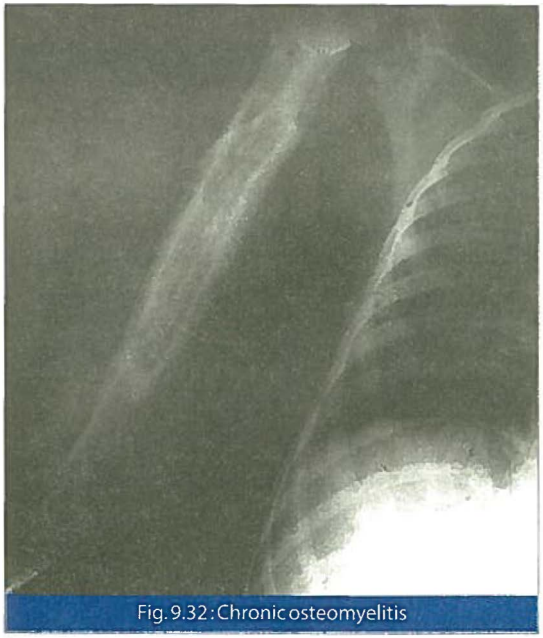


Fig. 9.32: Chronic osteomyelitis

1. Bone destruction with sclerotic reaction
2. Sequestrum: Dense, devascularized bony fragments lying within the pus and granulation
3. Involucrum: Peripheral shell of new supporting bone laid down by the periosteum

Tuberculosis of Bone

1. Diffuse loss of density of bone
2. Slight diminution in joint space
3. Trabeculae become indistinct and cortex is thinned out
4. Periosteal new-bone formation is absent and there is no massive sequestrum formation

Tuberculosis of Spine

1. Erosion of the affected vertebrae
2. Diminution of disc space
3. Paravertebral abscess
4. Wedge shaped collapse and angular kyphosis
5. Two affected vertebrae fuse into single wedge shaped bone.



Fig. 9.33: Tuberculosis of spine

Aneurysmal Bone Cyst

These are seen in several disorders. It usually indicates an autonomous parathyroid gland (primary or tertiary hyperparathyroidism).



Fig. 9.34 : Aneurysmal bone cyst

Scurvy

In scurvy there is adequate calcium but lack of osteoid tissue.

1. **Epiphysis:** The epiphysis has a dense margin with radiolucent centre *(ring sign or halo sign of Wimberger)*.
2. **Metaphysis:** the white line of metaphysis is wider than normal. '*Scurvy zone*' lies between the bone and the white line.
3. **Diaphysis:** There is uniform demineralization of the bone. The cortex is thinned out giving the bone a uniformed ground-glass appearance with penciled outline. Angular lateral bony spurs are present. These are defects in the cortex at the junction of diaphysis and metaphysis (*angle sign*).
4. **Subperiosteal hemorrhages** may occur which may lift the periosteum. It may calcify sometimes.

Rickets

1. **Epiphysis:** The epiphysis lacks a bony cortical margin and appears indistinct. There may be epiphyseal separation which is more common in renal rickets.
2. **Metaphysis:** The metaphysis is *splayed out*

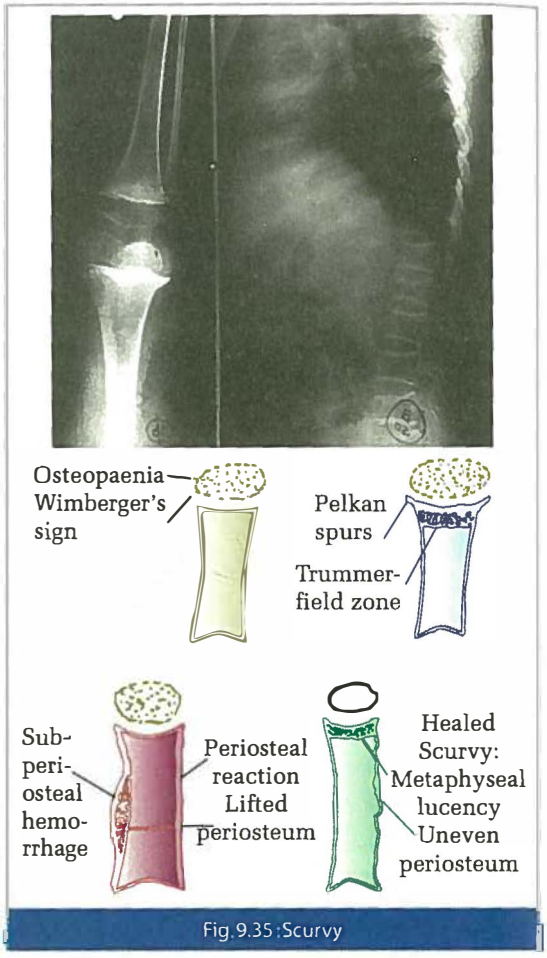


Fig. 9.35 : Scurvy

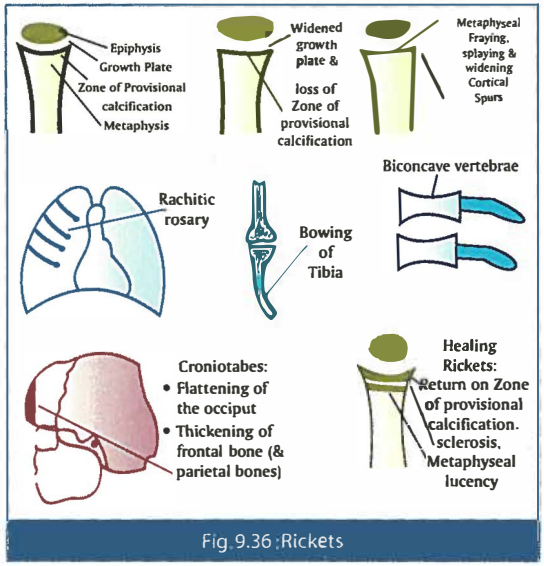


Fig. 9.36 : Rickets

and distally concave (*cupping*). The zone of calcification instead of forming a well-defined white line, is irregular and of low density. Its end appears arranged in longitudinal rows (*fraying or streaking*). Cortical spurs from the metaphysis may grow towards the displaced epiphysis resulting in deformity.

3. **Diaphysis:** There is generalized decalcification of the bones resulting in increased radiolucency between the diaphysis and epiphysis.
4. **Green-stick fractures** with bending and deformities may occur.

Osteomalacia

Definition: Osteomalacia is a disorder characterized by failure of the bony matrix to mineralize normally and promptly.

Features

1. Generalized decalcification of the bone
2. Vertebral bodies are biconcave (*cod-fish vertebrae*)
3. *Looser's zones* or pseudo-fracture may be present. They are 1-3 mm wide transradiant zones extending 1 cm into the bone at right angle to the cortex and look like incomplete fracture. They occur in ischio-pubic rami, axillary borders of the scapula, ribs, femur, humerus and lower third of tibia and fibula
4. Deformities of limb and pelvis (*triradiate pelvis*) may be present.
5. If chronic renal failure is the cause of osteomalacia there may be sub-periosteal bony erosions in middle phalanges and sclerosis of the vertebral end plate (*rugger jersey spine*).

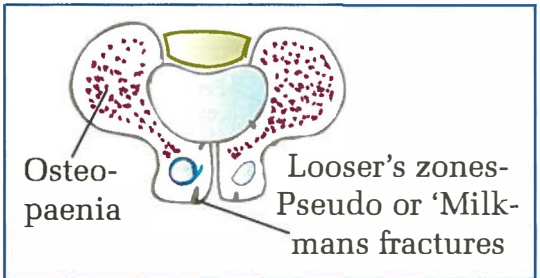


Fig. 9.37: Osteomalacia

Osteoporosis

Demineralization of bone with thin cortices and delicate medullary trabeculae.

Causes:

1. Endocrine: Cushing syndrome, thyrotoxicosis, hypogonadism
2. Metabolic: Mucopolysaccharidosis, homocystinuria
3. Deficiency: Famine, scurvy, hypocalcemia
4. Blood diseases: Leukemia, myeloma, lympho-sarcoma, secondaries, histiocytosis
5. Drugs: Heparin, steroids
6. Idiopathic
7. Osteomalacia

Osteosclerosis

Causes

1. Fluorosis
2. Secondaries from malignancy of prostate, breast, bronchus, gut and Hodgkin's disease
3. Marble bone disease
4. Osteopoikilosis
5. Mastocytosis


Fig. 9.38: Osteosclerosis

Bony Metastasis

1. Erosion without bone reaction or periosteal new bone formation
2. In the vertebrae it may cause vertebral collapse with intact disc space
3. Sclerosing bony metastasis have to be distinguished from Paget's disease

Table 9.4 : Differences between Sclerosing Metastasis and Paget's Disease

		Sclerosing metastasis	*Paget's disease*
1.	Width of bone	Normal	Increased
2.	Trabeculae	Normal	Wider and spaced at greater intervals
3.	Softening of bones	Absent	Present, causing deformities

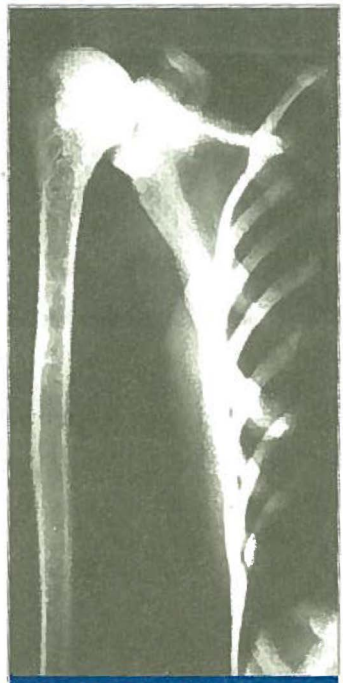


Fig. 9.39 : Sclerotic metastasis

Fluorosis

1. Osteosclerosis of the spine and pelvis
2. Ground-glass appearance of the bones
3. Calcification of the interosseous membrane of the forearm, intervertebral ligaments, sacrospinous and sacrotuberous ligaments



Fig. 9.40 : Calcification of interosseous membrane in fluorosis

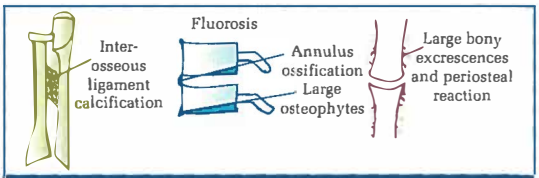


Fig. 9.41 : Fluorosis

Cretinism

1. Delayed appearance of the epiphyses which may be hypoplastic or stippled
2. X-ray spine: Intervertebral disc and the vertebral bodies are of same size
3. Mandible is ill-formed

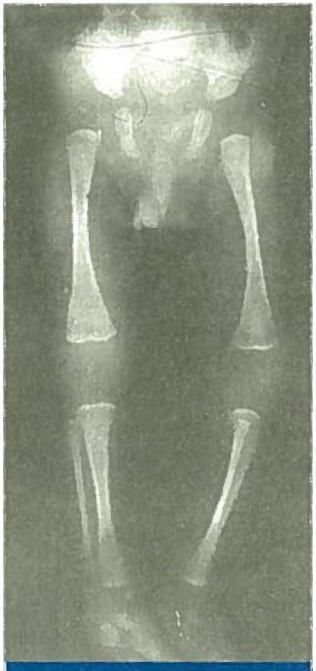


Fig. 9.42 : Cretinism

Rheumatoid Arthritis

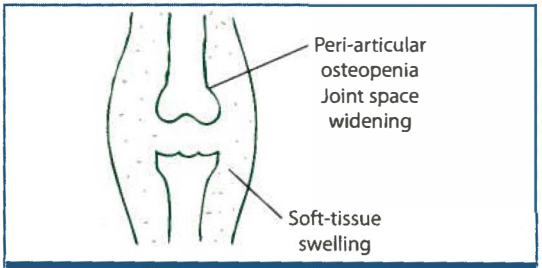


Fig. 9.43 : Rheumatoid arthritis



Fig. 9.44: Late phase of rheumatoid arthritis

Early phase	Late phase
1. Slight demineralization	1. Massive destruction
2. Joint effusion	2. Subluxation
3. Pericapsular swelling	3. Fibrous ankylosis
4. Marginal erosion	

Osteoarthritis

1. Loss of joint space
2. Bony marginal lipping may be present.
3. Sclerosis of subarticular bone.

Ankylosing Spondylitis

1. Sacro-iliac joint space initially wide, later narrow.
2. Fusion of anterior and lateral ligament gives an appearance of bamboo spine or railroad tract.
3. Demineralization along the joint surface with bone.

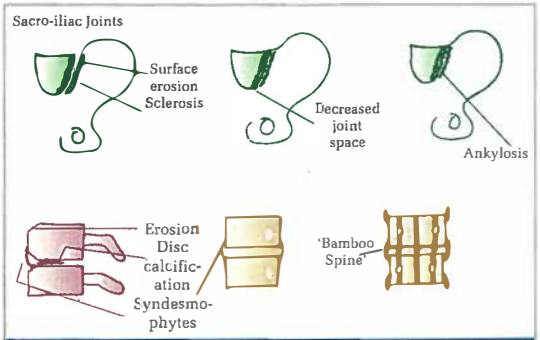


Fig. 9.45: Ankylosing spondylitis (Still's disease)

Gout

1. Capsular swelling leading to gross destruction of the joint usually affecting the distal interphalangeal joint.
2. Small, well-defined, punched-out areas without a white rim of sclerotic bone near the articular ends of the bone. These are caused by urate deposits.
3. Tophi within the soft tissues.

Septic Arthritis

1. Joint effusion with joint swelling
2. Rapid loss of cartilage and subchondral bone

Psoriatic Arthritis

1. Affects the distal interphalangeal joints
2. Joint space will be narrow
3. Marginal splaying out of the base of the terminal phalanges with punched out erosions (sharpened pencil appearance) may occur

Hyperparathyroidism

Sub-periosteal resorption of the bone seen in hands and skull.

1. In the hands decalcification of the cortical bone is seen in the middle and distal phalanges



Fig. 9.46: Subperiosteal bone resorption

2. In the skull there is fine granularity with demineralization and radiolucent cystic areas.

7 › X-ray Skull

The X-ray of the skull must be viewed as follow:

I. Calvarium and Base
   A. Normal radiolucencies e.g. Sutures and vascular markings
   B. Fractures: Linear, depressed or basilar

II. Sella Turcica
   A. Shape and size: It is ballooned in pituitary tumors
   B. Mineralization: It is demineralized in pituitary tumors
   C. Erosion of posterior clinoids

III. Calcification

Raised Intracranial Tension

In children:

1. Widened sutures
2. Prominent convolutional markings
3. Erosion of posterior clinoids. Sella turcica is shallow

In adults:

1. Erosion of posterior clinoids
2. Silver beaten appearance (Fig 9.47)

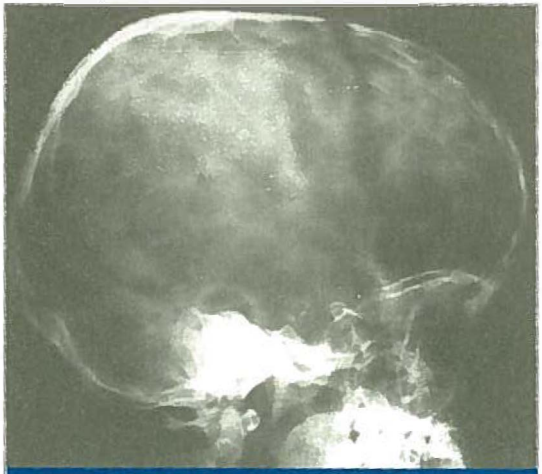


Fig. 9.47: Silver beaten appearance

Intra-sellar Space-occupying Lesions

Widening and deepening of the sella. Sellar ballooning (Fig 9.48) is seen in chromophobe and eosinophil adenomas.



Fig. 9.48: Sellar Ballooning

Acromegaly

1. The long bones are wide, thick, with coarse bony trabecular pattern & tufting of the terminal phalanges.

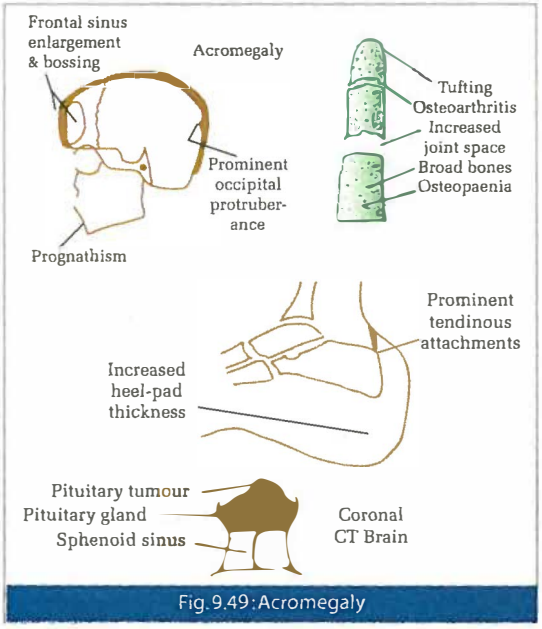


Fig. 9.49: Acromegaly

2. The vault of the skull is increased in thickness, paranasal sinuses are large, mandible shows prognathism and malocclusion of teeth and sella turcica is widened, deep and ballooned.

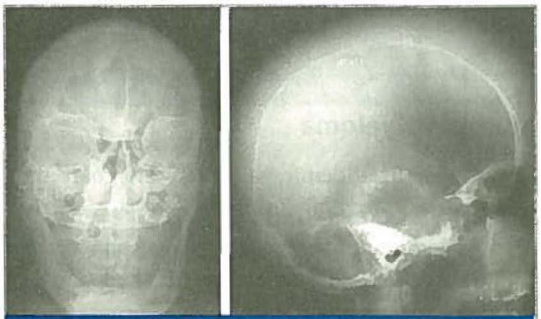


Fig. 9.50: Skull in acromegaly

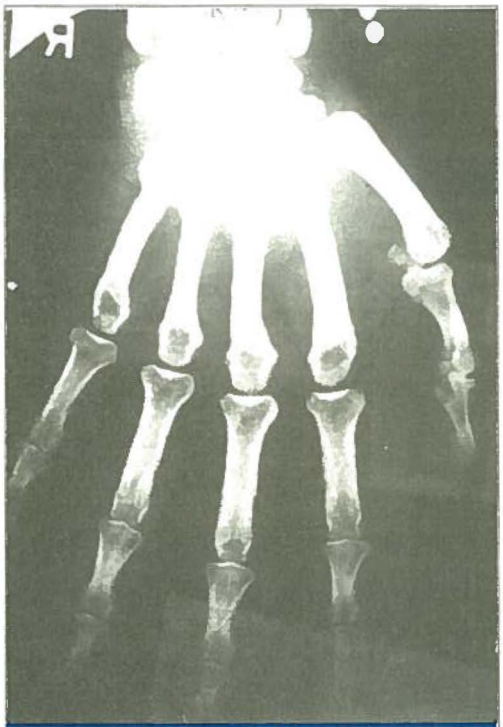


Fig. 9.51: Tufting of Phalanges in acromegaly

Hydrocephalus

1. Signs of raised intra-cranial tension.
2. Skull may be enlarged in size. Sutures may be separated.
3. Pituitary fossa may be distended and clinoid processes may be eroded.



Fig. 9.52: Hydrocephalus

Intracranial Calcification

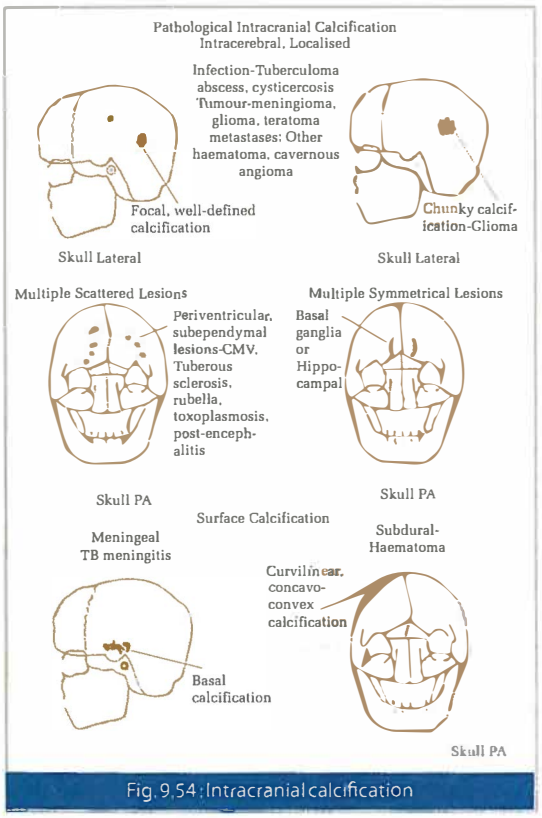


Fig. 9.54: Intracranial calcification



Fig. 9.53: Calcified tuberculoma

Normal

1. Pineal body
2. Falx cerebri
3. Choroid plexus
4. Petroclinoid ligament
5. Lateral edges of diaphragm sellae

Abnormal

1. *Infections:* Tuberculosis, hydatid cyst, cysticercosis and toxoplasmosis
2. *Vascular:* Sub-dural hematoma, old infarct, arteriosclerosis, AV malformations
3. *Tumors:* Meningioma, dermoid, cranio-pharyngioma, etc.
4. *Miscellaneous:* Sturge Weber syndrome, tuberous sclerosis, hypoparathyroidism.

Thalassemia

1. **Skull:** The diploic space is widened with lack of definition of the outer table. In severe cases, outer table cannot be defined and the bony trabeculae tend to be arranged at right angles to the inner table giving hair-on-end appearance.
2. **Long bones:** The medullary cavity is wider with coarse trabeculae and thinned out cortex. This is best seen in phalanges which may lose its biconcave shape and become rectangular or biconvex.

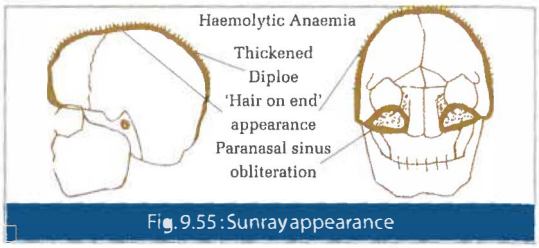


Fig. 9.55: Sunray appearance

Multiple Myeloma

1. Generalized demineralization and coarsening of the trabecular pattern.
2. Single or multiple, small, rounded, punched out areas of radiolucency best seen in skull, sternum, ribs, vertebrae and pelvis.
3. A drumstick expansion of the anterior ends of some of the ribs may be present over the radiolucent deposit.
4. Pathological fractures and vertebral collapse with spinal deformities may be present.

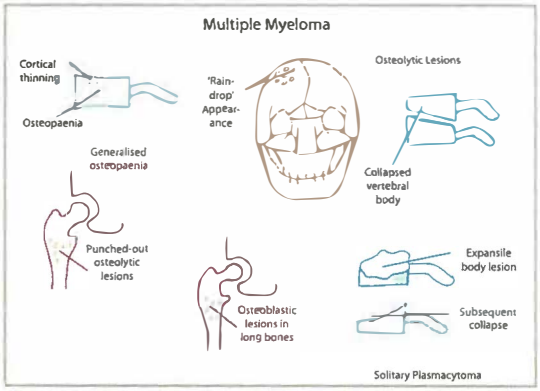




Fig. 9.56: Multiple myeloma showing multiple punched out areas

Instruments

10

1 › Endotracheal Tube

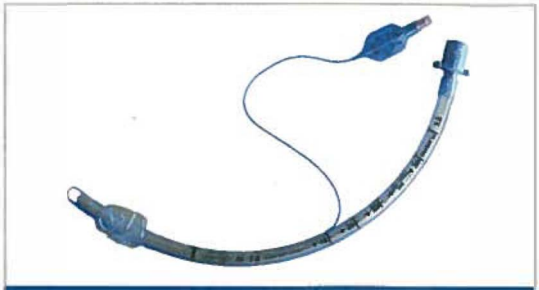


Fig. 10.1 : Endotracheal tube with a cuff

It is a tube made of India Rubber, Portex (polyethylene) or Polyvinyl chloride (PVC). The Portex and PVC tubes are softer and less irritant to the mucosa. They have a radio-opaque line along their length to assess the exact location of the tube. The tube has a smooth atraumatic tip. The end of the tube is beveled. The bevel usually faces left. There is also a sub terminal opening (eye) on the right in order to inflate the right lung.

There is a 1 cm graduation along the tube to indicate the depth of insertion. There is also a 2 cm mark (called the Vocal Cord Guide) at the distal end which helps in placement of the tube beyond the vocal cords.

The endotracheal tube may be cuffed or uncuffed. The cuffed tubes have a cuff at the distal end which can be inflated through a smaller tube which runs alongside the endotracheal tube or is embedded in its wall. There is also a pilot balloon with a one-way valve on the proximal end of the smaller tube which helps to assess the pressure of air injected into the cuff.

Endotracheal tubes may be for oral or nasal insertion.

Sizes

The size indicates the internal diameter of the tube in mm. Uncuffed tubes are available in sizes 2.5 to 10.0 mm with 0.5 mm increments. The cuffed tubes are available in 4.0 to 10.0 mm sizes with 0.5mm increments.

Sterilization

The India Rubber tubes can be boiled or autoclaved. The PVC or Portex tubes are available in gamma irradiated packs for single use.

Uses

1. Cardiopulmonary arrest to carry out artificial respiration
2. Respiratory failure due to severe pneumonia, chronic obstructive lung disease and respiratory muscle paralysis (Gullian Barre syndrome, myasthenia gravis, bulbar poliomyelitis, etc.)
3. To secure the airway and clear secretions to prevent aspiration in unconscious patients
4. To administer general anesthesia.
5. To suction the trachea in newborns in case of meconium aspiration

Method

The patient is kept in supine position with the cervical spine flexed and the head extended at the atlanto occipital joint. Standing at the head of the patient, the laryngoscope is inserted into the oral cavity and the vocal cords are visualised. The Endotracheal tube (with the cuff deflated), with the bevel facing left, is inserted through the vocal cords until the cuff passes through the cords. The Ambu bag is now connected to the endotracheal tube and ventilation is started. Bilateral air entry is checked for by 5 point auscultation (left and right anterior chest wall, left and right lateral chest wall and epigastrium).

If there is bilateral equal air entry, the cuff is inflated with 3-4 cc of air and the endotracheal tube is fixed with

adhesive tape to the corner of the mouth. An airway or mouth gag is inserted to prevent biting of the tube and also facilitate suctioning of secretions.

If bilateral equal air entry is not achieved, the tube is withdrawn by a few centimeters and rechecked. The tube might be in a bronchus (more often the right bronchus since it is shorter, wider and more vertical than the left). If bilateral equal air entry is still not achieved, the endotracheal tube should be withdrawn and reinserted. The tube was probably in the esophagus (no air entry bilaterally on chest auscultation and gurgling or bubbling sound in the epigastrium corresponding with the ambu bag ventilations).

Nasal V/s Oral Insertion

Advantages of Nasal Insertion:

- Does not obstruct the surgeons operative field in oro-facial operations
- Oral feeding is possible
- Biting of the tube does not occur

Disadvantages of Nasal Insertion:

- Blind insertion
- Nasal trauma
- Infection more common

Advantages of the Cuff

It provides a seal between the tracheal wall and the tube.

1. This prevents leakage of fluids into the trachea thus decreasing the chances of aspiration.
2. It also prevents leakage of gases around the tube thus increasing the efficiency of ventilation.
3. Secures the tube in place.

Precautions

1. The cuff is to be inflated with air only. No fluid can be used since in case the cuff ruptures, the fluid will cause aspiration.
2. An India Rubber tube can be kept in place up to 24 hours and a Portex tube up to 7 days. Beyond this period, a tracheostomy should be done.
3. Deflate the cuff every 2–3 hours for 1 -2 minutes to prevent tracheal necrosis.
4. Suctioning should be done every 15–30 min.

Complications

1. Infection
2. Trauma during insertion to the oral mucosa, teeth, pharynx, larynx and vocal cords
3. Blockage of the tube with secretion.
4. Undetected esophageal intubations can be catastrophic
5. Tracheal necrosis
6. Tracheal or sub-glottic stenosis
7. Collapse of one side of the lung due to wrong placement of the tube in one bronchus causing hypoventilation of the other lung
8. Difficult extubation (due to patients dependence on the ventilator)
9. Hoarseness of voice or vocal cord dysfunction after extubation
10. Laryngospasm following extubation commonly when the patient is in semiconscious state. Hence extubation should be done only when laryngeal reflex has returned

Contra-indications

1. Laryngeal spasm
2. Laryngeal edema
3. Upper airway trauma or cancer

2 › Tracheostomy Tube

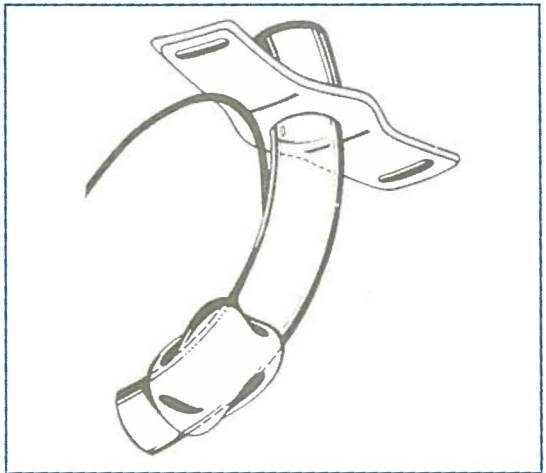


Fig. 10.2: Tracheostomy tube

Tracheostomy tube may be of Portex or rubber, cuffed or without cuff. A metal tube is also available which does not have a cuff.

The metal tube is used when permanent tracheostomy is required as following laryngectomy. It has an inner tube which be changed and cleaned.

The Protex tube has a cuff which can be inflated by injecting air through the outer tube. The balloon gets inflated and secures the tracheostomy tube in position. A plastic attached to the tube has ribbons which secures the tube around the neck.

Indications

1. Laryngeal spasm as in tetanus.
2. Prolonged artificial ventilation is required.
3. Airway obstruction due to trauma, tumor or secretions.

Complications

1. Tracheomalacia
2. Infection
3. Trauma to airways
4. Collapse of the lung

Uses of cuffed tracheostomy tube

1. Prevents leak of gases during positive pressure ventilation
2. Prevents aspiration
3. Secures the tube in place

Duration

Tracheostomy can be kept for 15-20 days.

Refer Pg. 502

3 › Laryngoscope

It consists of a handle and a blade with a light source. The handle has a rough surface for a better grip. It is usually short to prevent the handle from abutting the chest or breasts. The handle also contains the batteries which are required for the light source.

The Blade can be of two types: straight blade (Miller) or curved blade (Macintosh). The straight blade is preferred in infants and children younger than 8 years since the larynx is situated more anteriorly and



Fig. 10.3: Laryngoscope

cephalad than in adults. The blade has a slot at the base where is attached onto the handle. It can be fixed at 90 degrees to the handle. It has a long shaft which used to compress the soft tissues of the oral cavity and the pharynx. It has a blunt and slightly bulbous tip which is used to elevate the larynx.

The light source is usually a small light bulb which fits onto a socket on the blade and lights up when the blade is locked onto the handle and fixed at 90 degrees.

Uses

1. To pass an endotracheal tube
2. To visualize the upper airway upto the vocal cords (Direct Laryngoscopy)

Procedure

Patient is placed in supine position with the cervical spine flexed and the head extended at the atlanto occipital joint. Standing at the head end of the patient, the handle of the laryngoscope is held in the left hand and the mouth of the patient is opened with the right hand. The blade of the laryngoscope is passed into the oral cavity and the tip is placed between the base of the tongue and the epiglottis. The soft tissues of the oral cavity and pharynx are then elevated with upward movement of the handle of the laryngoscope in order to visualize the vocal cords.

At this time, a second helper provides Cricoid Pressure (Sellicks maneuver). The thyroid cartilage is located and the hard tissue just below it is the cricoid cartilage. Using the thumb and index finger, firm pressure is applied over the cricoid cartilage. This blocks the

esophagus with the firm cartilage of the trachea. It also allows the larynx and vocal cords to be visualized more easily.

With the vocal cords in view and the helper applying cricoid pressure, the endotracheal tube is passed between the vocal cords. The proper tube placement is confirmed by five point auscultation. Only after confirmation of proper tube placement and inflation of the balloon, is the cricoid pressure removed.

Sterilization

The blade and the handle (with the batteries removed) are sterilized by soaking in a solution of gluteraldehyde followed by properly rinsing them with warm water and drying the instruments with a clean soft cloth.

Complications

1. Local tissue injury that is to the lips, gums, teeth, tongue, palate pharynx, larynx or esophagus.
2. Dislocation of the cervical vertebra in case of vigorous mobilization of the neck.
3. Aspiration of a detached tooth, blood clots or the bulb of the laryngoscope.
4. Vagus nerve irritation causing changes in heart rate and blood pressure.

4 › Oxygen Mask and Oxygen Cannula (Nasal Prongs)

The oxygen mask consists of the mouth piece which snugly fits over the nose and the mouth through which oxygen can be administered. There are small openings on either side of the mask for expired air.

The oxygen cannula or nasal prongs consist of two prongs which fit into the external nares (nostrils) of the patient.

They are disposable and should not be reused.

Indications

They are both used to provide supplemental oxygen to a patient in respiratory distress, cardiac arrest or congestive cardiac failure.

Oxygen Concentration Delivered

Oxygen Cannula can provide upto 44% oxygen.

- 1 L/min – 24%
- 2 L/min – 28%
- 3 L/min – 32%
- 4 L/min – 36%
- 5 L/min – 40%
- 6-10 L/min – 44%

Oxygen Mask can provide upto 60% oxygen at 6 to 10 L/min

Oxygen Mask with Reservoir can provide 90 to 100% oxygen. There is a corrugated tube or reservoir bag attached to the mask in which oxygen is concentrated to deliver a higher percentage of oxygen to the patient.

- 6 L/min – 60%
- 7 L/min – 70%
- 8 L/min – 80%
- 9 L/min – 90%
- 10 L/min – nearly 100%

Precautions

Patients who are unconscious or in coma may vomit and aspirate the vomitus in case a tight fitting mask is used.

Refer to Chapter 11, Pg. 503 Oxygen Therapy.

5 › Nebulizer Chamber

This is a chamber which is connected to the nebulizer and oxygen mask on either side, so that when the patient breaths, along with oxygen, nebulized drug would also be inhaled.

Uses: In bronchial asthma and other respiratory illnesses, drugs like salbutamol beclomethasone and ipratropium bromide can be administered.

6 › Metered Dose Inhaler

This is a pressurized aerosol system. It consists of an L-shaped tube consisting of mouthpiece, which is taken in the mouth, and a tube to hold the canister of the medicines to be inhaled.

To administer the drug, the patient inhales after putting the mouthpiece in the mouth. The patient holds the breath, presses the canister and inhales through the mouth, the fixed dose of drug liberated.

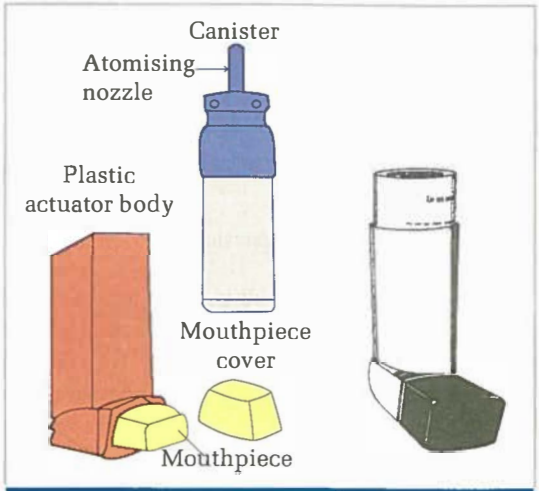


Fig. 10.4: Metered dose inhaler

The advantages over oral or parenteral drug administration are that there is a rapid onset of action, a smaller dose of drug is required, there is a lower incidence of side effects, the inhaler is easier to carry and it is cost-effective.

The biggest disadvantage with this method is that correct coordination from the patient is required.

The patient is adviced to rinse his mouth after each use in order to prevent oral candidial infections.

7 Spacehaler

This consists of a smooth plastic cylinder, at one end of which is mouthpiece through which the patient inhales the drug and at the other end the metered dose inhaler is placed. The procedure is like Metered Dose Inhaler.

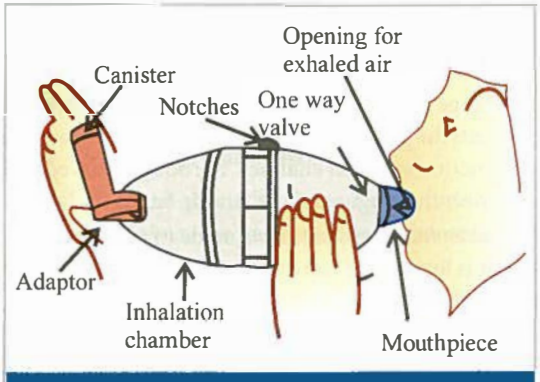


Fig. 10.5: Spacehaler

However, since the patient breathes in the cylinder a close coordination of the patient is not required. It also reduces the chances of candidal infection that occurs with inhaled steroids.

8 Rotahaler

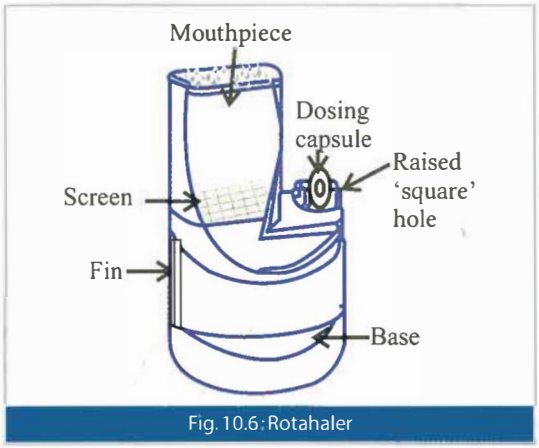


Fig. 10.6: Rotahaler

This is a dry powder inhaler (DPI) which is breath activated. The Rotacap is inserted into the raised square hole. On rotating the base, the two halves of the Rotacap separate and can be seen through the transparent body. The patientthen puts the mouthpiece between his teeth, seals his lips around it and breathes in through the mouth as deeply as possible. The rotahaler is easier to manipulate than the MDI and is specially suitable for children, elderly, arthritic patiens. The disadvantages are that it requires a minimal inspiratory flow rate of about 28 litres/min and since it is difficult to assemble in breathless or handicapped patients.

9 Nelson's Inhaler

This is an earthenware inhaler which is filled up to the base of the spout with three quarter cold water. The glass mouthpiece is boiled and inserted in the cork so that it points in a direction opposite to the spout. The patient inhales through the mouth only and exhales through the nose. The drug used is tincture benzoin, menthol, eucalyptus or pine. The inhaler is covered by a flannel bag which fits it. It is useful in respiratory ailments and coryza.

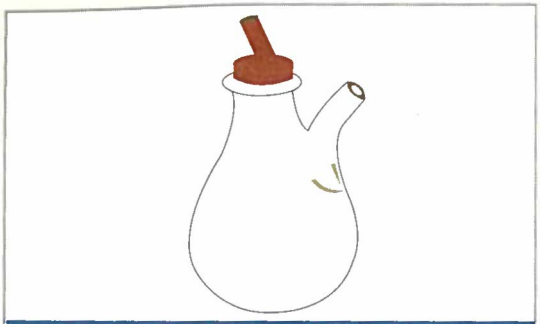


Fig. 10.7: Nelson's inhaler

10 › Ambu Bag (Self-inflating Ventillation Bag)



Fig. 10.8: Ambu bag

The AMBU Bag (Ambulatory Manual Breathing Unit) has the following parts:

1. Outlet (mask is attached to this end)
2. Two Valves
   - One-way Expiratory Valve (to prevent expirated air from entering the bag)
   - Pressure Release Valve or Pop off Valve (set at 30 – 45 cm of H_2O)
3. Self inflatable rubber bag (refills automatically after compression)
4. Two Inlets
   - Oxygen Inlet (for connection to the oxygen source)
   - Air Inlet (left open or attached to an oxygen reservoir)

Oxygen Delivery

- No Oxygen Source - Delivers 21% Oxygen (Room air)
- With Oxygen Source but Without Oxygen Reservoir - Delivers 40% Oxygen
- With Oxygen Source and Oxygen Reservoir – Delivers nearly 100% Oxygen

Sizes of the Bag

Pediatric Sizes (240 ml and 750 ml) and Adult Size

Indications

It is used to provide Intermittent Positive Pressure Ventilation

Procedure

When the bag is squeezed, air is driven into the lungs of the patient via the face mask, endotracheal tube or tracheostomy. The pressure release valve prevents high pressure ventilation thus preventing barotraumas. On releasing of the pressure the bag re-inflates automatically. The recoil of the chest causes the air to leave the lungs by the one-way expiratory valve. The Ambu Bag has to be cleaned after each use by soaking it in a disinfectant solution and then properly rinsing and drying it.

11 › Airway

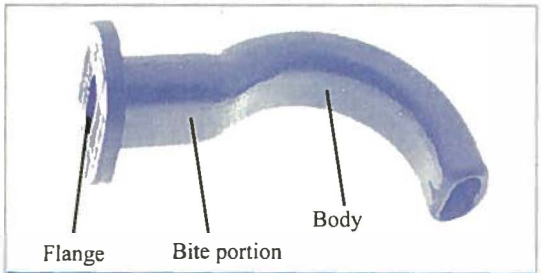


Fig. 10.9: Oropharyngeal Airway

The oropharyngeal airway is a plastic or metal instrument. It has 3 part: the flange, the bite portion and the body. The flange is a circular flat part at the oral end which prevents the airway from entering the oral cavity. The bite portion is a straight firm part between the flange and body. It is at the level of the teeth and prevents the patient from biting the airway and causing obstruction to the air channel. The body is curved and rests over the tongue and with the tip facing the larynx.

The nasopharyngeal airway is made of plastic or rubber. It is longer and has a flange and a body. The body is curved to fit in the nasopharynx.

The metal airways are sterilized by autoclaving or boiling. The plastic airways are disposable and meant for one time use.

Indications

- Airway maintenance in the unconscious patient
- Protects an endotracheal tube from being bitten
- Facilitates airway suctioning

Indications for Using a Nasopharyngeal Airway

The oropharyngeal airway is preferred except in the following situations

1. The mouth cannot be opened
2. There are loose teeth which might get detached and be aspirated
3. If there is macroglossia like in Pierre Robin Syndrome
4. In any pathology of the oral cavity

Procedure

The size of the *oropharygneal airway* is assessed by measuring the distance from angle of mouth to the angle of the jaw. The patient's mouth is opened with the left hand or using the chin lift maneuver. The oral airway is inserted upside down, so its concavity is directly upward, until the soft palate is reached. At this point the airway is rotated 180 degrees, the concavity is directed inferiorly and the airway is slipped into place over the tongue.

In children it is better to use a tongue depressor before inserting the airway in the correct position. The airway must not push the tongue backward and block the airway. It is then secured in place using adhesive tape attached to the bite portion.

The size of the *nasopharyngeal airway* is assessed by measuring the distance form the tip of the nose to the tragus of the ear and adding 2.5 cm to it. It is lubricated well and inserted into any nostril gently until it rests in the pharynx. It is then fixed in place.

Complications

1. *Oropharyngeal Airway*

- If the airway too long it may obstruct the larynx by pushing down the epiglottis against the posterior pharynx
- If the airway too short it may push the tongue backwards and cause obstruction
- Vomiting may be stimulated in a conscious or semiconscious patient.
- Laryngospasm – if the epiglottis or vocal cords are touched
- Local trauma to the lips, gums, teeth, tongue or soft palate.

2. *Nasopharyngeal Airway*

- A long airway may enter the esophagus and cause gastric hyperinflation and pulmonary hypoventilation (if bag and mask ventilation is being used)
- Vomiting may be stimulated in a conscious or semiconscious patient.
- Laryngospasm – if the epiglottis or vocal cords are touched
- Local trauma to the nasal cavity or soft palate

Precautions

1. Select the right size of the airway
2. Use it only in unconscious patients since vomiting may be stimulated in a conscious or semiconscious patients

12 〉 Mouth Gag

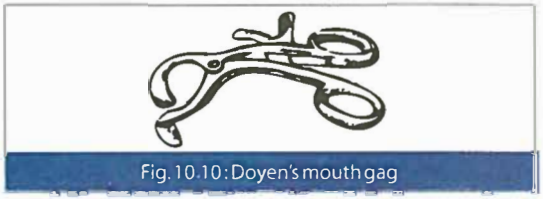


Fig. 10.10: Doyen's mouth gag

Types

1. Doyen's: Opening maintained with a ratchet.
2. Mason's: Opening maintained with a screw.
3. Ferguson's: Opening maintained with a ring.

Uses

1. To open the mouth in an unconscious patient for oral toilet and to free the airway.
2. To prevent tongue bite in an epileptic patient during attack.
3. In fibrous ankylosis of the temporomandibular joint, to open the mouth during oral surgery e.g. tooth extraction, tonsillectomy etc.

13 › Tongue Depressor



Fig. 10.11 : Tongue depressor

Uses

1. To examine the throat and oral cavity e.g. tonsils, palatal movements, posterior pharynx
2. To examine the gag reflex.
3. To test for the spasm of the masseter muscle in a suspected case of tetanus (captive tongue depressor).
4. To open the mouth in an unconscious patient for suction or oral toilet.

14 › Trocar and Cannula

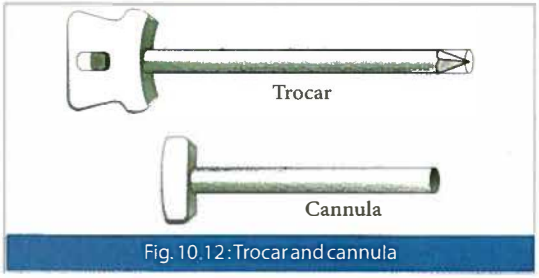


Fig. 10.12 : Trocar and cannula

Uses

1. To withdraw thick fluid form the body cavity e.g. ascitic tapping, when thick pus is suspected. (It is not required routinely as ordinary needles are adequate)
2. To aspirate pus in amebic abscess of the liver.
3. For suprapubic aspiration of urine from the bladder.

15 › Asepto Syringe and Bulb

It consists of a glass syringe with a capacity of 100 ml



Fig. 10.13 : Asepto syringe and bulb

and a rubber bulb. The asepto syringe has one tapering end to be fitted into the catheter and one broad end to be fitted with the rubber bulb. When the bulb is pressed, the air goes out and when released the fluid is sucked into it. It can be sterilized by autoclaving or boiling.

Uses

1. Bladder wash
2. Irrigation of wounds or cavities

Procedure

The solution used for bladder wash (Potassium Permanganate, Silver Nitrate or Betadine) is sucked into the asepto syringe by placing its tapering end into the solution and squeezing and releasing the bulb. The tapering end of the asepto syringe is connected to the urinary catheter which is inserted into the bladder. The asepto syringe is held vertically and the bulb is squeezed to push the air and fluid into the bladder. The bulb is then released and fluid is sucked back into the syringe. This procedure is repeated till the returning fluid is the same colour as the instilled fluid.

16 › Simple Rubber Catheter



Fig. 10.14 : Simple rubber catheter

This is also known as Nelatons or Robinson Catheter. It is a simple catheter made of India Rubber. It is closed at one end and has an eye at one end (sub-terminal opening). It has a single lumen. Sizes available are 1 to 12. It can be sterilized by autoclaving or boiling.

Uses

a) Urinary

1. Acute retention of urine: To relieve bladder

by evacuating urine from it. It cannot be retained in the bladder.

2. For bladder washes
3. To inject chemotherapeutic agents into the bladder e.g. Thiotepa, BCG
4. To collect urine from the bladder for Urine Culture Testing
5. To differentiate between retention of urine and anuria

b) Non Urinary

1. Oxygen Catheter: A thin simple rubber catheter can be used as a nasal oxygen catheter
2. Tracheal/ Laryngeal toilet or suction
3. Oral suction
4. Enema or High bowel wash: Larger bore, simple rubber catheter
5. Calorie Test: To infuse the warm or cold fluids into the ear
6. Tourniquet: It can be used as a tourniquet

17 Foley's Self-retaining Catheter

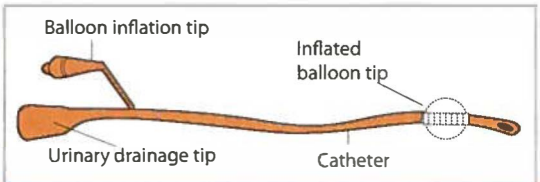


Fig. 10.15: Foley's self-retaining catheter

It is a double lumen, self retaining, disposable, sterile and ready to use catheter. It is made of latex. It has a sub-terminal balloon and an eye on one end and the other end is bifid. The catheter has two lumens, one big one for the passage of urine and the other smaller one for inflation of the balloon with sterile normal saline. The inflated balloon makes the catheter 'self-retaining' by resting at the bladder neck. The bifid end has two channels, one is for the passage of urine and is connected to the urosac bag and the other is smaller and connected to the balloon through the smaller lumen. The smaller channel has a valve which prevents the injected fluid from coming out.

It is also available as a siliconized tube which is more inert and non irritant than the latex tube. There may also be a triple lumen catheter in which the third lumen is used for irrigation of the bladder.

It is available in a gamma irradiated sterile pack covered with a plastic sheath. It is to be used only once.

Sizes

The most commonly used sizes are in the 'French system' indicated by the letter F. Sizes 8 F to 30 F are available in even numbers. 1F= 0.3 mm.

Common sizes used in males: 16, 18.

Common sizes used in females: 14, 16.

Other systems of caliberations are the English (E), American and German (Benique).

Balloon Capacity

The balloon can be filled from 5 to 50 cc. The maximum capacity is indicated on the smaller channel. Over-filling with saline can lead to rupture of the balloon, and a constant urge to defecate due to pressure on the rectum.

Uses

Urinary

1. Acute retention of urine: To relieve it and to differentiate it from anuria
2. UMN or LMN bladders: To prevent incontinence
3. Transverse myelitis: To prevent over-distention and atrophy of the detrussor fibers during neuronal shock. After neuronal shock, it is clamped and released at serially increasing intervals for training the automatic bladder. (Ref. Ch. 6: Urinary Bladder)
4. Ruptured urethra: For railroading to splint the urethra
5. Following prostate surgery: As a hemostat
6. Instilling chemotherapeutic agents into the bladder e.g. Thiotepa, BCG
7. Supra-pubic cystostomy
8. For monitoring urine output in cases of shock, burns, renal failure, etc.
9. To give bladder washes
10. To obtain urine for culture sensitivity testing

Non Urinary

1. Epistaxis: For nasal packing
2. As a Sengstaken Blakemore tube in children to control esophageal variceal bleeds
3. As an enema tube in children

Procedure

- The parts are shaved beforehand. Consent is not needed if done in an emergency. With sterile precautions (wearing two pairs of gloves), the parts are cleaned an antiseptic solution. The prepuce is retracted and the glans is also cleaned. The outer pair of gloves should be discarded. 10cc of Lignocaine jelly is injected into the urethra and retained for about 2 minutes.
- The assistant strips the outer unsterile plastic cover off the Foley's Catheter. The doctor takes out the Foley's Catheter holding the sterile inner plastic cover and exposes the tip by removing the plastic along the dotted line.
- Lignocaine jelly is applied on the tip of the catheter and it is inserted along the floor of the urethra until the bifurcation. The doctor only touches the sterile inner plastic sheath, not the catheter directly. This is called the 'No Touch Technique'.
- The balloon is inflated with 5 cc to 30 cc of sterile saline. The catheter is now GENTLY pulled until resistance is felt. This resistance implies the balloon is adequately filled and impinged on the base of the bladder making the catheter self-retaining.
- An urosac bag is applied to the catheter.
- The prepuce is replaced back over the glans.
- The catheter is taped to the inner side of the thigh. An antibiotic or Vaseline gauze dressing is given to the tip of the penis.

Precautions

1. The catheter should be inserted up to the bifurcation irrespective of the outflow of urine. The balloon is sub-terminal and the eye is distal to it. Hence there is a chance of the eye being in the bladder allowing the outflow of urine, while the balloon is still in the urethra. At this point if the balloon is inflated it will lead to rupture of the urethra.
2. The balloon should be inflated with saline and not air for the following reasons:
   - Air in the balloon will cause it to float on the urine in the bladder causing incomplete drainage of urine.
   - In case of rupture of the balloon, air could be absorbed through the vesical veins leading to an air embolism.
3. In females, the catheter can easily enter the vagina and get coiled. In this situation, no urine will come out from the catheter.

Care after Catheterisation

1. Patient should be instructed not to pull the catheter.
2. Daily dressings of the glans should be done by retracting the prepuce and cleaning the glans and the catheter with an antiseptic solution.
3. Bladder washes should be done frequently to decrease chances of cystitis

Changing the Catheter

The Latex Foleys catheter can be retained for a period of 1-2 weeks following which it should be changed. The siliconized catheter can be retained for 1 month.

Complications

1. Difficulty in deflating the balloon to remove the catheter.
   - Over-distend the balloon with saline or distilled water
   - Inject 1 ml of Ether. Being volatile it expands and ruptures the balloon. It is fat soluble.
   - Cut the catheter above the level of the valve. If obstruction is distal to the valve, it will be relieved.
   - Rupture the balloon with a guide wire
   - Rupture the balloon under ultrasonographic guidance (supra-pubic rupture)
2. Urinary tract infections : Cystitis, urethritis, pyelonephritis(rare)
3. Rupture of the urethra - if catheter is pulled by patient
4. Stricture of the urethra
5. Calculus formed at tip of the catheter due to precipitation of salts or crystals

6. Paraphimosis - if prepuce not replaced over glans after the procedure.

Contra-indications

1. Meatal Stenosis
2. Phimosis
3. Suspected Rupture of Urethra
4. Strictures of the urethra
5. Acute Urinary Tract Infections

18 › Malecot's Catheter



Fig. 10.16: Malecot's self-retaining catheter

It is a catheter made of India Rubber. It has a flower at one end with 2 straight and 4 curved petals. The curved petals can be straightened with an introducer for the insertion of the catheter (for removal it can be simply pulled out). It is sterilized by boiling or autoclaving.

Uses

Non Urinary

1. Inter-costal Drainage
2. Feeding gasterostomy or jejunostomy
3. Abdominal drain

Urinary

1. Suprapubic cystostomy
2. Condom catheter in males, along with a condom
3. Self retaining catheter in females (Foley's Catheter is preferred)

Disadvantages

1. It is highly irritant and thus cannot be used for long periods
2. It can be difficult to remove due to difficulty in straightening the flower.
3. The flower might get detached. This needs cystoscopic or ultrasonographic removal.

19 › Condom Catheter



Fig. 10.17: Condom Catheter

It can be prepared by making a small nick on a condom and passing a Malecot's catheter through it so that the flower rests on the nick.

Readymade catheters are also available which have a stiff condom which goes over the penis and an opening at the terminal end which can be directly connected to the urosac bag. It does not need attachment to the Malecot's catheter.

Uses

Chronic incontinence of urine where passage of a urinary catheter per urethra can lead to urinary tract infections.

Advantage

The bladder is not catheterized and hence the chances of urinary tract infections (cystitis and urethritis) are reduced.

20 › Urosac Bag

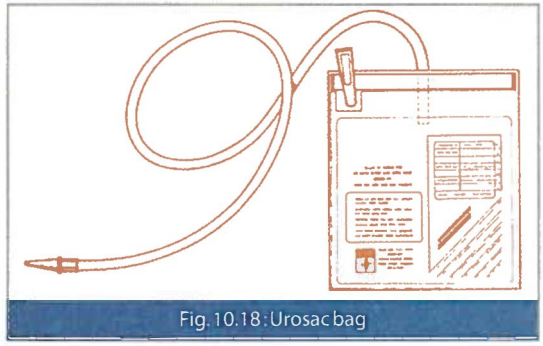


Fig. 10.18: Urosac bag

This is a calibrated bag with markings to indicate the volume filled. It has a 2 liter capacity. It has two tubes. The tube on the top is connected to the urinary catheter and has a non- return valve. The second tube is at the bottom or side and is used to empty the urine collected in the bag. It is kept closed otherwise. It is disposable, sterile and ready to use.

Uses

1. It is usedv to collect urine from a urinary catheter. The markings allow an accurate assessment of urine output.
2. It can be attached to abdominal or thoracic drains and is used to measure the output.

Advantages

1. It has a non-return valve which does not allow backflow of fluid into the catheter.
2. Its markings allow accurate quantification of urine output.
3. Its side tube allows easy emptying of urine.

21 › Stomach Tube

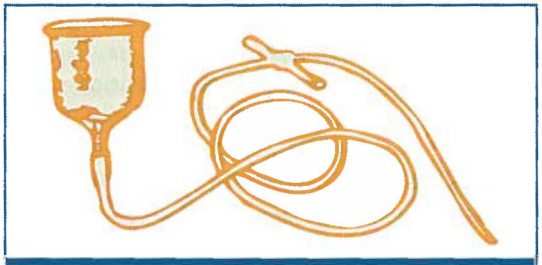


Fig. 10.19: Stomach tube

It is a thick tube, 75 cm in length, made of India Rubber. The distal end is solid and conical with two sub-terminal openings. To the proximal end, a funnel may be attached through which fluids may be poured when necessary. The tube is marked with a black ring at 45cm indicating the distance between the incisor teeth and the cardia of the stomach. It can be used with or without a mouth gag. It is sterilized by autoclaving or boiling.

Uses

1. Stomach washes in poisonings when the suspected poison is thick and viscous, (e.g. Opium, food poisoning) in which case the thinner tubes may get clogged.
2. Aspiration of gastric contents to prepare a patient for emergency surgery in case the stomach is full.

Procedure

The tip of the tube is lubricated. The tube is introduced into the mouth and pharynx and the patient is encouraged to swallow. The tube is gently pushed forward into the stomach. The tubes' place is confirmed by aspiration of the gastric contents or injecting air while auscultating the epigastrium. To give a stomach wash, the funnel is connected to the proximal end. The funnel is raised above the level of the stomach and the fluid enters stomach. To remove the fluid, the funnel is lowered below the level of the stomach and the fluid comes out by the siphon action.

22 › Ryle's Tube (RT) or Nasogastric Tube

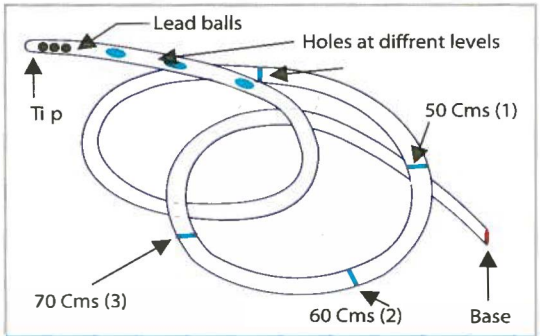


Fig. 10.20: Ryle's tube

It is a 75 cm long thin tube made of polyvinyl chloride (PVC) which is open at one end and has an oval tip at the other end with 3 – 4 sub-terminal openings. There are 2 or 3 lead balls which make the tip heavy, allowing easy passage of the tube into the stomach. There are 3 markings on the tube denoting the position of the tube at 50, 60 and 70 cm from the tip.

The cardia, the body and the pylorus are at 40, 50 and 57cm respectively from the incisor teeth. There is a blue or green line along the entire length which is radio opaque. This allows it to be seen on X-Ray. It is available in a gamma irradiated pack and is for single use.

The nasogastric tube was originally made of India Rubber. There is a modification called the Levine Tube which is longer, made of Portex and has no lead balls. The Levine Tube is suitable for insertion up to the duodenum.

Sizes

Available in sizes 8 to 22 French in even numbers, 8

being the smallest and 22 being the largest diameter. Regular Adult sizes are 14 – 16 F.

Uses

Diagnostic

- Upper gastro-intestinal bleeding: In cases of hematemesis or malena, the RT is inserted and gastric fluid is aspirated to diagnose upper GI bleeding.
- Gastric Analysis: To diagnose peptic ulcer disease, Zollinger Ellison syndrome, achlorhydria, etc.
- Poisoning: Aspirate sent for analysis
- Exfoliative cytology: For diagnosis of stomach cancer
- Tuberculosis in children: Acid Fast Bacilli (AFB) in the aspirate in children who cannot produce sputum or swallow it. Early morning aspiration is preferred.
- Tracheo-esophageal fistula: In newborns, there will be an obstruction to the passage of the RT or the RT will coil up in the blind esophagus.

Therapeutic

- Enteral feeding of nutrients or drugs for patients who cannot ingest it orally
- Gastric lavage or stomach washes in case of poisoning and hematemesis.
- Gastric decompression in intestinal obstruction, paralytic ileus, acute gastric dilation, peritonitis or post operatively.
- In acute cholecystitis or acute pancreatitis: to give rest to the bowel

Contra Indications

- Corrosive poisoning
- Kerosene poisoning

Procedure

With the patient sitting up, the more patent or larger nostril is selected. It is properly cleaned and then anesthetized by instilling lignocaine jelly. The RT is removed from the pack and the tip is lubricated with lignocaine jelly on it.

The tip is now gently pushed along the floor of the nose and the patient is encouraged to swallow as the tube passes into the throat and into the esophagus. This closes the epiglottis and allows the RT to pass into the esophagus. The RT gently pushed further until the 2nd mark is at the nostril.

Confirm the RT is in place by the following methods and then secure it with adhesive tape:

- Aspirating Gastric contents from the RT
- Injecting air through the RT while simultaneously auscultating the epigastrium
- Putting the nasal end of the RT into a bowl of water. If the RT is in the trachea, there will be air bubbles.
- Tracheal intubations will result in coughing as the RT irritates the trachea or bronchi.
- Plain X Ray of the Abdomen will show the radio opaque line along the RT and the lead shots.

Precautions

RT Feeding: The patient has to be propped up. There should be 2 hours between feeds. Before feeding, aspirate the gastric content to check if at least one third the contents have been emptied or not. If not, the feed should be delayed. The RT should be flushed after the feeding. The patient should be propped up for at least half an hour after the feed.

Complications

1. Epistaxis, rhinitis
2. Pharyngitis
3. Esophagitis, esophageal perforation, rupture and bleeding of esophageal varices
4. Reflux esophagitis since lower esophageal sphincter is incompetent
5. Gastritis, gastric bleeding (if over-zealous suction done rapidly)
6. Aspiration pneumonia if tracheal insertion not detected
7. Hypokalemic, hypochloremic, metabolic acidosis if overzealous suction

23 › Sengstaken-Blakemore Tube (S.B. Tube)

It is a 50 cm long latex tube. Its distal end has 4 subterminal holes for gastric aspiration. It has 2 balloons

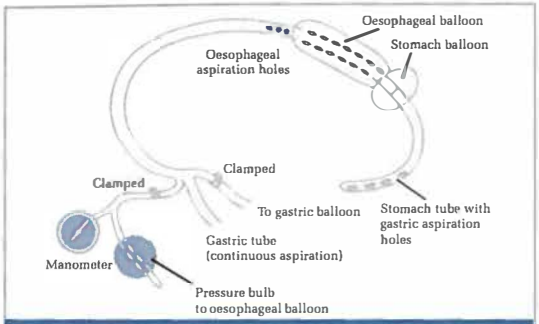


Fig. 10.21 : Sengstaken-Blakemore tube

and 3 channels. There is a distal gastric balloon and a proximal esophageal balloon. The central channel is for gastric aspiration or lavage. The other two channels are for inflating the gastric balloon (capacity 120 ml) and esophageal balloon (capacity 30 ml).

Modifications

- Minnesota modification has an additional channel for esophageal aspiration. It has holes on the tube just proximal to the esophageal balloon for esophageal aspiration.
- Linton Nahas Tube has only a gastric balloon but no esophageal balloon. It has only 2 channels.

Uses

To obtain hemostasis by pressure in cases of bleeding esophageal or gastric varices. Hemostasis is achieved by pressure.

Procedure

The tube can be passed through the mouth or preferably the nose. The larger nostril is anesthetized using lignocaine jelly. The tip of the tube is also coated with lignocaine jelly and the tube is passed along the floor of the nose through the pharynx into the stomach. Once in the stomach, the gastric balloon is filled with air. The tube is now withdrawn until the gastric balloon tightly occludes the cardia. The esophageal balloon is then inflated with air. The catheter is put under traction using external weights. Aspiration of the gastric contents indicates whether the bleeding has stopped or not.

Precautions

1. It should not be kept in place for more than 48 to 72 hours.
2. The gastric and esophageal balloons should be deflated alternately after 24 hours to prevent pressure necrosis.
3. The saliva which cannot be swallowed due to the esophageal balloon should be continuously suctioned out.
4. If the bleeding does not stop or if the patient re-bleeds, emergency surgical or endoscopic intervention should be undertaken

Complications

1. Pressure necrosis of the esophagus or stomach mucosa if retained more than 48 to 72 hours.
2. Aspiration pneumonia due to saliva collection proximal to the esophageal balloon.
3. Air embolism due to rupture of the balloons

24 › Infant Feeding Tube

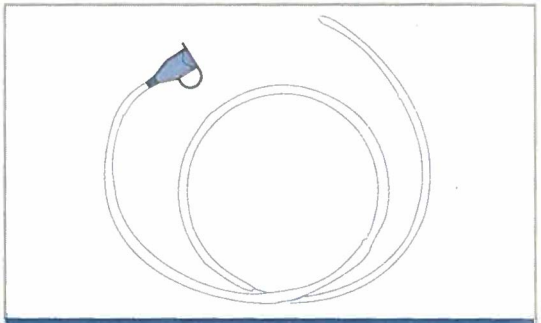


Fig. 10.22: Infant feeding tube

It is a thin polyethylene tube with a blunt tip and subterminal openings. There are no lead shots like in Ryle's tube. It is 52 cm in length. It is disposable, sterile and ready to use. The sizes are 5 – 12 F.

Uses

Diagnostic

1. Tracheo-esophageal fistula: passage of the tube is met with resistance
2. Choanal atreisa: Passage of the tube is met with resistance
3. Imperforate anus: Passage of the tube is met with resistance

4. Tuberculosis: Gastric secretion aspirated for detection of acid fast bacilli
5. Poisoning: Gastric aspirate for analysis
6. Upper gastro-intestinal bleeding: Blood in the gastric aspirate

Therapeutic

1. Enteral feeding in children
2. Venesection
3. Decompression of the stomach in intestinal obstruction or before emergency surgical procedures or after resuscitation
4. Suction through an endotracheal or tracheostomy tube in children
5. As an oxygen catheter in children

25 Record Syringe and Needle



Fig. 10.23: Record syringe

It consists of a piston made of metal and a glass body with a long tapering nozzle that is also made of metal. It derives its name from the fact that for the first time in the history of medicine, something could be recorded. It is available in sizes 2, 5, 10 and 20 cc.

Advantage

The piston does not come out of the body and break.

Disadvantage

It cannot be autoclaved as it is partly glass and partly metallic. The cement between the glass and the metal melts on autoclaving and as glass and metal expand differently, the syringe can be damaged. Hence, they are rarely used today.

26 B.D. Syringe and Needle

B and D stand for Beckton and Dickinson, who


Fig. 10.24: B.D. syringe

manufactured it. The B.D. Syringe is made of glass. It has a piston and a barrel with a nozzle. The barrel is calibrated according to the capacity of the syringe. The barrel has a flattened flange at one end to give a grip while injecting. The nozzle may be eccentrically or centrally placed. The piston is floating since it is hollow. It is available in 2, 5, 10, 20, 50 and 100 cc. sizes. Glass syringes are sterilized by boiling or autoclaving.

Plastic syringes are also available for one time use. They are disposable, sterile and ready to use and are available in gamma irradiated packs. They are not to be sterilized and reused.

The B.D. needle has a bevel, body and shoulder. The number of the needle varies inversely with the thickness. The lower the number, the thicker is the needle, e.g. number 18 needle has a thickness of $1/18^{th}$ of an inch.

The needle can be fitted directly to the nozzle or can be locked together by applying a metallic Leur Lock to the needle which prevents slipping of the needle. If the syringe has a Leur Lock, it cannot be autoclaved or boiled since it is metal.

Uses of Syringes

1. 2 cc Syringe:
   a. Injection: To administer drugs
      eg. Analgesics-(Paracetamol, Deriphyllin), Antibiotics- (Gentamycin), Vitamins-(Vitamin K, Vitamin B complex, etc.), others- (diazepam)
   b. Aspiration of blood for Arterial blood gas analysis
2. 5 cc Syringe:
   a. Injection – to administer drugs
      eg. Antibiotics (streptomycin, cephalosporins, chloroquine), Analgesics (diclophenac), local anesthesia, Vaccine (Antirabies Vaccine), Vitamins, etc.
   b. Aspiration
      - Blood collection
      - Fine Needle Aspiration Cytology

3. 10 cc Syringe:
   a. Injection
      - Electrolytes - (calcium gluconate, sodium bicarbonate); Antibiotics - (crystalline penicillin, cefalosporins)
      - Chemotherapy
      - Vaccines- Antirabies Vaccine
      - Sclerosants in sclerotherapy
      - Exchange Transfusions
      - To inject Air into a Ryle's tube to check if it is in the stomach
      - To inflate the bulb of the Foley's catheter with saline or distilled water
      - Preparing diluted solutions e.g. 1:100 or 1:1000 solutions
   b. Aspiration
      - Blood Collection
      - Bone Marrow Aspiration
      - Fine Needle Aspiration Cytology
4. 20 or 50 cc Syringe:
   a. Injection:
      - Chemotherapy
      - Aminophylline 0.25gms in 20cc of 10% Dextrose IV
      - Feeding through the Ryle's Tube
      - Injecting fluid or blood in case of hypovolemic shock
   b) Aspiration
      - Pleural Fluid, Pericardial Fluid or Ascitic Fluid Aspiration
      - Blood Collections
      - Stomach Washes

Uses of Needles

1. No. 12 -16: Aspiration of thick fluids or pus, bone marrow aspiration
2. No. 18: Blood collection from donors, I.V. fluids, aspiration of fluids from body cavities
3. No. 20 – 21: Blood collections (small amounts, routinely), I.V. Fluids
4. No. 22 – 23: I.M. injections, F.N.A.C.
5. No. 24: I.M. injections in children
6. No. 26: Tuberculin testing, Insulin, BCG, intradermal or subcutaneous injections

27 › Tuberculin Syringe



Fig. 10.25: Tuberculin syringe

It is a 1cc syringe with a blue piston.

Uses

Mantoux Test to inject old tuberculin (OT) or purified protein derivative (PPD) intra-dermally in a dose of 0.1ml containing 5TU (tuberculin units). It may also be used to give test doses before giving a drug.

28 › Insulin Syringe



Fig. 10.26: Insulin syringe

It is a 1 ml syringe made of plastic or glass with a white or red piston. It is available in graduations of 40, 80 or 100 units. It is available with or without a 26 number needle attached. It is disposable, sterile and ready to use.

Uses

1. To inject Insulin (insulin is available in 40, 80 or 100 units per ml hence the calibrated needle makes insulin administrations easier)
2. Mantoux testing (to inject the tuberculin-OT or PPD)
3. To give BCG, TT, DPT or Hepatitis vaccination
4. To give intra-dermal test dose (before giving certain drugs like penicillin)
5. Allergy testing
6. To give drugs: Inj. Adrenaline 0.5 – 1 ml, Vitamin K 0.1 ml in a newborn
7. To collect blood for Arterial Blood Gas Analysis

29 Lumbar Puncture Needle



Fig. 10.27: Lumbar puncture needle & stilette

It is a B.D. needle, 10-12 cms in length, made of platinum or German alloy. The stilette of the needle has a pin which fits into the slot of the head of the needle.

Uses

1. For lumbar puncture
2. For cisternal puncture
3. For carotid angiography
4. For splenoportogram
5. In trigeminal neuralgia, if Harrey's needle is not available it can be used to inject alcohol
6. For tapping fluids from the cavity e.g. ascites or pleural fluids

N.B.:

1. In children, an ordinary B.D. needle is often used for lumbar puncture.
2. The advantage with the lumbar puncture needle is that the stilette helps to keep the lumen of the needle patent.

30 Cisternal Puncture Needle



Fig. 10.28: Cisternal puncture needle

This needle is similar to the lumbar puncture needle except that it has, in addition, markings on the needle to prevent deep penetration and injury to the medulla oblongata.

31 Vim-Silverman's Needle



Fig. 10.29: Vim Silverman's needle: Top: stillette; Middle: cannula; Bottom: bifid needle

Parts:

1. Stillette.
2. Cannula
3. Bifid needle

Uses:

1. Liver biopsy.
2. Kidney biopsy
3. Lung biopsy - rarely

Advantage: Large liver tissue is obtained and failure rate is low.

Disadvantage: Complications are more compared to Menghini needle.

32 Menghini's Needle and Syringe

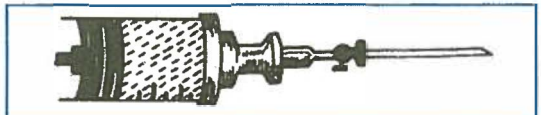


Fig. 10.30: Menghini's needle

Parts

1. Sterile syringe with 3 cc of fluid
2. Menghini's needle

Use: Same as Vim-Silverman's needle. The syringe flushes any skin fragment after it has penetrated the intercostal space.

Advantage: Patient gets minimal discomfort and complications are rare.

Disadvantage: Failure rates are high.

33 Bone Marrow Aspiration Needle

Parts

1. Thick body with nail.

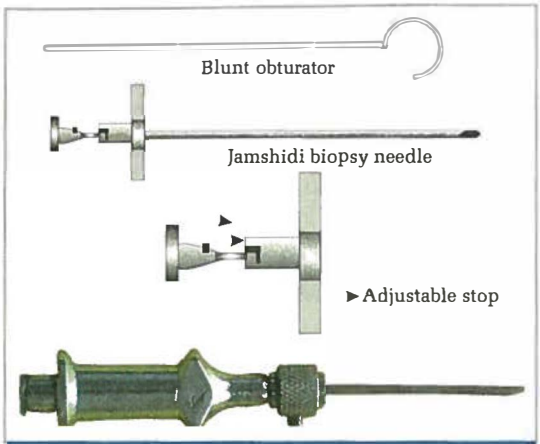


Fig. 10.31: Bone marrow aspiration needle

2. Guard 2 cms from the tip. (Guard prevents through and through penetration of the bone)
3. Stilette

34 › Pleural Biopsy Needle

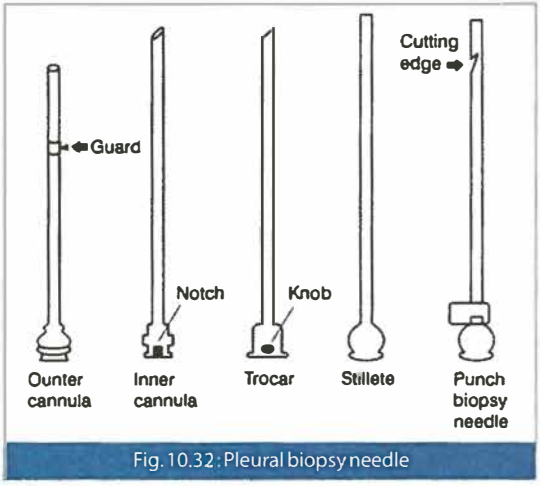


Fig. 10.32: Pleural biopsy needle

Types: Abraham, Cope, Rajah

Parts

1. Outer cannula with guard
2. Inner cannula
3. Trocar
4. Stilette
5. Punch biopsy needle

Uses

1. Pleural malignancy
2. Tuberculosis

35 › Trucut Needle

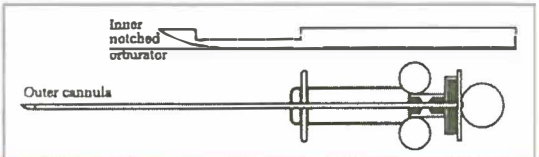


Fig. 10.33: Trucut needle

This needle has sliding knife edge and is used for Kidney or Liver Biopsy. It is less traumatic and helps to obtain a better specimen.

36 › Southey's Tube and Needle



Fig. 10.34: Southey's tube and needles

These are tiny needles put together in a tube. Each needle has shoulder to which a thread can be tied. The other end is pointed and the body is hollow.

It was used in the past to remove edematous fluid from the cutaneous tissue. The disadvantage was the severe infection which sometimes followed. Now with diuretics, this is an obsolete needle.

37 › Tourniquet

It is a Latex tube.

Uses

1. **Blood Collection:** To be tied proximal to the site of blood collection for filling up the veins.
2. Varicose veins examination
3. **Snake Bite:** Applied proximally to the site of the bite (if bite is on the extremities)
4. **Trauma setting:** As a sling or a splint to a fracture site

38 Venesection Needle



Fig. 10.35: Venesection needle

This is a needle with a cannula. Just above the tip it is bulbous, to which a polyethylene tube snugly fits. (The other end of the polyethylene tube is pushed in the vein after venesection). As the name suggests it is used during venesection.

39 Scalp Vein Needle

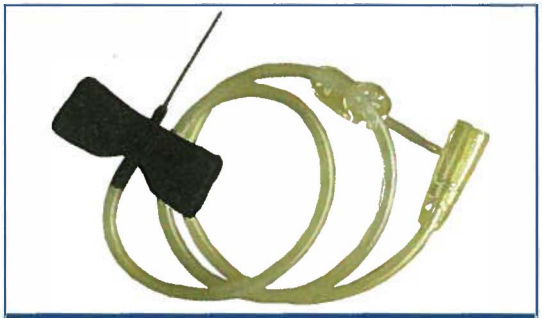


Fig. 10.36: Scalp Vein needle

It consists of a short beveled siliconized stainless steel needle connected to a polyethylene tube which has a stopper at the end. Between the needle and the tube are plastic butterfly shaped wings which is used to give a better grip while inserting and to fix the needle to the skin. The tube can be closed with the stopper. They are disposable, sterile and ready to use. Sizes available are 18 to 25 G (gauge). The smaller the number, the larger the bore of the needle.

Uses

1. To get venous access for a short period (24 – 48 hours) for administration of intravenous fluid, drugs
2. For Blood Collection, specially in children

Procedure

Choose an appropriate vein. Clean the site with spirit. Give proximal pressure with a tourniquet to distend the veins. Holding the scalp vein needle with the butterflywings folded, the needle is inserted with the bevel facing upwards. As soon as blood starts coming into the tube, the tube is kinked. The scalp vein needle is fixed with adhesive tape to the skin. The tube is then flushed with saline or 0.5ml of heparin. When used in children, the hand has to be splinted to prevent movement since movement can cause counter-puncture.

Complications

- Counter-puncture detected by hematoma (swelling) formation just distal to the scalp vein needle or by resistance felt during flushing with saline or heparin
- Thrombophlebitis due to infection or irritation by drugs or fluids

40 Pleural or Ascitic Aspiration Needle

These are long BD needles. The 18 number needle is used for pleural or ascitic fluid aspiration when the fluid is thin. Whereas 13-14 needle is used when the fluid is likely to be thick.

41 Intravenous Cannulas (Venflow or Angiocath)

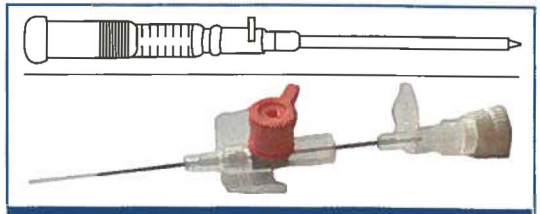


Fig. 10.37: Angiocatheter

It consists of a beveled siliconized stainless steel needle and an outer cannula (sheath) made of PTFE (Poly Tetra Fluoro Ethylene). The needle snugly fits into the outer sheath. They are available in two forms.

- with wings and an injection port (VENFLOW)
- without wings and without injection port (ANGIOCATH)

The wings make it easier to fix the needle to the skin. The IV cannula without wings can be rotated and maneuvered. They are disposable, sterile and ready to use.

Sizes

14 -24 G in even increments. Smaller the number, larger the bore of the needle.

Uses

To get venous access for a longer period (48 – 72 hours) for the administration of intravenous fluid, intravenous drugs, blood and blood products, multiple fluids or drugs together

Procedure

After choosing an appropriate vein, the site is cleaned with spirit. Proximal pressure is given with a tourniquet to distend the veins. Holding the venflow with the index finger and the middle finger at the wings and the thumb at the proximal most end, the venflow is inserted into the vein. Once blood starts coming into the sheath, the venflow is held steady in place. The needle is withdrawn slightly (but not all the way out; it should still be in the sheath). The venflow is then pushed in all the way, so the needle supports the sheath but does not counter-puncture the vein. Occluding the vein distal to the inserted venflow, the needle is withdrawn from the sheath. A three way is now attached to the sheath and it is flushed with saline to rule out counter-puncture. The venflow with the three way is attached to the skin with adhesive tape.

Complications

- Counter-puncture: Detected by hematoma (swelling) formation just distal to the scalp vein needle or by resistance felt during flushing with saline or heparin
- Thrombophlebitis due to infection or irritation by drugs or fluids

42 › Three Way

It is a T-shaped instrument. It consists of two inlets and one outlet. By a screw, either or both of the inlets can be connected to the outlet. It is disposable, sterile and ready to use.

Uses

- It is commonly connected to an I.V. Cannula where thorough one inlet I.V. fluids pass and through the other inlet medications can be given or the CVP can be monitored.
- It is also useful to connect the three way whilst aspirating fluid from body cavities e.g. pleural tap. Through one inlet fluid is withdrawn from the body cavity into a syringe and by changing the direction of the screw, the fluid from the syringe can be pushed into a kidney tray.
- Exchange transfusion: Two three ways have to be used simultaneously



Fig. 10.38: Three way

Precaution

The three way should always be screwed shut when not being used. If the screw is wrongly placed leaving it open or it is accidentally shifted, bleeding can occur from the vein.

43 › I. V. Set

The I.V. Set has three parts: the proximal limb, Murphy's chamber and the distal limb. The proximal limb has a

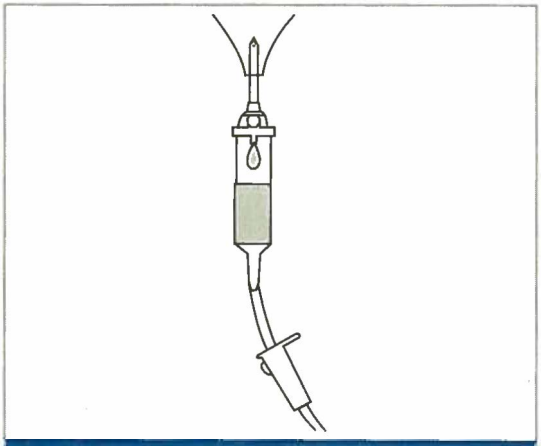


Fig. 10.39: I.V. Set with Murphy's chamber

sharp pointed tip which is used to puncture the outlet of the I.V. Fluid bottle or bag.

The Murphy's chamber is a glass chamber that is used to regulate the flow of fluid by adjusting the number of drops falling per minute.

The distal limb is consists of a long tubing with a nozzle at the end which is attached to the venous access (scalp vein, angiocath or three-way). It also has a regulator which is used to adjust the rate of flow through the Murphy's chamber. There may be a rubber tip just at proximal to the nozzle so that any drug can be injected bolus through it if necessary. They are disposable, sterile (gamma irradiation) and ready to use.

Types

The main difference is in the Murphy's chamber.

1. *Macrodrip Set*

The Murphy's chamber is normal. 16 drops constitute 1ml.

Uses

1. Fluid administration such as colloids (albumin, hemaxcele, Dextran) or crystalloids (normal saline, ringer lactate, DNS)
2. I.V. drug administration (antibiotics, iron, etc.)

2. *Microdrip Set*

The Murphy's chamber has a thin needle coming into it from the top. 16 micro drops constitute 1ml.

Uses : Accurate small quantities of drugs have to be given I.V. (nitroglycerine, sodium nitroprusside, dopamine, dobutamine, adrenaline, noradrenaline, insulin, heparin, etc.)

3. *Blood Transfusion Set*

The Murphy's chamber has a filter in it to filter out any clots.

Uses

Transfusion of blood and blood products (whole blood, packed cells, platelets, fresh frozen plasma, cryoprecipitate, coagulation factors, etc.)

Precautions With Murphy's Chamber

Before connecting the I.V. Set to the venous access, the regulator should be fully opened and the fluid should be allowed to fill the Murphy's chamber up to a certain level and fill the tubing. This drives all the air in the tubing out and prevents air embolism. The fluid level in the Murphy's Chamber will prevent the air from the proximal part to enter the venous access. Thus a fluid level should always be maintained.

44 › Clinical Thermometer

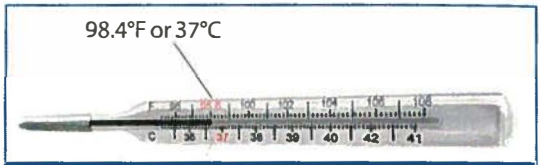


Fig. 10.40: Clinical thermometer

Clinical thermometer is used to record temperature. In a clinical thermometer there is a constriction just beyond the bulb. When the thermometer bulb is placed in the mouth, mercury within expands and this force of expansion is great enough to force the expanding mercury past this constriction. The part of the mercury which has expanded beyond the constriction remains in position and indicates patient's temperature. The mercury must be jerked back into the bulb before the thermometer is used again.

Clinical thermometer is calibrated over the range 95-108°F, since the body temperature does not vary much from its normal values of 98.4°F. Since the bulb is thin and small, the thermometer is quick acting, reaching the body temperature in about 1 min. The quantity of mercury used is small and the capillary tube must therefore have a very fine bore. To enable the thermometer to be read, the front of the glass is shaped so as to produce a magnified image of the thread.

After being washed and wiped it should be stored in a glass jar partly filled with a disinfectant like 70% isopropyl alcohol with 1% iodine. The jar should have a piece of cotton wool at the bottom.

Recording the temperature:

After cleaning the thermometer and shaking it to bring the column of mercury down to about 2° below nor-

mal, the temperature is recorded in the axilla, groin, mouth or rectum.

1. *In the axilla or groin:* When either of these parts is used it must not be exposed for washing for at least half an hour before recording the temperature. Perspiration, if any, is wiped away and the bulb of the thermometer is carefully placed in position and the arm brought across the chest and kept there, the patient supporting his elbow with his other hand. If the groin is used the legs should be crossed at the knees. The thermometer is less likely to be broken by a sudden movement of the patient, and a correct temperature is obtained if it is placed high in the axilla and the stem laid against the chest, parallel to the arm and between the two. The thermometer is left in position for 3-5 minutes.
2. *In the mouth:* The bulb of the thermometer is placed under the tongue. The patient must close his lips but not teeth. If the lips are not kept closed, cold air will enter and wrong temperature may be recorded. Hence this method is used only if the patient can breathe comfortably through the nose. No drink should be given for 10 minutes before the thermometer is used. It should never be used in unconscious patients or young children as they may bite it
3. *In the rectum:* This is the most reliable method. To reduce the risk of injury, the thermometer should have a rounded or pear-shaped bulb. The rectum must be empty of feces and the instrument must be oiled and introduced for 4 cms and left in position for 1-2 minutes. Thermometers used in taking rectal temperature should be reserved for that purpose.

   Rectal temperature is 1°F higher than mouth temperature which is 1°F higher than axillary or groin temperature.

45 › Flatus Tube

It is a stout tube made of India Rubber. It is 45 cm (18 inches) long and is open at both ends. In addition it has one or two eyes (sub-terminal openings) at one end to facilitate expulsion of gas. It can be sterilized by autoclaving or boiling.



Fig. 10.41: Flatus tube

Uses

It is used to help passage of flatus e.g. in typhoid tympanitis.

Procedure

With the patient in left lateral position with lower leg extended & upper leg flexed a lubricated flatus tube is inserted (with the end having sub terminal openings) into the anus up to 10 to 20 cm. The end (without the eye) which is outside should be placed in a bowl of water or potassium permanganate (preferable since it acts as a good deodorant) and the number of bubbles produced should be counted. Usually 8 bubbles per minute or more than 60 bubbles totally are good results.

Contra-indications

Painful perianal conditions

46 › Proctoscope



Fig. 10.42: Proctoscope

Parts

1. The Body or Flange: It is funnel shaped with a handle at an obtuse angle to it.
2. The Obturator: It has a bulbous tip which when inserted into the flange protrudes outside the flange. This creates a smooth rounded surface of the assembled proctoscope, thus preventing the mucosa of the rectum and anal canal from being caught in the distal end.
3. Torch or Source of light

Uses

For proctoscopic examination to diagnose condition like hemorrhoids, anal fistulas, anorectal strictures or ulcers and for internal banding of hemorrhoids.

Procedure

The patient is placed in the left lateral position. The upper leg is flexed and the lower leg is extended. Per rectal examination is done to exclude painful pathology of the anus and anal canal. The assembled proctoscope is lubricated and inserted in the anus in the direction of the umbilicus, asking the patient to take deep inspirations. The obturator is withdrawn and through the flange light is thrown into the rectum to visualize any pathology. Gradually, the flange is withdrawn and the rectum and anal canal are visualized.

Precaution

The flange must not be pushed in without the obturator as the sharp end of the flange might cause trauma to the anorectal mucosa.

47 Stethoscope

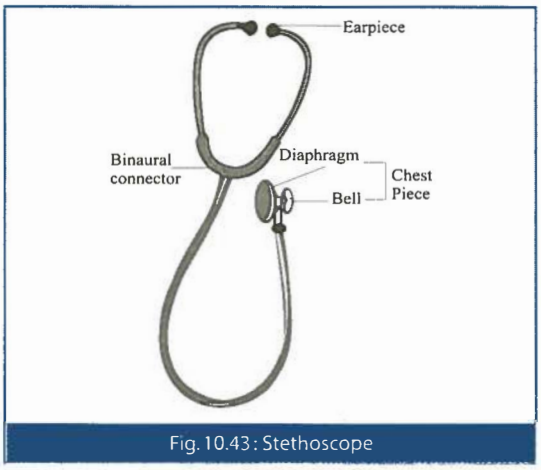


Fig. 10.43: Stethoscope

The stethoscope was invented by Laenec. This was a wooden instrument. Electronic and magnetic stethoscopes are also available.

It has a dual chest piece with a valve that allows switching from the bigger diaphragm to the smaller bell. There is tube connecting the chest piece to the binaural connector and earpieces. The tubing length should be 12 inches. Double lumen tubes are ideal. The bell is usually 1 inch in diameter and the diaphragm is 1½ inches in diameter.

Uses

The stethoscope is used in auscultation of the chest or abdomen. The bell is used for low frequency sound 30 to 150 Hz = S3, S4, MDM and the diaphragm is used for high frequency sound > 300 HZ = S1, S2, clicks, OS, systolic murmur, early diastolic murmurs.

48 Central Venous Catheter

They are available in sterile disposable packs with the equipment required to insert them into a vein.

Seldinger's Technique

The Central Venous Catheter is a long thin tube which is inserted into the vein. It has marking along its length at an interval of 5 cm. It also has a radio-opaque line which can be seen on X-rays. It usually contains the central line, the guide wire, introducer, needle and dilator.

1. The guide wire is a slender wire which is used to cannulate the vein first. Its tip is curved into a 'J' shape so as to make it non traumatic and also so that the tip is not caught in any valves in the veins. It is threaded into the introducer, which is spiral, making the long guide wire easier to handle.
2. The needle is usually 18 or 20 No. and is hollow so that the guide wire can go through it.
3. The dilator is usually a plastic device with a tapering tip which can be cannulated over the guide wire in order to dilate the site of puncture allowing the central line to be passed without resistance into the vein.

Catheter Through Sheath Technique

They usually contain a needle, sheath and the central venous catheter.

1. The Needle is a large bore needle, No. 16. The needle can be inserted into the sheath.
2. The Sheath is made of polyethylene and is shorter than the needle so that the tip of the needle

protrudes out of it when the needle is inserted into the sheath.

3. The Central Venous line is similar to the one above but it also has an inner wire to prevent it from kinking while being inserted into the vein.

Indications

1. Measurement of central venous pressure (CVP)
2. Venous access when no peripheral veins are available or venous access is required for a prolonged time
3. Administration of vasoactive/inotropic drugs which cannot be given peripherally
4. Total parenteral nutrition
5. Hemodialysis/plasmapheresis

Method of Insertion

After having selected the site, skin is cleaned painted and draped. Local anesthesia is infiltrated.

Seldinger's Technique:

The Heparinised Needle with a syringe attached is inserted into the vein and blood is aspirated. The Guide Wire is threaded through the needle into the vein with the J shaped end first. The Needle is then removed. The Dilator is passed over the guide wire in a twisting motion to dilate the site of skin puncture. A small incision in the skin may be necessary to introduce the dilator. The dilator is removed and the Catheter is passed over the guide wire. The guide wire is then removed. After confirming blood can be aspirated freely, the catheter is flushed properly with heparinized saline. The catheter is secured in place with a suture and a sterile dressing is given.

Catheter Through Sheath Technique:

The Needle inside the Sheath is inserted into the vein and blood is aspirated. The Needle is withdrawn holding the Sheath steadily inside the vein. The Catheter is threaded into the vein through the sheath. The inner wire is removed from the central catheter followed by the sheath. After confirming blood can be aspirated freely, the catheter is flushed properly with heparinized saline. The catheter is secured in place with a suture and a sterile dressing is given.

Method of Insertion of the Needle According to the Site Selected:

1. ***Internal Jugular Vein:*** With the patient in head low position and with the head turned to face the left. The right Internal Carotid artery is palpated in the lateral to the cricoid cartilage. This falls within a triangle formed by the two heads of the sternocleidomastoid muscle and the clavicle below. Starting at the apex of the triangle, keeping a finger gently over the artery, the needle is inserted just lateral to the pulsations at an angle of 30-40° to the skin and advance it downward in the direction of the nipple on the same side.
2. ***Subclavian Vein:*** The needle should be inserted into the skin 1cm below the junction of inner & middle $^1/_3$ of the circle. The needle is kept horizontal and is directed to sternal notch.
3. ***Antecubital Vein:*** A tourniquet is applied to the upper arm to distend the veins. The one which is best visible is selected and the needle is introduced.
4. ***Femoral Vein:*** The femoral artery pulsations are felt 1 – 2 cm below the inguinal ligament. Keeping a finger gently over the femoral artery, the needle is inserted just medial to the pulsations at an angle of 30 degrees.

Complications

1. Hematoma formation or bleeding
2. Pneumothorax (specially with Subclavian Venous access)
3. Infection
4. Cardiac Arrhythmias
5. Air embolism
6. Catheter or guide wire embolism
7. Injury to surrounding structures

Procedures 11

1 › Transvenous Pacing

Transvenous pacing can be done through the antecubital, subclavian or external jugular veins. The antecubital vein technique is much easier especially in the sick patient, but there is a risk of electrode displacement, which could be reduced by strapping the arm to the side.

Procedure

1. The right or the left antecubital fossa is selected and venesection is performed on the median cubital vein.
2. A catheter is introduced through the cutdown. The position of the catheter is monitored under fluoroscopy, as it approaches the heart.
3. The catheter is advanced into the right atrium and a loop is formed. The catheter is then manipulated through the tricuspid valve and the electrode is placed at the apex of the right ventricle.
4. The catheter is connected to the external pacemaking unit, which is set to demand mode.
5. The rate and the current are adjusted to the lowest setting and then the pacemaker is turned on. The rate is then gradually increased unit it exceeds the patient's intrinsic heart rate and the current is also gradually increased until capture is demonstrated. The threshold for pacing is judged by turning down the output voltage by 0.1 volt decrements until a minimum voltage to obtain consistent pacing is found. Usually the patient is placed at a voltage 2-2 1/2 times that of the pacing threshold.
6. After pacing and sensing are demonstrated, the patient should be asked to cough and move about, after which pacing and sensing are checked again. If the pacemaker function is unstable, the electrode position is changed and the procedure repeated.
7. Once pacing is stable, the electrode is secured to the arm or chest and sterile dressing is applied to the wound. The heart rate should be maintained between 70-80/min.

Complications

1. Ventricular premature beats, tachycardia or fibrillation may occur during insertion of the catheter as it enters the right ventricle. Hence a working D-C defibrillator must be at hand and the above procedure performed in an intensive cardiac care unit.
2. Perforation of the ventricle causing pericarditis or cardiac tamponade.

2 › Cardioversion

Cardioversion can be done with the help of a D-C defibrillator, which should be checked regularly and kept in working condition. It should be set on synchronized mode so that the shock is delivered on the R or S wave and not on the T wave. Usually the energy setting is of 100 joules at the beginning and then it is gradually increased up to 400 joules. **NB: If the patient is on digoxin it is much safer to start with a much smaller dose of 10-20 joules.**

Pre-requisites

In an elective case, the following pre-requisites are necessary:

1. Digoxin should be stopped for at least 48 hrs.
2. Anticoagulants like heparin and warfarin should be started and continued for at least 6-12 weeks

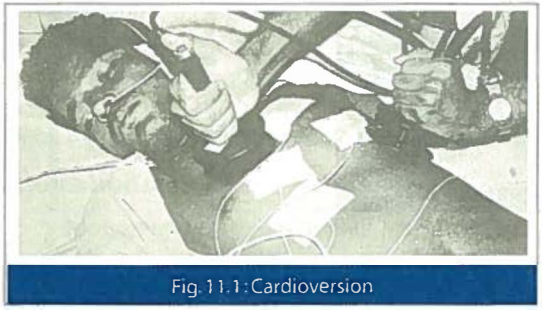


Fig. 11.1: Cardioversion

to prevent systemic embolization following successful cardioversion.

3. If the patient has slow ventricular rate or atrial fibrillation of prolonged duration, atropine sulfate 1-2 mg should be given intravenously.
4. The patient should be fasting overnight.
5. Diazepam 5-10 mg should be given intravenously. Halothane as an anesthetic agent should avoided as it may precipitate arrhythmias. In an emergency, if cardioversion has to be done in a patient on digoxin, the following drugs should be given immediately before the shock:
   a) Beta blockers like propranolol 1 mg intravenously.
   b) Diphenylhydantoin 100 to 250 mg intravenously.

Procedure

1. The procedure must be explained to the patient because the idea of receiving an electric shock creates a great deal of anxiety.
2. In male patients with a hairy chest, the chest should be shaved to improve the contact with the skin.
3. The patient is strapped and an ECG is connected.
4. The electrical jelly is applied well on the chest wall anteriorly over apex and pulmonary area
5. The paddles are placed over the site where the jelly is applied and taking care that no part of the operator touches the patient or his bed, the switch is pressed and current given.
6. If the arrhythmia is not corrected, the same procedure is repeated after 5 minutes with a higher current.

Complications

1. Serious arrhythmias may occur if the patient has been receiving digoxin.
2. Hypertension and pulmonary edema may sometimes occur.
3. Burning of the skin of the chest wall may occur if adequate jelly is not applied.

3 › Lumbar Puncture

Lumber puncture is aspiration of cerebrospinal fluid (CSF) from the spinal sub-arachnoid space by puncturing the spaces between lumbar 2 and 3 or lumbar 3 and 4 vertebrae.

Indications

I. Diagnostic

A. *Absolute:*
   1. Meningitis
   2. Subarachnoid hemorrhage

B. *Relative:*
   1. Neurosyphilis
   2. Unexplained coma
   3. Guillain Barre syndrome
   4. Multiple sclerosis

C. *Radiological:*
   1. Myelography
   2. Pneumoencephalography (P.E.G.)

II. Therapeutic

A. To introduce drugs:
   1. Methotrexate 0.25 mg/kg biweekly in leukemia
   2. Gentamicin 10-20 mg in gram negative meningitis
   3. Crystalline Penicillin 10,000-20,000 units in pyogenic meningitis

B. To reduce raised intro-cranial tension in hypertensive encephalopathy

C. To administer spinal anesthesia

Contra-indications

1. Raised intracranial tension (as shown by

papilledema) because of the risk of herniation of brain through foramen magnum, and damaging the vital medullary centres causing death.

2. Marked spinal deformity
3. Local infections
4. Suspected cord compression

Procedure

1. *Position:* The patient is placed on his side at the edge of the bed with the knee drawn up and the head flexed. It can also be done with the patient sitting and bending forward.
2. *Site:* In the 3rd lumbar space. This space lies in the plane which joins the highest points on the iliac crest. The skin over the back from the lower thoracic vertebrae to the coccyx is sterilized with Cetavlon, ether, iodine and spirit. The part is draped.
3. *Local anesthesia:* The skin to be punctured is infiltrated with 5 ml of 2% lignocaine. Infiltration is done up to ligamentum flava.

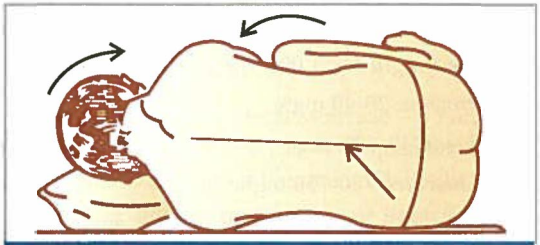


Fig. 11.2: Position for lumbar puncture with patient lying down

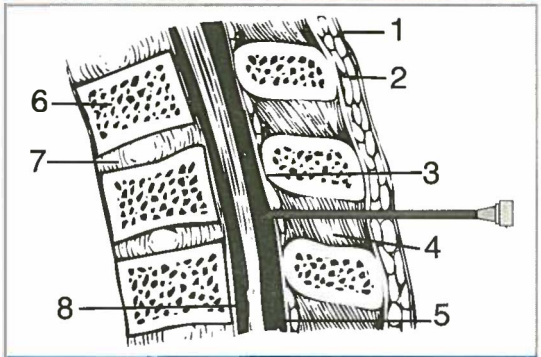


Fig. 11.3: Section of the spinal cord showing L.P. needle in the third lumbar space 1. Skin, 2. Supraspinous ligament, 3. Ligamentum flavum, 4. Interspinous ligament, 5. Dura mater, 6. Vertebral body, 7. Disc, 8. Posterior longitudinal ligament.

4. *Puncture:* A lumbar puncture needle with a stilette is introduced after 2-3 minutes into the anesthetized space, with the cutting edge of the bevel in the direction parallel to the fibers of the ligamentum flava. The needle is introduced (slightly upwards and forwards at 5° to avoid injury to the disc) through the resistance of supraspinous ligament. The interspinous ligament is then easily negotiated. At about 4-7 cm, the firmer resistance of ligamentum flavum popping sensation as the dura is breached. The stilette is then withdrawn and the fluid is collected slowly in 4-5 bulbs for biochemical, cytological and serological tests.
5. *Seal:* The needle is withdrawn and the puncture mark is sealed with a tincture benzoin seal
6. *Post-procedure orders:*
   a. Plenty of fluids are to be taken by mouth.
   b. Head low position, with half to one block to prevent headache
   c. Salicylates, if headache

Problems

I. Dry Tap

A. The needle is blocked: Re-insert the stilette to dislodge any flap of dura that may have blocked the needle.

B. Faulty technique: Repeat the procedure.

C. Subarachnoid block

II. Bloodstained CSF

A. Trauma to the spinal blood vessels.

B. Subarachnoid hemorrhage.

To distinguish between these two conditions. CSF must be collected in 2 parts is separate test tubes. The appearance of more blood in one sample compared to the other suggests trauma; in subarachnoid hemorrhage it is uniform.

Complications

1. *Headache* is the commonest problem. To minimise this, plenty of fluids should be taken orally, head-low position is to be given and salicylates if required. In neurosyphilis, headache never occurs following lumbar puncture.

Table 11.1 : CSF Picture in Various Diseases

Test	Normal	MENINGITIS				
		Pyogenic	T.B.	Viral	Fungal	Syphilitic
Appearance	Clear /Colourless	Turbid	Clear or Slightly opaque	Clear	Clear	Clear
Pressure	60-150 mm of CSF	↑	↑	N	↑	↑ or N
Proteins	20-40 mg%	↑↑↑	↑↑↑	↑	↑↑	↑
Sugar	40-70 mg%	↓↓↓	↓↓↓	N	↓	N
Chlorides	720-750 mg%	↓	↓	N	↓	N
Cells	0-5 L Per cu mm	Polymorphs large number	L large number	L 100-200	L 100-200	L 100-200
Culture	S	Organisms	Mycobacterium	S	Cryptococci	S
V.D.R.L.	-ve	-ve	-ve	-ve	-ve	+ve
Colloidal Gold Curve	-ve	M	M	-ve	M	M

↑ = Increased ↓ = Decreased N - Normal L - Lymphocytes M - Meningitic P - Paretic T - Tabetic or leutic
-ve - Negative +ve - Positive S - Sterile X - Xanthochromia R - RBC Abs - Absent

2. Backache
3. Infection: Often causing gram-negative meningitis
4. Medullary herniation leading to death
5. Injury to the blood vessels, spinal cord or intervertebral disc
6. Aggravation of symptoms from which the patient is suffering eg root pains, paraplegia, etc.

Queckendstedt's 'Test'

A manometer is attached to the lumbar puncture needle. Pressure is applied over one jugular vein and then the other. This raises the intra-cranial venous pressure, which also raises intraspinal venous pressure, and this is reflected in the manometer if the pathway between the skull and L.P needle is patent. The fluid will rise quickly by about 100 mm and falls less quickly on release of pressure. A delay signifies a spinal block.

If pressure is applied on one jugular vein, and the pressure on the manometer vises, it indicates lateral sinus thrombosis. This is a positive Toby-Ayer's test.

Normal CSF

Daily 1500 ml of CSF is formed.

1. *Volume:* 130-150 ml. (The whole volume of CSF is replaced several times a day)
2. *Color:* Clear
3. *Pressure:* 60-150 mm of C.S.F in supine and 200-250 mm of C.S.F in sitting position
4. *pH:* 7.35
5. *Specific gravity:* 1.007
6. *Proteins:* 20-40 mg%
7. *Sugar:* 40-60% mg
8. *Chlorides:* 720-750 mg%
9. *Cells:* 0-5 epithelial cells, which appear like lymphocytes

Cohen's Law of Meningitis (1929)

Substances which are more in C.S.F than blood diminish in meningitis and substances which are less in C.S.F than blood increase in meningitis (except sugar which is low in meningitis because it is used by the organisms and is also required for the increased metabolism of the brain).

The following substances are less in C.S.F than blood: Protein, Sugar, Cholesterol, Urea, Calcium and Phosphorus.

The following substances are more in C.S.F than blood: Chlorides and Magnesium.

The following substances are never seen in C.S.F as they do not cross the blood-brain barrier: antibodies, enzymes, penicillin, streptomycin, etc.

Table 11.1 : CSF Picture in Various Diseases *(Contd...)*

	G.P.I.	Tabes Dorsalis	Subarachnoid haemorrhage	Brain abscess	Spinal tumour	Guillain Barre Syndrome
Appearance	Clear	Clear	Blood stained	Clear	X	X
Pressure	↑ or N	N	↑	↑	↓	N or ↑
Proteins	↑	↑	↑	↑	↑	↑↑
Sugar	N	N	N	N	N	N
Chlorides	N	N	N	N	N	N
Cells	L 100-200	L 100-200	R	L 100-200	Abs	Abs : Cyto-albumin-ergic dissociation
Culture	S	S	S	S	S	S
V.D.R.L.	+ve	+ve	-ve	-ve	-ve	-ve
Colloidal Gold curve	P	T	-ve	-ve	-ve	-ve

Site of CSF Formation

1. Choroid plexus of the lateral ventricles-95%
2. Choroid plexus of the third and fourth ventricle.
3. Perivascular spaces of the brain.
4. Lymphatics around the roots and peripheral nerves.

Circulation of CSF

Choroid plexus of lateral ventricle → Foramen of Monroe → Third Ventricle → Acqueduct of Sylvius → Fourth Ventricle → Foramen of Luschka and Magendie → Sub-arachnoid space → Basal Cisterns → Circulation over brain and spinal cord.

Absorption of CSF

C.S.F is absorbed by the arachnoid villi that sit over the venous sinuses.

Functions of CSF

1. Nutrition
2. Excretion
3. Shock absorption
4. Regulation of intracranial pressure

Abnormal CSF

I. Pressure:

A. *Increased:*

1. Brain tumor
2. Meningitis, encephalitis
3. Neurosyphilis
4. Subarachnoid and intracerebral hemorrhage
5. Hypertensive encephalopathy
6. Venous sinus thrombophlebitis
7. Hydrocephalus
8. Benign raised intracranial tension
9. Uremia
10. Emphysema

B. *Decreased:*

1. Repeat L.P. soon after the first one
2. Subarachnoid spinal block
3. Subdural hematoma

II. Appearance

A. *Turbid:* Pyogenic meningitis

B. *Cobweb:* T.B meningitis

C. *Blood tinged*

1. Subarachnoid hemorrhage
2. Trauma to spinal blood vessels
3. Bleeding diathesis

D. *Xanthochromia* (Yellow tinting of the CSF).

1. Following hemorrhage in the CSF
2. High protein content of the C.S.F e.g. Guillain Barre syndrome, spinal block, neurofibroma, etc.
3. Jaundice.

4. Tumors near the cauda equina, around the ventricles and acoustic neuroma.

III. **Proteins**

A. *Increased:*

1. Meningitis
2. Encephalitis including poliomyelitis
3. Disseminated sclerosis
4. Guillain Barre syndrome
5. Neurosyphilis
6. Spinal cord compression
7. Intra-cranial tumor
8. Cerebral arteriosclerosis

B. *Decreased:* (Not known)

IV. **Sugar**

A. *Increased:*

1. Diabetes mellitus
2. Following I.V glucose administration
3. Encephalitis

B. *Decreased:* Meningitis

V. **Chlorides**

A. *Increased:* (Not known)

B. *Decreased:*

1. Purulent and tuberculous meningitis
2. Systemic hypochloremia

VI. **Cells**

A. *Polymorphonuclear leucocytosis:*

1. Pyogenic meningitis.
2. Acute syphilitic meningitis
3. Acute poliomyelitis (early stage)
4. Epidural abscess

B. *Lymphocytosis:*

1. Meningitis-tuberculous, viral, syphilitic and late stages of pyogenic
2. Encephalitis
3. Poliomyelitis-later stages
4. Disseminated sclerosis
5. Cerebral tumor
6. Cortical venous thrombophlebitis

C. *Eosinophil:* Cerebral or spinal cysticercosis

D. *Malignant cells:* Cerebral or spinal malignancy

4 › Cisternal Puncture

Cisternal puncture is aspiration of C.S.F from the cisterna magna by puncturing in midline, half an inch above the second cervical vertebra.

Indications

1. Diagnostic: Same as for lumbar puncture. Lumbar puncture is preferred to cisternal puncture. If L.P has been traumatic or if there is spinal deformity and LP is difficult, cisternal puncture is done.
2. Spinal block: When there is spinal block demonstrated by a myelogram from below, myodil is introduced also from above after a cisternal puncture to know the upper limit of the block.

Contra-indications: Same as for L.P.

Procedure

1. *Position:* The patient is placed on his side at the edge of the bed with his head flexed.
2. *Site:* In the mid-line half an inch above the second cervical vertebra and in the plane of the tip of the mastoid. Hair is shaved over the back of the head below external occipital protuberance and the part is sterilized with Cetavlon, ether, iodine and spirit.
3. *Local anesthesia:* The skin and the subcutaneous tissues are punctured with 1% lignocaine
4. *Puncture:* The cisternal puncture needle with calibrations and short bevel is introduced in the midline, half an inch above the second cervical vertebra. It is pushed for about 4-5 cms in the plane of tragus and nasion when it enters cisterna magna and CSF comes out.

5 › Liver Biopsy

Liver biopsy is removal of a bit of the liver tissue percutaneously for histological examination.

Indications

1. *Cirrhosis of liver:* To distinguish fatty liver from cirrhosis and to diagnose the type of cirrhosis.
2. *Hepatic malignancies:* To diagnose hepatoma in cirrhotic patients, as they are prone to develop hepatoma.
3. *Granulomas:* eg. Tuberculosis, sarcoidosis, schistosomiasis.
4. *Metabolic and storage disease:* e.g. Wilson's disease, amyloidosis, Hodgkins.
5. *Reticulo-endothelial diseases:* e.g. leukemias, multiple myeloma, Hodgkin's disease.
6. *Unexplained fever* with hepatomegaly as occurs in amebiasis, cholangitis, tuberculosis, brucellosis, etc.
7. *Unexplained jaundice:* If jaundice persists after 2-3 weeks, and diagnosis is not obvious on clinical and biochemical tests.
8. *Jaundice due to chronic hepatitis:* To differentiate post-necrotic cirrhosis from other sequelae.
9. Screening relatives of patients with familial diseases of liver.

Contra-indications

1. Bleeding diathesis.
2. Protracted severe hepatocellular jaundice because hepatic precoma may be precipitated.
3. Infections in liver, peritoneum, biliary tract, right lung base and right subphrenic abscess.
4. Hydatid cyst in liver is suspected.
5. Hemangioma of liver is suspected.
6. Chronic passive congestion of the liver.
7. Gross ascites.

Pre-requisites

1. The following investigations must be done: Bleeding time, clotting time and prothrombin time. If they are high, the patient must be given injection Vit K 10 mg I.M. for 3 days. If the prothrombin time does not return to normal fresh frozen plasma must be given to the patient.
2. Blood should be sent for grouping and cross-matching.
3. If ascites is present, it must be tapped first and then the biopsy done.

Procedure

1. Pre-anesthetic medication: Injection atropine 0.6 mg and injection phenobarbitone 50 mg must be given intramuscularly half an hour before the procedure.
2. Position: Patient lies on his back in the bed with the right side very near the edge of the bed.
3. *Site:* Ninth or tenth inter-costal space in the midaxillary line. The area is sterilized with Cetavlon, ether, iodine and spirit.
4. *Local anesthetic:* The skin, subcutaneous tissue and the tissues up to the capsule of the liver are infiltrated with 1% lignocaine.
5. *Biopsy method:* This may be done by either Vim-Silverman's or Menghini's method.
   a. *Vim-Silverman's method:* The trocar and cannula are penetrated through the liver substance. The trocar is removed and the split needle, which cuts the liver tissue, is introduced. The cannula is then rotated over the split needle so that the cut liver tissue remains between the two blades of the split needle. The cannula and the split needle are now rotated and the needle withdrawn. The tissue is collected in Bouin's fluid, which is composed of picric acid (75 parts) acetic acid (5 parts) and formalin (25 parts). Throughout the procedure, the patient must hold his breath.
   b. *Menghini's method:* 3 ml of sterile saline solution is drawn into a syringe with the

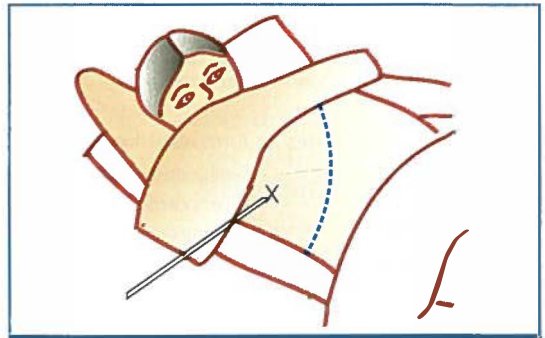


Fig. 11.4 Site for liver biopsy

needle attached. The needle is inserted up to the intercostal space but not through it. About 2 ml of the solution in the syringe is injected to clear the needle of any skin fragment. Aspiration is now begun and maintained. With the patient holding his breath in expiration the needle is quickly inserted into the liver substance and then quickly with-drawn, placing the tip of the needle under saline in a glass receptacle. By this method there is little distortion of the biopsy material and it causes less discomfort to the patient.

6. *Seal:* After the biopsy, the punctured skin is sealed with a tincture benzoin seal.
7. *Post-procedure orders:* T.P.R., B.P to be recorded half hourly and the patient should not be given feeds for the next 4 hours. If there is pain, analgesics may be given.

Failure of the Liver Biopsy

Causes:

1. Wrong technique
2. Very tough liver tissue as in cirrhosis
3. Emphysema

In case of failure the biopsy must be repeated if:

1. Experienced person is doing the biopsy
2. Patient is co-operative
3. Menghini's needle is used
4. Patient does not have jaundice

Table 11.2 : Naked Eye Appearance of the Biopsy Material

1. Biopsy material floats in water	- Fatty liver
2. Fragmented small pieces	- Cirrhosis of liver
3. Dull-white colored	- Malignancy
4. Green color	- Biliary cirrhosis Obstructive jaundice
5. Chocolate colored	- Dubin Johnson's syndrome
6. Congested	- Cardiac cirrhosis

Complications

1. Hemorrhage
2. Infection
3. Injury to the liver, gall bladder (causing biliary peritonitis), colon, kidneys, blood vessels and nerves
4. Precipitation of hepatic coma

6 › Kidney Biopsy

Kidney biopsy is removed of bit of the kidney tissue percutaneously for histological examination.

Indications

1. **Diagnostic:**
   a. Asymptomatic proteinuria (more than 1 gm/day)
   b. Recurrent isolated hematuria with proteinuria, where I.V.P and cystoscopy do not show the source
   c. Acute nephritis with persisting oliguria
   d. Nephrotic syndrome in adults. In children only if proteinuria persists after a trial of corticosteroids
   e. Acute renal failure where there is no obvious cause and renal tract obstruction is excluded
   f. Chronic renal failure where kidneys are normal on radiographs
2. **Prognostic:**
   a. Follow-up cases of glomerulonephritis
   b. To assess the effects of steroids or immunosuppressants in glomerulonephritis or nephrotic syndrome

Contra-indications

1. Unilateral kidney
2. Shrunken kidney
3. Infections: Peri nephritic abscess, pyonephrosis etc.
4. Cystic diseases: Hydronephrosis, polycystic disease of the kidneys or large solitary cyst

5. Hypernephroma
6. Bleeding diathesis

Pre-requisites

1. Bleeding, clotting and prothrombin time (PT) must be done. If high, injections of 50 mg of vitamin K are given for 3 days and PT is repeated. If it is still high, biopsy must be postponed.
2. Blood must be sent for grouping and cross matching.
3. Plain X-ray abdomen or sonography must be done to determine the size of the kidneys.
4. Renal function tests must be done e.g. routine urinalysis, blood urea, serum creatinine, etc.

Procedure

1. *Pre-anesthetic medication:* Injection atropine 0.6 mg and injection phenobarbitone 50 mg must be given intramuscularly half an hour before the procedure.
2. *Position:* Patient lies prone with pillows below the abdomen. The middle of the table may be broken if possible so that the spine flexes completely.
3. *Site:* This is determined by plain X-ray abomen or I.V.P. The side where the disease is suspected is the side of the biopsy. In case a bilateral lesion is suspected, the biopsy is preferably performed on the left side. The area is sterilized with Cetavlon, ether, iodine and spirit.
4. *Local anesthetic:* The skin, sub-cutaneous tissues and the tissues up to the renal capsule are infiltrated with 5 ml of 2% lignocaine. When the needle penetrates the renal tissues it moves on respiration
5. *Biopsy:* This is performed exactly in the same way as for liver biopsy
6. *Seal:* As for liver biopsy
7. *Post-procedure orders:*
    a. T.P.R. and B.P. to be recorded half-hourly and no feeds are to be given for the next 4 hours.
    b. Supine position for the next 24 hours.
    c. Plenty of fluids must be taken for the next 24-48 hours to maintain urine output over 3 liters.
    d. Alkaline mixture must be given to make the urine pH alkaline.
    e. The patient mustbe informed that he will have hematuria for the next 24-48 hours and if he does not have it, it signifies that the biopsy was a failure.

Complications

1. Local pain
2. Hematuria
3. Infections causing renal abscess
4. Injury to the ileo-inguinal nerves which causes intense pain.
5. Peri-renal hematoma, causing dull pain and swelling in the loin, which may require surgical drainage
6. Transient intra-renal A-V fistulas.

7 › Bone-marrow Aspiration

Bone-marrow aspiration is aspiration of the bone marrow, the histological examination of which is useful in the diagnosis of various hematological conditions.

Indications

I. **Diagnostic:**
    A. *Bone-marrow examination essential for the diagnosis:*
        1. Aplastic anemia
        2. Megaloblastic anemia
        3. Aleukemic leukemia
        4. Myelofibrosis
        5. Myelosclerosis
        6. Multiple myeloma
    B. *Bone-marrow examination helpful but not essential for the diagnosis:*
        1. Anemias:
            a. Refractory anemia
            b. Iron deficiency anemia (To differentiate from other hypochromic anemias)
            c. Hemolytic anemias
        2. Leukemias: To differentiate the types of leukemias

3. Thrombocytopenic purpura
4. Agranulocytosis
5. Hypersplenism
6. Tropical diseases like malaria, kala azar
7. Malignancy-secondary carcinoma
8. Infiltrative disorders eg. Gaucher's disease

II. **Prognostic:**
1. Agranulocytosis
2. Aplastic anemia
3. Leukemia

III. **Therapeutic:** Bone marrow transplant

Contra-indications

Blood dyscrasias especially hemophilia

PRE-REQUISITES: Bleeding, clotting and prothrombin times, including platelet count

Procedure

1. *Pre-anesthetic medications:* As in liver biopsy.
2. *Sites:*
   A. Sternal puncture: mid-manubrium - commonest
   B. Spinous process of the lumbar vertebrae.
   C. *Iliac crest:* In children.
3. *Position:* Patient is supine. The chest is shaved and prepared with Cetavlon, ether, iodine and spirit.
4. *Local anesthetic:* The skin, sub-cutaneous tissues and periosteum over the manubrium are infiltrated with 2% lignocaine.
5. *Aspiration:* After 2-3 minutes when the local anesthetic effect is apparent, the bone-marrow aspiration needle, with guard half an inch from the tip, is pushed vertically through the sternal plate with a boring motion. When the needle has entered the marrow, the stilette is withdrawn and 0.2-0.5 ml of bone-marrow is aspirated with a 1 ml syringe. The needle is withdrawn and smears are prepared with the marrow. Hemostasis is assured by maintaining pressure over the site for 3-5 minutes.
6. *Seal:* As for liver biopsy.
7. *Post-procedure orders:*
   a. T.P.R., B.P. half hourly for 4 hours
   b. Nil by mouth for 4 hours
   c. Analgesics for pain

Complications

1. Bone pains
2. Hematoma
3. Infection (Osteomyelitis)
4. Transfixation of the sternum and injury to the great vessels (This is prevented by the guard)

Causes of Dry Tap

1. *Faulty technique*
2. *Pathological changes in the bone-marrow:*
   a. Myelofibrosis and myelosclerosis.
   b. Carcinomatous infiltration of the bone-marrow.
   c. Hyperplasia of the marrow-leukemia.
   d. Hypoplasia of the marrow.

Composition of Normal Bone-marrow

1. Blood cells: Nucleated cells 20,000 - 1,00,000 per cu.mm
2. Blood vessels
3. Fatty tissue
4. Reticulum
5. Nerves

Look for the Following in a Bone Marrow Smear

1. Number and type of erythropoiesis, leucopoiesis and megakaryocytes.
2. Cellularity of the marrow
3. Myeloid-Erythroid ratio (Normally 3:1 or 4:1)
4. Presence of tumor cells, plasma cells, etc.
5. Presence of parasites: L.D bodies, malarial parasites, etc.

8 › Pleural Fluid Aspiration

Indications

1. Large pleural effusion up to the clavicles

2. Bilateral pleural effusion
3. Cardio-respiratory embarrassment
4. When pleural effusion is suspected to be infected (persistence of fever and constitutional symptoms) or hemorrhagic
5. Acute pulmonary edema
6. Persistent pleural effusion inspite of anti-tuberculous therapy

Contra-indications: None

Procedure

1. *Pre-anesthetic medication:* As for liver biopsy.
2. *Position:* Patient sits up against a backrest or leans forward resting the arms on the tip of a bed-table.
3. *Site:* Seventh or eighth intercostal space in the mid-axillary or scapular line. The part is prepared with Cetavlon, either, iodine and spirit.
4. *Local anesthetic:* Skin, subcutaneous tissue and parietal pleura are infiltrated with 2% lignocaine.
5. *Puncture:* The aspiration needle is introduced at right angles to the skin, mid-way between the two ribs, and advanced till parietal pleura is punctured which is indicated by a 'give in'. The needle is now attached to a 50 ml syringe with a two-way stop cork and about 800-1000 ml of fluid is removed at a time. Aspiration must be stopped if the patient coughs or complains of tightness in the chest.
6. *Seal:* As for liver biopsy
7. *Post-procedure orders:* As for liver biopsy

Complications

1. Pleural shock due to vagal inhibition
2. Air embolism
3. Pulmonary edema
4. Circulatory collapse due to a high negative intrapleural pressure, which may occur if there is pulmonary fibrosis as this prevents expansion of lung
5. Injury to the intercostal vessels
6. Pneumothorax
7. Hemoptysis
8. Infection

9 › Aspiration of Pneumothorax Cavity

Aspiration of pneumothorax cavity is removal of air from the pleural cavity.

Indications

1. Tension pneumothorax causing cardio-respiratory embarrassment.
2. Massive pneumothorax, unlikely to resolve spontaneously.

Procedure

1. *Pre-anesthetic medication:* Same as pericardial aspiration.
2. *Position:* The patient should be in an upright position with a backrest.
3. *Site:* Second intercostal space in the mid clavicular line or in the posterior axillary line at the level of the apex beat.
4. *Local anesthetic:* Same as pericardial aspiration.
5. *Aspiration:* The skin of the anterior chest wall on the affected site is prepared with Cetavlon, iodine and spirit. With the scalpel a small nick is made in the skin in the second intercostal space a little outside the midclavicular line. With the help of a trocar and canula, a disposable plastic thoracic tube or a rubber catheter is introduced into the intercostal space and connected to an underwater seal. The incision should be just above the upper border of the lower rib to avoid injury to the upper border of the lower rib to avoid injury to the intercostal nerves and blood vessels.

   If the incision is too near the midline, fatal penetration of the superior vena cava on the right side may occur.

   In emergency, as in tension pneumothorax, any large needle or even a stethoscope tube inserted through the stab may save the patient's life.
6. *Wound closure:* The skin incision is sutured.

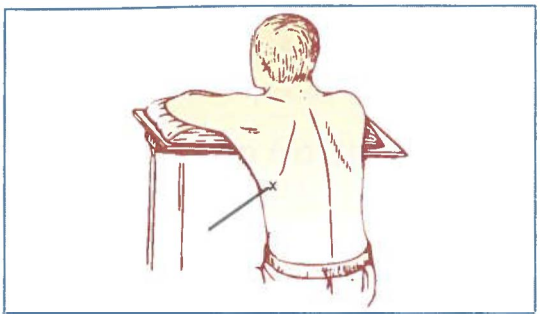


Fig. 11.5: Site for pleural tapping

7. *Post-procedure orders:* Same as pericardial aspiration.

Complications

1. Injury to blood vessels and nerves.
2. Subcutaneous emphysema.
3. Infection and development of pyopneumothorax.

10 › Pericardial Aspiration

Pericardial aspiration is removal of fluid from the pericardial sac.

Indications

1. Cardio-respiratory embarrassment
2. Rapid accumulation of fluid
3. Rheumatic effusion that has not been absorbed in 4 weeks

Sites

1. *Anteriorly:* In the fifth left intercostal space outside the apex beat but inside the outer edge of the cardiac dullness
2. *Epigastric:* Between the ensiform cartilage and the left costal margin
3. *Posterior:* Near inferior angle of the scapula.
4. *Sternal:* In the fourth left intercostal space lateral to the sternum

Procedure

1. *Pre-anesthetic medication:* Injection atropine 0.6 mg with injection pethidine 100 mg is given intramuscularly half an hour before the procedure.
2. *Position:* The patient is put in the supine position.
3. *Site:* Any of the above sites are selected but usually the epigastric position is preferred.
4. *Local anesthetic:* The skin and the subcutaneous tissue are infiltrated with 1% lignocaine.
5. *Aspiration:* The needle is inserted to the left of the xiphoid process and directed at an angle of 45° posteriorly towards the midclavicular line. It is advisable to attach an ECG electrode to the needle so that on contact with the heart, the needle would show a negative deflection. The needle is slightly withdrawn, when the ECG shows a normal tracing, fluid is aspirated from the pericardial sac.
6. *Seal:* After the procedure the needle is removed and the punctured skin is sealed with a tincture benzoin seal
7. *Post-procedure orders:* TPR and BP must be recorded every half hourly. No feeds must be given for 4 hours. If there is pain, analgesics may be given

Complications

1. Laceration of the coronary artery and hemopericardium
2. Penetration of the cavity of the heart
3. Ventricular tachycardia
4. Shock

11 › Ascitic Tapping

Indications

Diagnostic

Therapeutic (LVP - Large Volume Paracentesir)

1. Marked abdominal discomfort and cardio-respiratory embarrassment
2. Ascites refractory to medical line of treatment
3. Diagnostic
4. All patients with new onset ascites.

Contra-indications

Severe jaundice with impending hepatic coma

Pre-requisite

The patient must be asked to evacuate the bladder

Procedure

1. Antiseptic precautions with betadine solution and
2. *Position:* Supine or semi-reclined with a backrest.
3. *Site:* In the flank mid-way between the anterior superior iliac crest and umbilicus.
4. *Local anesthesia:* with 2% Xylocains.
5. *Puncture:* A large bore needle about 3 1/2 inches in length is introduced and the ascites fluid is drained slowly through the rubber tubing connected to the needle.
6. *Seal:* As for liver biopsy
7. *Post-procedure orders:* As for liver biopsy

Complications

1. Hemodynamic instability: If the fluid is removed rapidly
2. Acute liver cell failure and precipitation of hepatic coma
3. Infection: Peritonitis (rare)
4. Perforation of a viscus (rare)
5. Renal dysfunction if intravascular volume depletion with decreased renal perfusion.

12 › Gastric Analysis

Indications

1. To diagnose achlorhydria in suspected cases of pernicious anemia
2. To diagnose peptic ulcer
3. To diagnose pyloric stenosis
4. In suspected cases of gastric carcinoma
5. In suspected cases of Zollinger Ellison's syndrome
6. To determine the completeness of vagotomy by Hollander's insulin test.

Contra-indications

(For gastric intubation)

1. Esophageal lesions: Varices, stenosis, malignancy, diverticula, etc.
2. Aneurysm of aorta.
3. Recent gastric hemorrhage
4. Congestive cardiac failure
5. Pregnancy

Procedure

1. Starve overnight
2. Ryle's tube is passed into the stomach and the stomach is emptied. The volume of the stomach aspirate is noted and tested for mucus, bile, blood, starch, etc.
3. The tube is taped onto the patient's face and the stomach aspirated every 15 minutes for 1 hour and titrated for acid. This is the basal acid output (BAO)
4. *Augmented Test:*
   a. *Augmented histamine test:* Antihistaminics are given to block the H1 receptors of histamine. Then 2.4 mg of histamine is injected every 15 minutes for the next 1 hour. This is replaced nowadays by the Pentagastrin test.
   b. *Pentagastrin test:* 6 mcg/kg. of pentagastrin is given intramuscularly and secretions are collected every 15 minutes for the next 1 hour. Peak acid output (PAO) is calculated from the highest two consecutive acid output collections.
   c. *Hollander's insulin test:* Blood is collected for blood-sugar estimation and this is followed by injection plain insulin 0.2 units/kg. Every 15 minutes for the next 1 hour gastric samples are collected and acid output is noted.

Interpretation

I. **Volume:** Fasting volume is normally 50 ml. If it is more than 250 ml it suggests pyloric stenosis or hypersecretion of the gastric juice.

II. **Odor:** Normal gastric juice has a faintly pungent odor.
   A. Foul and acid smell suggests pyloric stenosis
   B. Offensive fecal odor suggests small intestinal obstruction or gastro-colic fistula

C. Ammoniacal odor suggests uremia

D. No odor suggests achlorhydria

III. Color:

A. Blood red due to blood, confirmed by chemical test. It may be due to:

1. Trauma by the procedure
2. Hemorrhage fro
   a) Peptic ulcer
   b) Carcinoma of stomach
   c) Esophageal varices

B. Coffee-ground due to conversion of hemoglobin to acid hematin

C. Dark green color due to bile, confirmed by chemical test and, on adding water to the aspirate, the green color is apparent. It occurs due to regurgitation of the intestinal contents into the stomach

IV. Mucus: It is normally present and responsible for the viscosity of the gastric juice. It is present in excess in:

A. Swallowing of saliva and nasopharyngeal secretions

B. Gastritis

C. Gastric retention

V. Hydrochloric Acid (HCL) Normal: 2 mmol/hr. for men and 1 mmol/hr. for women.

A. Duodenal ulcer: BAO is twice normal or more and PAO is very high, about 25 mmol/hr.

B. Zollinger Ellison's syndrome: BAO is 15 m mol/hr. PAO is the same as BAO.

C. Test for complete vagotomy: After Hollander's test if PAO is greater than BAO it suggests vagotomy is incomplete. If vagotomy is complete PAO=BAO

D. Achlorhydria: It may be false or true:

1. False- Acid is secreted but is neutralized by saliva, mucus or regurgitated intestinal juice. Hence on histamine injection, acid is present
2. True- No rise in acidity following histamine or pentagastrin injections

Causes of Acholrhydria:

1. Idiopathic
2. Pernicious anemia
3. Sub-acute combined degeneration of spinal cord
4. Gastritis
5. Carcinoma of stomach
6. Gastrectomy
7. Chronic infections: cystitis, salpingo-oophoritis, appendicitis, etc
9. Rheumatoid arthritis
10. Pellagra
11. Radiation
12. Hyperthyroidism or Myxedema
13. Old age and debility
14. Pregnancy

VI. Microscopic Examination: It must be done to detect RBC, WBC (suggest infection), epithelial cells, malignant cells or parasites.

13 › Glucose Tolerance Test (G.T.T.)

Glucose tolerance test is a measure of the capacity of a person to dispose off glucose administered orally or intravenously.

I. Oral Test

A. Patient is fasting overnight after 3 days of high carbohydrate diet.

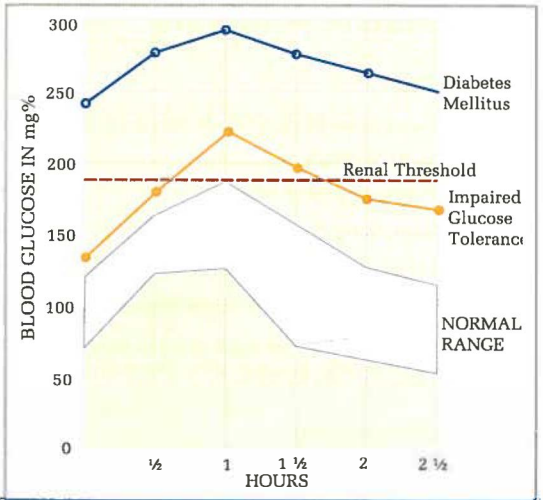


Fig. 11.6: Glucose tolerance curve

B. Next morning 3 cc of fasting blood and urine are collected.

C. A solution of 100 gm of glucose in 200-300 ml of limewater is given by mouth.

D. Blood and urine specimens are obtained every half hourly for 2-2 1/2 hours.

E. Blood sugar is estimated and urine sugar is qualitatively analysed.

F. A curve is prepared of time in hours against blood sugar levels in mg% (Fig. 11.6).

II. **Intravenous Test** is carried out in patients who have inadequate absorption of sugar, as in steatorrhoea. After overnight fast, 20-30 gm of glucose are injected I.V and blood sugar estimated every half hourly for 2 hours. In normal subjects blood sugar reaches fasting level in 1 hour.

III. **Cortisone G.T.T.:** Patient ingests 50 mg cortisone acetate 8 hour and 2 hour before the test. The test is then carried out as for oral test. This is a stress test as cortisone increases neoglycogenesis in the liver and raises the blood sugar level, which stimulates the beta cells to secrete more insulin. Hence it tests the reserve of beta cells.

Table 11.3 : Blood Glucose in mg%

	Fasting		*2 hrs PP*
Normal	<100	And	<140
Impaired GT	<100	And	140-200
Impaired FG	100-125	And	<140
Overt DM	>126	OR	>200

DM: Diabetes mellitus; GT: Glucose Tolerance; FG: Fasting glucose

14 › Intravenous Therapy

A. Venepuncture

Indications

1. To introduce or replace fluids into circulation.
2. To provide a route for administering parenteral medication or nutrition, usually in intensive care.

Site

Normally veins on the forearm or wrist are selected. If these are difficult, veins of ankle or feet are used.

Procedure

1. *Venepuncture:* After the clothes have been removed from the limb a tourniquet should be applied to distend the veins. The site of puncture is cleaned with a spirit swab. Heavy hair growth should be shaved before this is done. The needle is inserted slightly obliquely through the skin; pressure causes the bevel to enter the vein. Blood will enter the syringe. Now the syringe is removed and the clip set is attached, fixed and dressed.
2. *Post procedure orders:* The site should be examined daily for inflammation. Adding 500 units of heparin to each 500 ml of fluid infused, reduces the incidence of sepsis.

   Giving sets should be removed after 3-4 days and immediately after a blood transfusion, as clot remains in the filter chamber and may harbour microorganisms.
3. *Problems:*
   a. No veins are visible
   b. Failure to penetrate the veins
   c. Failure to flow
   d. Appearance of inflammation

Discontinuing the Infusion

The clip should be turned off to stop the intravenous needle is removed and a small sterile dressing is applied.

Dangers and Complications

1. Overloading the circulation
2. Thrombophlebitis
3. Hematoma
4. Infection
5. Local swelling and edema if the needle is displaced out of the vein
6. Air embolism if a new bottle is connected to the empty tubing directly instead of changing the set first.

B. Venesection

Indications

1. To replace fluids into the circulation when veins are collapsed and the venepuncture is difficult.

Table 11.4 : Composition of Commonly used Parenteral Solutions

CONSTITUENTS	% Solution	gm/L	mEq of the ion per litre of solution							
			Na	K	Ca	NH_4	Glucose	Cl	HCO_3	Lactate
NaCl	0.9	9.0	155	-	-	-	-	155	-	-
Sodium lactate M/6	1.87	18.7	167	-	-	-	-	-	-	167
Ammonium chloride	0.9	9.0	-	-	-	170	-	170	-	-
Sodium bicarbonate	7.5	75.0	900	-	-	-	-	-	900	-
Potassium chloride	14.5	145	-	2,000	-	-	-	2,000	-	-
5% Glucose	5.0	50.0	-	-	-	-	50 gm	-	-	-
5% Glucose in normal saline	5.0	50.0	155		-	-	50 gm	155	-	-
Ringer lactate			130	4	3.5	-	-	110.5	-	27
Ringer solution										
NaCl	0.85%	8.5	145	-	-	-	155	-	-	-
KCL	0.03%	0.3	-	4.0	-	-	-	-	-	-
$CaCl_2$	0.033%	0.033	-	-	6.0	-	-	-	-	-

2. To provide a route for administering parenteral medication with concentrated solutions.
3. To monitor central venous pressure (CVP).

Sites

Saphenous vein over the ankle or cephalic vein over the arm is usually selected. The basilic vein is selected when CVP is to be monitored.

Procedure

1. Local anesthesia: The skin and subcutaneous tissue are infiltrated with lignocaine.
2. Incision: For the saphenous vein, an incision is made half an inch above and lateral to the medial epicondyle between the biceps and triceps muscle. The incision is made at right angles to the long axis of the limbs.
3. The skin and the subcutaneous tissues are displaced with the artery forceps. Saphenous vein is very superficial and easily reached. Cephalic vein lies in the groove between the biceps and triceps muscles and superficial to the brachial artery.

   An aneurysm needle is passed below the vein and two threads are passed around the vein. In the upper limb, before proceeding further, radial pulsations are checked on compressing the "cephalic veins". They are not obliterated unless brachial artery is mistaken for cephalic vein.
4. The distal end of the vein is tied and the proximal end is caught between the thread. A nick is made in the vein and through it the polythene tube is passed for a short distance or up to the superior vena cava (in upper limbs).
5. I.V. drip is connected to the venesection needle. Skin is sutured and bandaged.

Discontinuing Venesection

I.V. fluids are stopped. The polythene tube is gently pulled out. The area is cleaned and one to two stitches are taken if required. They are removed after 8 days.

Calculations of Fluid and Electrolytes and its correction:

Sodium Deficit

Deficit = (Normal serum Na-Actual serum Na) x wt (kg) e.g. if serum sodium is 1200, in a man of 60 kg.

Deficit = (140 - 120) x 60

= 20 x 60

= 1200 units

Two-thirds is given as NaCl and one third as N/6 sodium lactate, i.e 5 liters as NaCl (Normal Saline) and 2 1/2 liters as N/6 sodium lactate.

Potassium lactate

It is extremely difficult to calculate potassium deficit. However it has been estimated that a deficit of 200-4000 mEq of potassium is required before the serum potassium is reduced to less than 3 mEq/L.

In diabetic ketosis gross deficits of potassium may exist with normal serum potassium.

Whenever possible, potassium deficit must be corrected by oral administration of potassium. If required, potassium may be given I.V at a rate not more than 20 mEq hour.

15 › Subcutaneous Infusions

Considerable quantities of liquid can be given subcutaneously if the rate of absorption into the body is hastened by mixing hylase with the fluid

Site

1. Outer aspect of the thigh
2. Abdominal wall
3. Lateral

Insertion

The set is first prepared. The skin is cleaned and the needle is inserted just under and parallel to the skin. The set is then connected to the subcutaneous needle, the clip turned on and the infusion commenced at 80 drop per minute.

A small gauze dressing is placed under the hilt of the needle and straping is placed over the hilt to secure the needle in position.

Discontinuing the Infusion

The needle is removed and small occlusive dressing applied over the site of injection.

Problems and Complications

1. Pain at the site of injection
2. Infection
3. Slow absorption of fluids

16 › Tracheostomy

Definition: Tracheostomy is an operation by which a stoma or window is made in the tracheal wall for the purpose of respiration.

Indications

1. Respiratory paralysis where prolonged intubation is required or in patients kept on a respirator
2. Tetanus
3. Acute laryngeal edema: e.g. Diphtheria, chemical burns, and inhalation of irritant gases.
4. Excessive tracheobronchial secretions
5. Foreign body in airway
6. Injury to or pressure on larynx
7. Bilateral abductor paralysis of the vocal cords

Procedure

1. *Preanesthetic medications:* Inj. atropine 0.6 mg half an hour before tracheostomy.
2. *Position:* The patient is put supine with neck over-extended and chin in the midline.
3. *Site:* Below isthmus of the thyroid gland
4. *Local anesthesia:* The part selected is prepared and infiltrated with 2% lignocaine
5. *Procedure:* A vertical mid-line incision is taken about 4 cms long, starting from the suprasternal notch. The skin, platysma and the superficial fascia are cut. The inner margin of the sternohyoid muscle is identified and the deep layer of cervical fascia is cut. Pretracheal fascia is cut and separated from trachea. The isthmus is cut between clamps and its ends ligated. 0.5-1.0 ml of 1% lignocaine is injected into the lumen of the trachea. The trachea is kept steady with fingers and the fourth and third tracheal rings incised from below upwards. A small portion of 1 to 2 rings is clipped off. The edges of the tracheal wound are held apart and a proper sized tracheostomy tube (with tapes already threaded) is introduced. The hooks are removed and tape is

tied. The wound and the tracheostomy are kept free of secretions by repeated suctions. The skin is sutured at the upper or lower extremity only. The wound is dressed. A reel of gauze with an encircling tape is placed around the tube and changed whenever soiled.

Complications

A. *During surgery:*
   1. Injury to the trachea and esophagus
   2. False passage

B. *Post-operative:*
   1. Blocked tracheostomy tube
   2. Surgical emphysema
   3. Infection, hemorrhage and ulcerations
   4. Pulmonary: Bronchopneumonia

Post-operative

1. Inner tube is removed and cleaned at least twice a day.
2. Outer tube is removed for cleaning on the 10th day and immediately another tube is introduced. Later, outer tube is cleaned once a week and then once a fortnight.

17 › Oxygen Therapy

Indications

A. **Decreased tension of oxygen in arterial blood:**
   1. High altitude
   2. Anesthesia
   3. Failure of respiration
   4. Hypoventilation
   5. Respiratory disease
   6. Right to left shunt

B. **Decreased oxygen content in arterial blood:**
   1. Anemia
   2. Carbon monoxide poisoning
   3. Cyanide poisoning
   4. Methemoglobinemia
   5. Sulfhemoglobinemia

C. **Decreased cardiac output:**
   1. Shock
   2. L.V.F.
   3. Cardiac arrest
   4. Cardiac arrhythmias
   5. Poor coronary perfusion

D. **Increased oxygen requirement:**
   1. Hyperpyrexia
   2. Hyperthyroidism

In patients with right to left shunt the increase in oxygen content is restricted to the fraction of oxygen dissolved in plasma. This fraction can be increased from 3 ml per blood when breathing air, to 20 ml per blood when breathing 100% oxygen.

Methods

I. **Administration by nasal tube:** A flow of 4 liters/min. is aimed which will produce 33% oxygen in alveolar air as compared to 14% oxygen during normal breathing. A 20 cu ft cylinder will last over 2 hours. Since oxygen makes mucous membranes dry it is best given moist and warm with the help of a Wolfe's bottle.

The disadvantages are:
   1. Nasal catheters are irritating
   2. Catheter may be blocked by mucus
   3. High oxygen concentration cannot be obtained

II. **Administration by mask:** Oxygen can be administered by a B.L.B apparatus, which consists of three parts:
   1. Rubber face mask and head-band
   2. Metal connecting device with air-regulating mechanism with the help of three ports and expiratory valve
   3. A rebreathing rubber bag (730-800ml): If a high concentration of oxygen is needed all

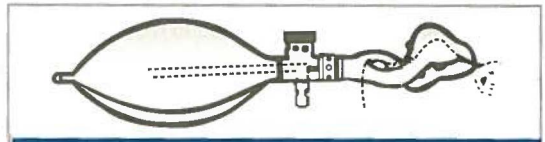


Fig. 11.7: BLB apparatus

the ports are closed and the flow of oxygen is adjusted so that the bag does not empty completely before the end of inspiration. If lower concentration suffices one or more port may be kept open so that the patient breathes partly from the bag and partly through the atmosphere. A fine adjustment valve regulates the flow of oxygen.

III. **Administration by tent:** Oxygen tents are more comfortable and efficient than nasal administration. It is of value in those patients who are restless or disoriented and interfere with mask and catheters. It is useful to treat severe shock, pneumonia and collapse.

Humidification

Techniques of oxygen administration should take into consideration the fact that the oxygen is completely dry and if administered without adequate humidification, will take up moisture from the mucosa of the respiratory tract with which it comes into contact. This may lead to drying, crusting and inspissation of secretions within the respiratory tract. Dried secretions may block the airways leading to atelectasis, ventilation-perfusion disturbances and provides a nidus for infection.

Techniques

1. Bubble humidifier: Oxygen is moistened by bubbling it through a large quantity of water.
2. Blower humidifier (Temperature of saturated air is 37°C).
3. Nebulizer: It suspends water droplets (1-10 mm in diameter) in air. Larger droplets are useless as they are deposited within the delivery tube.
4. Saline drip through tracheostomy tube at 10-12 drops/min.

Complications of Oxygen Therapy

1. Respiratory depression
2. Circulatory depression by stopping excess sympathetic activity
3. Drying secretions
4. On the lungs:
   a. Alveolar and interalveolar edema
   b. Atelectasis
   c. Fall of compliance
   d. Paradoxically fall in PaO_2
5. Retrolental fibrosis.

18 › Enema

Definition : Enemas are liquid preparations that are injected into the rectum.

Types

1. *Evacuant enemas* are intended to be returned
2. *Retention enemas* are intended to be retained

Table 11.5 : Types of Enemas

Evacuant	*Retention*
1. Warm water	1. Starch opium
2. Enema saponis	2. Normal saline
3. Glycerine	3. Astringent
4. Olive oil	4. Drugs-Chloral hydrate paraldehyde
5. Castoroil	5. Nutrient
6. Turpentine	6. Magnesium sulphate
	7. Barium

Evacuant Enemas

A. **Warm water** at 37°C is injected into rectum.

B. **Enema saponis** is made by dissolving 15 ml of green soap in 500 cc of warm water at 37°C. At least 5 mins should be taken in injecting it. It is used to empty the lower bowel in constipation and in preoperative preparations of patients. It is sometimes helpful in urinary retention. It has now replaced by Dulcolax suppositories.

C. **Glycerine:** 2-4 drachms of glycerine is mixed with equal volume of water and given rectally. It acts by irritating the wall of the rectum.

D. **Olive oil:** 5-10 ft oz of olive oil warmed at 37°C is given to soften the hard scybala. It should be followed by soap and water enema in 2-3 hrs.

E. **Castor oil:** 1-2 ft oz of castor oil is well mixed with 2-4 fl oz of olive oil and given slowly. It should be retained for 2-3 hours and followed by soap and water enema. It is used in severe constipation with impacted feces.

F. **Turpentine:** Oil of turpentine 1/2 fl oz is mixed with starch or soap and water enema (15 fl oz for and adult). There must be no floating globules. Petroleum jelly should be smeared around the anus to prevent irritation. It is useful in postoperative distension and in distension following enteric fever.

Dangers

1. Ulceration of the rectum
2. It may get absorbed and damage the kidneys.

Retention Enemas

A. **Starch opium enema:** This is prepared by taking 3 gm of starch and making a smooth paste with cold water is added (about 2 fl oz). To this 10-40 minims of opium is added and heated to 37° C. It is injected by glass syringe or catheter rubber tubing, and syringe barrel. It is given for relief of pain or to treat excessive diarrhea.

B. **Normal saline enema:** This is sometimes given to counteract shock or dehydration. Patient can absorb up to 2-3 liters of fluids in 24 hours and the danger of I.V. infusion is avoided. N/5 normal saline is used.

C. **Astringent enema:** It is ordered in sydentary and ulcerative conditions of rectum and colon. It is injected very gently and the patient is encouraged to retain it as long as possible. The amount is gradually increased up to 1-2 $^{1}/_{2}$ liters. Silver nitrate in distilled water (1:5000 increased to 1:500 tannicacid (3%) or alum (3%) maybe used. The patient lies on the back with hips raised. A morphine or cocaine suppository may be given earlier.

D. **Medicinal enema:** Chloral hydrate, paraldehyde and some antibiotics may be given rectally. Initially bowel is cleared with an evacuant enema. After 1 hour medicinal enema is given. A pad of cotton wool is pressed on the anus when the tube is removed to assist retention.

E. **Barium enema:** A low residue diet is given for three days preceding the examination. Two bowel washes are given, one on the previous evening and the other in the morning on the day of the examination. Rectum must be evacuated thoroughly till the returning fluid is clear; as fecal residues in the colon and rectum may simulate new growths during the X-ray examination. Two Dulcolax suppositories 1 hour prior to the procedure may be used instead. Two lbs of barium sulphate mixed with mucilage of tragacanth is diluted with two liters of hot water to bring the mixture of 37°C. This is injected slowly into the rectum by a rubber catheter and funnel. The column of fluid is watched by intermittent screening and radiographs are taken later. The flow of barium can be regulated by a control clip. At the end of the examination of contents of the lower bowel can be siphoned off into the pail.

F. **Nutrient enema:** Predigested food can be given rectally as rectum can absorb fluids.

G. **Magnesium sulphate:** Epsom salts 1-2 oz is dissolved in 4-8 fl oz of boiling water and cooled. It is used to reduce raised intracranial pressure by osmotically drawing fluid into the gut. It should be given slowly and retained as long as possible.

Procedure

Position: The patient is brought on the right side of the bed and turned to his left side with knees bent up. The foot end of the bed may be raised to ensure that the fluid may travel to the cecum.

Procedure: The temperature of the solution is tested and the tip of the catheter lubricated. Some of the solution is allowed to run through the apparatus to remove it. The catheter is nipped and the left forefingers placed on the anus, the catheter is placed for 8-10 cm into the rectum. The can is then raised about a foot above the level of the patient and at least 5 min are taken to give the enema.

After giving the enema, the tube is withdrawn and the patient is covered. Premature return of enema can be prevented by pressing a folded towel against the anus or holding the buttocks together. The bedpan is placed under the patient when he asks for it.

The result of the enema should be noted-whether the fluid has been returned clear, colored or accompanied by a stool, and whether distension, if present, is relieved.

After use, the rectal tube should be flushed throughly with cold water, washed with warm soapy water to remove the lubricant and boiled for 5 minutes.

19 › Parenteral Hyperalimentation

In a critically ill patient, increased metabolic demands leads to negative nitrogen balance, if the increased calories and proteins demands are not met with. Parenteral hyperalimentation is a therapeutic method of providing these to the critically ill patient. The usual 500 ml of 5% dextrose solution only provides 25 gm of glucose and 100 calories. Even if 3 liters of such fluid is given only 600 calories would be provided, whereas the minimum requirement would be 1400 calories. Hence parenteral solution should be so composed as to provide at least 1500 calories per day.

Composition of Fluid

The fluid for hyperalimentation should contain energy containing substrates like carbohydrates and fat, nitrogenous source (amino acids), electrolytes, minerals, vitamins, trace elements and water.

Glucose is the most physiological, cheapest and least toxic energy substrate. However, 5% glucose solutions would be inadequate and concentrated glucose solutions are hyperosmolar and cause irritation and thrombosis when injected in the peripheral vein. Hence, concentrated glucose is administered only into the central jugular vein or superior vena cava via a catheter.

A mixture of all essential and non-essential amino acids in appropriate proportion must be given to promote protein synthesis and achieve positive nitrogen balance. The calorie-nitrogen ratio is 150 calories to 1 gm nitrogen. The ratio of essential and non-essential amino acids is 2 : 3. It is given as casein hydrolysate or a mixture of crystalline synthetic amino acids.

Intravenous fats are as effective as glucose in sparing proteins and providing positive nitrogen balance. It has low osmolality and provides essential fatty acids, phosphate and concentrated source of energy. It can be given as 10% Safflower oil or 10% soya bean oil (Liposyn; Intralipid). A 1 : 1 mixture of glucose and lipids curtails the problems related to infusion of larger amount of glucose as well as lowers plasma fatty acids concentration.

About 2-3 liters of fluids are required daily. Sodium and chloride are required to maintain osmolality and acid base balance. Potassium, magnesium and phosphates are required for nitrogen retention and tissue formation. Calcium prevents demineralization of bones and tetany. Vitamins and trace elements like zinc, copper, chromium, selenium and iodides also must be infused.

Indications

I. **Disturbed gastro-intestinal continuity**
   1. Fistula - Pancreatic, biliary or entero-cutaneous
   2. Short bowel syndrome - Extensive intestinal resection, intestinal obstruction.

II. **Disturbed function of gastro-intestinal tract**
   1. Malabsorption Syndrome
   2. Inflammatory and Granulomatous lesion - Ulcerative colitis, regional enteritis, diverticulitis, etc.

III. **Malnutrition:** When more than 10% of his usual weight is lost coupled with inability to eat or absorb food.

IV. **Hypermetabolic states**
   1. Stress
   2. Sepsis
   3. Extensive burns

V. **Miscellaneous**
   1. Adjuvant to chemotherapy and radiation.
   2. Acute pancreatitis, hepatic failure, cardiac failure, acute renal failure.
   3. Anorexia nervosa.
   4. Prolonged coma.
   5. Patients undergoing gastrointestinal surgery.

NB: Parenteral hyperalimentation is not indicated in patients who are able to eat or can obtain adequate nutrition through nasogastric tube.

Patient Monitoring

During parenteral hyperalimentation the patient should be carefully monitored as follows:

1. Vital signs: Temperature, Pulse, Respiration and blood pressure.
2. Intake and output charts and weight.

3. Intravenous tube should be changed daily. Catheter dressing should be changed with all aseptic precautions on alternate days.
4. Blood sugar, urea, electrolytes, creatinine, acid-base status, blood count, prothrombin time, calcium, phosphorus, magnesium and iron must be estimated at regular intervals.

Complications

I. Metabolic

1. Hyperglycemia and glycosuria
2. Hyperosmolar hyperglycemic non-ketotic dehydration
3. Rebound hypoglycemia
4. Hyperchloremic acidosis, hyperammonemia and pre-renal azotemia
5. Essential fatty acid deficiency, fatty liver, cholestasis
6. Hypokalemia, hypophosphatemia, hypercalcemia

II. Mechnical due to central venous catheterization

1. Superior vena cava thrombosis
2. Pneumothorax or hemothorax.
3. Respiratory distress.
4. Air embolism

III. Sepsis

Hematology 12

1 › Blood Collection

Blood for hematological investigations can be collected either from a peripheral vein, an artery or capillaries.

Venous blood is preferred for most hematological investigations. *Capillary blood* can be nearly as accurate as venous blood if a free flow of blood is obtained and there is no dilutional error due to tissue fluids. However, it is used only in infants under 1 year or when it is not possible to collect venous blood.

Peripheral Venous Blood

1. The upper part of the arm is constricted by applying a tourniquet to hinder the venous return without obstructing the radial pulse.
2. The forearm area is cleaned with spirit (70% ethanol) and the patient is asked to clench the fist to make the veins prominent. The median cubital vein is most commonly used.
3. The vein is fixed by slight traction and the needle (20 or 21G) with the bevel upwards is inserted at an angle of 15^0 to the skin. The needle hub is colored according to its gauge (e.g. pink: 18G, yellow: 20G, green: 21G, black: 22G)

   A scalp vein needle ("butterfly" needle or "Winged Infusion Set") is sometimes used for infants and for patients with small veins or veins that may have a tendency to collapse.
4. Blood will flow into the syringe when the needle enters the vein correctly. The clenched fist is released.
5. After collecting the required quantity of blood, the tourniquet is released and the needle is quickly withdrawn. Pressure is applied with cotton wool over the puncture site for 3-5 mins.
6. Blood is transferred to the appropriate containers and the last few drops put on slides for preparing direct peripheral smears.

Complications of Venepuncture

Syncope, hematoma, bleeding (if bleeding disorder present), thrombophlebitis, thrombosis of vein, transmission of hepatitis/AIDS (if contaminated needles or syringes used).

Capillary Blood

1. The site selected is usually the fingertip or earlobe in adults or the big toe or heel in infants.
2. The selected site is massaged or warmed and cleaned with spirit or alcohol.
3. The skin is air dried because if it remains wet, blood will run all over and not collect into a drop. Residual alcohol can also cause hemolysis.
4. The skin is raised into a ridge. The sterile lancet or blade is plunged to a depth of 2-3mm with the index finger and then released. The blade should cut transversely to the axis of the finger.
5. From the wound large drops of blood should exude spontaneously. If the flow of blood is not spontaneous, pressure should be exerted on the skin in an outward direction to open the wound more widely. Squeezing should be avoided as it stops the flow and also adds tissue fluid to the blood, making cell counts inaccurate.
6. The first two drops are wiped off (since they contain excess tissue fluid) and when a sufficiently large drop has again accumulated, it is used for filling the required capillary tube or pipette.
7. Direct smears can be made from drops collected onto slides.

8. When all the required blood has been collected the finger should be cleaned with a cotton swab and pressure applied until bleeding stops.

Arterial Blood

Only arterial blood accurately reflects the amount of pO_2 transferred from the lungs. Arterial blood gases consist of three tests (pO_2, pCO_2 and pH) and provide useful information about the respiratory status and the acid base balance of patients with pulmonary (lung) disease and other critically ill patients.

Sites for collection

1. Radial artery (most convenient)
2. Brachial artery
3. Femoral artery (largest of the three)

2 › Preparation of Blood

I. Blood Smear

Preparation (slide method)

1. A drop of venous or capillary blood (direct smear) or EDTA-anticoagulated blood (indirect smear) is placed about 1 or 2 cm from one end of a pre cleaned slide. A greasy slide should not be used (it causes uneven smear preparation).
2. Immediately, another slide with a smooth edge (spreader) is placed at an angle of 25⁰ to 30⁰ and moved backwards to make contact with the drop. A spreader with a ragged edge should not be used since it causes neutrophils to collect at the tail end of the smear ("tailing") and inaccurate differential counts.
3. The drop of blood should spread out along the line of contact of the spreader with the slide.
4. The blood film is then spread by a rapid, smooth, forward movement of the spreader until all the blood has spread or the edge of the slide is reached. The ideal thickness for the smear is such that there is some overlap of red cells throughout majority of the length of the smear with separation and no distortion towards the tail of the film. A thick smear, required for detecting malarial parasites and microfilaria, should be of such a thickness that printed matter can just be seen through the smear.

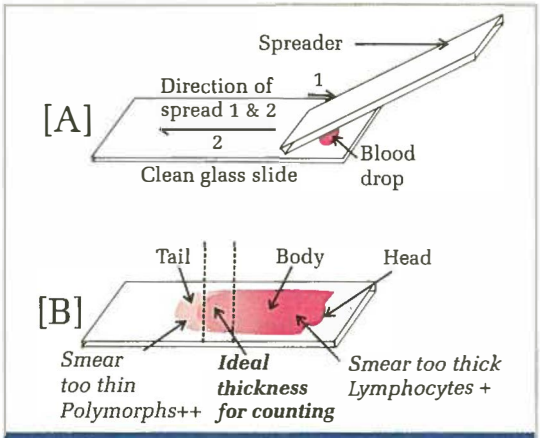


Fig. 12.1: (A) Preparation of peripheral smear; (B) A well-made smear

Fixing

The air-dried blood smear is fixed by covering the film with acetone-free methyl alcohol for 1 minute. This denatures proteins. It is required to prevent hemolysis of the RBCs when they come in contact with water in which some stains are dissolved, e.g. Giemsa's stain.

Methanol in a Coplin jar (4-6 dips of the slide) can also be used as a fixative.

Fixation is not separately required for Leishman's or Wright's stain as it is carried out simultaneously whilst staining.

Staining

Romanowsky dyes are used for staining blood films. They are made up of a combination of acid and basic dyes. Methylene blue or toluidine blue is used as the basic stain, whereas eosin or Azure B is used as the acid stain. The nucleus and the neutrophil granules are basophilic and stain blue. Hemoglobin is acidophilic and stains red.

Various modifications available are Leishman's, Wright's, Giemsa's and Jenner's stains. The pH is very critical in all the stains.

Composition of Leishman's stain

Leishman powder 1.5 g dissolved in 1 liter of methanol

Wright's or Leishman's staining

1. The slide is covered with the stain for 5 minutes taking care not to allow it to dry.
2. The stain is then diluted with an equal volume of buffered water (mixing the two by blowing on it through a pipette) and allowed to further act for 10 minutes.
3. The slide is then flooded with a stream of running tap water. Stain should never be poured off because a precipitate of stain will be deposited on the slide.
4. The slide is allowed to dry in a slanting position.

Giemsa's staining

1. The blood film is fixed with acetone-free methyl alcohol for 1 min and dried.
2. Giemsa's stain (1:10 dilution) is poured over the slide and kept for 20 minutes or longer.
3. The stain is washed off with distilled or tap water.
4. The slide is allowed to dry.

Thick Smear staining (Field's Stain)

This is a quick method for staining thick smears for malarial parasites.

1. The smear is allowed to air-dry for 30 minutes.
2. It is then immersed in a jar of polychromed methylene blue stain for 3 seconds. The slide is then immersed in tap water and gently shaken.
3. The slide is dipped in eosin stain for 3 seconds, washed in tap water and allowed to dry.

Buffy Coat Preparation

This is used to study the morphology of WBCs, platelets or abnormal cells after concentrating them. To detect LE cells for the diagnosis of SLE, blood is defibrinated using glass beads and then a buffy coat is prepared.

Method

1. EDTA anticoagulated blood or defibrinated blood is filled in Wintrobe's tube and centrifuged at 3000 rpm for 10 mins.
2. The topmost serum/plasma layer is discarded.
3. The next layer, above the packed red cell

Table 12.1 : Blood Preparations Required for Hematological Investigations

I. Blood smear
   1. Red cell examination
   2. Differential leucocyte count (DLC) & morphology
   3. Platelet count (Indirect method) & morphology
   4. Identification of blood parasites.

II. Anticoagulated blood
   1. Hemoglobin estimation
   2. Erythrocyte sedimentation rate (ESR)
   3. Hematocrit examination
   4. Sickle cell examination
   5. Hemoglobin electrophoresis
   6. Fetal hemoglobin determination
   7. Blood grouping, Rh typing
   8. Direct Coomb's test
   9. Osmotic fragility tests
   10. Coagulation studies
   11. Arterial blood gases
   12. Blood smear preparation (indirect smear)
   13. Reticulocyte count

III. Diluted blood
   1. Red (blood) cell count
   2. White (blood) cell count
   3. Eosinophil count
   4. Hemoglobin estimation
   5. Platelet count

IV. Plasma
   1. Coagulation studies
   2. Confirmation of hemoglobinemia (e.g. in PNH)

V. Serum
   1. Biochemical studies, Blood chemistry.
   2. Serological studies
   3. Electrolyte estimation
   4. Electrophoresis of proteins, immunoglobulins, lipoproteins
   5. Indirect Coomb's test
   6. Blood banking

VI. Cell suspension
   1. Serological tests
   2. Blood banking

VII. Whole blood (no preparation)
   1. Hemoglobin determination
   2. Osmotic fragility test
   3. Clotting time, Clot retraction
   4. Microbiological studies (sterile)
   5. Blood sugar estimation using glucometer
   6. Blood smear preparation (direct smear)

layer, contains the WBCs and platelets, is carefully pipetted onto slides (Fig 12.2).

4. This buffy coat is spread on a slide to make a smear.
5. The slides are air-dried and stained as above.

II. Anticoagulated Blood

A number of anticoagulants are available for various investigations.

1. **EDTA:** (Ethylenediamine tetra-acetic acid): It is used as disodium or dipotassium salt 1.2 mg per ml of blood. Dipotassium EDTA is more soluble than sodium EDTA and is therefore preferred for ***cell counters*** and other investigations. It is the most powerful calcium-chelating agent and gives the best preservation of ***cell morphology***. ***Smears*** can be made up to 3 hours after blood collection. Platelet clumping is inhibited so it is preferred for ***platelet counts***.
2. **Citrate:** It is used as a 0.106 M trisodium citrate dihydrate solution (3.2%); hence it dilutes the cellular elements and is not useful for cells counts. It is useful for ***coagulation studies and Westergren ESR*** estimations. In the former, 1 part of citrate to 9 parts of blood is taken, whereas in the latter, 1 part of citrate to 4 parts of blood is taken. It acts by binding calcium in a soluble unionized complex.
4. **Heparin:** It inhibits all the steps of coagulation reversibly; hence its effect slowly disappears as heparin is neutralized or metabolized. It is used in the concentration of 15 ± 2.5 IU per ml of blood and used for ***osmotic fragility tests, electrolyte estimation, immuno-phenotyping and arterial blood gases.***
5. **Double Oxalate:** Potassium oxalate causes shrinkage of the red cells whereas ammonium oxalate causes swelling. To balance these two effects, a mixture of the two in the ratio of 3 parts of ammonium oxalate to 2 parts of potassium oxalate is used at a concentration of 2 mg/ml of blood. Oxalate prevents clotting by binding calcium to form an insoluble salt. WBC morphology is not well preserved because the neutrophils often phagocytose the precipitated calcium oxalate.
6. **ACD solution** (Acid Citrate Dextrose Solution) is used in ***blood banking***.
7. ***CPDA solution*** (Citrate phosphate dextrose adenine solution) is used in ***blood banking***.
8. ***Sodium fluoride-potassium oxalate*** combination is used for ***plasma glucose*** determination. Fluoride inhibits glycolytic enzymes and prevents lowering of glucose. Oxalate acts as an anticoagulant.

III. Diluted Blood

Visual counting of red cells, white cells, eosinophils, reticulocytes and platelets require dilution of the anticoagulated blood using an appropriate pipette. Colorimetric estimation of hemoglobin also requires diluted blood.

IV. Plasma

1. The collected blood is transferred to test tube containing the specified type and quantity of **anticoagulant**.
2. The blood and anticoagulant are mixed by inverting the test tube several times.
3. The blood is centrifuged at 2000-3000 rpm for 10 mins.
4. The supernatant plasma is transferred to another test tube and stored on ice till tested.

Table 12.2 : Differences between Plasma and Serum

	Plasma	*Serum*
Blood Used	Unclotted blood	Clotted blood
Anticoagulant during collection	Added	Not added
Fibrinogen	Present	Absent
Clotting Factors	Present (except calcium)	Absent
Uses	Coagulation studies Confirmation of hemoglobinemia (e.g. in PNH)	Biochemical studies Blood chemistries Serological studies Electrolyte studies Electrophoresis of proteins, Igs, lipoproteins

V. Serum

1. The collected blood is transferred to a **plain glass or plastic test tube** and allowed to clot undisturbed for 1-2 hrs at 37° C.
2. If the clot has not completely retracted, it is gently detached from the walls of the test tube by means of a toothpick or an applicator stick or a sealed Pasteur pipette.
3. The tube containing the clotted blood is then centrifuged at 2000-3000 rpm for 10 mins.
4. The supernatant serum is carefully removed with a pipette and stored at 4°C till tested.

VI. Cell Suspension

1. A few drops of fresh anticoagulated blood or capillary blood is mixed with about 4 ml of physiological saline.
2. If washed red cell suspension is required, the red cell are washed 4 times in five times their volume of physiological saline with high-speed centrifugation between each wash. After the final wash, the red cells are suspended in saline to give a 10% suspension and used within 2 hrs.

3 Hemoglobin Estimation

The hemoglobin (Hb) content in a blood sample may be determined by measurement of its color, its power of combining with oxygen or carbon monoxide or by its iron content. The clinical methods for routine purposes are all based on color or light intensity matching techniques.

I. Sahli's Method (Acid-hematin)

Principle

Hemoglobin (Hb) is converted to acid hematin vby addition of **0.1 N hydrochloric acid** (HCI) and the resulting brown color is compared with standard brown glass reference blocks.

Method

1. 0.1 N HCI is placed in the special graduated tube to the 20% mark.
2. Capillary or EDTA blood is drawn up to the 20ml mark in the Sahli pipette. The blood is added to the acid in the tube, the pipette rinsed thoroughly and mixture is stirred well.
3. The mixture is allowed to stand for 10 min. for complete conversion to acid hematin.
4. The solution is diluted with a few drops of distilled water at a time, until the color matches with the standard glass reference block of the comparator of Sahli's hemoglobinometer. Natural light is used as a background.
5. The height of the solution in the graduated tube corresponds to the Hb content (Hb% or Hb g%) (100% Hb= 14.5 g/dl Hb)

Sources of Error

1. Visual error in color matching.
2. All hemoglobins are not converted to acid hematin by HCl acid, and therefore lower values.
3. Color is not stable and becomes lighter after 1 hour.

II. Cyanmethemoglobin Method

Principle

Hb, methemoglobin, carboxyhemoglobin (but not sulphemoglobin) are converted to cyanmet-hemoglobin when blood is diluted in a solution containing potassium cyanide and potassium ferricyanide. The absorbance of the solution is then measured in a photoelectric colorimeter at a wavelength of 540 mm or with a yellow-green filter.

Method

1. 20µl of blood are added to 5 ml of **Drabkin's** cyanide - ferricyanide **solution** and mixed well.
2. After 10 mins, the absorbance of the solution is read against a reagent blank (or distilled water) at 540 mm which is adjusted to an OD of 0.
3. A standard curve (or standard table) is prepared using cyanmethemoglobin graded dilutions of a reference solution of known concentration and using the same colorimeter. A straight line is obtained and Beer's Law is followed when absorbance (OD) is plotted against Hb conc.

4. The Hb value of the test sample can be then read on the standard graph/table.

Composition of Drabkin's solution

Potassium ferricyanide	200 mg
Potassium cyanide	50 mg
Potassium dihydrogen phosphate (anyhdrous)	140 mg
Nonidet-P40 or Sterox-SE	1 ml
Distilled water to	1 litre

pH 7.0 - 7.4; store at room temperature in a brown bottle. OD at 540 nm with DW blank should be zero.

Advantages

1. More accurate since visual matching is avoided
2. Certified standards of cyanmethemoglobin used
3. Hb, methemoglobin, carboxyhemoglobin (but not sulphemoglobin) are converted to cyanmet-hemoglobin by Drabkin's solution.
4. Cyanmethemoglobin is stable with time.

Sources of Error

1. Abnormal plasma proteins or a high leucocyte count may give erroneously high Hb content due to turbidity. The latter can be avoided by centrifuging the diluted sample. Abnormal plasma proteins can be solubilised by addition of a detergent e.g. Nonidet P40.
2. Technical errors in sampling, pipetting, calibration, etc.

III. Electronic Counters **(Refer Pg. 514)**

IV. Haldane's Carboxyhemoglobin Method

Hemoglobin is converted to carboxyhemoglobin (which is bright red in color), by exposing it to carbon monoxide (CO). It is a relatively accurate method but CO is dangerous.

V. Oxyhemoglobin Method

Hemoglobin is converted to oxyhemoglobin by mixing blood with a dilute solution of sodium carbonate or ammonium hydroxide. The intensity of color obtained is measured colorimetrically. It is a fast and accurate method.

VI. Alkali-hematin Method

Hemoglobin, methemoglobin, carboxy-hemoglobin and sulphemoglobin are converted to alkaline hematin by addition of sodium hydroxide - a strong alkali. It forms a true solution and the brown color can be read against comparable standards or in a colorimeter. Fetal hemoglobin and Hb-Barts are alkali-resistant, but can be converted by heating in a boiling water bath for 4 mins or by collecting the blood first into acid and then adding alkali (acid-alkali method).

NORMAL HEMOGLOBIN
Males: 13.0 - 17.0 g/dl
Females: 11.5 - 15.0 g/dl

4 › Packed Cell Volume (PCV)

PCV or hematocrit value is the volume of packed red cells in a given sample of blood expressed as a percentage or fraction of the total blood volume.

I. Wintrobe's Method

1. EDTA or oxalated blood is filled in Wintrobe's tube (Fig. 12.2) up to the 100 mm mark using a thin and long Pasteur pipette starting from the bottom and gradually withdrawing the pipette as the blood is expressed. This prevents formation of air-bubbles in Wintrobe's tube.
2. The tube is centrifuged at 2300 g (3000 rpm) for 30 minutes.
3. Three layers can be seen:
   a) The lowermost layer of packed red cells (PCV). The height of this is recorded as PCV. The "10" mark represents 100% PCV.
   b) The middle layer of WBC and platelets (buffy coat).
   c) The uppermost layer of plasma.

Significance

1. PCV is increased or decreased concomitantly with red cell count or hemoglobin.

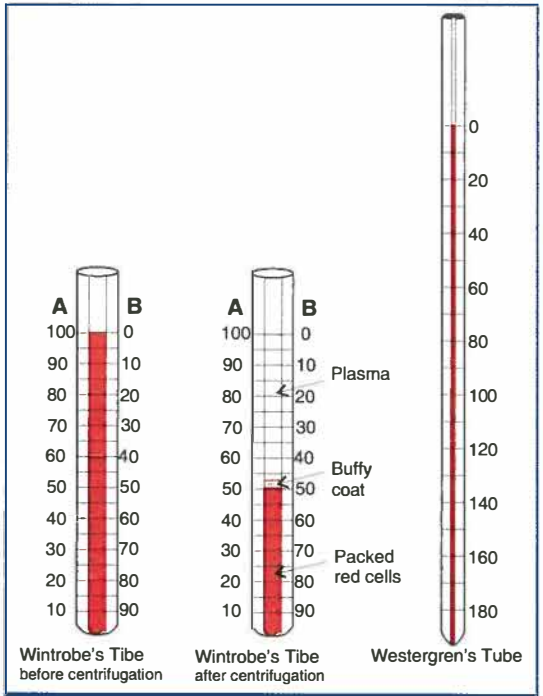


Fig. 12.2: Wintrobe's Tube: 110 mm long with 3 mm internal bore. Calibrated for PCV (A) and ESR (B). Westergren's Tube: 300 mm long with 2.55 mm internal bore. Calibrated for ESR

2. The buffy coat may be increased if platelets or leucocytes are increased.
3. The upper layer of plasma which is normally clear and straw-coloured, may be milky due to lipemia, yellow due to jaundice or reddish due to hemolysis/hemoglobinemia.

II. Microhematocrit Method

Two thirds of the capillary tube is filled with anticoagulated capillary or venous blood and the other end sealed with plasticine. The tubes are centrifuged at 12,000 g in a special centrifuge for 5 minutes. The hematocrit values are read by using special microhematocrit card readers.

Advantages

1. Capillary blood can be used.
2. Time taken for centrifugation is much less.
3. Smaller amount of blood is needed.

Sources of error

1. *Technical errors* due to improper mixing of blood, use of hemolysed sample, incorrect anticoagulant concentration, poor sealing causing leakage, etc.
2. Sample more than 6 hours old.
3. Error in reading, centrifugation speed and time, specimen mix up.

III. Electronic Counters

This can calculate the PCV from the mean red cell volume (MCV) and red cell count. The PCV obtained is usually 1.5 to 3% lower than the microhematocrit value since errors due to trapped plasma and inadequate oxygenation are eliminated.

NORMAL PACKED CELL VOLUME
Males: 40 - 52%
Females: 36 - 48%

5 Erythrocyte Sedimentation Rate (ESR)

When anticoagulated blood is allowed to stand undisturbed in a vertical tube, the red cells tend to fall to the bottom forming two layers - the lower red cell layer and the upper plasma layer. This occurs in three stages.

1. *Stage of aggregation:* The red cells form rouleaux. This is the most important stage and factors which affect this stage markedly alter sedimentation rate.
2. *Stage of sedimentation:* The larger the aggregates formed in stage 1, the faster the rate of fall.
3. *Stage of packing:* The individual cells and aggregates slow down due to crowding.

Methods

There are two common methods of measuring ESR. Westergren's method is more sensitive and accurate. Wintrobe's method uses smaller volumes of blood and the same tube can be centrifuged later for PCV and buffy coat.

Wintrobe's Method

1. Blood is drawn by venepuncture and then collected in a dry bulb containing Wintrobe's oxalate mixture.
2. After mixing with oxalate, blood is transferred

to the Wintrobe's tube with a Pasteur pipette up to mark 'O'.

3. The tube is placed vertically in its stand and the time is noted.
4. At the end of 1 hour, the reading corresponding to the top of the red cell layer (in mm) is the ESR.

Westergren's Method

1. 2 ml of blood is added into a tube containing 0.3 ml sodium citrate solution.
2. Blood is drawn into the Westergren's tube up to '0' mark.
3. The tube is placed vertically in a special stand in which a spring clip on the top firmly holds the tube against the rubber at the lower end.
4. At the end of 1 hour, the reading corresponding to the top of the red cell layer is noted in mm. This measurement is ESR. (Westergren 1 hr).

NORMAL ESR (using Wintrobe's Method)
Males: 0 - 7 mm/hour
Females: 0 - 14 mm/hour

NORMAL ESR (using Westergren's Method)
Males: 0 - 10 mm/hour
Females: 0 - 20 mm/hour

Factors Influencing ESR

1. *Plasma:* RBCs carry a negative electric charge, whereas plasma carries a positive charge. Any condition in plasma that increases its positive charge increases rouleaux formation and increases ESR by lengthening stage I. Fibrinogen, globulin and cholesterol accelerate whilst albumin retards sedimentation. Hence, ESR is increased in any condition that increases fibrinogen (tissue break-down as in infection and tuberculosis) or globulin (rheumatic fever, multiple myeloma and kala azar).
2. *RBCs:* Increase in blood counts as in polycythemia decreases ESR due to the jostling (or pushing one another) effect on the cells. Low blood counts in anemia tend to increase the ESR. However, altered shape of the RBC as in sickle cell anemia and microcytes in hypochromic anemia tend to prevent rouleaux formation and decrease ESR.
3. *Physiological variation:* ESR is low in infants, increases up to puberty, then decreases up to old age when again it increases. It is greater in women than men. It increases after the third month of pregnancy and returns to normal by about third week postpartum.

Causes of Increased ESR

1. Physiological: Pregnancy, menstruation, old age, females
2. Anemia
3. Infectious diseases: TB (maximum in miliary TB)
4. Inflammatory conditions, cell destruction, toxemia: Rheumatic fever, rheumatoid arthritis, SLE, ankylosing spondylitis, nephrosis.
5. Myocardial infarction
6. Shock
7. Post-operative states
8. Malignancies
9. Hypergammaglobulinemia : AIHA, multiple myeloma, Waldenstrom's macroglobulinemia

Causes of Decreased ESR

1. Physiological: Newborns due to polycythemia, males
2. Polycythemia
3. Congenital spherocytosis
4. Sickle cell disease
5. Hypofibrinogenemia
6. Allergic states

Significance of ESR

1. Changes in ESR indicates presence and *intensity of an inflammatory process*, they are not diagnostic of any specific condition.
2. ESR has *prognostic value*. Elevated ESR (as in rheumatic fever or tuberculosis), if returns to normal suggests improvement in clinical course.
3. *Extreme elevation of ESR* is seen in malignancies, hematological diseases (e.g. myeloma), renal diseases (e.g. azotemia), collagen diseases (e.g. RA, SLE, polymyalgia rheumatica), severe

infections (e.g. osteomyelitis, subacute bacterial endocarditis) drug fever, cirrhosis, etc.

Sources of Error

1. *Technical Errors:* Tilting of ESR tube, longer length of tube, high room temperatures and longer time increase ESR.
2. *Sample:* Anticoagulant concentration, clotted or hemolysed blood sample.
3. *Equipment:* Clean ESR tubes are essential.

6 Reticulocyte Count

Reticulocytes are juvenile red blood cells released into the blood stream from the bone marrow. They circulate for about 24 hours before maturing into erythrocytes. Reticulocytes are slightly larger than mature RBCs and contain a network of granular or filamentous reticulum which stains blue with **supravital staining** (i.e. staining of living cells). The reticulum contains ribosomal RNA from remnants of Golgi apparatus, mitochondria and other cytoplasmic organelles. Reticulocytes stain polychromatic with Romanowsky stains.

Reticulocyte Stain

Brilliant cresyl blue (or new methylene blue)	1.0 g (stains reticulum)
Sodium citrate	0.4 g (anticoagulant)
0.85% Sodium chloride	100 ml (iso-osmolality)

Method

1. Two drops of EDTA blood are added to two drops of just-filtered reticulocyte stain in a test tube.
2. This is mixed and incubated at 37° C for 30 mins.
3. A thin smear is made, air-dried and examined using the oil immersion objective.
4. Atleast 1000 RBCs (which stain pale blue) are counted and the number of reticulocytes (showing deep blue or purple reticulin precipitate or granules) is simultaneously counted.

$$\text{Reticulocyte count(\%)} = \frac{\text{No. of reticulocytes X 100}}{\text{No. of RBCs counted}}$$

Absolute Reticulocyte Count
= Reticulocyte count (%) X RBC count

Corrected Reticulocyte Count
(for patients with severe anemia)

$$= \frac{\text{Patient's Hb X Reticulocyte count (\%)}}{\text{Normal Hb value for that age}}$$

Significance

1. Diagnosis of bone marrow depression and ineffective erythropoiesis (reticulocytes decreased).
2. Therapeutic response to iron, folate or vitamin B12 therapy indicated by increase in retic count. The retic count increases by the 6th/7th day, indicating response to the specific therapy.
3. Response to erythropoietin can be monitored.
4. Response after bone marrow transplant can be monitored.
5. In alpha thalassemia, HbH inclusions stain with supravital stain.
6. Heinz bodies are seen in unstable hemoglobin disease, G6PD deficiency and on exposure to oxidant drugs or chemicals.

NORMAL RETICULOCYTE COUNT
Adults: 0.5 - 2.5 %
Cord blood: 2.0 - 5.0 %

Increased Reticulocyte Count (Reticulocytosis)

1. Effective erythropoietic activity, increased RBC production or recovery after blood loss.
2. Therapeutic response to iron for iron deficiency anemia or to folate/vitamin B12 therapy for megaloblastic anemia.
3. Hemolytic anemias, hemolytic crisis

Decreased Reticulocyte Count

1. Ineffective erythropoietic activity, decreased RBC production.
2. Megaloblastic anemia, Fanconi's anemia, pure red cell aplasia, aplastic anemia
3. Severe autoimmune type of hemolytic disease
4. Alcoholism
5. Myxedema

7 › Osmotic Fragility of RBCs

Osmotic fragility is an index of resistance offered by red blood cells to hemolysis.

When RBCs are placed in 0.85% saline, there is no change in the water content of RBCs. If the salt concentration is increased, water passes out of the red cells which become crenated. If the salt concentration is reduced, water enters the red cells which then hemolyse.

Method

1. Heparinized or defibrinated blood is used for the test (Additional salt in oxalated or citrated blood alters the toxicity, hence they are avoided).
2. 12 test tubes are taken. Each is filled with 5 ml of different concentrations of sodium chloride (0.80, 0.75, 0.65, 0.55, 0.50, 0.45, 0.40, 0.35, 0.30, 0.20, 0.1 and 0.0 per cent) solutions, pH 7.4.
3. To each test tube 0.5 ml of well-aerated blood is added, mixed and allowed to stand for 30 minutes at room temperature.

NORMAL OSMOTIC FRAGILITY OF RED CELLS

- Hemolysis begins at about 0.50% and is complete at 0.30% concentration (at RT for 30 mins).
- Mean Corpuscular Fragility (MCF) is 0.45% or slightly lower.

4. The amount of hemolysis in each tube is noted in a photoelectric colorimeter with a green filter (540 nm). The supernatant fluid from 0.80% (Tube 1) is used as a blank as there is no hemolysis and that for 0.0% (Tube 12) is used as 100% hemolysis.

$$\text{Percent hemolysis} = \frac{\text{O.D. of individual tube} \times 100}{\text{O.D. of tube with 100\% hemolysis}}$$

5. A fragility curve is drawn by plotting percent hemolysis on the Y-axis and concentration of sodium chloride on the X-axis.
6. The mean corpuscular fragility (MCF) is the concentration of NaCl which causes 50% hemolysis.

Significance

1. Spherocytes which are spherical in shape are unable to swell further, hence they are highly fragile and osmotic fragility is increased. Hemolysis may start at 0.75% and be completed at 0.40%. MCF is 0.5% or higher.
2. Target cells of thalassemia as well as hypochromic cells of iron deficiency anemia are relatively flat, and can swell a lot before rupturing. Hence fragility is decreased to below 0.30%. MCF is 0.35 to 0.40%.

8 › Total Red Cell Count

The RBC count is done with the improved Neubauer's chamber, a coverslip and an RBC pipette.

The Neubauer's chamber has two ruled stages separated by a small gutter. Each chamber has a large ruled area of 9 sq mm on each chamber stage. The center square, which is used for RBC counting, is divided into 25 squares, each of which is further divided into 16 squares.

The pipette has three marks, 0.5, 1.0 and 101. It contains a red glass bead inside to facilitate mixing of the blood and diluent.

RBC diluting fluid

Composition of Hayem's fluid:

Sodium chloride: 0.5 g (provides isotonicity)

Sodium sulphate: 2.5 g (anticoagulant)

Mercuric chloride: 0.25 g (preservative)

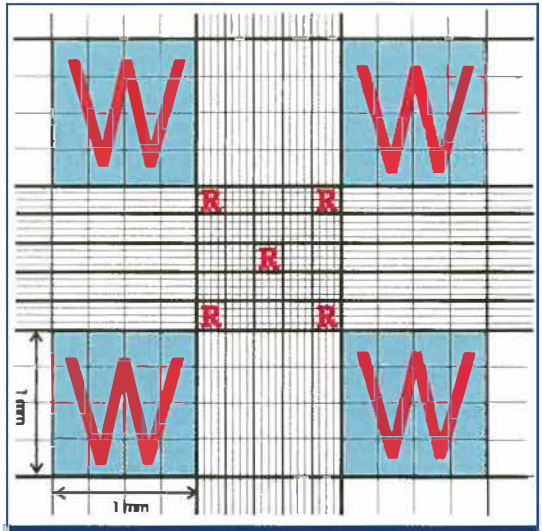


Fig. 12.3: Neubauer's chamber (improved): Blue areas (W): white cell count and red areas (R): RBC count

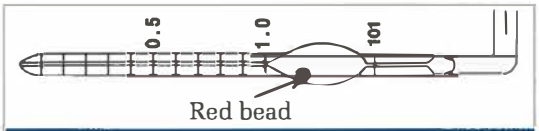


Fig. 12.4: RBC Pipette

Distilled water to 100 ml

Composition of Dacie's fluid:

Sodium citrate: 3.0 g (anticoagulant and isotonicity)

Formalin: 1 ml (fixative and preservative)

Distilled water to 100 ml.

Method

1. Capillary or EDTA blood is drawn into the pipette exactly up to the 0.5 mark.
2. RBC diluting fluid is then drawn up to the mark 101 (the blood has been diluted 1:200).
3. Fluid in the bulb is mixed by rapidly rotating the pipette between the fingers. The first few drops from the stem of the pipette are discarded because they have not completely mixed with blood.
4. The Neubauer chamber with the cover slip is charged by holding the pipette slightly inclined and gently releasing the pressure to allow a small volume of fluid to flow down. This will be attracted under the coverslip by capillary action. It is important to avoid air bubbles under the coverslip and not to overrun the fluid into the gutters.
5. The cells are allowed to settle for 2-3 mins.
6. The ruling is at first brought into focus using the low-power objective. The central large square is brought into the field of vision and the high power objective is now used to count RBCs in five (the central and four corner) squares. Each of these is divided into 16 squares and thus 80 small squares are counted. Depth of fluid is 0.1 mm below the cover slip.

Calculation

Area of each square = 1/5 X 1/5 = 1/25 mm^2

Area of 5 squares = 5 X 1/25 = 1/5 mm^2

Depth of chamber = 1/10 mm

Volume of 5 squares = 1/10 X 1/5 = 1/50 cu mm

In 1/50 cu mm, number of RBCs counted = N

$\therefore$ In 1 cu mm, number of RBCs = N X 50

Dilution is 1:200

$\therefore$ Total no. of RBCs in 1 mm^3 of blood

= N X 50 X 200 = N X 10000 per mm^3

= N/100 millions/ml (or X 10^{12} /liter)

NORMAL RBC COUNT
Males: 4.5 - 6.5 x 10^{12} per litre
Females: 3.9 - 5.6 x 10^{12} per litre

Causes of Increased RBC Count

1. Physiological: In neonates, high altitude, after exercise
2. Hemoconcentration: e.g. Burns, dehydration
3. Polycythemia rubra vera
4. Secondary polycythemia due to:
   - high altitude hypoxia, heavy smoking
   - renal diseases
   - central cyanotic states e.g. chronic lung diseases or congenital cyanotic heart diseases
   - uterine fibromyomata
   - cerebellar hemangioblastoma

Causes of Decreased Red Cell Count

1. Physiological: Old age, pregnancy, hemodilution
2. Anemias
3. Leukemias

9 Total White Cell Count

Total WBC count or TLC (total leukocyte count) is done with Neubauer's chamber and WBC pipette. Since WBCs are present in much smaller numbers than RBCs the dilution required is much less.

A WBC pipette has three marks 0.5, 1.0 and 11. It contains a white glass bead inside to facilitate mixing of the blood and diluent.

WBC diluting fluid (Turk's fluid) composition

1. Glacial acetic acid 2.0 ml (hemolyses RBCs)

2. 1% gentian violet 1.0 ml (stains the WBC nuclei)
3. Distilled water to 100 ml

Method

1. Capillary or EDTA blood is drawn into the WBC pipette (with the white bead) up to the mark 0.5
2. WBC diluting fluid is then drawn up to the mark 11.
3. Fluid in the bulb is mixed by rapidly rotating the pipette between the fingers. The first few drops from the pipette are discarded.
4. The Neubauer chamber is charged as for the RBC count.
5. The cells are allowed to settle for 2-3 mins.
6. The ruling is brought into focus by using the low power objective. The cells in the four large corner squares (4 sq. mm) of the Neubauer-ruling are counted.

Calculation

Area of each square = 1 mm X 1 mm = 1 mm^2

Area of 4 squares = 4 mm^2

Depth of chamber = 1/10 mm

Volume of 4 squares = 1/10 X 4 = 4/10 cu mm

In 4/10 cu mm, number of WBCs counted = N

$\therefore$ In 1 cu mm, number of RBCs = N X 10/4

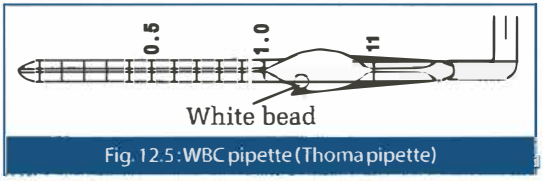


Fig. 12.5: WBC pipette (Thoma pipette)

Dilution is 1:20

$\therefore$ ***Total no. of WBCs in 1 mm^3 of blood***

= N X 10/4 X 20 = N X 50 per mm^3

= N/20 X 10 ^{9}/liter

NORMAL TLC: 4.0 - 11.0 X 10 ^{9}/litre

Corrected TLC for increased normoblasts

Normoblasts (nucleated RBC) do not get lysed by the diluting fluid. Hence, if the normoblast count is greater than 4 per 100 WBCs in the DLC, a correction is needed in the TLC.

Corrected TLC

$$= \frac{\text{Uncorrected TLC X 100}}{\text{100 + No. of normoblasts per 100 WBCs}}$$

Causes of Leucocytosis/Leucopenia

The most common cause is an increase/decrease in neutrophils.

Causes of Neutrophil Leucocytosis

(Neutrophils >11.0 x 10^9/L)

A. ***Physiological:*** Exercise, pregnancy, neonatal period, exposure to cold.

B. ***Drugs:*** Epinephrine, steroids, GCSF

C. ***Pathological:***
   1. Infection with pyogenic organisms
   2. Non-infective inflammations
   3. Vascular: Myocardial infarction, pulmonary embolism, acute hemorrhage
   4. Trauma and following surgery
   5. Toxic: Uremia, hepatic coma, chemicals
   6. CML, polycythemia vera, myelofibrosis
   7. Malignant neoplasms

Causes of Neutrophil Leucopenia

(Neutrophils <4.0 x 10^9/L)

1. ***Starvation and debility***
2. ***Overwhelming infections and toxemia*** in old people
3. ***Infections*** like typhoid, measles, malaria, kala-azar, hepatitis, influenza, etc.
4. ***Hypersplenism***
5. ***Bone marrow failure:*** aplastic anemia, leukemia, chemotherapy, megaloblastic anemia
5. ***Drugs:*** Sulphonamides, chlorpromazine, diuretics

Sources of Error in Counts using Neauber chamber

1. *Equipment errors:* Inaccurate pipette graduations or depth of ruled area of chamber, unclean chamber.
2. *Blood sampling errors:* Inadequate mixing of blood, blood clots in sample
3. *Technical errors:* Improper charging of chamber,

inadequate wiping of pipette, overflowing of chamber, contamination of diluting fluid.

4. *Field errors:* Unequal distribution of cells
5. *Calculation errors*

10 〉 Platelet Count

A peripheral smear prepared from EDTA anticoagulated blood helps to judge roughly whether adequate platelet are presents. Usually, if 2 to 10 platelets per 100 red cells or if clumps of platelets are present, it suggests that platelets are adequate. The size and morphology of the platelets can also be studied by peripheral smear examination. They are bluish spherical or oval structures, 2 - 4 microns in diameter. With Romanowsky's stain azure granules are seen in the hyaline, light blue cytoplasm; no nucleus is present.

Platelet counts can be made by visual counting or electronic counters. Accuracy in visual counting (direct or indirect method) is only achieved by scrupulous cleanliness during blood collection and preparation and by experience in differentiating platelets from extraneous matter. Phase contrast microscopy helps considerably in recognising and counting platelets.

Direct Method

1. 0.02 ml (20 ml) of EDTA anticoagulated blood is diluted and mixed with 2 ml of diluting fluid (same as RBC diluting fluid with 1-2 drops of 1% brilliant cresyl blue). Dilution is 1:100.

   Capillary blood and an RBC pipette can be used to prepare a dilution of 1:200.

   1% ammonium oxalate can also be used as a diluent in which red cells are lysed.
2. After 2 minutes an improved Neubauer's chamber is charged and placed under a petri dish with moist filter paper for 20 minutes. This allows the platelet to settle on the surface of the counting chamber. The moist filter paper keeps the air moist and prevents drying of the chamber.
3. Platelets appear as *highly refractile particles* under the high power lens. Platelets are counted in one square mm (central large square). At least 100 platelets must be counted.

Calculation

If N cells are counted in 1 sq. mm (0.1 µl volume) of 1:100 dilution of blood, then the platelet count per litre is:

$$= \frac{\text{No. of platelets counted X dilution X } 10^6}{\text{Volume (µl)}}$$

$= N \times 100 \times 10^6 / 0.1\ \mu l$

$= N \times 10^9$ (per litre)

Sources of Errors

1. Same as for RBC/WBC counts using Neubauer's chamber.
2. If platelet clumps are present, specimen should not be used.
3. Platelet count should roughly tally with the peripheral smear observation.

Indirect Method

1. A drop of 14% magnesium sulfate is placed on the fingertip and the finger is pricked through it to dilute the blood at once in order to prevent the clumping or disintegration of platelets.
2. With a drop, a thin smear is prepared and stained with Leishman's or Wright's stain.
3. With another drop of blood, the RBC count is done simultaneously.
4. On the smear 1000 RBCs are counted and the number of platelets seen whilst counting is noted.

Platelet count (per litre)

$$= \frac{\text{Number of platelet counted X red cell count}}{1000}$$

NORMAL PLATELET COUNT
150 - 450 X 10^9 per litre

Causes of the Thrombocytosis

1. During infections, at high altitudes, after severe muscular exercise
2. Immediately after surgery and following bleeding.
3. Iron deficiency anemia.
4. Chronic myeloid leukemia
5. Polycythemia vera
6. Myelofibrosis
7. Idiopathic thrombocytosis

Causes of Thrombocytopenia (TP)

A. **Congenital (rare):**
   1. Congenital aplastic anemia, congenital CMV or rubella infection
   2. TAR (thrombocytopenia with absent radii) syndrome
   3. Wiskott Aldrich syndrome

B. **Acquired:**
   1. **Aplastic anemia, megaloblastic anemia, viral infections, drugs** (e.g. sulphonamides, thiazides, NSAIDs), **chemotherapy, radiotherapy, myelodysplasia**
   2. **Immune Thrombocytopenia:** Autoimmune thrombocytopenia (AITP) or Drug-induced immune thrombocytopenia (e.g. heparin, quinine) caused by platelets being coated with antibodies & destroyed by macrophages. AITP includes:
      a) ***ITP:* Idiopathic thrombocytopenic purpura (acute/chronic)**
      b) *Secondary AITP* (chronic lymphocytic leukemia, lymphomas, solid tumors, HIV, chemo/radiotherapy, bone marrow transplant, SLE, Evan's syndrome)
      c) *Acute (post-viral) AITP* (e.g. malaria, HIV, EBV)
   3. **DIC (Thrombotic Thrombocytopenia (TTP), hemolytic uremic syndrome (HUS)**
   4. **Vasculitis** due to thrombosis in small vessels

11 › Electronic Cell Counters

The advent of electronic cell counters (hematological autoanalysers) has revolutionised the complete blood count (CBC). It has increased the accuracy, practicability and diagnostic value of red cell counts. In addition, most counters also determine white cell counts, hemoglobin concentration, hematocrit (PCV), red cell indices (MCV, MCH, MCHC) and platelet counts. More advanced counters offer DLC, red cell size distribution, platelet size distribution and abnormal cell information. Standardisation and strict quality control in all electronic counters is very important.

Visual counting is still used in some laboratories and as a reference method for calibration of electronic counters. The basic principles of electronic cell counters are based on one of the three principles:

1. **Electrical Impedance Principle (*Coulter Principle*)**: Blood is highly diluted with a particle-free buffered electrolyte solution and made to flow through an aperture tube of specific dimensions.

   A constant electric potential is maintained between an electrode in the sample container and one inside the aperture tube. Blood cells are poor conductors of electricity and when a cell displaces some of the conductive fluid in the aperture tube, the electrical resistance is increased. Each increase in resistance is read as a pulse, the amplitude of which is directly proportional to the cell volume. An amplitude discriminator selects the minimal pulse height to be counted.

   For leucocyte counts and hemoglobin estimation the red cells are lysed and Hb converted to cyanmethemoglobin.

2. **Optical Principle** (e.g. Technicon system): A diluted red cell suspension is allowed to flow through a cuvette in the form of an optical chamber, which is aligned to a dark field condenser. The impulses produced due to the light scattered by each cell, as it passes the focussed light, are converted into electrical impulses in a photomultiplier tube and then amplified and counted.

3. **Laser Principle** (e.g. Ortho system): A diluted red cell suspension is injected into a stream of buffered saline in which the cells flow in single file past a laser beam. A photovoltaic cell detects the light, which is scattered and diffracted by the cells. The pulses (whose magnitude is proportional to cell volume) are electronically accumulated and counted.

12 › Red Cell Indices

The mean corpuscular volumes (MCV), mean corpus-

cular Hb (MCH) and mean corpuscular Hb concentration (MCHC) are 'Absolute' values calculated from the results of Hb content, total red cell count and PCV and are used in the classification of anemias.

MCV : *Volume of the average erythrocyte (femtolitres)*

$$= \frac{\text{PCV (\%)} \times 10}{\text{Red cell count (x } 10^{12} \text{ per litre)}}$$

MCH : *Weight of Hb in the average erythrocyte (picograms)*

$$= \frac{\text{Hb (g/dl)}}{\text{Red cell count (x } 10^{12} \text{ per litre)}}$$

MCHC : *Hb concentration of the average erythrocyte (g/dl)*

$$= \frac{\text{Hb (g/dl)} \times 100}{\text{PCV (\%)}}$$

The initial diagnostic approach to hematological disorders is peripheral smear (PS) examination and blood cell counting. PS examination includes:

- Red cell morphology
- Differential leucocyte count (DLC)
- Platelet morphology and assessment of count
- Abnormal cells
- Parasites and microfilaria

NORMAL RED CELL INDICES
MCV 78 - 95 femtoliters (fl) or cu micron
MCH 27 - 32 picograms (pg) or mmg
MCHC 30 - 35 g/dl or %

13 Red Cell Morphology

An area of the blood smear where the cells are well separated is selected to study the morphology of the cells. The smear is therefore examined first under low to high power which helps to detect parasites like microfilaria and helps to select a suitable area for the study of red cell morphology. A drop of oil is then placed on the slide which is examined under the oil immersion lens (100 X)

A. Size

Normal RBCs

They are 6.0 to 8.5 microns in diameter and are called ***normocytes*** (Fig 12.6). They are roughly the size of the nucleus of small lymphocytes. Their biconcave shape gives an approximately one-third central pale area. MCV is 78-95 fl. Mature red cells have no nucleus.

Microcytes

These are smaller (less than 6 microns in diameter) cells which are found in iron deficiency anemia, various types of thalassemia, spherocytosis, severe anemia of chronic disease. MCV is less than 78 fl.

Macrocytes

These are larger cells (> 9 microns in diameter) which are found in megaloblastic anemias, liver disease, alcoholism, increased erythropoiesis (reticulo-cytosis), myelodysplasia. MCV is greater than 95 fl.

Anisocytosis

This refers to an increase in variation of red cell size. It is a common, non-specific abnormality in many hematological disorders. Anisocytosis may be due to microcytes, macrocytes or both being present.

B. Shape

Normal red cells are shaped like biconcave discs.

Poikilocytosis

Abnormal shaped red cells are called poikilocytes.

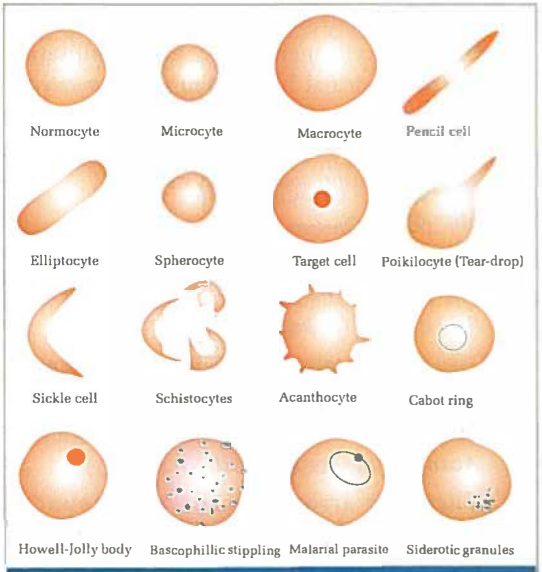


Fig. 12.6: Red cell morphology

Poikilocytosis is a non-specific abnormality in many hematological disorders. Marked poikilocytosis is found in myelofibrosis, dyserythropoietic anemias, extramedullary hemopoiesis.

Spherocytes

These are small spherical cells with no central pallor, found in hereditary spherocytosis, autoimmune hemolytic anemia, ABO hemolytic disease of the newborn, septicemia. Usually MCV is decreased and MCHC is increased.

Target cells (or codocytes)

These have a central round area stained pink around which is a colorless zone rimmed by a border of normal pink. They are found in thalassemia, sickle cell anemia, hypochromic anemia, following splenectomy or dehydration and in liver diseases.

Elliptocytes (or ovalocytes)

These are oval-shaped cells, found in large numbers in hereditary elliptocytosis. Macro-ovalocytes are seen in megaloblastic anemia.

Dacrocytes (or tear drop cells)

These are tear drop shaped cells, found in fibrosis, severe dyserythropoiesis, some hemolytic anemias.

Sickle cells (or drepanocytes)

These are sickle or crescent shaped cells found in sickle cell anemia due to crystallisation of the abnormal hemoglobins at low oxygen tension. These cells are best demonstrated by adding a drop of blood and then preparing a wet preparation sealed with vaseline.

Stomatocytes

These have a narrow slit-like central area and are found in stomatocytosis. They may be artefacts.

Schistocytes (or keratocytes)

These are irregular red cell fragments found in microangiopathic hemolytic anemias (e.g. DIC, HUS, TTP, burns, snake bite).

Acanthocytes (or spur cells)

These are irregular cells with rounded projections seen in uremia, liver disease, abetalipoproteinemia, chorea-like hereditary neuropathy, etc.

Echinocytes (or Burr cells or crenated cells)

These are ameba-shaped cells seen in uremia, liver disease or post-splenectomy. They are usually artefacts.

Rouleaux formation

Red cells look like a pile of coins. It is characteristic of hypergammaglobulinemia and if found, myeloma or macroglobulinemia is suspected. ESR is usually high.

C. Color

Normal red cells have a central one-third area of pallor.

Hypochromia is when this pale area is increased and suggests decreased hemoglobin concentration or abnormal thinness of the red cells e.g. in anemias, thalassemias, chronic infections, etc.

Hyperchromia is when cells appear without central pallor. This does not indicate increased hemoglobin concentration but suggests altered shape of the cell or altered thickness of the membrane (megaloblastic anemia, spherocytosis, neonatal blood).

Polychromatophilia is when the red cells stain blue. It indicates reticulocytosis.

Erythrocyte dimorphism is the presence of normal and hypochromic microcytic cells. It can occur in iron deficiency anemia responding to iron therapy, following blood transfusion or in sideroblastic anemia.

D. Inclusions

Basophilic stippling

These are small blue or black granules in red cells seen in thalassemia, aplastic anemia, lead poisoning, megaloblastic anemia, unstable hemoglobins, liver disease, infections, etc.

Howell-Jolly bodies

These are remnants of the nucleus seen as small, round, dark pink-purple particles near the periphery of the cell. They are found following splenectomy and in severe anemia.

Pappenheimer bodies

Siderocytes are RBCs with Pappenheimer bodies, which are siderotic purple round granules containing iron found at the periphery of red cells. They show blue-green iron granules on

iron staining with Prussian blue. They are found in sideroblastic anemia, thalassemia, etc.

Cabot ring

These are pale-staining nuclear remnants in the form of rings or figure of eight seen in hemolytic anemia, megaloblastic anemia, leukemias, post-splenectomy.

Heinz bodies

These are single inclusions containing residues of denatured Hb and stain only with supravital stains (e.g. cresyl violet). They are found in unstable Hb disease, G6PD deficiency, drug-induced hemolytic anemia, etc.

HbH inclusion bodies

These are found in alpha thalassemia demonstrated by the reticulocyte supravital staining.

Parasites

They may be present in the RBC (Malaria), WBC (leishmania) or outside the cells (filaria).

Nucleated Red Cells

(Normoblasts/erythroblasts)

These are present in the blood in:

1. Normal cord blood
2. Severe anemias (except aplastic anemia)
3. Hemolytic disease of newborn
4. Thalassemia major
5. Sickle cell disease
6. Leukemia
7. Myeloproliferative diseases
8. Post-splenectomy

Anemia refers to a decrease in hemoglobin and the total number of red blood cells as compared to the normal for that age and sex. Symptoms of anemia are pallor, weakness, fatigue, dysnea on exertion, headaches, angina, pica and menorrhagia, depending on the speed of onset, age and severity. Older patients may have tachycardia and sometimes congestive heart failure.

14 Anemias

Classification of anemias according to morphology

1. ***Hypochromic microcytic anemias***
   (MCV<80 fl, MCH<27 pg)
   a. Iron deficiency anemia
   b. Thalassemias, hemoglobinopathies
   c. Sideroblastic anemia
   d. Anemia of chronic disorders
   e. Lead poisoning
   f. Vitamin B6 deficiency
2. ***Normochromic normocytic anemias***
   (MCV 80-95 fl, MCH>26 pg)
   a. Anemia due to acute blood loss
   b. Hemolytic anemias
   c. Anemia due to bone marrow failure, renal disease, etc.
   d. Anemia of chronic disorders
3. ***Macrocytic anemias***
   (MCV>95 fl)
   a. **Megaloblastic anemia:** Vitamin B12 or folate deficiency
   b. **Non-megaloblastic anemias:** Liver disease, myelodysplasia, aplastic anemia, drug-induced anemia, hemolysis, hypothyroidism, alcoholism, etc.

Iron Deficiency Anemia

Iron deficiency anemia is the commonest cause of anemia. It is a microcytic hypochromic anemia.

Stages

1. *Negative Iron Balance:* Demand of iron increases above the ability to absorb iron. Hemoglobin, serum iron and TIBC are normal. serum ferritin is reduced.
2. *Iron Deficiency Erythropoiesis:* Iron stores are depleted. Hemoglobin is normal, serum iron is reduced, TIBC is increased, serum ferritin is reduced and protoporphyrin is increased.
3. *Iron Deficiency Anemia:* Hemoglobin also decreases (see Tables 12.3 and 12.4).

Causes

1. *Increased Requirement:* Infancy, pregnancy,

Table 12.3 : Basic Haematological Parameters in Various Red Cell Disorders

Disorder or Disease	Hemoglobin Level	RBC Count and RBC Morphology	WBC Count and Morphology	Platelet Count	Reticulocyte Count	Red Cell Indices
1. **NORMAL**	M: 13-17 g/dl F: 11.5-15.0 g/dl	M: 4.5-6.5 X 10^{12}/1 F: 3.8-5.6 X 10^{12}/1	4-11 X 10^9/1	150-400 X 10^9/1	0.5-2.5%	MCV 76-96 fl MCH 27-32 pg MCHC 30-35 g/dl
2. **Iron Deficiency Anemia**	Decreased	Decreased. Microcystosis, Hypochromia, anisocytosis, Target cells, poikilocytosis	Usually normal Marginal granulocytopenia	Usually increased	Normal or increased	MCV decreased MCH decreased MCHCdecreased
3. **Thalassemia Trait**	Slightly decreased	Increased. Microcytosis, Hypochromia, Antisocytosis, Target cells, Basophilic stippling	Usually normal	Normal	Normal or increased	MCV decreased MCH decreased MCHCdecreased
4. **Megaloblastic Anemia**	Decreased	Decreased. Macrocytosis macroovalocytosis, anisocytosis.Poikilocytosis, Polychromatophilia, teardrop cells, Nucleated red cells.	Normal todecreased. Normal to Hypersegmented neutrophils	Normal or Decreased	MCV increased decreased	MCH increased MCHC normal
5. **Hemolytic Anemia**	Decreased	Decreased. Normocytic, Polychromatophilia, Nucleated red cells, Spherocytes or sickle cells may be present	Increased. Shift to the left	Increased. Often abnormal in morphology	Greatly increased	All normal or decreased
6. **Aplastic Anemia**	Markedly decreased	Decreased. Normocytic or lightly macrocytic Normochromic	Decreased	Decreased	Decreased	All normal MCV sometimes decreased

lactation, chronic infections, chronic inflammatory diseases, chronic renal diseases,

2. *Blood Loss:*
   a. Reproductive System: Menorrhagia, repeated miscarriages, etc.
   b. GI Tract: Bleeding due to **hookworms,** oesophagitis, varices, hiatus hernia, peptic ulcer, hemorrhoids, carcinoma, etc.
   c. Nose: Epistaxis
   d. Hemostatic disorders: Hemophilia, von Willebrand's disease, platelet disorders
   e. Lungs: Hemoptysis
   f. Iatrogenic: Hemodialysis, phlebotomy for polycythemia
   g. Frequent blood donation
3. *Inadequate dietary intake*: Poor economic status, anorexia, elderly, vegans.
4. *Decreased iron absorption:* gastrectomy, achlorhydia, intestinal malabsorption, (sprue, Chrohn's disease)

Symptoms and Signs

1. Fatigue, bodyache, decreased excercise tolerance, palpitations
2. Pallor (Refer Pg. 22)
3. Koilonychia (Refer Pg. 30)
4. Cheilosis (fissuring of angles of mouth)
5. Inadequate growth in children
6. Symptoms and signs of etiology e.g. of chronic blood loss, worms in stool, etc.

Laboratory Investigations

These should be undertaken after a complete clinical history and physical examination is done.

Table 12.4 : Haematological Parameters in Various Red Cell Disorders

Disorder/ Disease	*Serum Iron*	*TIBC*	*Transferrin Saturation*	*Serum Ferritin*	*Other Hematological Tests*
1. **Normal**	35-140 µg/dl	245-400 µg/dl	20-60 %	Men: 30-350 ng/ml Women: 20-250 ng/ml	HbA_2 1.0 - 3.5% HbF < 1% Bone marrow iron present
2. **Iron Deficiency Anemia**	Decreased	Increased	<16%	Decreased (<15 ng/ml)	Hb electrophoresis normal Bone marrow iron stores absent
3. **Thalassemia Trait (α or β)**	Normal	Normal	Normal >15 ng/ml	Normal	HbA_2 > 3.5% in β thal trait Bone marrow iron present
4. **Thalassemia**	Increased major	Normal	Increased	May be normal at diagnosis. Increases later with transfusion	HbF >90% and HbA: Absent HbA_2 Variable Indirect bilirubin increased Bone marrow iron increased
5. **Sideroblastic Anemia**	Increased	Normal	Increased	Increased	Bone marrow iron present: Ring sideroblasts Hb electrophoresis normal
6. **Anemia of Chronic Disorders**	Decreased	Decreased	Normal	Normal or Increased	Hb electrophoresis normal Bone marrow iron reduced
7. **Megaloblastic Anemia**	Normal	Normal	Normal	Normal or increased	Serum B12 reduced (B12 deficiency) Serum folate reduced (folate deficiency) Bone marrow iron may be increased. Unconjugated bilirubin & LDH increased
8. **Hemolytic Anemia**	Normal	Normal	Normal	Normal	Increased unconjugated serum bilirubin, urinobilinogen, fecal stercobilinogen. Serum haptoglobins absent.

1. **Blood Picture**
   a. Hypochromic, microcytic red cells with pencil cells, tear-drop cells and occasional target cells.
   b. Platelet count increased or normal
   c. Red cell indices all decreased
   d. Red cell protoporphyrin is the intermediary in the pathway of heme synthesis. In iron deficiency it accumulates in the red cells and is >100 mg/cell (normal upto 30 mg/cell)
2. **Bone Marrow Picture**
   a. *Cellularity*: Normal
   b. *Erythropoiesis*: Sometimes erythroblasts are increased, small and have ragged cytoplasm.
   c. *Iron stores* by Perl's staining: Absent with no siderotic granules.
3. **Hematinic assays:** Serum iron, total iron binding capacity, serum ferritin (see Table 12.4)
4. Blood urea, electrolytes, liver function tests
5. Stools: Hookworm ova, occult blood
6. GI tract: Endoscopy and/or radiology
7. History of menorrhagia, repeated pregnancies, bleeding disorders, hematuria.

Treatment

1. *Treatment of the cause*
2. *Diet:* Green leafy vegetables (e.g. spinach), nuts, dates, custard apple, meat, liver
3. *Iron therapy:*
   a) Oral
   Preparations:
   Fe sulphate 200 mg (60 mg elemental): best absorbed
   Fe gluconate 300 mg(35 mg elemental): better tolerated)

Fe fumarate 200 mg (65 mg elemental): better tolerated)

Acidity of stomach, citric acid, etc. facilitate absorption and phytates, calcium, etc. retard absorption.

Requirement:

Upto 200-300 mg of elemental iron per day of which about 50 mg is absorbed.

Replacement:

Continue tablets for 6 months after anemia is treated to replenish stores (upto 0.5 - 1.0 g stores should be present)

Side effects:

Nausea, vomiting, abdominal pain, constipation, diarrrhoea, black stools.

Response:

Reticulocyte count increase by 4-7 days, peaks at 10 days and hemoglobin returns to normal

b) Parenteral:

Indications:

- Intolerance to oral iron
- Rapid replenishment of iron needed
- Ongoing blood needed
- Impaired iron absorption

Preparations:

For I.M. (stretch skin, insert needle deep IM, release skin and then inject to prevent discoloration of skin):

- Iron dextran (Imferon)
- Iron Sorbitol citrate (Jectofer)
- Ironcarbohydratecomplex(Uniferon)

For I.V. (in 5% dextrose or normal saline):

- Iron dextran (Imferon)
- Iron gluconate (Ferrlecit)

Dose calculation:

2.38 X body wt (kg) X 15 - Hb (g/dl) + 500 mg or 1000 mg for stores

Test dose 25 mg before injection is essential

Complications:

Anaphylaxis, injection abscess, discoloration of skin

4. *Blood transfusion:*

Transfusion of packed red cells can be given if there is excessive blood loss, congestive cardiac failure or immediate replenishment is required. Diuretics and antihistamines may be given simultaneously to prevent fluid overload and allergic reactions. Hemoglobin starts rising in three days.

Megaloblastic Anemia

Megaloblastic anemias are a group of anemias characterised by abnormalities in the peripheral blood and bone marrow - maturation of the nucleus is delayed compared to that of the cytoplasm - due to deficiency of vitamin B12 and/or folate.

Causes

1. *Vitamin B12 Deficiency*
   - a) Inadequate dietary intake
     - i) Vegetarian
     - ii) Malnutrition
   - b) Decreased absorption
     - i) Achlorhydria, atropic gastritis
     - ii) Partial gastrectomy
     - iii) Decreased production of intrinsic factor
       - Pernicious anemia
       - Total gastrectomy
     - iv) Disorders of terminal ileum
       - Tropical sprue
       - Non-tropical sprue
       - Intestinal resection
       - TB, other infections of terminal ileum
       - Fish tapeworm (D. latiem)
       - Selective B12 malabsorption (Imerslund Grasbeck syndrome)
     - v) Blind loop syndrome, strictures, divert
     - vi) Neoplasms
     - vii) Drugs: Colcicine, neomycin, nitrous oxide
   - c) Others
     - i) Enzyme deficiency e.g. methyl malonyl CoA mutase
     - ii) Transcobalamine II deficiency

2. *Folic Acid Defieciency*
   a) Inadequate intake
      i) Alcoholism
      ii) Malnutrition
      iii) Excessive cooking
   b) Inadequate absorption
      i) Tropical sprue
      ii) Non-tropical sprue
      iii) Drugs: Phenytoin, barbiturates, methotrexate, trimethoprim, ethanol, zidovudine, etc.
   c) Increased requirement
      Infancy, pregnancy, lactation, neoplasms
   d) Others
      i) Dihydrofolate reductase deficiency
      ii) Hemodialysis, hemolytic anemia
      iii) Alcoholism
3. *Other Causes*
   a) Impaired DNA metabolism due to drugs
      i) Purine antagonists: 6 mercaptopurine, azathioprim
      ii) Pyramidine antagonists: 5 fluorouracil, cytosine arabinoside, etc.
   b) Miscellaneous: Lesch Nyhan syndrome, Di Gugliemo's syndrome (AML M6), congenital dyserythropoetic anemia

Symptoms and Signs

1. *Symptoms of anemia*
   Fatigue, weakness, bodyache, vertigo, tinitus, palpitations, angina, pallor, icterus due to high erythroid turnover in marrow, systolic flow murmur, tachycardia
2. *Gastrointestinal*
   Smooth, beefy tongue, diarrhoea, anorexia, weight loss
3. *CNS*
   a) Subacute combined degeneration (demyelination, axonal degeneration and neuronal death of peripheral nerves, posterior and lateral columns, cerebellum)
      i) Parasthesia in ectremities
      ii) Loss of vibration in left limb, K.J. brisk, A.J. lost, plantars extensor
      iii) Dementia, irritability, psychosis, decreased mentation, geographical apraxia
      iv) Ataxia
4. *Others*
   a) Knuckle pigmentation
   b) Retinal hemorrhages

Laboratory Diagnosis

1. *Blood:* Hemoglobin decreased, macrocytosis, anisocytosis, poikilocytosis, ovalocytosis, low reticulocyte count, TLC and platelet count may be reduced. Occasional hypersegmented neutrophils present.
   Arneth Count: The number of neutrophils with more than 5 lobes are counted. In megaloblastic anemia they are >5% (Normal <1%)
   MCV inreased, MCH increased, MCHC normal or reduced.
2. *Bone Marrow Picture*
   a. *Cellularity*: Hypercellular, decreased M:E ratio.
   b. *Erythropoiesis*: Erythroid hyperplasia, *megaloblasts with fenestrated chromatin network* (nuclear maturation lags behind), nucleated RBC precursors, HJ bodies.
   c *Giant metamyelocytes* may be present.
   d. *Megakaryocytes*: Normal
   e. *Iron staining* shows increased number of iron granules but no ring sideroblasts.
3. *Biochemistry*
   A) Serum Vitamin B12 and Folate Levels
      a) Serum vitamin B12 is reduced in vitamin B12 deficiency (Normal range 160-925 ng/l, less than 100 ng/l is indicative)
      b) Serum folate is reduced in folate deficiency (Normal range 6.0-20.0 ng/ml, less than 4.0 ng/ml is significant).
      c) Red cell folate is reduced in folate deficiency (Normal range 160-640 mg/l). It may be normal or low in vitamin B12 deficiency.
      d) Serum bilirubin (unconjugated)

and serum LDH increased due to ineffective erythropoiesis

e) Serum methylmalonic acid and serum homocysteine levels are both raised in vitamin B12 deficiency and serum homocysteine level is raised in folate deficiency

f) Urinary formiminoglutamate (FIGLU) levels increased

4. *Schilling Test*

Absorption test which indirectly measures urinary exretion of B12 and detects intrinsic factor deficiency (pernicious anemia).

1. Patient is given radiolabelled B12 orally and one hour later unlabelled B12 is given IV (to saturate the tissue sites). If patient has normal intrinsic factor, then B12 will be absorbed and excreted in the urine. 24 hour urine exretion is normally 10% or more. In pernicious anemia or malabsorption syndrome, urinary excretion is < 10%.
2. The patient is then given B12 bound to intrinsic factor orally. The urinary excretion is measured. If it returns to normal, patient has pernicious anemia. If it remains <10%, patient has malabsorption syndrome (bacterial overgrowth or ileal disease).

5. *Microbiological Assay*

Sample to be assayed is added to a medium with all growth factors for a B12 dependant organism, *Euglena gracilis*. The growth of the organism is compared to a standard.

Lactobacillus sp., which requires 5 methy tetrahydrofolate (folic acid coenzyme), is used for folate deficiency testing.

Treatment

1. *Treatment of B12 deficiency*
   a) Diet: Non-vegetarian food, dairy products
   b) Replacement therapy: 1000 µg B12 I.M, once a week for 8 weeks -> 1000 µg B12 I.M, once a month for life.
2. *Treatment of Folic Acid deficiency*
   a) Diet: Green leafy vegetables, nuts, meat, liver
   b) Replacement therapy: 5 mg/day for 2-4 months
   c) Folinic acid 100-200 mg/day used in patients on treatment with methotrexate or trimethoprim.
3. *Treatment of Cause*

   e.g. folic acid 5-10 mg/day in pregnancy, antibiotics for blind loop syndrome, niclosamide 500 mg 3 tablets stat for D latum.
4. *Packed cell transfusion*

   Given in cases of severe anemia. (Whole blood transfusion causes circulatory overload)

Prognosis

Symptoms of anemia disappear in 2-3 days. Reticulocyte count increases by 4th day and peaks on 7th day. Peripheral neuropathy may improve in a few weeks. Neuronal damage does not improve.

Pernicious Anemia

Most common cause of Vitamin B12 deficiency is due to the absence of intrinsic factor (IF), due to atrophy of gastric mucosa or autoimmune destruction of parietal cells which produce the IF. Only B12 bound to IF is absorbed by terminal ileum.

It is more common above 60 yrs age and in children < 10 yrs (juvenile pernicious anemia)

It is associated with Graves disease, myxedema, Hashimoto's thyroiditis, vitilligo and has a higher incidence in relatives.

Clinical features are of B12 deficiency with increased incidence of gastric polyps and gastric cancer.

Diagnosis by anti-parietal antibody test (90%) and anti-intrinsic factor antibody test (60%). The latter is more specific.

Treatment is lifelong Vitamin B12 replacement therapy. Glucocorticoids may be helpful.

15 › Differential Leucocyte Count

A good peripheral blood smear is important to perform the differential leucocyte (white cell) count (DLC) and to study the morphology of normal and abnormal

leucocytes. It should be done under oil immersion after first scanning the smear under low or high power to detect the area where the cells are separated and can be seen with good details.

The different types of white cells present in the blood are counted and each type of cells counted (usually 100). Absolute counts can be calculated by multiplying by the total white cell count.

1. *Neutrophils:* Nucleus is divided into 2-5 lobes. Granules in the cytoplasm stain violet-pink with Romanowsky stains. Cell size 10-12 μ.

   Arneth Count is the number of cells per 100 WBCs with more than 5 lobes in the nucleus (hypersegmented neutrophil). Normal Arneth count <1%. In megaloblastic anemia it is >3%.

   Sex chromatin consists of a drumstick appendage (1.2-1.5 μ) attached to one of the nuclear lobes by a thin strand. Present in males <0.3% and females 3-6% of neutrophils.
2. *Eosinophils:* Nucleus has usually 2 lobes in a spectacle arrangement and the cytoplasm has large orange granules. Cell size 10-15 μ.
3. *Basophils:* The cell is slightly smaller than the above two. The nucleus is kidney shaped or lobulated and the cytoplasm has large, round, deep purple to black granules.
4. *Monocytes:* This is the largest cell, twice the size of a neutrophil. The nucleus is kidney shaped, stains pale violet and has a fine chromatin arrangement. The cytoplasm stains pale grayish blue and may contain vacuoles and fine pinkish blue granules. Cell size 14-20 μ.
5. *Lymphocytes:* These may be large (12-16 μ) or small (8-10 μ). Large lymphocytes have an indented nucleus with dense smudgy chromatin and abundant, pale blue cytoplasm. The small lymphocyte's nucleus is slightly indented & has no visible chromatin pattern. The cytoplasm is a scanty rim around the nucleus.

Leukocyte Abnormalities

Causes of Neutrophila (Neutrophil Leucocytosis)

(Neutrophils >7.5 x 10^9/L)

A. Physiological: Exercise, pregnancy, neonatal period, exposure to cold, stress.
B. Drugs: Epinephrine, corticosteroids, GCSF
C. Pathological:
   1. *Acute infections* with pyogenic organisms
   2. *Non-infective inflammations*
   3. *Vascular:* Myocardial infarction, pulmonary embolism, acute hemorrhage, hemolysis
   4. *Trauma and following surgery*
   5. *Toxic:* Uremia, hepatic coma, chemicals
   6. *Hematopoietic disorders:* chronic myeloid leukemia, polycythemia, myelofibrosis
   7. *Malignant neoplasms*

NORMAL RANGE OF DLC	
Neutrophils	40 - 80%
Lymphocytes	20 - 40%
Monocytes	2 - 10%
Eosinophils	1 - 6%
Basophils	0 - 2%

Toxic Granules

Dark staining, coarse, toxic granules (strongly peroxidase positive) are found in severe bacterial infections and some hereditary disorders.

Dohle Bodies

Small, pale blue or grey, round or oval structures (2-3 μ) in the cytoplasm are seen in bacterial infections, burns, May-Hegglin anomaly, exposure to cytotoxic drugs, etc.

Leukemoid Reaction

This is a *benign reactive leucocytosis* characterised by the presence of immature WBCs (*left shift*) in the peripheral blood of a person who does not have leukemia. Clinical features of the underlying cause are generally present and those of leukemia are absent. It is important to distinguish this from CML.

Causes of Myelocytic Leukemoid Reaction

1. *Severe or chronic infections:* Endocarditis, pneumonia, septicemia, leptospirosis, etc.
2. *Severe hemolysis or hemorrhage*
3. *Toxic:* Burns, eclampsia, mercury poisoning

4. *Malignant diseases:* Hodgkin's disease, multiple myeloma, myelofibrosis, bone metastases

Causes of Lymphoid Leukemoid Reaction

1. *Infections:* Infectious mononucleosis, infectious lymphocytosis, pertussis, chickenpox, TB, CMV infection, measles, etc.
2. *Malignant diseases:* Stomach or breast cancer
3. *Dermatitis herpetiformis*

Causes of Monocytic Leukemoid Reaction

1. *Infections:* TB
2. *Mediastinal teratoma*

Causes of Neutropenia

(Neutrophils <1.8 x 10^9/L)

1. *Starvation and debility*
2. *Overwhelming infections and toxemia* in old people
3. *Infections:* Typhoid, measles, malaria, kala-azar, hepatitis, influenza, HIV, miliary TB, etc.
4. *Hypersplenism, liver cirrhosis, SLE.*
5. *Bone marrow failure:* Aplastic anemia, leukemia, megaloblastic anemia, myelo-dysplasia, myelofibrosis.
6. *Drugs:* Sulphonamides, antibiotics, analgesics, bone marrow depressants, arsenicals, anti-thyroids, anticonvulsants, etc.
7. *Physical agents* (e.g. radiation) and *chemical agents* (e.g. benzene).
8. *Anaphylactic shock.*

Causes of Lymphocytosis

Absolute lymphocytosis

1. *Infections:* Tuberculosis, brucellosis, syphilis, pertussis, toxoplasmosis, mumps, rubella, infectious mononucleosis, infectious lymphocytosis, CMV infection, etc.
2. *Hematopoietic disorders:* CLL, other lymphoid leukemias, lymphosarcoma
3. *Drugs*

Relative lymphocytosis

1. All causes of *neutropenia* (relative)
2. *Convalescence from acute infections*
3. *Thyrotoxicosis*
4. *Infective hepatitis*
5. *Infants* with infections, malnutrition and avitaminosis

Viral Lymphocytes

These are transformed lymphocytes with a deep blue cytoplasm.

Infectious Mononucleosis

The diagnosis is suspected if sore throat, fever, lymph-adenopathy, splenomegaly and atypical lymphocytes (absolute count 10-20 X 10^9/L) with moderate lymphocytosis are present. The "reactive" lymphocytes which are present represent T-lymphocytes reacting to Epstein-Barr virus infected B cells. Paul-Bunnell test is positive.

Causes of Lymphopenia

1. *Severe bone marrow failure*
2. *Immunosuppressive therapy, chemotherapy, corticosteroid therapy.*
3. *Hodgkin's disease*
4. *Irradiation*
5. *Viral infection:* e.g. HIV
6. *Infections*

Causes of Monocytosis

1. *Infections:* TB, bacterial endocarditis, malaria, kala-azar, syphilis, typhus, rickettsial infections, viral infections.
2. *Convalescence from acute infection.*
3. *Hematopoietic disorders:* Acute monocytic (AML M5) or myelomonocytic leukemia (AML M4), chronic myelomonocytic leukemia (CMML), myelodysplastic syndrome (MDS)
4. *Hodgkin's disease, malignant neoplasms*
5. *Chronic inflammatory conditions:* RA, SLE, Crohn's disease, ulcerative colitis.

Causes of Basophil Leucocytosis

1. *Hematopoietic disorders:* Chronic myelogenous leukemia (CML) (Fig. 52), polycythemia vera,

myeloid metaplasia, Hodgkin's disease, post-splenectomy.

2. *Myxedema*
3. *Chickenpox, smallpox, ulcerative colitis*
3. *First sign of blast crisis* in CML.

Causes of Eosinophilia

1. *Allergic disorders:* Hay fever, urticaria, bronchial asthma, food sensitivity
2. *Drug hypersensitivity* to gold, sulphonamides, penicillin, nitrofurantoin, etc.
3. *Parasitic infections:* Trichinosis, Hookworm, hydatid cyst, amebiasis, filariasis, etc.
4. *Skin diseases:* Dermatitis herpetiformis, psoriasis, pemphigus, eczema, drug rash
5. *Collagen diseases:* Polyarteritis nodosa
6. *Hematopoietic disorders:* Hypereosinophilic syndrome, eosinophilic leukemia, Hodgkin's disease
7. *Tropical eosinophilia, Loffler' syndrome*
8. *Malignancies*

16 › Leukemias (Refer Pg. 202 and Tables 12.5 & 12.6)

17 › Parasites in Blood

Malaria (Refer Pg. 90)

Kala-azar (Refer Pg. 95)

Filarsasis

Wuchereria bancrofti (microfilariae) causes filariasis (elephantitis, lymphedema). The larvae of these worms are transmitted by mosquito to humans, where they can be demonstrated in blood (peripheral smear, thick blood smear, unstained wet preparations or blood concentration technique).

African trypanosomiasis (sleeping sickness) is caused by *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense.* American trypanosomiasis (Chagas' disease) is caused by *Trypanosoma cruzi.* Both can be demonstrated by examining wet preparations of

Table 12.5 : Cytochemical Stains used in Diagnosis of Acute Leukemias

Cytochemical Stain	*Specificity*	*Significance*
Myeloperoxidase/Sudan Black B	Stains primary and secondary granules in cytoplasm of cells of **neutrophil lineage**, eosinophil granules, monocyte granules, Auer rods. AML M0 blasts negative.	Myeloblast cytoplasm stains **positive in AML M1-M6.** Lymphoblasts and erythroblasts are negative. Useful to differentiate between AML and ALL.
Periodic Acid-Schiff (PAS)	**Lymphoblasts of ALL show coarse block positivity.** T-ALL blasts may be negative. Myeloblasts, monoblasts, megakaryoblasts, normal erythroblasts are negative or show diffuse or granular positivity.	Useful to differentiatie between AML and ALL. **Positive in ALL.** Strong, diffuse block PAS positivity in **erythroleukemia (AML M6).**
Acid Phosphatase	Variety of hemopoietic cells show diffuse acid phosphatase activity. **T-lineage blasts in acute and chronic leukemias show strong focal positivity.**	Diagnosis of **hairy cell leukemia** which show +veTRAP (tartarate resistant acid phosphatase) activity. **T-ALL & T-CLL show polar positivity & -ve TRAP**
Non-specific esterase (α–naphthyl acetate esterase)	**Monocytes** and macrophages, megakaryocytes and platelets, T-lymphocytes, T-lymphoblasts	Diagnosis of **AML M4 and M5**
Leukocyte (neutrophil) alkaline phosphatase (LAP/NAP score)	Cytoplasm of neutrophils. Specific secondary and tertiary granules give positive reaction.	Normal Range: 25-100 in adults **High Scores** in leukemoid reaction, **blast crisis in CML**, myelofibrosis, P. vera, ITP, Down's syndrome, pregnancy. Low Scores in PNH, chronic phase of CML, AML

Table 12. 6 : Basic Hematological Parameters in Peripheral Blood in Acute and Chronic Leukemias

Disorder	*Hemoglobin Level*	*RBC-Count and Morphology*	*WBC-Count and Morphology*	*Platelet Count*	*Reticulocyte Count*	*Red Cell Indices*
ACUTE MYELOID LEUKEMIA (AML)	Decreased Normochromic	Decreased. Normocytic, Anisocytosis. Nucleated red cells.	Increased, normal or low. Immature myeloid series, specially myeloblasts	Usually decreased	Normal or slightly increased	Normal
ACUTE LYMPHOCYTIC LEUKEMIA (ALL)	Decreased	Decreased. Normocytic, Normochromic	Increased, normal or low. Immature lymphocytic series, specially lymphoblasts	Usually decreased	Decreased	Normal
CHRONIC MYELOID LEUKEMIA (CML)	Decreased	Decreased. Normocytic, Normochromic, Anisocytosis. Nucleated red cells.	Markedly increased. All stages of neutrophilic series. Mostly segmented and band forms	Normal or increased	Normal or increased	Normal
CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)	Slightly decreased	Normal or decreased. Normocytic, Normochromic	Markedly increased. Usually small lymphocytic cells predominate. Few immature cells	Normal or decreased	Normal or decreased	Normal

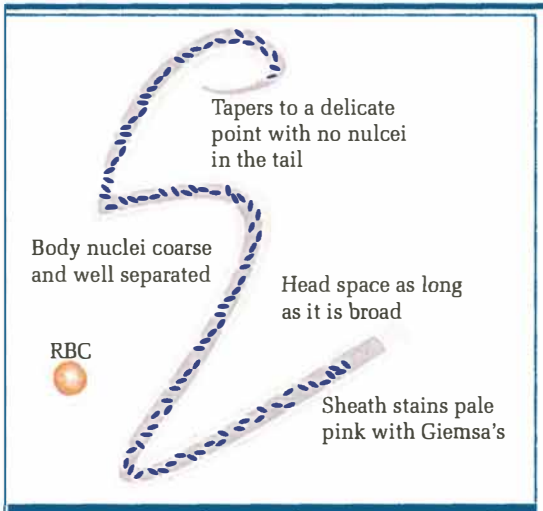


Fig. 12.7 : Wuchereria bancrofti 200-300 X 8-10 mm with RBC on left for comparison of size

blood or lymph node fluid. Thick-stained blood films or chancre aspirates can also be examined.

18 › Multiple Myeloma

Multiple myeloma is a malignant proliferation of plasma cells characterised by increased plasma cells (>15%) in the bone marrow, osteolytic bone lesions and the presence of paraproteins (monoclonal protein or M-protein) in the serum and/or urine.

Blood Picture and Serum Electrophoresis

1. Normochromic normocytic anemia with rouleaux formation and increased background staining due to increased globulin.
2. Neutropenia, thrombocytopenia in advanced disease.
3. Plasma cells may spill over into blood.
4. Serum globulin is increased, albumin is low.
5. ESR is markedly increased.
6. M-band (M-protein: IgG>70 g/l or IgA>50 g/l) seen on serum protein electrophoresis. Bence-Jones protein (free light chains) in urine found in 2/3rd of patients.
7. Serum calcium increased.
8. Blood urea, creatinine raised if renal damage present.

Bone Marrow Picture

1. Plasma cells constitute 15-20% of total cells.
2. Plasmacytoma may be found on biopsy.

19 › Coagulation Studies

The normal hemostatic response to blood vessel dam-

age depends on closely linked interactions between the blood vessel wall, circulating platelets and blood coagulation factors (Figs. 12.9 and 12.10 and Table 12.7). The fibrinolytic system and inhibitors of coagulation limit the coagulation to the site of injury (Table 12.8).

Defective hemostatic plug formation with spontaneous hemorrhage or abnormal bleeding following trauma or surgery may result from:

1. Thrombocytopenia
2. Platelet dysfunction
3. A deficiency or defect of coagulation factors
4. The presence of inhibitors (in the blood) to the action of coagulation factors.
5. Excessive fibrinolysis.
6. A combination of some of the above defects.

Table 12.7 : Plasm Clotting Factors

Factor	
I.	Fibrinogen
II.	Prothrombin
III.	Thromboplastin (tissue factor)
IV.	Calcium
V.	Proaccelerin (labile factor)
VII.	Proconvertin (stable factor)
VIII.	Antihemophilic factor (AHF) (VIII:C) von Willebrand Factor (vWF)
IX.	Christmas factor (plasma thromboplastin component)
X.	Stuart - Prower factor
XI.	Plasma thromboplastin antecedent
XII.	Hageman (contact) factor
XIII.	Fibrin-stabilising factor Prekallikrein (Fletcher factor) HMWK (High molecular weight Kininogen) (Fitzgerald factor)

Table 12.8 : Plasma Clotting Inhibitors

Protein C
Protein S
Tissue Factor Pathway Inhibitor (TFPI)
Antithrombin III
Heparin Cofactor II
α_2- microglobulin

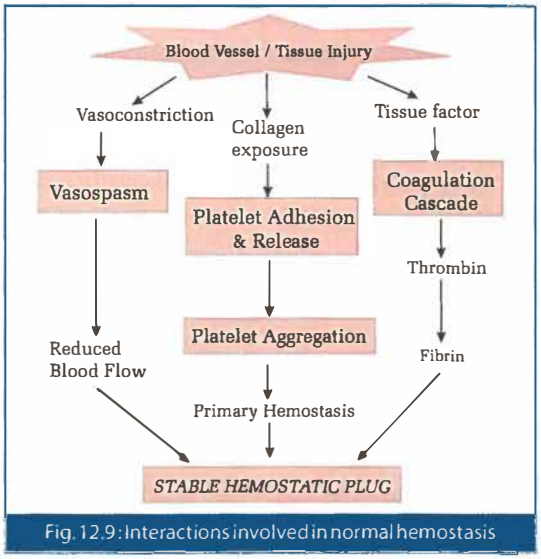


Fig. 12.9: Interactions involved in normal hemostasis

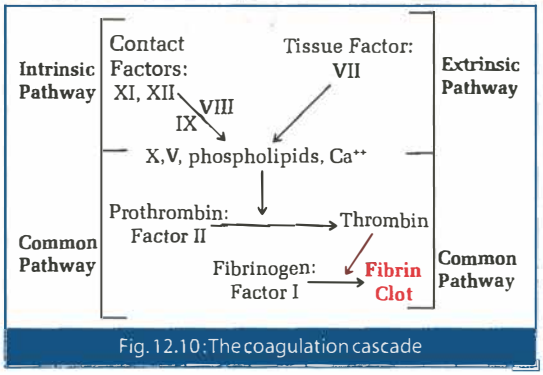


Fig. 12.10: The coagulation cascade

Laboratory Diagnosis

Screening Tests

These should be undertaken only after a full clinical assessment including family history. The results of these screening tests provide a presumptive diagnosis which can be confirmed with further tests. (Fig 12.11 and Table 12.10).

The tests and the normal ranges are given in Table 12.9.

Blood Collection

Blood collection is very critical as the test results are affected by many variables. Venous blood should be collected using a clean venepuncture in 3.8% sodium citrate. The ratio of plasma to anticoagulant is critical. PCV correction for severe anemia or polycythemia is

Table 12.9 : Screening Tests

	Test	Normal Range
1.	Platelet Count	150-400 X 10^9/litre
2.	Bleeding Time (Ivy's Method)	2-7 min
3.	Whole Blood Clotting Time	5-11 min
4.	Clot Retraction Test	Good ++
5.	Prothrombin Time (PT)	10-14 sec (INR 1.0)
6.	Activated Partial Thromboplastin Time (APTT)	30-40 sec
7.	Thrombin Time (TT)	12-16 sec
8.	Fibrinogen Level	200-400 mg/dl
9.	Factor XIII Urea Clot Solubility Test	Insoluble
10.	Tests for Fibrinolysis	
	FDP	< 10 ug/ml
	D-Dimer	< 500 units
11.	Ristocetin Aggregation Test (15mg/dl ristocetin)	Positive

essential and adequate anticoagulant should be added as per standard charts. History of warfarin, heparin, aspirin, etc. is essential.

Platelet Count

Accurate platelet counts are important for diagnosis of bleeding disorders(Refer Pg. 513). Direct peripheral smear examination is essential in patients with low counts to exclude pseudo-thrombocytopenia and to observe large platelets as in Bernard Soulier syndrome.

Bleeding Time (BT)

This test detects abnormal platelet function in vivo. It measures the time taken for a standardized skin wound to stop bleeding. Duke's, Ivy's, Template methods are used.

Duke's Method is not very accurate. It uses a finger prick method (Refer Pg. 501). A 5 mm deep puncture is made and the bleeding time is recorded as in steps 3 and 4 below.

Ivy's Method

1. A sphygmomanometer cuff is inflated over the patients' arm and maintained at 40 mm Hg throughout the test.
2. The volar surface of the foreman, devoid of superficial veins, is cleaned with 70% ethanol and allowed to dry. It is stretched and punctured up to 3 mm depth with a sterilised standard lancet.
3. Every 30 seconds, the blood adjacent to the wound is gently blotted with a filter paper until bleeding stops.
4. Bleeding time is recorded.

Note:

1. BT is falsely prolonged in patients with history of aspirin injestion within a week prior to the test.
2. In hemophilia A and B, delayed bleeding from the puncture site may be observed after 24 hours, even though bleeding time is normal.

Template Method is the same as above, but uses a template made of plastic with a 9 mm slit. The blade is introduced into the slit and an incision 1 mm deep is made.

Causes of Prolonged Bleeding time

1. Thrombocytopenia (Platelet count < 50 x10^9/L prolongs bleeding time)
2. Platelet Function Disorders
   a. Hereditary (von Willebrand's disease, Glanzmann's thrombasthenia, Bernard Soulier syndrome)
   b. Acquired:
      i) Drugs (aspirin, NSAIDs, anticoagulants, tricyclic antidepressants, high dose beta-lactams, phenothiazines, anesthetics, etc.)
      ii) Uremia
      iii) DIC, liver disease
      iv) Malignancy
      v) Waldenstrom's macroglobulinemia
3. Dysfibrinogenemia, afibrinogenemia
4. Vascular disorders

Capillary Fragility Test (Tourniquet Test/HESS"s Test)

This test indicates the degree of permeability of the capillary walls and any defect in them.

Method

1. A sphygmomanometer cuff is applied around the upper arm and inflated to pressure midway between systolic and diastolic blood pressure.
2. After 7 mins, if more than 20 purpuric spots (petechiae) apppear in an area of 3 cms in diameter, below the antecubital fossa, the test is positive.

Causes of Positive Capillary Fragility Test

Thrombocytopenia, platelet function disorders, vascular disorders, Glanzmann's thrombasthenia, scurvy.

Whole Blood Clotting Time (CT)

This is the time taken for whole blood drawn from a vein to clot in vitro. The surface of the glass tube initiates the clotting process. This test is sensitive to the factors involved in the **intrinsic pathway.**

Clotting time is prolonged in:

1. Deficiency of factor VIII, IX, XI or XII
2. Afibrinogenemia, dysfibrinogenemia, hypofibrinogenemia
3. Vitamin K deficiency
4. Deficiency of factor II, V or X, von Willebrand's disease may prolong clotting time.
5. Liver disease, warfarin therapy.

Note:

It is an insensitive method for screening abnormalities of coagulation as it is normal in nearly one-third of hemophilia patients. However, besides serving as a control over blood collection techniques, observation of the clot in these tubes after one hour and 24 hours gives insight into the platelet number and function and accelerated fibrinolysis respectively.

Lee and White Method

1. 1 ml of freshly collected is transferred directly from the syringe (without the needle) into two glass clotting tubes.
2. After 2 minutes the tubes are examined every 15 secs. by very gently tilting them.
3. Clotting time is noted when the tube can be completely inverted without fluid loss.
4. **Clot retraction and clot size** are also observed after one hour and 24 hours.

Prothrombin Time (PT)

This is the time taken for platelet-poor citrated plasma to clot after adding calcium and tissue (brain) thromboplastin. This is an important screening test for defects of the extrinsic and common coagulation pathways since the intrinsic pathway is bypassed by adding tissue factors and calcium.

PT is used to monitor oral anticoagulant therapy.

Normal PT is 10-14 secs.

Prothrombin time is prolonged in:

1. Congenital deficiencies of one or more of factors II, V, VII or X
2. Therapy with coumarin or inadanedione (anti coagulant) drugs.
3. Obstructive jaundice
4. Hemorrhagic disease of the newborn.
5. Liver disease
6. Fibrinogen deficiency
7. Vitamin K deficiency

Method

1. 0.1 ml brain extract is mixed with 0.1 ml plasma in a glass test-tube placed in a water bath at 37°C.
2. After 1 min. 0.1 ml of warm 0.1 M $CaCl_2$ is added to the above mixture and the stop watch is simultaneously started.
3. The end point is obtained by tilting the tube in a regular consistent manner and stopping the stopwatch the moment a clot appears.
4. The test must be performed in duplicates with test and control plasmas and the average values noted.

Partial Thromblastin Time PTT/APTT

(Kaolin Cephalin Clotting Time).

Platelet poor citrated plasma is preincubated with a surface activating agent (e.g. ellagic acid, particulate silicates or kaolin) and phospholipid prior to adding calcium. This test is used to detect defects of coagula-

tion in the intrinsic and common pathways. PTT is used to monitor heparin therapy.

It is known as partial PTT because platelet substitutes (which are partial thromboplastins), are used. They are not capable of activating the extrinsic pathway which requires complete tissue thromboplastin (tissue factor).

Normal PTT is 30-40 secs.

PTT is prolonged in:

1. Hemophilia A (Factor VIII: C deficiency)
2. Christmas disease (Hemophilia B) (Factor IX deficiency)
3. Von Willebrand's disease (Factor VIII: vWF deficiency)
4. Contact factor (XII) or factor XI deficiency
5. Heparin and oral anticoagulant therapy
6. Hepatic failure
7. Intravascular coagulation
8. Deficiencies in Factors II, V or X
9. Presence of acquired inhibitors e.g. in SLE

Method

1. Equal volumes of cephalin and kaolin are mixed. 0.1 ml of the mixture is added to 0.1 ml plasma and incubated at 37°C in a water bath for 5 mins.
2. 0.1 ml warm 0.025 M $CaCl_2$ solution is added and a second stopwatch started.
3. Clotting time is noted as for PT.
4. Duplicate test and control samples are simultaneously run and the values averaged and compared.

Mixing Tests

Prolonged clotting times in PT and PTT tests due to factors deficiency are corrected by the addition of normal plasma to the test plasma (mixing tests). If there is no partial correction, an inhibitor of coagulation is suspected.

Thrombin Time (TT)

In this test, thrombin is added to citrated plasma and the clotting time noted. This tests the conversion of fibrinogen to fibrin monomers by thrombin.

Prolonged TT is obtained in:

1. Hypofibrinogenemia.
2. Dysfibrinogenemia.
3. Heparin, fibrinogen or fibrin degradation products.
4. Chronic liver disease.
5. Multiple myeloma.
6. Intravascular coagulation.

Method

1. 0.1 ml diluted thrombin is added to 0.1 ml plasma diluted with 0.1 ml buffered saline at 37°C in a water bath. The clotting time is recorded.
2. Duplicate test and control samples should be tested simultaneously. The normal pool sample should give a clotting time of 15 - 20 secs.

Clot Solubility in Urea

Factor XIII cross links overlapping fibrin strands and make them resistant to solubilisation.

In this test, urea or monochloroacetic acid are added to the clot (plasma clotted with $CaCl_2$). If Factor XIII deficiency (<1%) is present, the clot will be soluble.

CONVERSION OF OLD UNITS TO NEW SI UNITS

	Old Units	*Multiplication by*	*New SI units*
Total Red cell count	Mill/ul	1	10^{12}/litre
Hemoglobin (Hb)	g/dl or g/100 ml	10	g/litre
Packed cell volume (PVC)	ml/100 ml (%)	0.01	litres/litre.(decimal fraction).
Mean cell volume (MCV)	Cubic micron	1	femtolitres (fl) *
Mean cell Hb (MCH)	Micromicrograms (μμg)	1	Picograms (pg) **
Mean cell Hb concentration (MCHC)	Per cent	10	g/litre
White cell count	per/ μl	0.001	(No. X 10^9/litre)
Platelet count	per/ μl	0.001	(No. X 10^9/litre)

*1 fl = 10^{-15} litre = 1 cu μ. **1pg = 10^{-12}g = 1 μμ g

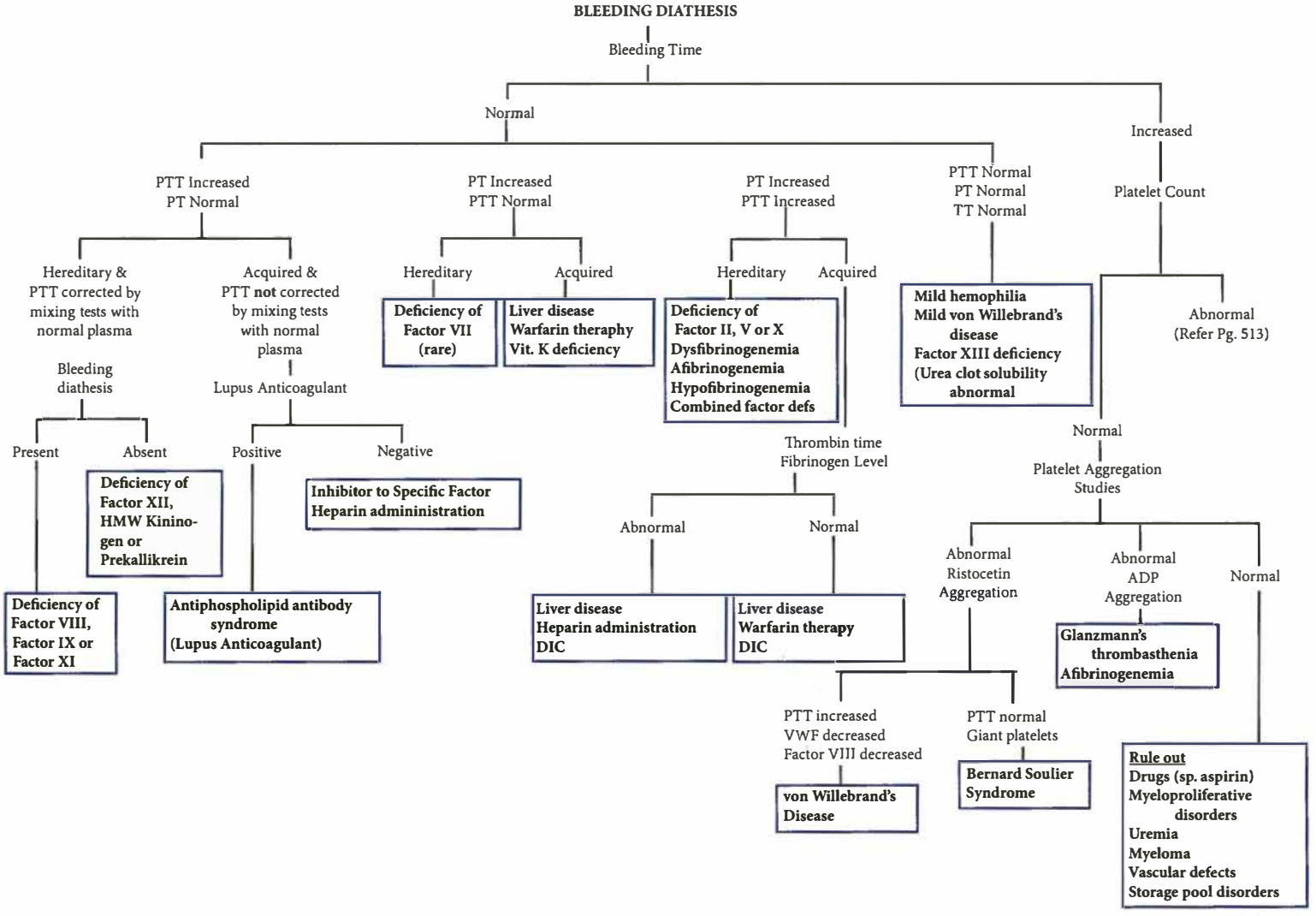

BLEEDING DIATHESIS
Bleeding Time
Normal
Increased
PTT Increased
PT Normal
PT Increased
PTT Normal
PT Increased
PTT Increased
PTT Normal
PT Normal
TT Normal
Platelet Count
Hereditary & PTT corrected by mixing tests with normal plasma
Acquired & PTT not corrected by mixing tests with normal plasma
Hereditary
Acquired
Hereditary
Acquired
Mild hemophilia
Mild von Willebrand's disease
Factor XIII deficiency
(Urea clot solubility abnormal
Abnormal
(Refer Pg. 513)
Deficiency of Factor VII (rare)
Liver disease
Warfarin theraphy
Vit. K deficiency
Deficiency of Factor II, V or X
Dysfibrinogenemia
Afibrinogenemia
Hypofibrinogenemia
Combined factor defs
Bleeding diathesis
Lupus Anticoagulant
Normal
Present
Absent
Positive
Negative
Thrombin time
Fibrinogen Level
Platelet Aggregation Studies
Deficiency of Factor XII, HMW Kinino-gen or Prekallikrein
Inhibitor to Specific Factor
Heparin admininistration
Abnormal
Normal
Abnormal Ristocetin Aggregation
Abnormal ADP Aggregation
Normal
Deficiency of Factor VIII, Factor IX or Factor XI
Antiphospholipid antibody syndrome
(Lupus Anticoagulant)
Liver disease
Heparin administration
DIC
Liver disease
Warfarin therapy
DIC
Glanzmann's thrombasthenia
Afibrinogenemia
PTT increased
VWF decreased
Factor VIII decreased
PTT normal
Giant platelets
Rule out
Drugs (sp. aspirin)
Myeloproliferative disorders
Uremia
Myeloma
Vascular defects
Storage pool disorders
von Willebrand's Disease
Bernard Soulier Syndrome

Table 12.10 : Interpretation of Coagulation Screening Tests for Bleeding Disorders

Platelet Count	*Bleeding Time**	*Tourniquet tests/Clot retraction*	*Clotting Time**	*PT*	*aPTT*	*TT*	*Presumtive Diagnosis*	*Ancillary Testsrequired*
N	N	N	uA	N	A	N	Hemophilia A or Christmas disease, very rarely factor XI or XII deficiency, lupus anticoagulant, acquired factor inhibitors	Factor VIII and Factor IX Assays, Lupus anticoagulant studies
N	uA	N	vA	N	A	N	Von Willebrand disease (vWd)	Factor VIII, vW factor assay, Ristocetin induced platelet aggregation test
N	N	N	vA	A	A	N	Deficiency of factor II, V, X, Vit. K deficiency Liver disease. Warfarin therapy	Specific assay for factor II, V, X Russel's viper venom time
N	N	N	N	A	N	N	Deficiency of Factor VII	Factor VII assay
N	uA	A	A	uA	uA	uA	Afibrinogenemia Dysfibrinogenemia Hypofibrinogenemia	Physio-chemical methods for fibrinogen estimation
N	N	N	N	N	N	N	With clinical evidence of bleeding; Factor XIII deficiency, mild coagulation defects, α2 antiplasmin deficiency	Fibrin Stabilising Factor test. Assay of factor XIII Thromboelastogram
N	A	A	N	N	N	N	Platelet function defect; Glanzmann's thrombasthenia	Platelet function tests
R	A	A	N	N	N	N	Thrombocytopenia; platelet count and function defects, Bernard Soulier syndrome, Wiscott-Aldrich syndrome, etc.	Platelet function tests Platelet Morphology
R	A	A	A	A	A	A	Liver disease, DIC	Liver function tests

Key: N = Normal; A = Abnormal(Increased); vA = Variably abnormal; uA = Usually abnormal; R = Reduced;
DIC= Disseminated intravascular coagulation
*Bleeding time and Clotting time Test gives abnormal results only in severe deficiencies and are not reliable by themselves if PT, aPTT and TT data are not available.

For details refer to P.J. Mehta's "Practical Pathology (Including Microbiology, Hematology & Clinical Pathology)"

Clinical Pathology 13

1 › Urine Examination

Collection of Urine

1. Random freshly voided sample is usually adequate for most tests. Early morning sample is usually preferred because not only is it most concentrated but also because it has a low pH, which preserves the formed elements.
2. A 24-hour sample is usually required for quantitative tests. The early morning urine is discarded and all the urine during the next 24 hours including the early morning urine the next day is collected.
3. A mid-stream sample is required for bacteriological tests. Before voiding, the patients must clean the glans penis or vulva properly. The initial urine is discarded and a clean-catch mid-stream sample is collected.

Preservation of urine

No preservative is required if urine is examined in 1-2 hours after voiding. Preservatives are required for 24 hours collection.

1. Toluene is the best preservative but it interferes with protein estimation by sulfosalicylic acid method.
2. Thymol, Formalin or Chloroform: 1 drop/30 ml. preserves sediments but interferes with sugar and acetone estimation.
3. Concentrated HCI (10 ml) is useful for all chemical examination especially calcium and nitrogen content.

Physical Examination

A. Quantity: Average urine output is 1,200-2,000 ml/day. Polyuria is increased urine output. Oliguria is decreased (less than 500 ml/day) urine output. Anuria is total suppression of urine (less than 50 ml/24 hr).

B. Color: Normal urine color is clear, pale yellow due to the presence of urobilin and urochromes. The depth of the color depends on the volume of urine voided and specific gravity of urine. Presence of blood, bile, lymph and drugs alter the color of urine. Cloudy urine may occur due to presence of amorphous phosphates and urates, pus, bacteria, fungi and chyle.

C. Odor: Normal fresh urine has a slight aromatic odor. When allowed to stand, urea is decomposed to form ammonia, giving a strong ammoniac smell. Ketone bodies, when present, may give a fruity odor.

D. Reaction: Normal urine is acidic in reaction with pH 6.0 due to the presence of weak organic acids. On standing, it becomes alkaline due to formation of ammonia.

Method: Blue and red litmus papers are put in urine. If blue turns red, urine is acidic. If red turns blue, urine is alkaline. pH paper has a range from 4.5-7.0.

E. Specific gravity: Normal specific gravity of urine varies from 1.003-1.030 and it can vary between 1.001-1.060. Substances influencing specific gravity are urea, sodium, chloride and phosphates. Albumin and sugar, when present, may also alter specific gravity. In end stage renal disease when the kidneys lose their ability to concentrate urine, the specific gravity may remain fixed at 1.010.

Method

1. Urine is poured into a cylinder or conical flask till it is three-fourths full.



Fig. 13.1 : Urinometer

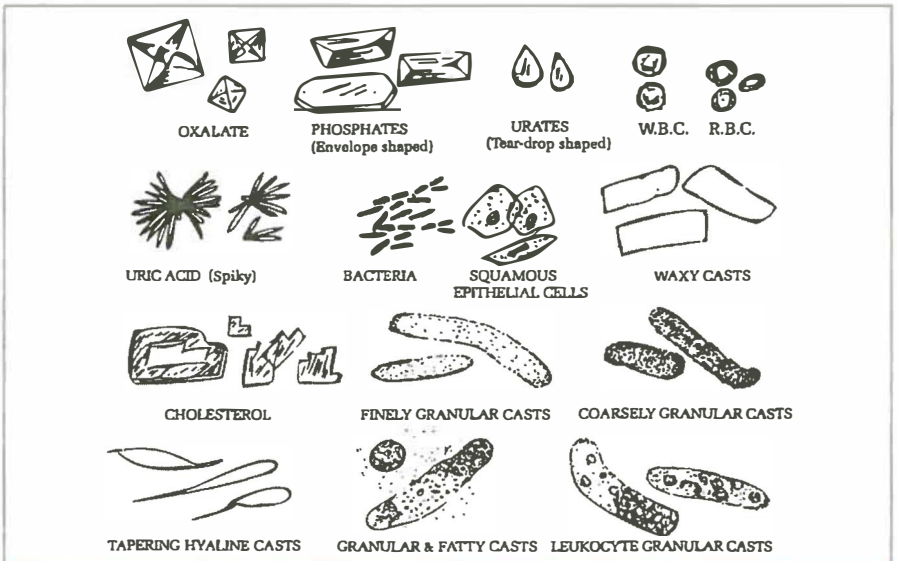


Fig. 13.2 : Urinary Sediments

2. *Urinometer,* which is a weighed cylinder with a scale in the stem reading from 1.001 to 1.060, is floated in the urine freely, without touching the bottom or sides (Fig. 13.1)
3. Reading is taken at eye level.
4. A refractometer can also be used.

Correction

1. *For temperature:* Urinometer is usually calibrated for a certain temperature, which is marked on it (usually 15° or 20°C). For each 3°C above this, 0.001 is added to the reading. For each 3°C below this, 0.001 is subtracted from the reading.
2. *For albumin:* For every 1 mg% albumin in urine 0.001 is deducted from the reading.

Chemical Examination

I. Proteins:

Normal 24-hour urine sample contains less than 50 mg of proteins, which is not detected by conventional tests described below. If proteins are detected by these tests it is abnormal and denotes proteinuria.

Method

A. *Heat test:*

1. If the urine is alkaline, it is made acidic by addition of 3% acetic acid.
2. If the urine is turbid it should be filtered.
3. Filtered urine is taken in a test-tube and the upper part of the column boiled.* A white cloud appears if proteins, phosphates or carbonates are present.
4. 2-3 drops of 3% acetic acid is added. If the white cloud persists it is due to proteins.
5. 3 drops of nitric acid is added. If the precipitate disappears it is due to nucleoproteins and mucin, whereas if it persists it is due to albumin or globulin.

---

* Upper part of the column must be heated and not the lower part for 2 reasons:

1. By convection currents hot liquid moves up and so if the lower part is heated it takes longer for proteins to precipitate than if only the upper part is heated.
2. If only the upper part is heated, the convection current does not affect the lower part which remains cold and unchanged and acts as a control to compare with the cloudiness in the upper part.

It is important to note that false negative results may be obtained:

a) If urine is alkaline, because proteins may

be converted to non-coagulable alkaline metaproteins on boiling.

b) If excess of acetic acid is added before boiling, because proteins may be converted to acid metaproteins which are also noncoagulable on boiling.

B. *Sulfosalicylic acid test:*

1. 2 ml of clear urine is taken and 3% sulfosalicylic acid is added.
2. Mixture is allowed to stand for 10 minutes.
3. Presence of proteins (as little as 5 mg) is indicated by cloudiness and precipitation.

C. *Heller's test*

1. Urine is added drop by drop to 1 ml. of concentrated nitric acid in a test tube.
2. Presence of proteins is indicated by the appearance of a white ring at the junction of acid and urine.

D. *Albustix, Clinistix or Labstix:* Urine is passed on these sticks and change of color indicates the presence of albumin. All these tests are based on the same principle. An indicator, tetra bromphenol blue, which has a yellow color at pH 3, changes to blue or green at the same pH in presence of proteins.

E. *Esbach's quantitative method:*

1. Specific gravity of urine is noted. If it is more than 1.008 it is diluted till it is less than 1.008.
2. Filtered, acidified urine of correct specific gravity is taken in Esbach's albuminimeter up to mark "U"
3. Esbach's reagent (which consists of 1 gm picric acid to precipitate proteins, 2 gm citric acid to dissolve phosphates and 100 ml water) is added to mark "R" and mixed.
4. The tube is corked and stood vertically for 24 hours when proteins settle down and the precipitate read off in gm/liter. If the urine was diluted, the figure must be multiplied by the dilution factor. If this is multiplied by total 24-hour urine volume in liters, it gives 24-hour excretion. If it is multiplied by 10, it gives gm% of proteins present.

F. *Kingsbury test:* This is rapid and more accurate than Esbach's test.

1. 2.5 ml of urine is taken in a test-tube and 7.5 ml of 3% sulfosalicylic acid is added.
2. The two solutions are mixed and allowed to stand for 5 minutes.
3. The turbidity is compared with the standards in a colorimeter and expressed as gm%.

II. Sugar

A. *Benedict's qualitative test:*

1. To 5 ml. of Benedict's qualitative reagent, 0.5 ml of protein free urine is added (8 drops). (Proteins interfere with precipitation of cuprous oxide). Measured amounts of Benedict's reagent and urine are taken, as this test is a semiquantitative test.
2. The mixture is boiled and a change of color, if any, from blue to green, yellow, orange or red and presence of precipitate is noted.
3. The results are noted as follows:

Negative: No change of color
Trace : solution pale green and slightly cloudy
+ : Cloudy green
++ : Yellow (less than 1%)
+++ : Orange (1-2%)
++++ : Brick red (more than 2%)

This test is based on the principle that sugars reduced blue copper sulfate in alkaline solution to insoluble yellow cuprous oxide.

False positive results occur in presence of:

a) Lactose, fructose or pentose.
b) Salicylates (This also gives +ve Gerhardt's test)
c) Homogentisic acid and melanogen

B. *Clinistix (test tape):* Glucose oxidase, peroxidase and orthotoluidine are incorporated into a cellulose strip along with a chromogen system. The strip is dipped for half a minute in the urine. Glucose is oxidised in the presence of glucose oxidase to gluconic acid and hydrogen peroxide which is liberated produces a blue color. The test is specific for glucose (when more than 15 mg%) but is more expensive than Benedict's test.

C. *Tablet test:*

1. 5 drops of urine and 10 drops of water are placed in a test tube.
2. One Clinitest tablet is added and the change of color is noted.
3. If the solution changes from orange to brown color more than 2% sugar is present.
4. If this change does not occur, the color of the solution, 15-30 seconds after the boiling stops, is compared with the standard chart provided to note the amount of sugar present.

   This test has a self-heating tablet which determines the presence of reducing sugar by reduction of copper sulfate.

D. *Benedict's quantitative test:*

1. If the qualitative Benedict's test is strongly positive, urine is diluted "X" times.
2. 25 ml of Benedict's quantitative reagent is taken in a conical flask and to it is added 15 gm of crystalline sodium bicarbonate and some broken porcelain. The mixture is boiled.
3. When sodium bicarbonate is completely dissolved, urine is run down from the burette slowly whilst the mixture is boiling, till all blue color is discharged.
4. The amount of urine required is noted: "Y" cc.
5. Since 25 ml of Benedict's solution requires 0.05 gm of sugar for reduction, the amount of sugar in urine is :

$$\frac{0.05 \times 100 \times X}{Y} = \frac{5X \text{ gm\%}}{Y}$$

X - dilution factor Y - Amount of urine.

III. Ketone Bodies

Ketone bodies are intermediate products of fat metabolism. Acetone, Diacetic acid and Beta hydroxybutyric acid are the ketone bodies found in urine when fat metabolism is deranged as in diabetes mellitus and following starvation.

A. *Rothera's test:*

1. 5 ml. of urine is fully saturated with ammonium sulfate.
2. 1 crystal of sodium nitroprusside is added.
3. Liquor ammonia is run down the side of the tube.
4. If permanganate color develops at the junction, acetone and/or diacetic acid are present.

B. *Gerhardt's test:*

1. 5 ml. of urine is taken in a test-tube and 10% ferric chloride solution is added drop-by-drop until further precipitate of ferric phosphate occurs.
2. The solution is filtered and to the filtrate more ferric chloride solution is added.
3. If a brownish red color develops, diacetic acid or salicylate is present.
4. The above test is repeated on another sample of 5 ml of urine to which 5 ml of water is added and the mixture boiled till the volume is reduced to 5 ml.
5. If the test, which is positive with unboiled urine, is negative with boiled urine, it is due to diacetic acid which on boiling is converted to acetone which evaporates. If the test is strongly positive both times it is due to salicylates.

IV. Bile Pigments

A. *Foam test:*

1. 10 ml of urine is taken in test-tube and shaken

Table 13.1 : Urine Picture in Common Disorders

Disease	Volume (daily)	Appear-ance ance & Colour	Odour	Specific Gravity	Albumin	Sugar	Acetone bodies	RBC	WBC	Casts	Bacteria
1. Normal	1-2 lit	Clear	Nil	1.004-1.025	Upto 100 mg/day	abs	abs	abs	abs	abs	abs.
2. Acute Glomerulo-nephritis	Oliguria Anuria	Smoky turbidity	Nil	High	About 2 gm/day	abs	abs	present	present	Hyaline, RBC	abs.
3. Chronic glomerulo-nephritis	Oliguria or Nor-mal	Gross haema-turia if Rapidly progres-sive	Nil	High or normal	Heavy, if rapidly progres-sive	abs	abs	Intermit-tently	Intermit-tently stages	Granular & waxy in terminal	abs.
4. Acute Pyelone-phritis	Normal	Grossly cloudy	Strong	High	Less than 2 gm/day	abs	abs	abs	present	WBC	Coliform
5. Acute Renal Failure	Oliguria or Anuria				Depend-ing on the under-lying cause						
6. Chronic Re-nal Failure	Polyuria	Clear	Nil	Low	Variable	abs	abs	abs	abs	abs	abs
7. Diabetes Mellitus	Polyuria	Maybe pale	Fruity	High	abs	+	+	abs	abs	abs	abs
8. Diabetes Insipidus	Polyuria	Colour-less	Nil	Low 1.010 or Less	abs	abs	abs	abs	abs	abs	abs
9. Nephrotic	Polyuria	Milky or opales-cent	Nil	High	More than 4.5 gm/day	abs	abs	abs	abs	Cel-lular or granular	abs

2. Yellow foam on the top indicates the presence of bile pigments.

B. *Gmelin's test:*

1. Half an inch column of yellow nitric acid in a test tube is brought in contact with an equal volume of urine.
2. A band or colored ring, especially green, indicates the presence of bile pigments.

V. Bile Salts

Hay's test:

This is based on the principle that bile salts lower surface tension and hence cause sulfur flowers to sink. It is important to remember not to use soap to wash the test tube since this will give false positive results. The test is performed as follows:

1. Sulfur flowers are sprinkled over urine.
2. If they sink in urine, bile salts are present.

VI. Urobilinogen

Ehrlich's aldehyde test:

1. 10 ml of urine is taken in a test-tube and 2.5 ml of barium chloride is added and the mixture filtered. (The filter paper removes bilirubin absorbed in barium chloride. If Fouchet's reagent is added to this, a green color develops in presence of bilirubin).

2. 2-3 ml of the filtrate is taken and 0.5 ml of aldehyde reagent is added and the solution allowed to stand for 3 minutes.
3. A pink color denotes the presence of urobilinogen.

VII. Blood

A. *Benzidine test:*

1. A saturated solution of benzidine in glacial acetic acid is prepared.
2. A few ml of the above solution and an equal amount of urine are mixed.
3. To this mixture, hydrogen peroxide is added. A blue color denotes the presence of blood.

B. *Orthotoluidine test:*

This test is similar to the benzidine test, except that instead of saturated solution of benzidine in glacial acetic acid, 0.5 ml. of 1% solution of orthotoluidine in glacial acetic acid is taken.

Microscopic Examination

Preparation of Smear

1. 10-15 ml of urine is taken in a conical centrifuge tube and centrifuged at 3,000 r.p.m. for 5 minutes to bring all the sediments to the bottom.
2. After centrifuging, the supernatant fluid is poured off and the fluid clinging to the sides of the tube is allowed to run down and mix with the centrifuged deposit.
3. This is then transferred to a glass slide and examined at first under the low power and then high power, preferably using a phase contrast microscope.

Urinary sediments

The various urinary sediments are:

A. Organised: Crystals.

B. Unorganised: Casts, red cells, pus cells, epithelial cells and bacteria.

Crystals Found in Acid Urine

1. *Uric acid and urates:* Uric acid crystals are yellowish whereas urate crystals are reddish granules.
2. *Calcium oxalate:* These are prism or dumbbell shaped crystals also found in alkaline or neutral urine.
3. *Cysteine:* These are refractile hexagonal plates.
4. *Leucine and Tyrosine:* These are spherical and fine needle respectively.

Crystals Found in Alkaline Urine

1. *Phosphate:* These are colorless, feathery or leaf-like if due to triple phosphate. If due to dicalcium phosphate, they are colorless prisms arranged as rosettes or stars.
2. Calcium carbonate and oxalate.

Casts

Casts are formed in the renal tubules by coagulation of albuminous material. They are usually cylindrical in shape and associated with pathological lesions in the kidney.

1. *Hyaline:* These are colorless, semitransparent casts which consist of coagulated protein material.
2. *Granular:* These are granular deposition on coagulated proteins. Granules are due to disintegration of white cells or epithelial cells of the tubules. They always indicate renal disease.
3. *Epithelial:* These are coagulated proteins in which are embedded epithelial cells from renal tubules.
4. *Blood:* These are red cells embedded in the coagulated protein in the tubules. This is found in acute glomerulonephritis.
5. *Pus cells:* These are pus cells embedded in the coagulated protein. This is found in suppurative conditions of the kidney.
6. *Fatty:* These are fat globules embedded in the coagulated protein. They are derived from degenerating epithelial cells.
7. *Waxy:* These casts resemble hyaline casts, but are more opaque with a dull waxy appearance. They are seen in end stage kidney disease.

Cells

1. *Red cells:* When in large number is always pathological.

2. *Pus cells:* These denote urinary infection or contamination with vaginal secretions.
3. *Epithelial cells:* When these are present in large numbers they denote destruction of the tissue in the urinary tract.

2 › Sputum

I. Naked Eye Examination:

A. *Quantity:* This varies from a few ml in the early morning sample to a liter in 24 hours. Large quantities are seen in lung abscess, bronchiectasis and tuberculosis.

B. *Odor:* It is usually inoffensive. It is offensive in bronchiectasis, lung abscess and gangrene of the lung.

C. *Consistency:* It may be serous, purulent, blood streaked, hemorrhagic or viscid, depending on the underlying disorder.

II. Microscopic Examination:

Normally there may be epithelial cells, leucocytes, fibrinous strands and bacteria.

Abnormal contents include large number of epithelial cells, pus cells, elastic fibres, malignant cells, Curschmann's spirals, Charcot Leyden crystals, fibrinous casts and parasites.

III. Concentration Method:

Petroff's Method: Treat a specimen of sputum with an equal volume of 4% sodium hydroxide. Keep at 37°C for 30 minutes until the mixture is homogenous. Neutralize the mixture with 8% hydrochloric acid and centrifuge. Take the deposit from the centrifuged sample and make a smear.

Gram's Stain

This is done to visualize gram positive and gram negative bacteria.

1. Make a smear of the sputum and fix it by heating over a flame.
2. Pour gentian violet over it for 3 minutes to stain.
3. Pour Gram's Iodine over this for 1 minute for mordanting action.
4. Drain off, wash and decolorize with alcohol.
5. Wash with water.
6. Pour safranin for 30 seconds for counterstaining.
7. Wash and dry the slide.
8. Mount under oil immersion.

Ziehl Neelsen's Stain

This is done to visualize acid-fast bacteria e.g. *Mycobacterium tuberculosis* and *Mycobacterium leprae.*

1. Make a smear of the sputum and fix it by heating over a flame.
2. Pour carbol fuchsin over the smear and heat it from below (till fumes rise) for 5 minutes, taking care not to char the smear.
3. Wash with water.
4. Decolorize with 20% H_2SO_4 (5% H_2SO_4 is used for M. leprae).
5. Wash and counterstain with Loeffler's methylene blue for 1 minute.
6. Wash and dry the slide.
7. Mount under oil immersion.

3 › Feces Examination

Collection of Sample: The sample of feces is preferably collected in a disposable cardboard container. Examination should not be delayed for more than a few hours especially when amoebae are to be looked for.

Naked Eye Examination

A. Quantity: Bacteria normally make up one third to one half of the dry weight of feces. Bulkier stools occur with vegetarian diet.

B. Color: Normal feces are light to dark brown in color due to the presence of bile pigments. Clay colored stools occur in obstructive jaundice due to absence of bile pigments in the stools. Tarry or black stools occur in upper gastro-intestinal hemorrhage due to altered blood. Tarry stools also occur following iron administration.

C. Consistency: Normal stools are well formed.

Watery stools occur in diarrhea. Hard feces suggest constipation. Flattened and rib-bon-like stools occur in obstruction in the lumen of the bowels. Pale, bulky, semi-solid, frothy stools, occur in malabsorption syndrome.

D. **Odor:** Normal odor of feces is due to the presence of indole and skatole, which is stronger after a meat diet. In nursing infants, a typical sour odor due to the presence of fatty acids occurs.

E. **Blood and Mucus:** Small amounts of mucus may be normally present. When large amounts of mucus are present, especially with blood, it suggests lesions of the large gut especially amebic or bacillary dysentery. Rarely it may be due to uremia or cancer.

F. **Parasites:** Stools may contain worms or segments of worms e.g. roundworm, tapeworm, etc.

Table 13.2 : Differences Between Amoebic and Bacillary Dysentery

		Amebic Dysentery	*Bacillary dysentery*
1.	Number of Stools	6-8/day	More than 10/day
2.	Amount	Copious	Small
3.	Odor	Offensive	Odorless
4.	Color	Dark red	Bright red
5.	Fecal matter	Present	Absent or very little
6.	Reaction	Acidic	Alkaline
7.	Adherence to Container	Absent	Present
8.	Red cells	Clumps	Discrete or Rouleaux Formation
9.	Pus cells	Scanty	Plenty
10.	Macrophages	Few	Plenty
11.	Parasites	E. histolytica	Absent
12.	Charcot Leyden Crystals	Present	Absent

Chemical Examination

1. Reaction: Normal stools are slightly acidic or slightly alkaline.
2. Benzidine test for occult blood: Refer Pg. 538

Microscopic Examination

A. *Saline preparation:* A bit of fecal matter is taken on the end of narrow stick and a thin emulsion in a drop of saline is prepared on the slide. A coverslip is put and the smear is examined to detect the motility of E. histolytica and other organisms.

B. *Iodine preparation:* This is done in a similar

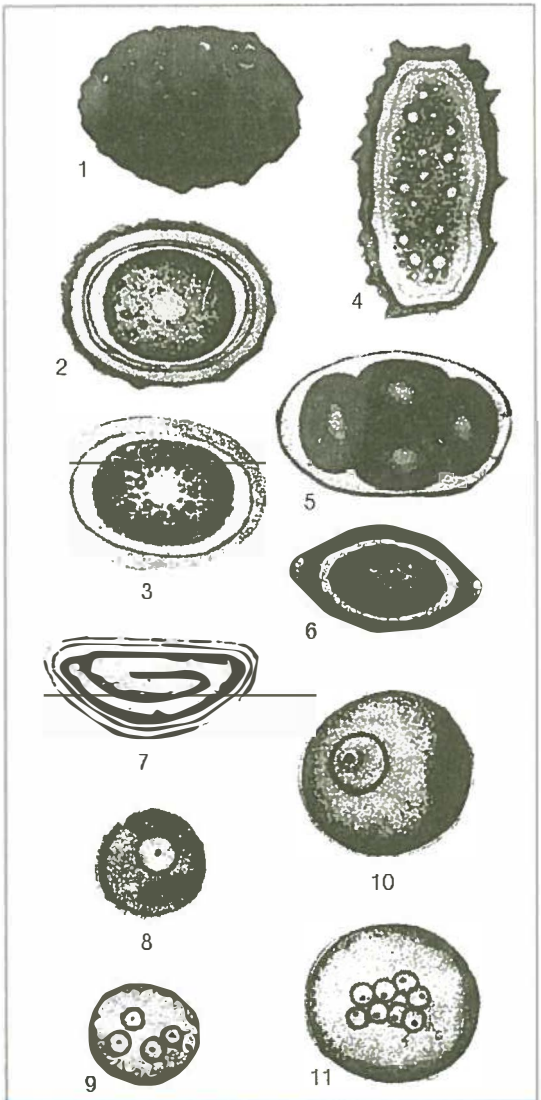


Fig. 13.4: Ova in stools - 1, 2 and 3: Fertilised eggs of A. lumbricoides. 4: Unfertilised eggs of A. lumbricoides. 5: A. duodenale 6: T. trichura 7: E. vermicularis 8 and 9: E. histolytica (uni and quadrinucleate forms). 10 and 11: E. coli (uni and octo-nucleate forms).

manner as saline preparation except that instead of saline, Gram's iodine is used. Iodine stains nuclear structures making identification simpler. However, this preparation kills the organisms and hence motility cannot be detected.

C. *Hanging-drop preparation:* A bit of diluted fecal material is taken on a coverslip, which is inverted on a special slide and then examined under the microscope. This helps to examine the darting motility of Vibrio cholera.

D. *Concentration method:*

1. 1 ml of feces is taken in a flat-bottomed vertical ledged container of 15-20 ml capacity with a diameter of not more than 1 1/2 inches.
2. A few ml of saline are added and an even emulsion is prepared.
3. Gradually more saline is added till the receptacle is full.
4. A glass slide is then placed across the mouth of the receptacle so that the centre is in contact with the fluid.
5. The preparation is kept for 20-30 minutes (eggs take 20-30 mins to come to the surface of the fluid).
6. The glass slide is quickly lifted up and smoothly turned to avoid spilling of the liquid
7. The slide is then examined under the microscope for detection of the eggs.

4 Helminthic Infections

Round Worm
(Ascaris lumbricoides)

Morphology

The adult worm resembles an ordinary earthworm, 20-30 cm in length.

Life-cycle

Eggs of the round worm matures in the soil and infects green vegetables. Man eats the eggs containing larvae. Larvae bore through the intestinal mucosa and through the portal circulation reach the heart and lungs. They re-enter into the stomach by breaking the alveoli and going up the trachea, pharynx and oesophagus. In the intestines the larvae mature into adult worms. After fertilization, the gravid female lays eggs which pass out through the feces and enter the soil.

Clinical Features

The clinical features are divided into two groups:

1. Those due to migrating larvae.
2. Those due to Adult worms.

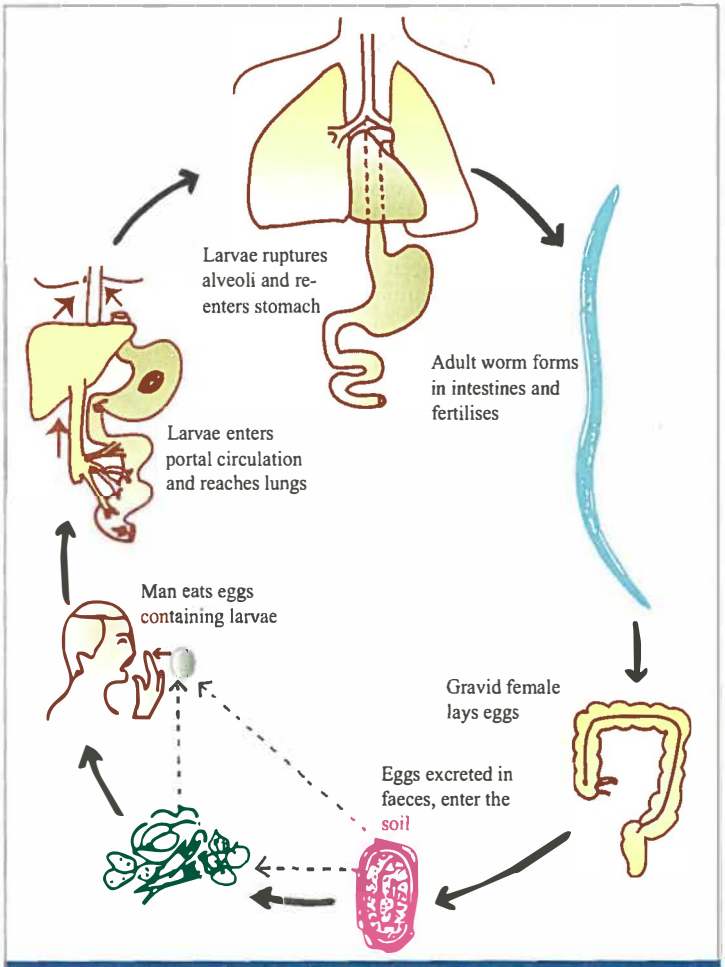


Fig. 13.5: Life-cycle of roundworm

Migrating Larvae in the lungs are responsible for cough and fever. If the infection is severe there may be dyspnea, urticaria and eosinophilia.

If the migrating larvae enter the general circulation through the pulmonary capillaries, they may lodge in various organs like brain, heart, kidneys, etc. causing disease of that organ.

The Adult Worms are present in the upper part of the small intestine and hence cause gastro-intestinal symptoms like vomiting, diarrhea, anorexia, loss of weight and dull aching pain in abdomen. Mechanical effects like intussusception or intestinal obstructions may occur. Allergic manifestations like urticaria, cough & conjunctivitis and signs of hypoproteinemia and vitamin deficiency may also be present.

Rare symptoms are appendicitis, obstructive jaundice and respiratory suffocation due to the passage of worms from the esophagus to the pharynx.

Diagnosis

1. Adult worm may be present in stools or in the vomitus. Stools may also show the eggs.
2. Hemogram may show anemia and eosinophilia.
3. Adult worm may be seen in the intestines on barium studies.

Effective drugs

1. Piperazine citrate 3-4 gm daily for 2-3 days.
2. Bephenium hydroxynaphthoate 5 gm, mixed with fruit juices is given once especially if there is simultaneous roundworm and hookworm infestation.
3. Mebendazole 100 mg twice daily for 3 days Pyrantel albendazole and tetramisole are other useful drugs.

Thread Worm
(Enterobius vermicularis)

Morphology

The adult worm is small and white in color. It is spindle shaped and resembles a piece of thread. The egg is flat on one side and convex on the other.

Life-cycle

The adult threadworms mature in the cecum in 2-3 weeks. The gravid female travels down and lays eggs around the anus. During scratching of the anal region, the fingers get contaminated. The eggs containing larvae are swallowed and the latter are liberated into the cecum.

Clinical Features

Children are commonly affected. The symptoms are due to the female worm creeping out of the anus and laying eggs in the perianal region. This causes intense itching around the anal region especially at night. In female patients genitals may be affected. Sometimes appendicitis may occur.

Diagnosis

Inspection of the anal region at the time of perianal itching may reveal the gravid female. Stool examination may show the presence of eggs or adult worms.

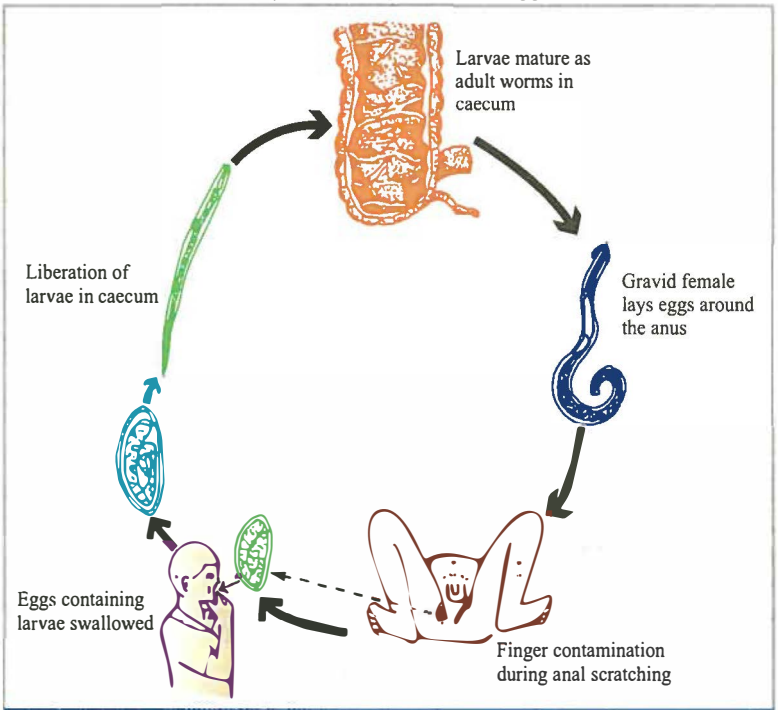


Fig. 13.6: Life-cycle of threadworm

Effective drugs

1. Piperazine citrate 1-1.5 gm daily for 7 days.
2. Mebendazole 100 mg once only.
3. Pyridinium pamoate 250-500 mg. once every 15 days for three doses.

Hook Worm
(Ancylostoma duodenale)

Morphology

The adult worm is small, grayish white and cylindrical in form. The egg is oval in shape and contains four blastomeres.

Life-cycle

The eggs develop in the soil into larvae, which infects man through the skin of the bare foot. It enters the blood stream and reaches the lungs. Larvae break through lung capillaries and travel up the respiratory tract to reach pharynx. They are swallowed back into the stomach and mature as adult worms in the intestines in about 3-4 weeks. They attach to the intestinal walls and suck blood. After fertilization, gravid female discharges eggs, which are passed in the feces and then into the soil.

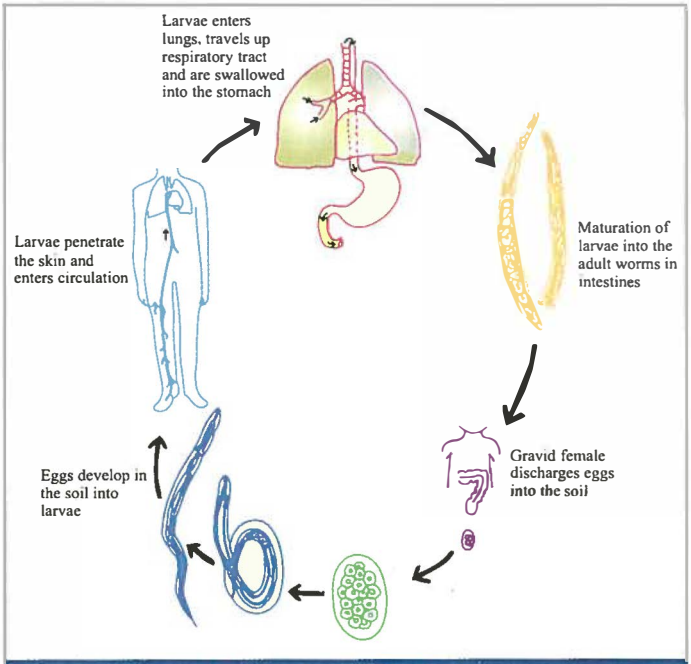


Fig. 13.7: Life-cycle of hookworm

Clinical Features

1. The patient often presents with anemia. The parasites remain attached to the intestinal mucosa by means of powerful buccal armatures, through which it continuously sucks blood and causes chronic hypochromic microcytic anemia.
2. The larvae at the site of entry through the human skin may produce dermatitis or ground itch.
3. In the lungs, bronchitis and broncho-pneumonia may occur due to the migrating larvae.

Diagnosis

1. Examination of stool may show adult worm or characteristic hookworm eggs.
2. Blood examination would reveal hypochromic anemia and eosinophilia.

Treatment

This consists of expulsion of the worms and treatment of anemia. If anemia is severe, it should be treated first. The drugs acting on hookworms are tetrachlorethylene, bephenium hydroxynaphthoate, thiabendazole and mebendazole.

1. *Anemia* should be treated with oral iron therapy along with vitamin B complex and folic acid. If it is severe blood transfusions should be given.
2. *Effective drugs*
   a) Tetrachlorethylene 5 ml is given after an overnight fast and may be repeated in heavy infestation.
   b) Bephenium hydroxynaphthoate 5 gm is given orally with fruit juices because it is very bitter.
   c) Mebendazole 100 mg twice daily is given for three days.

Whipworm
(Trichuris Trichiura)

Morphology

Adult worm in general appearance resembles a whip.

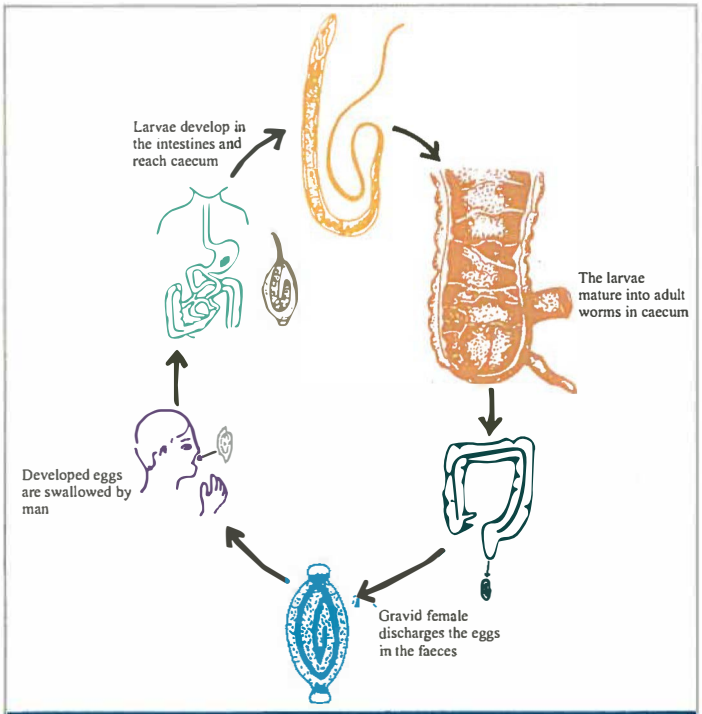


Fig. 13.8: Life-cycle of whipworm

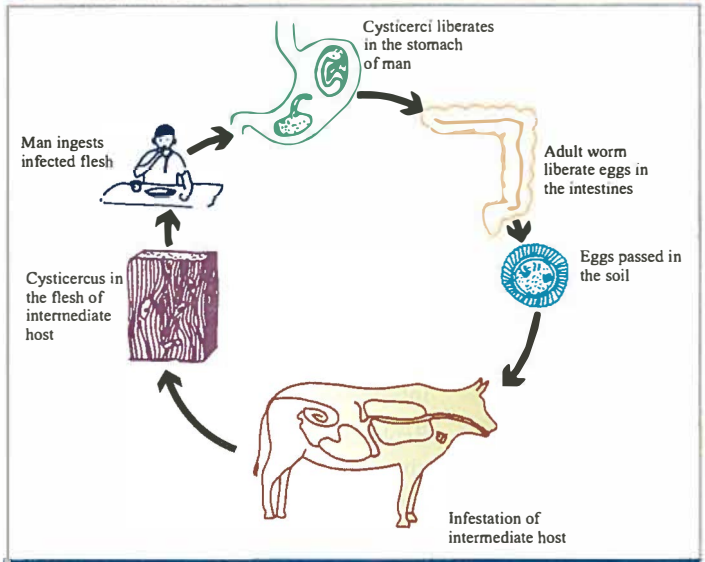


Fig 13.9: Life-cycle of tapeworm

It measures 3-5 cm in length. The egg is barrel shaped with a mucus plug at each end.

Life-cycle

The larvae develop into mature worms in the cecum. After fertilization, the gravid female liberates eggs which are passed in the feces. In the soil, eggs develop and are swallowed by man. They develop into larvae in the intestines and reach the cecum.

Clinical Features

There are usually no symptoms. In heavy infections abdominal pain and diarrhea may be present.

Diagnosis

Examination of the stool shows characteristic barrel shaped eggs.

Treatment

Stilbazium iodide, thiabendazole and mebendazole.

Tapeworm

(Taenia Saginata and Taenia Solium)

Morphology

Adult Worm: Taenia saginata is white and semitransparent, measuring 5-8 meters in length. Taenia solium measures about 2-4 meters in length.

Eggs: The eggs are spherical having outer thin transparent wall and inner embryophore, thick walled and radially striated.

Life Cycle

The life cycle is same in T. solium and T. saginata, excepting the intermediate host which in T. saginata is cow and in T. solium is pig.

The adult worms fertilize in the small intestines of man. Gravid female liberates eggs, which are passed in the feces. The eggs are swallowed by the intermediate host (cow for T saginata and pig for T solium) whilst grazing in the field. The eggs develop in the stomach and then reach the muscles as cysticercus. The meat of the intermediate host, when eaten by man causes liberation of these cysticerci in the stomach.

Cysticerci reach the small intestines and mature into adult worms.

Clinical Features

Adult worms in the intestine usually produce the symptoms. The patient may notice segments of the tapeworm in feces.

Cysticercus Cellulose

The larval form of T. solium though occurs in pig, man may become infested either by drinking contaminated water or by eating uncooked vegetables infected with eggs.

In the stomach the shells of the ova are digested and larvae are liberated. The larvae penetrate the intestinal mucosa and reach any part of the body. They are usually concentrated in the skin and muscles. They can be palpated as nodules. They may be found in the brain causing epileptic fits. The cysts die in about five years and become calcified.

Treatment

The effective drug is mepacrine. Other drugs used are dichlorophen and niclosamide.

Hydatid Worm

The dog tape worm (Echinococcus granulosa)

Morphology

The adult worm is 3.5 mm in length. The egg is oval in shape resembling the egg of Taenia.

Life-cycle

The adult worm develops in the small intestines of dog (definitive host) and gravid female liberates eggs, which are passed in the feces. Handling of dog by man (intermediate host) leads to ingestion of eggs. The eggs develop in the stomach and form hydatid cysts in liver, lung, brain, etc. Since human flesh is not ingested by dogs, the cycle may end. However, if the eggs develop in other intermediate hosts like sheep, cow, pig, etc., ingestion of their flesh by dogs causes liberation of eggs in the stomach of the dog.

Clinical Features

The larval stage of hydatid cyst usually occurs in sheep and cattle. Dog, by ingesting cysts is the definitive host. Man is infested either by a direct contact with infested dog or by taking uncooked vegetable contaminated with infected canine feces.

The infection is acquired in the childhood.

The hydatid cyst grows very slowly. The most commonly affected organ is liver. The lungs and the brain are the other affected organs.

The cyst usually remains symptomless. At the site, it may cause pressure symptoms. The cyst may rupture or suppurate.

Diagnosis

1. Blood examination shows eosinophilia.
2. Casoni's Intradermal test consists of intradermal injection of 0.2 ml of sterile hydatid fluid. A large wheal (5 cms) indicates positive test.
3. Radiology : X-rays of lungs and liver may reveal cyst in the form of a circular shadow.

Treatment

There is no specific treatment. The cyst, if causing pressure symptoms necessitates surgical removal. Mebendazole 600 mg TDS for 21 days has been found effective in hydatid cyst of the liver.

Pathology Specimens

14

When observing any specimen one should observe the following:

I. *Size:* Whether normal, small, enlarged, or only a portion of the entire viscera has been preserved.

II. *Shape:* Whether normal or distorted. If distorted, whether they are normally found there or not.

III. *Position:* The relation of organs and surrounding tissues to each other.

IV. *Surface:* Whether the surface is smooth or not. Normally pericardium, pleurae and peritoneum are smooth, shiny and transparent.

V. *Capsule:* Whether the organ or tissue has a capsule or not and whether it is normal or thickened, opaque and adherent.

VI. *Cut section:* If the organ has been cut one should make a note of the following:

A. Whether it is cut longitudinally, transversely or obliquely

B. The normal areas

C. The abnormal areas

D. Whether there are any contents and if present whether they are normally found there or not.

1 Central Nervous System

1. Meningitis

Gross

There will be exudate over the base of the brain. In *tuberculous meningitis* it is thick and may be organized enmeshing the structures at the base. There may be small tubercles extending on the surfaces of the brain.

In *pyogenic meningitis* the exudate may extend to cover the lateral surfaces of the brain and may be greenish, and less thick, than the tuberculous exudate.

Microscopic

In *tuberculous meningitis* there is predominantly mononuclear exudate in the meningeal space. There may be tubercle like lesions.

In *pyogenic meningitis* there is a predominantly polymorphonuclear exudate in the meningeal space.

II. Cerebral Abscess

Gross

There is an area of softening and congestion. There may be evidence of cerebral edema like flattening of gyri and obliteration of sulci.

The cut section shows an abscess-like area with necrotic areas and pus formation.

Microscopic

There is an area of necrosis with an acute inflammatory infiltration, predominantly polymorphs and macrophages.

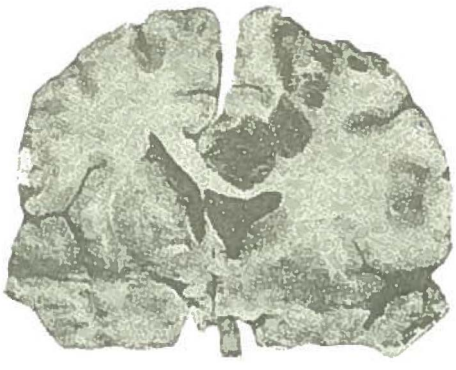


Fig. 14.1 : Brain abscess

2 Cardiovascular System

I. Pericarditis

Gross

The most commonly encountered specimen is that of fibrinous pericarditis. The external surface of the heart is covered with a fibrinous exudate, which may have undergone organisation and may form adhesions. When the layers of the pericardium are pulled apart they are likened to a bread and butter appearance, as they resemble two slices of buttered bread being pulled apart.

Other exudates that may be seen are serous, hemorrhagic or purulent if watery fluid, blood or pus respectively is seen in the pericardial cavity.

II. Rheumatic Heart Disease

Gross

The essential lesion in rheumatic endocarditis is the presence of rheumatic nodules in the endocardium of the valves. There is diffuse thickening of the cusps and there may be rheumatic vegetations. These are tiny, bead - like, warty nodules arranged in a row along the margin of contact of the cusps i.e. on their proximal aspect.

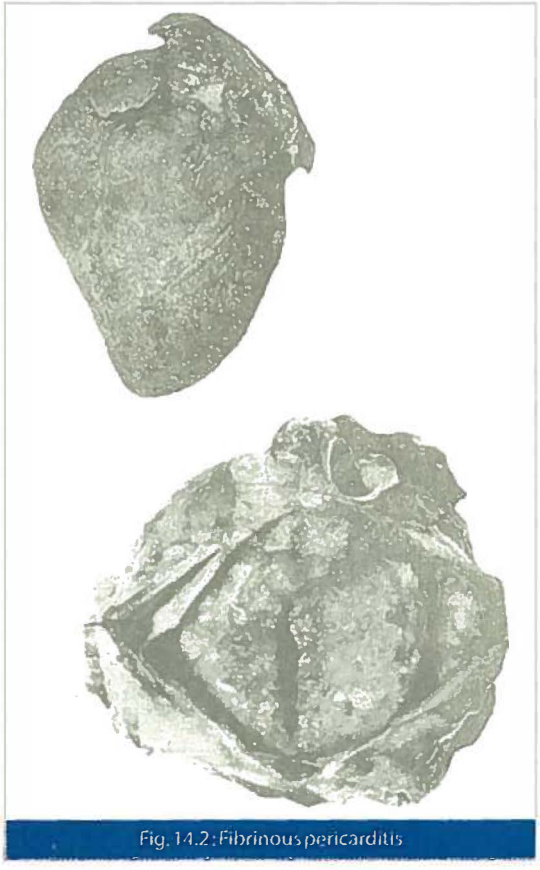


Fig. 14.2: Fibrinous pericarditis



Fig. 14.3: Acute rheumatic endocarditis

There may be associated pericarditis. There may be associated valvular stenosis, usually the mitral, often also the aortic. Calcification of the valves also may be seen.

There may be a MacCallum patch i.e. a rough thickened whitish patch on the posterior wall of the left atrium just above the mitral valve. There may be thickening and shortening of the chordae tendineae.

Microscopic

There may be a pancarditis i.e. inflammation of all the layers. The vegetations consist of platelet thrombi-deposited on the raw surfaces of the endothelium, later becoming organized.

Aschoff bodies may be seen in the myocardium, usually around the blood vessels. They consist of a central necrotic, reticulated area, lymphocytes, plasma cells and the characteristic, large multinucleated Aschoff cells. The Anitschkow cells with its serrated bar of chromatin in the centre of the nucleus ('caterpillar nucleus') may also be seen. Usually fibroblastic tissue and collagen fibers are seen in the later stages.

III. Bacterial Infective Endocarditis

Gross

The lesions affect mainly the mitral and sometimes the aortic valve.



Fig. 14.4: Subacute bacterial endocarditis

The characteristic lesions are large, polypoid, brownish, friable vegetations which originate from the line of contact, but may cover the valve and spread to the mural endocardium.

Microscopic

The vegetations consist of amorphous masses consisting of fused platelets and fibrin. The valve is infiltrated by inflammatory cells, mostly mononuclear cells. Bacterial colony clumps may be seen at places.

IV. Atherosclerosis of the Aorta

Definition

Atherosclerosis is a patchy and irregularly disposed process usually involving the intima of large elastic and muscular arteries.

Gross

Usually the abdominal aorta is affected because there is a maximum trauma and eddying of the blood in that region. There may be yellow fatty dots and/or streaks, wax-like plaques, ulcers, calcification or hemorrhage depending on the stage reached. There may be narrowing and occlusion of branches arising from the main trunk. There may be thrombi overlying the lesions.

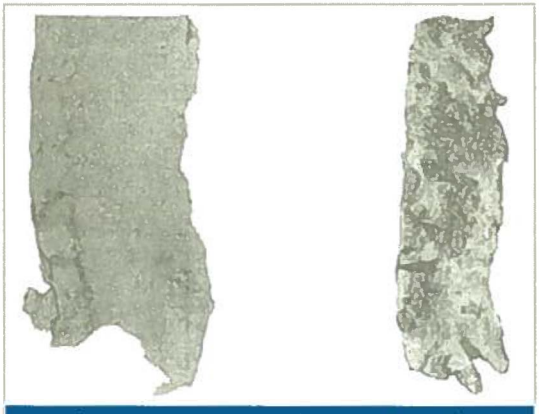


Fig. 14.5 and 14.6: Early and late atherosclerosis

Microscopic

1. There is lipid accumulation in the cytoplasm of intimal smooth muscle fibers transforming them into foamy lipophages.
2. Aggregates of lipophages disintegrate leading to release of thin lipid content which is degraded to cholesterol giving rise to the typical slit like spaces of the cholesterol crystals. A slight inflammatory exudate may be seen around.
3. A sclerotic layer forms over the intimal lipid accumulation.
4. There is vascularization from the arterial wall beneath the plaque.
5. Calcification, hemorrhage and overlying thrombosis may be seen.

V. Syphilis of the Aorta

Gross

The characteristic findings may be obscured by superimposed atherosclerosis. Very often both syphilis and atherosclerosis may occur in the aorta simultaneously.

Usually the ascending aorta is involved, often associated with aortic valvular affection, the valve displaying thickened, rolled, foreshortened cusps and widened commissures.

The aorta shows thickening of the aortic wall and longitudinally disposed linear depressions of the intima interspersed with elevated, gray-white fibrotic plaques. There may also be radially disposed fissures. The appearance of the aorta has been described as a 'tree bark appearance'.

Microscopic

There is both a periarteritis and an endarteritis with some atrophy of the media. The intima shows marked uniform thickening and

endarteritis obliterans. There is gumma formation with a mantle of lymphocytes and plasma cells especially around the lymphatic channels and vasa vasorum.

VI. Aneurysms of the Aorta

Definition

An aneurysm is an abnormal roughly circumscribed dilatation of an artery due to structural weakening.

Gross

A true aneurysm (where the sac is formed by the wall of the vessel) must be differentiated from a false one (where the sac is formed by the surrounding tissues).

Usually fusiform (elongated or spindle-shaped) aneurysms are associated with atherosclerosis, and saccular (rounded or sac-like) aneurysms occur in syphilis. It may be eroding adjacent structures eg the body of the vertebrae, or, may have ruptured resulting in a tear surrounded by blood clots or there may be lamellated blood clots within the aneurysmal sac.

Dissecting aneurysms are not true aneurysms, as the vessel is not dilated. Here hemorrhage occurs in the media of the aorta between the middle and outer thirds, commencing at the base and spreading along the vessel for a variable distance splitting the media into two layers in its passage.

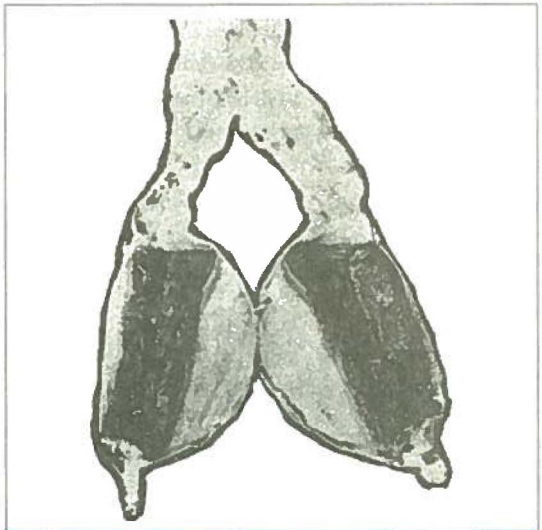


Fig. 14.7: Aneurysm of aorta

3 › Lung

The lung is identified by the presence of pleura, hilium, bronchovascular structures and black pigmentation distributed throughout the parenchyma.

I. Lobar Pneumonia

This is a progressive process beginning at the hilum and proceeding to the periphery involving one or more lobes or both lungs. (Usually one lobe with a clear demarcation is seen). One or more stages may be seen at a time.

Gross

A. *Stage I: Acute congestion and edema*

The region is grayish red with frothy blood stained fluid exuded on squeezing.

B. *Stage II: Red hepatization (2-4 days)*

The cut surface is dry, granular, red, airless, has the consistency of liver and retains straight, sharp edges. Fibrinous pleurisy may be seen.

C. *Stage III: Gray hepatization (4-8 days)*

The cut surface is dry, granular, gray, airless, has the consistency of liver and retains straight, sharp edges. Fibrinous pleurisy may be seen.

D. *Stage IV: Resolution*

The cut surface is gray or brown with a mottled look. Large amounts of frothy, creamy fluid exude on pressure.

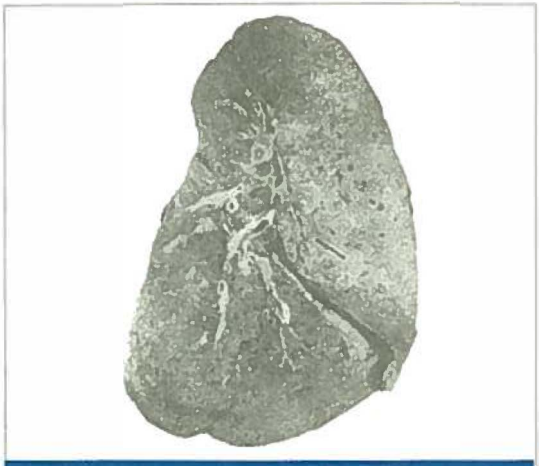


Fig. 14.8: Lobar pneumonia (gross)

Microscopic

A. *Acute congestion and edema:*

Prominent alveolar capillaries with alveoli filled with eosinophilic fluid and a few neutrophils. Gram's stain may divulge the organisms.

B. *Red hepatization* (2-4 days):

Replacement of alveolar fluid by marked neutrophilic infiltration, few fibrin strands and few erythrocytes.

C. *Gray hepatization (4-8 days):*

Mostly fibrin, fewer neutrophils, and retraction of the exudate from the region of the alveolar septae.

D. *Resolution:*

Shrunken fibrin masses with a large number of macrophages engulfing the debris and neutrophils.

II. Lung Abscess

Gross

A. *Site:* Abscesses of inhalational origin are usually found in the right upper lobe or the right lower lobe apex due to the more vertical course of the right bronchus.

Abscesses following pneumonia may be found anywhere, not necessarily in relation to a bronchus as found above. Septicemic abscesses are usually small and scattered in both lungs.

B. *Appearance:* In early stages the abscess is yellow or white, and firm. It may have a thin red rim.

Once liquefaction occurs there is pus formation with a ragged, yellow lining.

Chronic abscesses have firm, fibrosed walls with a fairly smooth lining and surrounding organizing pneumonia.

Microscopic

Acute abscesses show destruction of the parenchyma with a dense polymorphonuclear infiltration and varying numbers of macrophages. Chronic abscesses also show a surrounding fibrous zone.

Differential Diagnosis : The microscopic picture will prove the diagnosis, but on gross examination:

A. *Granulomas* will be firm, show evidence of chronicity, will not have a red rim or show liquefaction.

B. *Necrosis in a tumor:* Tumorous area may be seen around, probably in relation to a bronchus with evidence of tumor infiltration into surrounding tissue. No red rim is seen.

C. *Tuberculosis in lung:* There is caseation necrosis as opposed to liquefaction necrosis with pus formation. If lymph nodes are kept along with the lung specimen there will be caseation there too. Again this is a smooth walled cavity as compared to acute lung abscesses.

III. Tuberculosis of the Lung

This may show in a variety of forms of gross morphology, most usually associated with involvement of overlying pleura.

Gross

A. *Miliary tuberculosis*

The lungs are studded with firm white tubercles about 1 mm in diameter which may later appear as numerous caseating tubercles slightly larger in size. The pleurae may be thickened, opaque and adherent.

B. *Chronic fibrocaseous tuberculosis*

Usually first cavities are formed at the apex. The cavity walls are smooth and may be traversed by bronchi and blood



Fig. 14.9 : Miliary tuberculosis



Fig. 14.10: Lung tuberculosis with cavitation

vessels. There is central cavitation and caseation (Cheesy material). Pleurae may be involved with thickening, adherence & opacity. Bronchioles may show softening and dilatation.

C. *Acute tuberculous caseous pneumonia*

The lesions ulcerate through bronchial walls in many places with widespread caseous areas fusing to form larger ones. The entire lung may appear pneumonic.

D. *Tuberculoma*

A nodular area of caseous necrosis with a fibrous capsule, usually solitary and in an upper lobe. The cut surface shows dry, caseous areas with calcified parts.

Microscopic

A typical tubercle consists of a central area of caseation necrosis surrounded by a rim of epithelioid cells, lymphocytes and Langhans giant cells with surrounding fibrosis of varying degrees.

IV. Bronchiectasis

This is either localized or generalized permanent pathological dilatation of bronchioles.

Gross

Bronchiectasis invariably affects bronchi running in a vertical direction and is usually found in the lower lobes. Dilatation may be cylindrical, fusiform or saccular. Bronchioles also may show mucosal flattening. Surrounding lung tissue may show pneumonitis. Bronchiectatic cavities are dilated and filled with pus.



Fig. 14.11: Bronchiectasis

Microscopic

The mucosa may be hypertrophic or atrophic. There is destruction of the bronchial musculature and elastic tissue (causing dilation) and replacement by fibrous tissue in later stages.

V. Emphysema

Gross

The lung is airy, voluminous, pale, dry and distended. Large bullae may be formed, especially subpleurally and more often along the sharp edges of the lung, on the mediastinal or diaphragmatic surfaces.

Microscopic

Thin broken alveolar septae with large, distended, clear alveoli.



Fig. 14.12: Lung emphysema

VI. Bronchogenic Carcinoma (B.G.C.)

Gross

Commonly a firm, grayish white tumor arising from a bronchus (usually hilar in region) which may cause blockage of the bronchus by projecting into its lumen or pressure from the exterior.

Bronchogenic carcinoma usually infiltrates irregularly into the surrounding lung. The bronchial lymph nodes may show enlargement and involvement. Secondary changes like atelectasis, bronchiectasis and abscess formation may be associated with it.

The overlying pleura may be thickened, opaque and adherent. Usually epidermoid carcinoma arise centrally, and adenocarcinomas peripherally.

Microscopic

A. *Epidermoid carcinoma:*

Usually sheets or cords of squamous cells. These appear like irregular large eosinophilic cells with intracellular bridges, mitotic figures, and epithelial pearls (formed by keratin).

B. *Adenocarcinoma:*

Varying pictures are seen. Better-differentiated varieties show single layered tall columnar cells lining alveolar septae with small hyperchromatic nuclei. The cytoplasm may be pale or contain mucin. Mucin may also distend some alveoli. Less differentiated forms show hyperchromasia, pleomorphism and mitoses.

C. *Anaplastic carcinoma:*

Sheets of small or large undifferentiated pleomorphic cells.

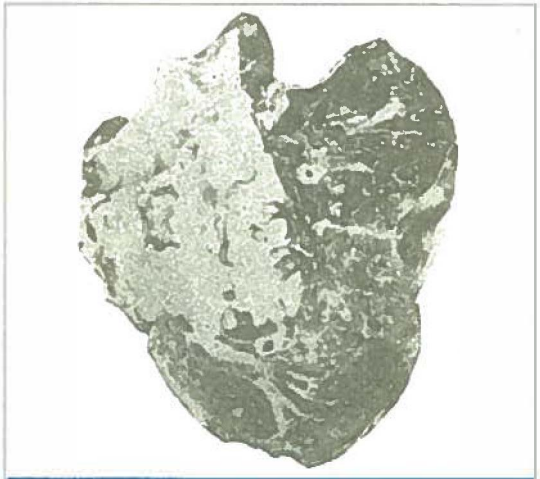


Fig. 14.13 : Bronchogenic carcinoma

4 › Small Intestine

I. Typhoid Lesion

Gross

The small intestine, mainly ileum and ileocecal regions are affected. There is hypertrophy of the Peyer's patches and ulceration, the ulcers lying along the long axis of the intestine (vertical ulcers). Perforations may be seen.

Microscopic

The mucosa is ulcerated, and submucosa heavily infiltrated with macrophages. There is hypertrophy of Peyer's patches.

II. Tuberculous Lesion

Gross

Initial lesions appear at the ileocaecal junction.



Fig. 14.14 : Typhoid ulcers

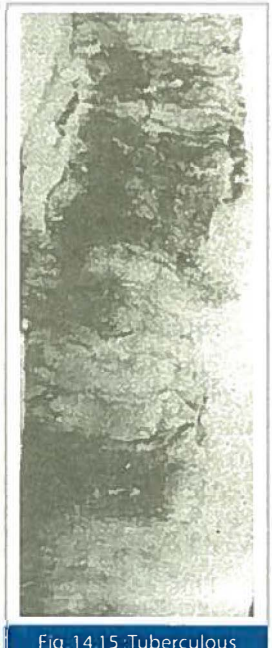


Fig. 14.15 : Tuberculous ulcers

From here they spread up and down. Small gray tubercles appear in the Peyer's patches and solitary follicles, and eventually break down and undergo caseous necrosis forming ulcers with ragged undermined edges. Usually the ulcers are transverse. There may be small tubercles on the overlying serosal aspect. Stricture formation may be present.

Microscopic

The mucosa shows ulceration with typical tubercles extending sometimes upto the serosal layer. These show central caseation, with surrounding lymphocytes, epithelioid cells and Langhans type of giant cells.

5 Large Intestines

I. Amoebic Dysentery

Gross

The initial lesion shows raised areas on the mucosal surface, which ulcerate forming large, irregular, ragged, flask shaped ulcers with undermined edges. The intervening mucosa appears normal. The overlying peritoneum is thickened.

Microscopic

There is flask shaped ulceration with demonstration of the trophozoite forms, which appear as small eosinophilic bodies at the edges of the lesion. These may be seen invading fairly deeply.

II. Bacillary Dysentry

Gross

The lesions are usually suppurative with generally shallow ulcers with sharp edges and an inflamed intervening mucosa.

Microscopic

There is acute pyogenic inflammation that may progress from edema and leucocytic infiltration of the mucous membrane to necrosis and ulceration, usually superficial.

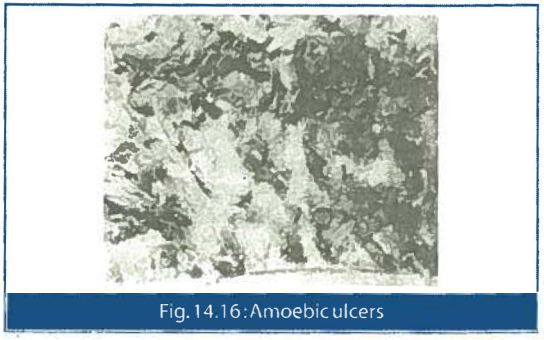


Fig. 14.16: Amoebic ulcers

6 Liver

I. Fatty Liver

Gross

The liver is enlarged, soft, yellowish and has rounded edges and tense capsule. The cut surface is yellow, greasy with indistinct lobular markings.

Causes

1. Malnutrition
2. Alcoholism
3. Diabetes
4. Wasting diseases
5. Poisons

II. Cirrhosis of Liver

Gross

The liver may be increased or decreased in size. The surface may be finely nodular (micronodular) or have coarse, irregular, large nodules (macronodular). In biliary cirrhosis, the liver is greenish in colour.

There is resistance on cutting. The normal lobular architecture is destroyed. There are nodules and fibrous bands running across the cut surface.

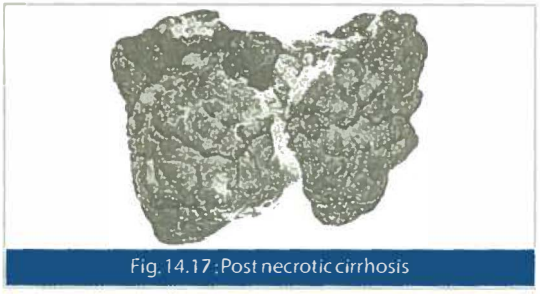


Fig. 14.17: Post necrotic cirrhosis

III. Chronic Passive Congestion

Gross

The liver is normal in size, firm and dark, reddish

brown in colour. The surface is finely granular and has thickened capsule. The cut surface would show mottled grayish yellow areas alternate with reddish brown zones. The hepatic vessels are dilated and may show thickened walls and thrombi. The typical appearance is of nutmeg because blackish pinpoint areas of necrosis alternate with yellowish area of fatty change that occurs due to anoxia.

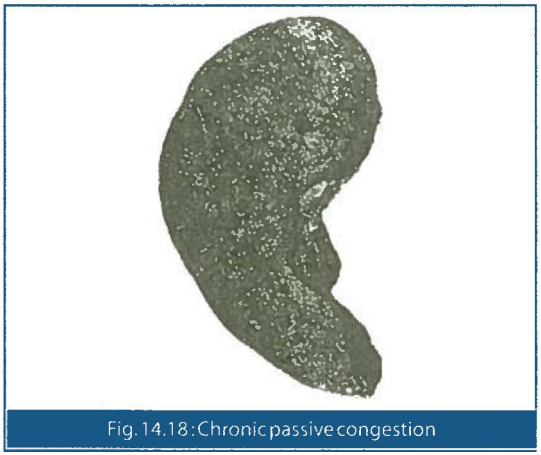


Fig. 14.18: Chronic passive congestion

IV. Amoebic Liver Abscess

Gross

The abscess may be visible from the outer surface or may appear as a bulge or softened area. The cut section would show a large loculated abscess filled with brownish "anchovy sauce" material with an irregular shaggy wall surrounded by an area of congestion.

V. Pyemic Liver Abscess

This resembles amebic abscess and is often mistaken for the same. However, here there are multiple, small, purulent and necrosed area scattered irregularly throughout the liver parenchyma.

VI. Hepatoma (Hepatocellular Carcinoma)

Gross

Hepatomas are commonly seen in cirrhotic livers. The liver is irregularly enlarged. The tumor may be massive, nodular and diffuse, more common in the right lobe. There may be a single large nodule surrounded by multiple small seedling tumors. There may be extension into the blood vessels or bile duct.

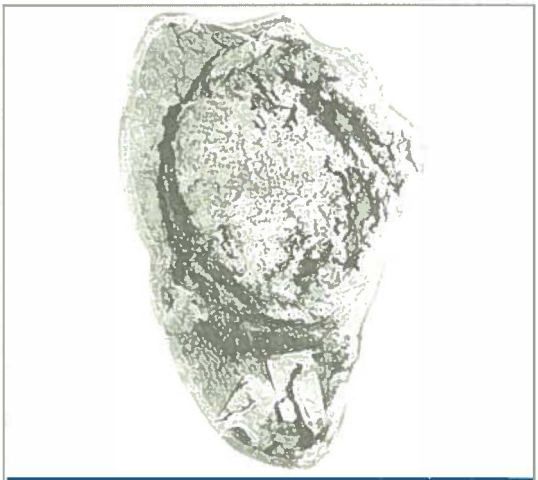


Fig. 14.19: Amebic abscess of liver

VII. Metastasis of Liver

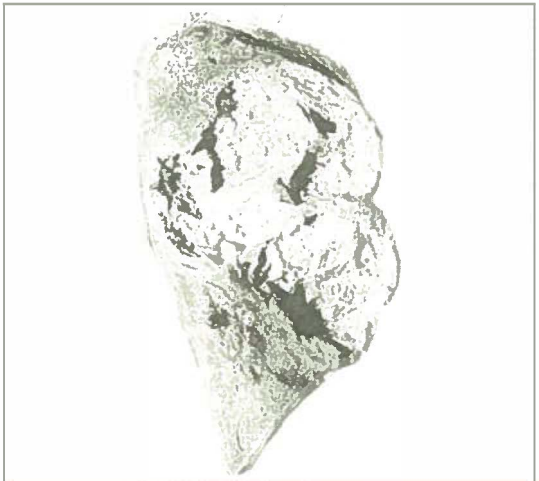


Fig. 14.20: Pyemic abscess of liver



Fig. 14.21: Multiple metastases in liver

Gross

Metastatic tumors are usually multinodular and may resemble the parent tumor. They are irregular

nodules showing central umbilication or pitting due to rapid tumor growth. Umbilication differentiates metastatic nodules from the large irregular nodules of post-necrotic cirrhosis and hepatomas.

On section, usually the nodules are grayish white. However, they may resemble the primary e.g. black (melanoma metastasis), mucinous (carcinoma colon or stomach metastasis).

7 › Kidney

I. Small Contracted Kidney:

Gross:

In the final stages of chronic renal failure one sees a small contracted kidney, the etiology of which is difficult to make out, but the following causes should be kept in mind.

Causes

A. Chronic glomerulonephritis
B. Chronic pyelonephritis
C. Nephrosclerosis

Distinguishable features include:

A. *Chronic glomerulonephritis:* the surface is finely granular with an adherent capsule. The cut section shows irregularity and atrophy of the cortex.
B. *Chronic pyelonephritis:* the surface is coarsely and irregularity scarred with an adherent capsule. The cut section shows involvement of the cortex and medulla.
C. *Nephrosclerosis* - The appearance resembles that of chronic glomerulonephritis but in the latter the granules appear to be finer due to the diffuseness of the lesions.

Microscopic

A. *Chronic glomerulonephritis:* The glomeruli show sclerosis of differing degrees. Few hypertrophied glomeruli may be seen.
B. *Chronic pyelonephritis:* There is periglomerular fibrosis. The tubules may contain albumin casts. The interstitium is infiltrated with collections of chronic inflammatory cells.
C. *Nephrosclerosis:* There is hyaline degeneration, best seen in the smallest vessels (e.g. afferent arterioles) and a smooth, well-defined subintimal acidophilic thickening. The internal elastic lamina shows reduplication or splitting into several layers.

II. Large White Kidney

GROSS

The kidney appears enlarged, smooth, pale and soft.

Causes:

A. Amyloidosis
B. Infective subacute glomerulonephritis
C. Circulatory disturbances like renal vein thrombosis
D. Toxemia of pregnancy
E. Degenerations and infiltrations eg fatty, cloudy changes
F. Nephrotic syndrome
G. Leukemic infiltrations

Microscopic

This depends on the underlying causes.

A. Amyloidosis shows waxy pale translucent pink deposits in glomeruli and around the blood vessels.
B. Subacute glomerulonephritis shows proliferation of Bowman's capsule epithelium forming the typical crescents.

III. Flea-bitten Kidney



Fig. 14.22: "Flea-bitten" kidney

Gross

The kidney is enlarged, soft, and has a surface mottled with tiny dark red to blackish areas giving a 'flea-bitten' appearance.

Causes

A. Subacute bacterial endocarditis.

B. Focal thrombotic glomerulonephritis - following bacteremia (as in endotoxic shock), accidents of childbirth (as in abruptio placenta and amniotic fluid embolism) and hematological conditions like hemolytic uremic syndrome and thrombotic thrombocytopenic purpura.

C. DIC

D. Septicemia

E. Malignant hypertension

Microscopic

This depends on the underlying cause. The basic pathology shows small focal glomerular thrombi.

IV. Acute Glomerulonephritis

Gross

The kidney is moderately swollen and is pale or congested. The cut section shows cortical swelling.

Microscopic

The glomeruli are swollen and distend the Bowman's capsule obliterating the Bowman's space. They are hypercellular with increased mesangial and endothelial cells.

There is stuffing of capillaries with inflammatory cells and a few red cells.

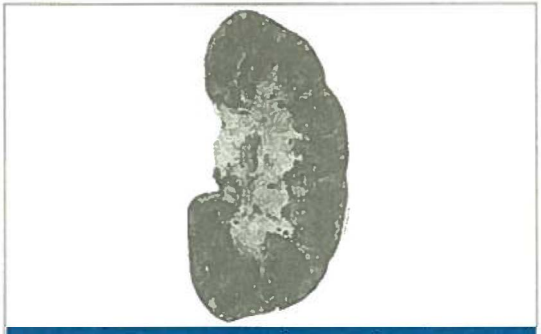


Fig. 14.23: Cortical necrosis

V. Acute Pyelonephritis

Gross

The kidneys show wedge shaped areas of inflammation, extending through the cortex and medulla to the pelvis, which is red and inflamed and may contain pus.

Microscopic

There is interstitial infiltration with acute inflammatory cells, mostly polymorphonuclear cells.

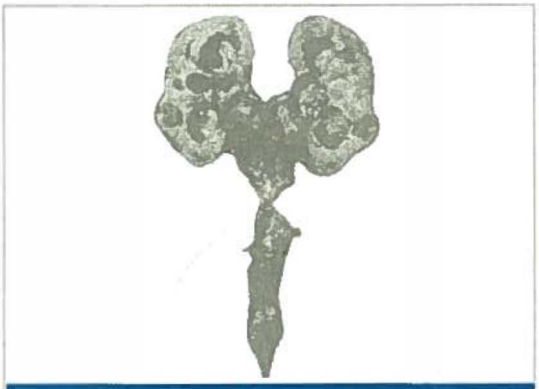


Fig. 14.24: Pyonephrosis

VI. Polycystic Kidney

This is a congenital malformation, which may involve one or both kidneys and may manifest later in life.

Gross

The kidneys are moderately to massively enlarged, with an irregular outline. On section, numerous irregular, variable sized cysts filled with greenish yellow gel may be seen. Usually normal kidney tissue is not visible.

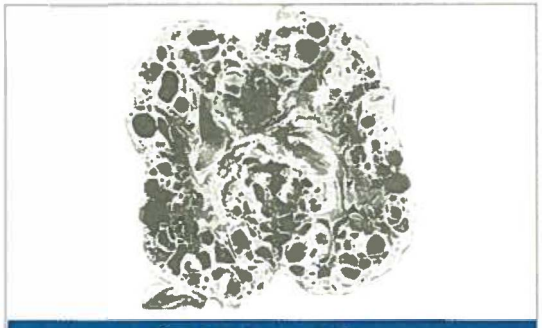


Fig. 14.25: Polycystic kidney

Drugs

15

CARDIOVASCULAR DRUGS

INOTROPIC DRUGS

Drug/Dose	Action	Side Effects	Uses
1. DIGITALIS			
I. *Rapid* a) DIGOXIN 1.5 mg initially 0.5 mg 6 hrly till digitalization b) DIGITOXIN 0.4 mg orally0.2 mg. 6 hrly till digitalization c) OUABAIN I.V. ultra-short acting II. *Slow* a) DIGOXIN 0.25 - 0.5 mg. initially 0.25 mg/day till digitalization b) DIGITOXIN 0.2 mg initially 0.2 mg. 8 hrly till digitalization III. *Maintenancedose* a) DIGOXIN 0.25 mg/day 10-20 µgm/kg body wt b) DIGITOXIN 0.1-0.2 mg/d	1. It increases the force of systolic contraction and decreases the oxygen expenditure for a given work output. 2. Heart rate is decreased. 3. Conduction through the A.V. node and Purkinje's fibers is depressed. 4. Refractory period of atria and ventricles is decreased and that of AV node is increased (QT interval shortens). It acts by inhibiting the sodium-potassium ATPase. This causes faster release of calcium which enhances the automaticity, contractibility ectopic pacemaker activity.	*Cardiac:* Premature beats atrial and ventricular tachycardia and fibrillation. Heart blocks, sinus bradycardia *Gastrointestinal:* Anorexia, nausea, vomiting (of central origin) and diarrhea *Neurological:* 1. Vertigo 2. Visual hallucinations, colour vision defects and blurring 3. Headache 4. Neuralgic pains *Miscellaneous:* 1. Skin rashes, eosinophilia 2. Gynecomastia 3. Premature labour with ECG changes in fetus	1. Congestive cardiac failure 2. Left ventricular failure 3. Atrial fibrillation and flutter 4. Premature beats 5. Supra-ventricular tachycardias *Contra-indications:* 1. High output states 2. Partial heart (AV) block 3. Ventricular tachycardia 4. Constrictive pericarditis 5. Myocarditis/Diphtheria 6. Hypersensitivity 7. WPW syndrome 8. Hypokalemia
2. AMRINONE 0.5 µg/kg IV bolus injection followed by 2 to 20 µg/kg/min infusion **MILRINONE** **VESNARINONE** 60 mg/day orally	It inhibits the enzyme phosphodiesterase which metabolises cyclic 3,5 AMP to the inactive cyclic 5 AMP. Causes vasodilatation with fall in systemic vascular resistance. It increases the force of contraction & velocity of relaxation of cardiac muscle. Inhibits phosphodiesterase (as above). Enhances influx of Ca ions through Ca-channels	1. Hypotension on IV administration 2. Myocardial ischemia 3. Thrombocytopenia	Cardiacfailure Now withdrawn due to toxicity. Mega studies have shown increased mortality
3. DOPAMINE 2.5-20 µg/kg/min. Up to 4 µg/kg/min: Renal dose 4-10 µg/kg/min: Inotropic dose with β action >10 µg/kg/min: α + β action	It is a direct beta-1 agonist which stimulates the heart and causes renal, mesenteric and cerebral vasodilation. Low doses increase renal blood flow, but large doses stimulate alpha receptors causing vasoconstriction and reduction of renal blood flow.	1. Nausea, vomiting 2. Angina, palpitations 3. Arrhythmia (less than with catecholamines) *Contra-indications:* 1. Pheochromocytoma 2. VF/VT	1. Cardiogenic shock 2. Chronic refractory congestive cardiac failure 3. Low doses in renal failure 4. Dilated Cardiomyopathy

The other drugs used in heart failure are ACE inhibitors, vasodilators and diuretics, which are discussed elsewhere.

Drug/Dose	Action	Side Effects	Uses
4. DOBUTAMINE			
2.5-10 μg/kg/min. rate or peripheral vascular	It increases the cardiac output without increasing the heart release endogenous nor-actions.	As dopamine, but causes less tachycardia as it does not heart failure epinephrine. *Contra-indications:* HOCM	1. Cardiogenic shock 2. Chronic refractory congestive cardiac failure 3. Dilated Cardiomyopathy

ANTI-ARRHYTHMIC AGENTS

1. CLASS IA AGENTS

a) QUINIDINE QUINIDINE SULFATE 200-400 mg 4-6 hrly. orally. Total dose not more than 4 gm (Tab 100 mg, 200 mg; Inj. 0.3 mg/ml) Therapeutic serum levels: 1.3-5 μg/ml Initially give test dose QUINIDINE GLUCONATE 80 mg vol. diluted in 5% glucose. IV. 25 mg/min. Total dose up to 800 mg/day.	1. Depresses the entry of sodium into the cell during depolarisation, hence decreases diastolic depolarisation. Has negative inotropic effect by depressing the entry of calcium into cardiac muscle cells. 2. Prolongs refractory period of atria but decreases that of AV node, hence it abolishes arrhythmias due to circus movement, but increased conduction through AV node may cause sudden rise of ventricular rate.	*Cardiac:* 1. Bradycardia 2. Ventricular tachycardia 3. Ventricular fibrillation 4. V.P.B. 5. Hypotension 6. Torsades de pointes *Extra-Cardiac:* 1. Intolerance: Skin rash, fever, thrombocytopenia 2. Cinchonism: Ringing in ears, vertigo, blurred vision, tremors, light-headedness 3. G.I.: Nausea. vomiting, diarrhea 4. Respiratory failure 5. Cerebral: Convulsions	1. Atrial fibrillation 2. Atrial flutter 3. Paroxysmal tachycardia 4. Atrial, nodal & ventricular premature beats 5. Ventricular fibrillation 6. Malaria (If quinine not available) *Contra-indications:* 1. Heart block 2. Hypotension 3. Stokes Adams syndrome 4. Quinidine intolerance/ idiosyncrasy 5. H/O Embolism 6. Myasthenia gravis *Drug Interactions:* 1. Increases digitalis level 2 X 2. Potentiates effect of warfarin 3. Phenobarbitone and eptoin reduce its half-life
b) **PROCAINAMIDE** 0.25-0.5 gm 4-6 hrly. orally. 100 mg. IV stat & every 4 min. Total dose 1 gm. 250-500 mg IM 6 hrly. Therapeutic serum levels: 8-12 μg/ml Toxic level 30 μg/ml	Similar to quinidine, but safer for IV use.	*Cardiac:* Similar to quinidine Torsades de pointes *Extra-Cardiac* 1. Intolerance, skin rash 2. GI: Nausea, vomiting, diarrhea 3. Agranulocytosis 4. Lupus like syndrome/SLE 5. Psychosis 6. Exacerbation of myasthenia	Similar to quinidine *Drug Interactions*: Absent with digoxin or warfarin
c) **DISOPYRAMIDE** 150-300 mg orally 6 hrly Maximum 1.8 gm/day. Therapeutic serum levels: 2-4 μg/ml	Cardiac depressant and has marked anti-cholinergic action compared to quinidine. No α blocking property.	1. Urinary retention 2. Dry mouth 3. Blurred vision 4. Constipation	1. Ventricular arrhythmias 2. VPC 3. PSVT 4. WPW syndrome 5. Recurrent VT 6. Atrial fibrillation/flutter *Drug Interactions:* 1. Phenytoin lowers plasma levels 2. Digoxin levels unaffected
d) **MORICIZINE** 200 mg. 8 hrly up to 900 mg/day	Inhibits the rapid rise of action potential (phase 0)	1. Dizziness 2. Postural hypotension 3. Nausea vomiting	Not effective for ventricular tachycardia & utility for atrial tachycardia needs further study

2. CLASS IB AGENTS

a) **LIGNOCAINE** 1-2 mg/kg (IV bolus) followed by IV infusion 1-4 mg/min .Therapeutic serum levels 2-6 μg/ml.	Depresses the automaticity in ventricular tissue. No action on SA node, AV node or atria.	*Cardiac:* Hypotension. dizziness, twitching, convulsions.	Ventricular arrhythmias in myocardial infarction.

Drug/Dose	Action	Side Effects	Uses
b) **PHENYTOIN SODIUM** 1 gm IV given at < 50 mg/min followed by 100 mg every 8 hrly Therapeutic serum levels 10-20 μg/ml. Toxic levels : 20 μg/ml.	1. Depresses ventricular automaticity. 2. Accelerates AV conduction. 3. Does not decrease conduction velocity like quinidine or procainamide.	1. I.V. Phenytoin causes local phlebitis due to alkaline diluent 2. Hypotension 3. Gum hypertrophy 4. Megaloblastic anemia 5. Cerebellar ataxia 6. Nystagmus 7. Lupus	1. Digitalis-induced arrhytmias because it does not increase A.V. block 2. Premature beats 3. SVT and VT 4. Ventricular arrhythmia after GA and surgery 5. Congenital QT syndrome (when β blockage has failed) 6. Epilepsy with arrhythmias
c) **TOCAINIDE** 400-800 mg orally every 6-8 hourly. 500-750 mg IV in saline drip. Therapeutic serum levels: 4-10 μg/ml	Similar to lignocaine	1. Twitches, tremors, diplopia 2. Skin rash 3. Interstitial pneumonia 4. Nausea vomiting 5. Leucopenia, anemia	Ventricular arrhythmias
d) **MEXILETINE** 400-600 mg initially. 200 mg 6 hourly orally. 250 mg IV slowly. 250-500 mg in saline drip. Therapeutic serum levels : 0.75-2 μg/ml	Similar to lignocaine	1. Nausea, vomiting, unpleasant taste. 2. Drowsiness, dizziness, diplopia, confusion, ataxia. 3. Hypotension, bradycardia and atrial fibrillation.	Ventricular arrhythmias. It can be used with quinidine. *Drug Interaction:* 1. Phenytoin and Rifampicin reduce plasma levels 2. Increases theophylline levels
3. CLASS IC AGENTS			
a) **ENCAINIDE:** 25 mg 8 hrly orally up to 200 mg/day	Depress the rate of rise of phase 0 of the action potential and slows conduction in His-Purkinje system, AV node and ventricle. Prolongs the refractory period of accessory pathway. Hence useful in WPW synd.	1. Nausea 2. Headache, blurred vision dizziness 3. Sinus node dysfunction 4. Exacerbation of ventricular arrhythmia 5. Cardiac failure	1. Supra-ventricular tachycardia 2. W.P.W. syndrome 3. Ventricular tachycardia
b) **FLECAINIDE** 100 mg twice a dayincreased to maximum of 400 mg/day. Therapeutic serum levels: 0.4-0.9 μg/ml	As above	As above	As above
c) **PROPAFENONE** 150 mg 8 hourly up to 300 mg 8 hrly.	As above	1. As above 2. Bronchospasm	As above
4. CLASS II AGENTS - BETABLOCKERS			
a) **PROPRANOLOL** 1 mg. IV slowly every 5 min up to 0.1 mg/kg 40-320 mg orally	1. Decreases automaticity 2. Decreases conduction velocity 3. Increases refractory period 4. Stabilises the membrane	1. Cardiac failure 2. Bronchospasm 3. Hypoglycemia 4. Light-headedness, depression, paresthesias 5. Nausea Vomiting 6. Impotence	Tachyarrhythmias due to 1. Digitalis 2. Sympathetic overactivity - emotion or anesthesia
b) **ESMOLOL** **(Ultrashort acting)** 5 gm in 500 ml dextrose 0.5 mg/kg over 1 min, folowed by 50 μg/kg infusion over 4 min, followed by 1 mg/kg over 4 min upto 2 mg/kg	As Propranolol	(As propranolol) Due to ultrashort action, very few side effects.	Useful for emergencies Effect occurs in 2 min and after termination of infusion recovery from beta blockade occurs in 10-20min.
5. CLASS III AGENTS			
a) **AMIODARONE** 200 mg tds orally, x 4 weeks and then gradually reduced	Broad-spectrum, long-acting. Class III type of antiarrhythmic agent which prolongs the dura	1. Allergic reactions 2. Benign yellowish brown corneal micro-deposits	1. Ventricular arrhythmia and WPW syndrome even in presence of cardiac failure

Drug/Dose	Action	Side Effects	Uses
to 200 mg daily or alternate days or 300-400 mg IV slowly over 1/2 3 min or in a drip.	tion of the cardiac action potential	3. Slate-grey discoloration of skin & retinal pigmentation 4. Bradycardia, hypotension and conduction defects 5. Extrapyramidal effects, pripheral neuropathy, vetigo, insomnia etc. 6. Pulmonary Fibrosis 7. Liver damage 8. Hypo- & hyperthyroidism	2. Refractory paroxysmal tachyarrhythmias 3. Atrial flutter and fibrillation 4. VPC's 5. Recurrent cardiac arrest
b) **BRETYLIUM** 5 - 10 mg/kg IV bolus; IV 0.5-2 mg/min. 80-160 mg oral 12 hrly	Adrenergic neuron blocking agent. It increases ventricular fibrillation threshold.	1. Hypotension 2. Nausea and vomiting	1. Life threatening ventricular arrhythmias 2. CPR
c) **SOTALOL** 80 to 320 mg orally every 12 hrly	Non selective β adrenergic receptor antagonist that also prolongs cardiac action potentials by inhibiting delayed rectifies and other K^+ currents	Similar to Propranolol Torsades de pointes	Life threatening ventricular arrhythmias
6. CLASS IV AGENTS			
VERAPAMIL 40 or 80 mg TDS orally OR 5 mg - 10 mg IV for paroxysmal atrial tachycardia	1. Causes coronary dilatation and reduces myocardial oxygen consumption. 2. Interferes with inward displacement of clacium & delays the conduction within AV node	1. Constipation 2. Hypotension 3. Vertigo 4. Nervousness	1. SVT: Atrial tachycardia, Atrial fibrillation 2. Premature beats 3. IHD: Angina 4. Hypertension
7. MISCELLANEOUS			
a) **ADENOSINE** 6- 12 mg IV as a rapid bolus, followed by 12 mg after 2 min if no effect. 30 mg (10 ml amp)	Purine analogue ideal for Re-entry tachycardia 1. Inhibits sinus node automaticity 2. Prolongs AV nodal refractoriness	1. Facial flushing 2. Dyspnea and chest discomfort 3. Nausea & light headedness 4. Sweating	Re-entrant supra ventricular tachycardia *Interaction* 1. Effects antagonized by theophylline and caffeine 2. Effects potentiated by dipyridamole & carbamazepine
b) **ISOPRENALINE** 2 mg in 500 ml 5% dextrose OR 10-15 mg QDS sublingually.	1. Enhances the rhythmicity of sinus, nodal and ventricular pace-makers 2. Enhances A.V. conduction 3. Increases heart rate and cardiac output.	1. Palpitation, flushing 2. Headache 3. Angina	1. Second degree A.V. block 2. Ventricular tachycardia with block
ANTI-ANGINAL AGENTS			
1. NITRATES			
GLYCERYL TRINITRATE SL 0.15 to 0.6 mg. Buccal 1 mg every 3 to 5 hr. Sustained release 2.5 to 9 mg 2 to 4 times a day. Ointment - 2% 4 to 8 hr. I.V. 5 µg/min. DISC/TTS patch (2.5-15 mg) OD **ISOSORBIDE DINITRATE** Sublingual 2.5 - 10 mg every 2 to 3 hrs. Sustained release 40 - 80 mg every 8 to 12 hr Oral 10 to 40 mg every 6 hr **ISOSORBIDE MONONITRATE** 10 mg, 20 mg, 40 & 60 mg SR	Increases coronary blood flow decreased oxygen consumption of the heart by decreasing the preload and afterload. **ERYTHRITYL TETRANITRATE** 5,15 mg TDS upto 30-60 mg **PENTA-ERYTHRITOL PENTANITRATE** 20-40 mg BD	1. Headache, halitosis 2. Methemoglobinemia 3. Glaucoma 4. Hypotension and syncope *Contra-indications* 1. Acute myocardial infarction 2. Severe anemia	1. Angina pectoris 2. Pulmonary hypertension 3. Cyanide poisoning 4. Paroxysmal nocturnal dyspnea 5. As spasmolytic 6. Achalasia cardia 7. Chronic stable angina 8. Portal hypertension prophylaxis

Drug/Dose	Action	Side Effects	Uses
2. K-CHANNEL OPENERS			
a) **NICORANDIL** 10-20 mg BD. (10 mg tablet) b) **PINACIDIL** 37.5 mg BD	1. ATP dependant K channel opener or activator 2. Nitric oxide donor	1. Headache, flushing 2. Nausea, vomiting, dizziness	Coronary artery disease-angina
3. BETA-BLOCKERS			
PROPRANOLOL 10 mg - 40 mg TDS upto 100 - 200 mg/day Dose titration till pulse<60	Refer Pg. 562 1. Reduces O_2 consumption. 2. With nitrates produces hypotension since it does not allow cardiac response to sympathetic stimulation secondary to hypotension by nitrates	1. L.V.F., C.C.F. 2. Bronchial asthma 3. Bradycardia 4. Hypoglycemia 5. Uterine hypomotility	1. Angina 2. Hypertension 3. Arrhythmia
4. CALCIUM BLOCKERS			
a) **NIFEDIPINE** 10-60 mg. orally or Sublingually, SR or GITS preparations	Potent calcium antagonist. Reduces O_2 consumption and reduces cardiac work by causing peripheral vasodilatation and reducing the peripheral resistance	1. Headache, lethargy 2. Flushing 3. Tachycardia 4. Hypotension	*Cardiovascular Uses:* 1. Angina Pectoris 2. Hypertension 3. Peripheral vascular disease 4. Achalasia cardia 5. Raynaud's phenomenon 6. Migraine 7. Nocturnal leg cramps 8. High altitude pulmonary edema 9. LVH, arrhythmias, valvular diseases, cerebrovascular diseases, post-MI *Non-cardiovascular Uses:* 1. Esophageal motility disorders 2. Supraventricular arrhythmias 3. Extrinsic bronchial asthma 4. Biliary or renal colic 5. Epilepsy 6. Alzheimer disease 7. Bone pain in transplant recipients 8. SAH, nocturnal enuresis
b) **VERAPAMIL, AMLODIPINE NICARDIPINE, ISRADIPINE, FELODIPINE, NIMODIPINE**	Refer Pg. 562	1. Headache, flushing, edema and hypotension. 2. Depression of A.V. nodal conduction 3. Bradycardia	
c) **DILTIAZEM** 30-60 mgTDS	It increases the coronary blood flow, decreases myocardial contractility, reduces peripheral resistance and BP, thus increasing cardiac output due to decreased afterload. It increases exercise tolerance.		
d) **PERHEXILINE MALEATE** 100-200 mgTDS	Not known. Reduces exercise-induced tachycardia. Causes vasodilatation of systemic & coronary vessels, decreases L.V. work & O_2 consumption.	1. Dizziness, headache 2. Hepatotoxicity 3. Impotence 4. Polyneuropathy, myopathy	
e) **OXYFEDRINE** 24-48 mg/day	It improves the myocardial microcirculation.	1. Weakness, headache, giddiness, insomnia, nausea, constipation	

ANTI-HYPERTENSIVE AGENTS

1. DIURETICS (Refer Pg. 567)			
a) HYDROCHLORTHIAZIDE 12.5 mg twice a day increased up to a maximum of 100 mg/day orally	Increased excretion of Na and Cl which reduces the vascular resistance direct relaxant action on the blood vessels. Mild carbonic anhydrase inhibitor	1. Muscular weakness 2. Electrolyte imbalance 3. Increase in blood sugar and uric acid levels	1. Hypertension 2. Refer Pg. 567
b) INDAPAMIDE 2.5 mg once a day orally	As above, vasodilatory diuretic	As above	As above
c) XIPAMID 20 to 40 mg once a day	As above	As above	As above
d) CHLORTHALIDONE 50-200 mg	As above	As above	1. As above 2. Hypocalcemia due to hypoparathyroidism

Drug/Dose	Action	Side Effects	Uses
2. BETA-BLOCKERS			
a) *Specific Beta-blockers:* SOTALOL, TIMOLOL b) *Beta-blockers with membrane-stabiling activity (MSA):* PROPRANOLOL 40-240 mg/day c) *Beta-blockers with MSA & Intrinsic sympathomimetic property:* PINDOLOL 5-20 mg/day; OXPRENOLOL, ALPRENOLOL d) *Cardio-selective:* ATENOLOL, ACEBUTOLOL 100-300 mg/day e) β-*blockers with α-blocking activity:* CARVEDILOL 25-100 mg/day; LABETOLOL 200-800 mg/day	1. Inhibits adenyl cyclase & decreases 3-5 cyclic AMP & hence causes bronchospasm 2. Reduces oxygen consumption of the heart and improves exercise tolerance. 3. Reduces BP by reducing cardiac output. 4. Membrane stabilizing effect (like quinidine) Depresses myocardium and may precipitate CCF 5. Intrinsic sympathomimetic action may prevent CCF 6. Crosses blood-brain barrier & causes sedative and anticonvulsant effect. 7. Alters mood	1. Bradycardia 2. CCF 3. Aggravates A-V conduction defects 4. Bronchospasm 5. Hypoglycemia. May also mask symptoms of hypoglycemia 6. Nausea, vomiting, constipation 7. Uterine hypomotility and prolonged labour 8. Fatigue, depression, hallucination 9. Thrombocytopenia, leucopenia	1. Angina 2. Hypertension 3. Cardiac arrhythmias 4. IHHS 5. Thyrotoxic crisis 6. Anxiety neurosis. 7. Migraine prophylaxis 8. Chronic open angle glaucoma 9. Fallot's Tetrad - in prevention of hypoxic spells
f) β *BLOCKERS USED IN EYE* 1. TIMOLOL 0.25-0.5% eye drops 2. BETAXOLOL 0.5% 3. METIPRANOLOL 0.1%	Decreases secretion of aqueous humor As above As above	— — —	Chronic open angle glaucoma Same as above Same as above
g) ESMOLOL (Refer Pg. 559)			
h) METOPROLOL 50 mg twice a day, maximum 250-300 mg	Cardioselective β blocker	Same as above	Same as above
i) BISOPROLOL 2.5-10 mg	Superselective β blocker	Same as above	Hypertension, arrhythmias, functional sympatheticotonic
j) CELIPROLOL 100 & 200 mg	β2 blocker, alpha agonist	Same as above	Cardiovascular disorders & can be safely used in heart failure
3. CALCIUM ANTAGONISTS			
a) NIFEDIPINE 20 mg. BD 5 mg sublingually in hypertensive emergencies	Refer Pg. 562	Refer Pg. 562	Hypertension and Refer Pg. 562
b) VERAPAMIL	Refer Pg. 562		
c) DILTIAZEM	Refer Pg. 562		
d) NITRENDIPINE 20-40mg OD	Similar to Nifedipine but longer acting and more specific for coronary and peripheral blood vessels.	Similar to Nifedipine	Hypertension and Refer Pg. 562
e) AMLODIPINE 2.5- 10 mg OD	Similar to Nifedipine but longer action	Similar to Nifedipine	Hypertension and Angina
f) NICARDIPINE 60-90 mg BD	Similar to Nitrendipine but shorter acting	Similar to Nifedipine	Hypertension, hypertensive crisis and Angina
g) ISRADIPINE 5-20mg OD	Similar to Nitrendipine. Dose has to be reduced in elderly & in kidney and liver damage.	Similar to Nifedipine	Hypertension, hypertensive crisis and Angina
h) FELODIPINE 10-20 mg OD	Similar to Nifedipine	Similar to Nifedipine	Hypertension, hypertensive crisis, angina, highly vasculo-selective
i) LACIDIPINE 2 mg - 4 mg OD	Superselective 3rd generation di-hydropyridine calcium antagonist	Similar to Nifedipine Rare, gum hypertrophy	Hypertension & Angina
j) NIMODIPINE 30 mg TDS 1 mg/hr IV infusion	Similar to Nifedipine, special cerebroselective action due to high lipophilic properties	Similar to Nifedipine	1. Hypertension 2. Sub-arachnoid hemorrhage 3. Acute ischemic stroke

Drug/Dose	Action	Side Effects	Uses
k) BENIDIPINE 4-8mg OD	Similar to Nifedipine, long-acting	Similar to Nifedipine	Hypertension & angina
l) NISOLDIPINE: 20-60 mg OD	Similar to Nifedipine	Similar to Nifedipine	
4. ACE INHIBITORS			
a) CAPTOPRIL 25 mg TDS increased every week up to a maximum of 450 mg/day.	Competitively inhibits angiotensin converting enzyme (ACE) & thus blocks the generation of angiotensin II. ACE also inactivates bradykinin. Hence increases bradykinin level that contributes to hypotensive effect.	1. Pruritus, skin rash 2. Disturbance of taste (ageusia) 3. Agranulocytosis 4. Proteinuria and renal insufficiency	1. Hypertension 2. Heart failure 3. Prevention of diabetic nephropathy in normotensive / hypertensive micro albuminuric patients
b) ENALAPRIL 2.5 - 20 mg OD	Similar to captopril but longer acting.	Lesser than captopril, longer acting.	Same as above
c) LISINOPRIL 5 - 40 mg. OD	Similar to captopril but longer acting and more effective.	Similar to Captopril but ageusia & thrombocytopenia does not occur. Cough, headache and diarrhea more with Lisinopril.	Same as above
d) PERINDOPRIL 4-8 mg OD	Similar to Captopril, but longer acting	Similar to Lisinopril	Same as above
e) RAMIPRIL 2.5-20 mg OD	Similar to Captopril. Dose adjustment reqd. in renal failure	Similar to Lisinopril. Lesser cough.	Same as above
f) FOSINOPRIL 10-80 mg OD	More tissue specific.	Similar to Lisinopril.	Same as above
g) BENAZEPRIL 10-40 mg OD	Similar to Captopril. Non-sulfodryl ACE inhibitor		
h) MOEXIPRIL 7.5-15 BDS			
i) QUINAPRIL 5-80 mg OD/BD			
j) TRANDOLAPRIL 1-4 OD			
5. ANGIOTENSIN II RECEPTOR ANTAGONIST			
LOSARTAN 25-100 mg OD or BD VALSARTAN 80-320 mg OD IRBESARTAN 150-300 mg OD	Antagonist of angiotensin II AT_1 type 1 receptor subtype present in vascular and myocardial tissue, brain, kidney and adrenal glomerular cells that secrete aldosterone.	1. Hypotension 2. Hyperkalemia 3. Reduces renal function 4. Does not produce cough associated with use of ACE inhibitors	1. Hypertension 2. Heart failure, esp. elderly 3. Prevention of diabetic nephropathy 4. Additional uricosuric action
6. VASODILATORS			
a) HYDRALLAZINE 75-200 mg. orally 20-40 mg IV or IM 25 mg tablets 1 ml ampoule=20 mg	1. Acts directly on the vascular smooth muscles and decreases the peripheral resistance. 2. Increases heart rate and renal, cerebral, coronary & splanchnic blood flow. 3. When vasomotor centre is severed in animals this drug does not act, hence it may also acts centrally.	1. *Cardiac:* Palpitations, tachycardia, angina 2. *G.I.:* Anorexia, nausea, diarrhea. Aggravates peptic ulcer 3. *Intolerance:* Fever, rash, anemia, pancytopenia 4. *CNS:* Headache, tremors, dizziness, paresthesias 5. Drug-induced Lupus (SLE)-Antihistone antibody +ve *Contra-indicated:* Severe IHD	1. Hypertension 2. Heart failure
b) DIAZOXIDE 300-800 mg/day orally 75-150 mg every 15 min. IV till BP is controlled.	1. Arterial vasodilator: Produces hypotension when given I.V. in hypertensive emergencies by causing peripheral vasodilatation. The effect may last 18-24 hrs. The effect cannot be reversed 2. Potassium channel opener.	1. Hyperuricemia 2. Brittle diabetes 3. Hirsutism 4. Refractory fluid retention 5. Acute pancreatitis It is *contra-indicated* in acute MI, pulmonary edema, diabetes, hyperuricemia	1. Hypertension 2. Hypoglycemia

Drug/Dose	Action	Side Effects	Uses
c) SODIUM NITROPRUSSIDE 200 µg/min. 50 mg of powder is to be dissolved in 500 ml of 5% dextrose just prior to administration. It is light sensitive and a paper bag over the IV container is necessary. It is given at 200 ug/min. 0.5-8 µg/kg/min IV drip	Relaxes both arteriolar and venous smooth muscles without any effect on the uterus or GI tract. It reduces the oxygen consumption of myocardium. The action is rapid in onset and of short duration. Hence the hypotensive effect is reversible on stopping the drug. It is useful in presence of MI, pulmonary edema and diabetes where diazoxide is contraindicated. It should not be used > 3-4 days.	Retching apprehension, twitching, hypothyroidism, methemoglobinemia. Hypotension, diaphoresis, nausea, vomiting, dizziness, tinnitus, blurred vision.	1. Hypertensive emergencies 2. Acute coronary syndromes with hypertensive crisis
d) MINOXIDIL 2.5 - 40 mg BD or ointment	1. Similar to hydralazine, but longer acting. It causes fluid retention, hence it has to be combined with a diuretic. 2. Potassium channel opener.	Pulmonary hypertension, hypertrichosis, headache	1. Hypertension 2. Baldness (Alopecia), specially ointment
7. ALPHA BLOCKERS			
NON-SELECTIVE α BLOCKERS			
a) TOLAZOLINE 25mg t.d.s. orally or 50 mg S.C. b) PHENTOLAMINE 5 mg I.M. or I.V. c) PHENOXYBENZAMINE 10-50 mg OD or BD orally	They are alpha-adrenergic blocking agents. They cause peripheral vasodilatation and increase force of contraction of myocardium.	1. Flushing, palpitation, sweating. 2. Postural hypotension. 3. Nausea, vomiting, diarrhea, aggravation of peptic ulcer 4. Precipitates myocardial infarction.	1. Peripheral vascular disease 2. Diagnosis and treatment of pheochromocytoma 3. Shock; Because blood flow to certain critical areas rather than B.P. is the important factor in survival from shock 4. Raynaud's syndrome 5. Scorpion bite 6. Male sexual dysfunction
SELECTIVE α BLOCKERS			
a) PRAZOSIN 0.5 mg twice a day maximum 5 mg oral. 5-20 mg in BPH	Direct relaxant of the vascular smooth muscles and alpha-receptor blockade. Selective blocker of α1 receptors. First dose hypotension.	Same as above but less likely to produce reflex reflex tachycardia	1-6. Same as above 7. Benign Prostatic hypertrophy (BPH) 8. Hypertension
b) TERAZOSIN 1 mg at bedtime max 10 mg/day oral.	Same as above Long acting	As above	Hypertension Prostatic hypertrophy
c) DOXAZOSIN 1-2mg OD upto 16mg	Same as above Long acting	As above	Same as above
e) INDORAMINE: 20 mg BD	Same as above	As above	Prostatic hypertrophy
8. CENTRALLY ACTING DRUGS			
a) ALPHA METHYL DOPA 250 mg-2000 mg. It is safe during pregnancy	1. Catecholamine synthesis inhibitor: Inhibits dopa decarboxylase which normally inhibits the conversion of dopa to dopamine & noradrenaline & thereby reduces sympathetic tone (vascular resistance). 2. Converted to alpha methyl noradrenaline which displaces noradrenaline from the granule stores. It acts as a false neuro-transmitter and due to its lesser potency produces relative hypotension. 3. Similar to clonidine	1. *CNS:* Headache, drowsiness, depression, Parkinsonism 2. *CVS:* Precipitates C.C.F. 3. *Hemolyticanemia* 4. *Miscellaneous:* Diarrhea, loss of libido, bradycardia. *Contra-indications:* 1. Pheochromocytoma 2. Liver disease 3. With MAO inhibitors	1. *Drug of choice in* Pregnancy-induced hypertension 2. Hypertension

Drug/Dose	Action	Side Effects	Uses
b) CLONIDINE 0.2-1.0 mg orally in hypertension, and 0.075-0.15 mg. orally in migraine.	Clonidine stimulates the alpha-adrenergic receptors in the vasomotor centre and this inhibits the peripheral sympathetic activity. It, however, maintains renal blood flow. It produces refractory sodium retention and therefore rapid tolerance to its antihypertensive effect occurs unless it is combined with a diuretic.	Drowsiness, depression, dry mouth, impotence, parotid pain Over-shoot hypertension on stopping it.	1. Hypertension 2. Migraine prophylaxis 3. Narcotic-morphine/drug addiction- withdrawal 4. Growth hormone stimulation test to diagnose GH deficiency 5. Irritable bowel syndrome 6. Menopausal hot flushes 7. Spinal cord spasticity
c) MOXONIDINE	1. Selective imidazole agonist (I-agonist) 2. Co-stimulates α-2 receptors 3. Similar to clonidine	Similar but far lesser side effects than clonidine	Hypertension, esp. with obesity, diabetes and hyperlipidemia
9. CATECHOLAMINE DEPLETORS			
RESERPINE (An alkaloid from Rauwolfia) 0.25-1 mg orally 0.5-2.5 mg I.M. or I.V. Orally, action takes 4 weeks. I.V., action in 10 min I.M. action in 2 hrs	Catecholamine depletor: The exact mechanism is not known. It depletes 5 H.T. from CNS and catecholamines from peripheral sympathetic nerve endings including that of heart and various other sites in the body. It prevents granular uptake (reversible) as well as granular storage (irreversible) of catecholamines. If given after MAO inhibitors or with it, it causes hypertension.	*Due to sympathetic blockade:* 1. Salivation, nasal congestion, cutaneous vasodilatation. 2. Increased gastric secretion and peptic ulcer. 3. Orthostatic hypotension, bradycardia. *Central action:* 1. Weight gain and increased appetite. 2. Mental depression. 3. Parkinsonism. 4. Feminization & impotence. *Allergic:* Thrombocytopenia.	Hypertension, rarely used due to side effects.
10. GANGLION BLOCKERS			
a) GUANETHIDINE 10 mg or 25 mg tablets once a day upto 100 mg/day	1. Inhibits the transmission of noradrenaline at sympathetic nerve terminals. 2. Depletes noradrenaline stores at sympathetic nerve endings. 3. Blocks the re-uptake of noradrenaline by sympathetic nerve endings.	1. *Due to sympathetic blockade:* Postural hypotension, diarrhea, nausea, vomiting, parotid tenderness and nasal congestion 2. *Impotency:* Impotence, failure to ejaculate 3. *CNS:* Mental depression. 4. *Polyarteritis nodosa.* *Contraindicated in:* 1. Pheochromocytoma 2. Severe IHD 3. CVA	Hypertension, rarely used due to side effects.
b) BETHANIDINE 5-10 mg BD	Similar to guanethidine, but shorter duration of action.	Similar to guanethidine, but diarrhea is rare.	Hypertension, rarely used due to side effects.
c) DEBRISOQUINE	Similar to guanethidine	Similar to guanethidine	Hypertension, rarely used due to side effects.
d) TRIMETHAPHAN 1-6 mg/min	Autonomic ganglionic blocker	1. Postural hypotension 2. Dry mouth 3. Constipation 4. Urinary retention 5. Impotence 6. Visual symptoms	Malignant hypertension

Drug/Dose	Action	Side Effects	Uses
ANTI-THROMBOTIC AGENTS			
1. STREPTOKINASE 7.5-15 lakhs IU I.V. Loading dose 2.5-5.0 lakhs IU followed by rest of the dose over 6 hrs. **2. UROKINASE** 2.5-7.5 lakhs IU I.V. Loading dose 2.5 IU over 10 mins followed by 5 lakhs IU over next 60 mins **3. TISSUE TYPE PLASMINOGEN ACTIVATOR/ ALTEPLACE (TPA)** 10 mg I.V. bolus followed by 50 mg over next 1 hour **4. ANISTREPLASE** (ACYLATED PLASMINOGEN STREPTOKINASE ACTIVATOR COMPLEX -APSAC) 30 units I.V. bolus over 2 mins **5. TENECTPLASE** 0.53 mg / kg IV over 10 seconds single dose **6. RETEPLASE** (rPA) 10 million units bolus IV over 2 - 3 minutes. Repeat after 10 minutes	Plasminogen activator. Plasminogen is the inactive enzyme in plasma which binds to fibrin during the formation of thrombus. This binding ensures fibrinolytic properties on the plasminogen-plasmin system.	1. Bleeding 2. Anaphylaxis 3. Allergy 4. Hypotension 5. Hemorrhagic stroke 6. Fever, rash, pruritus, wheeze 7. Arrhythmias *Contra-indications:* 1. Active bleeding 2. Bleeding diathesis 3. Recent trauma 4. Recent surgery/neurosurgery 5. Recent invasive procedure 6. Recent GI or genito-urinary bleeding 7. Recent prolonged CPR 8. Stroke or TIA in past 1 year 9. History of brain tumor, aneurysm or AVM 10. Active peptic ulcer 11. Pregnancy 12. Uncontrolled severe hypertension	1. Acute myocardial infarction 2. Deep vein thrombosis 3. Pulmonary embolism 4. Arterial thrombosis or embolism 5. Acute peripheral arterial occlusion 6. Occlusion of AV cannulae 7. Acute ischemic stroke 8. Acute coronary syndromes like unstable angina
HEPARINS / APROTININ			
1. HEPARIN (conventional) (Refer Pg. 566 for PE/DVT) 10,000 units I.V. followed by 5000 I.V. 6 hourly. Susequent doses depend on clotting time. CT should not exceed 12 min. Pitkin menstruum is a repository form of conc. heparin 20,000-40,000 units in dextrose-gelatin-acetic-acid base.	1. Anti-thrombin action. 2. Anti-prothrombin action. 3. Anti-thromboplastin. 4. Anti-polymer action of fibrin monomer. 5. Lipoprotein lipase: Heparin activates lipoprotein lipase which inhibits lipemia. Since lipemia inhibits fibrinolysis, heparin increases fibrinolytic activity	1. Allergic and Anaphylactic reaction: Asthma, urticaria 2. Hemorrhage from various sites 3. Alopecia 4. Diarrhea 5. Osteoporosis: (on a dose of 15,000 units per day for over 6 months)	Anticoagulant action starts immediately, reaching peak in 5-10 minutes & is normal in 2-4 hrs. 1. Acute coronary syndromes: unstable angina, AMI 2. Pulmonaryembolism 3. Deep vein thrombosis 4. Perioperative DVT prophylaxis 5. DIC. 6. Evolving stroke/TIA 7. LA or LV clot
2. LOW MOLECULAR WEIGHT HEPARINS			
a) DALTEPARIN 2500 - 10000 IU ; S.C./I.V. b) ENOXAPARIN 20-40 mg S.C. c) REVIPARIN SODIUM 1432 IU; S.C. d) PARNAPARIN 3200-6400 IU; S.C./I.V. e) NADROPARIN 3075 IU; S.C. f) TINZAPARIN	1. Molecular weights vary from 4000 to 6500 2. Longer duration of action 3. Predictable response 4. Lesser interaction with platelets 5. Minimal action against thrombin 6. Similar to heparin	Similar to heparin but far lesser	1. Domiciliary or outpatient heparin 2. Similar to heparin
3. APROTININ 10,000 - 20,000 Units I.V. followed by 5,000 - 10,000 units I.V. 6 hrly till satisfactory response	Plasmin inhibitor	Hypersensitivity reactions	1. Reduction of perioperative blood loss during open cardiac surgery. 2. Traumatic/hemorrhagic shock, Septic shock 3. Fulminant pancreatitis

Drug/Dose	Action	Side Effects	Uses
4. ABCIMAB IV 0.25 mg/kg	Platelet aggregation inhibitor. Platelet glycoprotein IIb/IIIa receptor blocker	1. Bleeding 2. Nausea, vomiting 3. Hypotension 4. Arrhythmias 5. Pneumonia, pleurisy	1. Adjunct to PTCA for prevention of RESTENOSIS
DIURETICS			
1. LOOP DIURETICS			
a) FUROSEMIDE 40-100 mg upto 2 gm orally, I.M. or I.V.	Acts on all sites of nephron, except distal tubules. It causes loss of Na, K, chloride, Ca, Mg & phosphates. Water is lost along with sodium. IV furosemide rapidly causes pooling of blood in peripheral deep veins. This effect occurs before diuresis & is important in treatment of pulmonary edema and acute LVF.	1. Hypokalemia, hyponatremia, hypochloremia 2. Hyperglycemia 3. Skin rashes 4. Bone marrow depression 5. Pancreatitis 6. Ototoxicity 7. Precipitation of Hepatic encephalopathy	1. Acute left ventricular failure 2. Edema disorders 3. Forced diuresis e.g. Barbiturate poisoning, etc. 4. Cardiac failure (CCF) 5. Acute renal failure 6. Anti-hypertensive
b) BUMETANIDE 0.5-4 mg BDS/TDS	Similar to furosemide, but more potent	Similar to furosemide	Similar to furosemide
c) ETHACRYNIC ACID 25-100 mg BDS/TDS	Similar to furosemide.	1. Similar to furosemide 2. Acute vertigo, tinnitus, deafness	Similar to furosemide.
d) MEFRUSIDE 12.5 to 50 mg orally once a day	Similar to furosemide, but more potent	Similar to furosemide	Similar to furosemide
e) TORESEMIDE 5-100 mg/day OD			
2. THIAZIDES			
a) HYDROCHLORTHIAZIDES 12.5-50 mg. OD b) POLYTHIAZIDES 2-4 mg.OD c) CHLORTHALIDONE 12.5-50 mg OD d) METOLAZONE 0.5-20 mg. OD e) INDAPAMIDE 1.25-5 mg OD	Acts mainly on sites proximal to those for exchange of sodium and potassium in distal tubules. Initially diminished sodium reabsorption from distal tubules and gradually reduces E.C.F. When this occurs, sodium reabsorption from proximal tubules increases, hence less sodium is delivered distally. This causes decrease in diuretic activity and resistance, has mild carbonic anhydrase inhibitory action.	1. Hypokalemia, hypochloremia, alkalosis 2. Allergic reaction 3. Hyperglycemia 4. Hyperuricemia 5. May precipitate renal or hepatic failure	1. Edema disorders 2. Hypertension 3. Hypercalciuria 4. SIADH: Inappropriate secretion of A.D.H. 5. Chlorthalidone is useful to correct hypocalcemia due to hypoparathyroidism
3. POTASSIUM SPARING			
a) SPIRONOLACTONE 25-100 mg/day orally. Maximum dose: 400 mg	Competitive antagonist to aldosterone due to similar structure. It acts on distal tubules where it decreases sodium reabsorption & potassium is retained	1. Gynecomastia 2. Drowsiness 3. Hyperkalemia (if renal failure)	1. Conn's syndrome. 2. In resistant oedema in combination with furosemide. 3. In cirrhosis and nephrosis where there is secondary hyperaldosteronism. 4. Hirsutism
b) TRIAMTERENE 25-100 mg/day.	Acts directly on the distal tubule. Depresses the excretion of potassium but increases the excretion of sodium and chloride.	1. Hyperkalemia 2. Diarrhea 3. Dry mouth 4. Skin rash	1. Edema disorders with diuretics. 2. Pseudo – aldosteronism.
c) AMILORIDE HYDROCHLORIDE 5-10 mg/day	Acts on proximal & distal tubule	Similar to triamterene	Similar to triamterene.

Drug/Dose	Action	Side Effects	Uses
4. CARBONIC ANHYDRASE INHIBITORS			
ACETAZOLAMIDE 0.25-0.5 gm day. METHAZOLAMIDE 50-100 mg TDS ETHOZOLAMIDE 50-200 mg/day DICHLORPHENAMIDE	Inhibit carbonic anhydrase which converts H_2CO_3 to H^+ and $H\ CO_2$. Hence H^+ is not available at distal tubule to exchange with Na^+. Hence, Na^+ and along with it, water is lost. HCO_3 cannot be reabsorbed and is lost in urine which is alkaline. Patient will develop metabolic acidosis which will stop the action of this diuretic due to excess H^+ now available for exchange distally. Hence it is a self-limiting diuretic.	1. Hypokalemia 2. Metabolic acidosis 3. Drowsiness, paresthesia 4. Skin rash, hypersensitivity 5. Blood dyscrasias 6. Stone formation	1. Diuretic 2. Glaucoma: It reduces intra-ocular tension by reducing fluid formation by inhibiting carbonic anhydrase. 3. Resistant epilepsy: It decreases C.S.F. formation 4. Emphysema: It helps by acting on CO_2 transport system 5. Periodic paralysis 6. Acute mountain sickness
5. OSMOTIC DIURETICS			
MANNITOL 25% solution 1.5-2 gm/kg body weight rapidly IV 100 ml, IV, 8 hrly GLYCEROL 1-1.5 gm/kg body weight Maximum:120 gm/day IV 10%in 500 ml saline Oral & IV	On intravenous administration it is rapidly filtered by the glomeruli where it exerts osmotic activity which prevents reabsorption of sodium and water. It also reduces medullary hypertonicity which also decreases the reabsorption of water.	Cardiacfailure	1. Barbiturate poisoning 2. Cerebral edema 3. Renal failure due to prerenal causes 4. To decrease intraocular pressure in ocular emergency 5. Hypertensiveemergency & encephalopathy 6. Raised intracranial tension: neurosurgery (cerebral edema) 7. Respiratory acidosis 8. Acute mountain sickness

AUTONOMIC NERVOUS SYSTEM

CATECHOLAMINES

1. EPINEPHRINE			
(ADRENALINE) 0.5-1.0 ml S.C. or I.M. 1:1000 in 1 ml	1. Increases the rate, force of contraction & cardiac output 2. Adrenaline stimulates adenyl cyclase and increases 3-5' cyclic AMP which causes bronchodilatation. 3. Causes contraction of radial muscles of iris causing pupillary dilatation. 4. Constricts blood vessels and controls local bleeding	1. Pallor, palpitation, tremors, anxiety, headaches 2. Anginal pains 3. Arrhythmias in patients with infarction 4. Sudden hypertension	1. Anaphylactic shock 2. Cardiac resuscitation 3. Bronchial asthma 4. Control of hemorrhage like epistaxis or following tooth extraction 5. With local anesthetics, reduces its systemic absorption, prolongs its action & reduces systemic side effects. 6. Open angle glaucoma
2. NOR-EPINEPHRINE (NOR-ADRENALINE) 4 mg, in 500 ml of 5% dextrose I.V.	Causes vasoconstriction and thus raises BP	Similar to epinephrine	Shock
3. ISOPROTERENOL (ISOPRENALINE) 5-20 ml of 1:200 solution 5-20 mg sublingually 0.5 ml of 1:200 solution by inhalation	Acts on β-receptors. Has very little action on α-receptors. Relaxes smooth muscles of GI tract & bronchi by stimulating adenyl cyclase & increasing 3-5 cyclic AMP. Diastolic BP falls but due to increased venous return & +ve inotropic & chronotropic effects, cardiac output is increased.	1. Palpitations, tachycardia, tremors, anxiety, headache 2. Angina 3. Arrhythmias	1. Status asthamaticus 2. AV block: Stokes-Adams 3. Cardiogenic shock: Reverse drug

Drug/Dose	Action	Side Effects	Uses
4. EPHEDRINE 30 mg orally or I.M. or S.C.	It stimulates cyclic AMP formation (by stimulating adenyl cyclase) which causes broncho-dilatation. Ephedrine is a less potent vasopressor agent than noradrenaline, but vasopressor response persists for a longer time.	Similar to adrenaline	1. Bronchial asthma 2. Hypotension 3. Nasal decongestant 4. Stokes Adams syndrome 5. Mydriatic 6. CNS stimulant in narcolepsy, by acting on reticular activating system 7. Nocturnal enuresis
5. AMPHETAMINE 5 mg twice a day, not to be given at night.	It increases mental and physical activity, elation, euphoria, tremors & confusion due to stimulation of reticular activating centre. It acts on the lateral feeding centre of the hypothalamus and reduces appetite.	1. Anxiety, confusion, psychosis 2. Habituation 3. Dry mouth, anorexia, nausea, vomiting, diarrhea	1. Narcolepsy 2. Obesity 3. Temporal lobe epilepsy
6. MEPHENTERMINE 15-30 mg. I.M. or S.C.	Beta-receptor stimulant. Increases B.P. by augmenting cardiac output.	Similar to adrenaline.	1. Vasopressor. 2. Nasal decongestant.
7. ALPHA AGENTS	Refer Pg. 564		
8. BETA BLOCKERS	Refer Pg. 562		

CHOLINERGIC AND ANTI-CHOLINERGIC AGENTS

1. ACETYL CHOLINE ESTERS a) CARBACHOL 1-4 mg, orally 0.25-0.5 mg. S.C. b) BETHANECHOL 10-30 mg, orally 2.5-5 mg S.C. c) METHACHOLINE 100-200 mg orally, 10-25 mg S.C. d) FUTRETHONIUM IODIDE 25 mg orally 5 mg S.C. (Above 4 have only muscarinic effects)	**A. MUSCARINIC:** 1. *CVS:* Bradycardia leading to cardiac arrest due to SAN depression. 2. *GI:* Increases peristalsis. and relaxes the sphincters. Increases secretions. 3. *Urinary*: Contracts urinary bladder & relaxes sphincters 4. *Bronchial*: Constricts bronchial muscles & increases the secretions. 5. *Eye*: Miosis & spasm of accommodation **B. NICOTINIC** 1. *Autonomic ganglia*: Stimulated to release noradrenaline and acetylcholine 2. *Skeletal muscles*: Induces contraction of skeletal muscle, but large doses lead to paralysis	1. Flushing, sweating, salivation, bradycardia 2. Hypotension and syncope 3. Cardiac arrhythmias and cardiac arrest, heart blocks 4. Bronchospasm. 5. Abdominal cramps, belching, nausea and vomiting 6. Eye: Ocular pain and spasm of accommodation	1. Paroxysmal atrial tachycardia 2. Peripheral vascular diseases 3. Gastric atony and paralytic ileus 4. Acute urinary retention. 5. Glaucoma 6. To stimulate pancreatic secretion for study of pancreatic function *Contra-indications:* 1. Hyperthyroidism 2. Peptic ulcer 3. Bronchial asthma 4. Myocardial infarction
2. ATROPINE ATROPINE SULFATE 0.5 mg/ml and 6 mg/ml 0.5 mg tablets. OXYPHENONIUM 10 mg orally, GLYCOPYROLLATE	Blocks the muscarinic effects of acetylcholine as it has the same affinity for muscarinic receptors as acetylcholine but poor intrinsic activity	1. Dry mouth, dysphagia, constipation, paralytic ileus 2. Urinary retention. 3. Blurred vision and precipites of glaucoma. 4. Allergic dermatitis. *Precautions:* 1. In elderly it precipitates glaucoma and urinary retention (if enlarged prostate). 2. In chronic lung diseases. it dries up secretion	1. Preanesthetic medication 2. Organophosphorus poisoning 3. Bradyarrhythmias 4. Motion sickness 5. Colic and dysmenorrhea 6. Peptic ulcer: Reduces HCl secretion and smooth muscles spasm. 7. Parkinsonism: To relieve tremors and rigidity. 8. To produce mydriasis & cycloplegia (e.g. fundus exam)

Drug/Dose	Action	Side Effects	Uses
PROPANTHELINE 15 mg thrice a day 30 mg at bedtime oral **PIRENZEPINE** 100 mg BDS orally	Decreases gastric acid secretion. Increases gastric emptying time, allows antacid to at on gastric mucosa for long time.	Less than atropine	1. Peptic ulcer 2. Abdominal colic
HOMATROPINE 1 to 2% eye drops mydriasis and cycloplegia Duration 24 to 48 hrs.	Paralyses the iris and ciliary muscle. Produces	Less than atropine	1. Pre anesthetic medication 2. OPC poisoning 3. Funduscopic examination 4. Iritis 5. Break adhesions between iris and ciliary body
EUCATROPINE 2% to 5% eye drops	Same as above Duration 12 to 24 hrs	Less than atropine	Same as above
3. NEOSTIGMINE 15-30 mg orally 0.5-2 mg I.M. or S.C. **PYRIDOSTIGMINE** 60-240 mg orally 1.5 mg S.C. or I.M. (Longer duration of action)	Inhibits both true and pseudo-cholinesterase and hence actions are similar to acetylcholine.	1. Salivation, sweating, lacrimation. 2. Nausea, abd. pain, diarrhea. 3. Constriction in chest, hypertension. 4. Tremors, paraesthesias and fasciculations.	1. Myasthenia gravis 2. Acute congestive glaucoma 3. Paralytic ileus and urinary retention 4. Treatment of curare poisoning. 5. Supraventricular tachycardia
4. EDROPHONIUM 10 mg/ml. 10 ml in a vial.	Similar to neostigmine, but rapid onset and short duration of action (10 min). It has a weak anticholinesterase activity as compared to neostigmine but it enhances neuromuscular transmission with a dose that is too low to affect the smooth muscles, myocardium & the glands.	Similar to neostigmine.	Diagnosis of myasthenia gravis.
13. OXIMES PAM (Pyridine aldoxime monostearate). 1 gm, I.V. slowly followed by 0.5 gm 6 hrly. DAM (di-acetyl monoxime)	Organophosphorous compounds cause irreversible inhibition of cholinesterase due to phosphorylation of the esteratic site. Oximes combine with these phosphor groups forming a soluble complex, thus setting free the esteratic site & causing a reactivation of enzyme.	1. Local irritation 2. Drowsiness, giddiness, diplopia 3. Tachycardia, hypotension	Antidote for organo-phosphorous poisoning - use in the first 48 hrs only.

DRUGS IN RESPIRATORY DISEASES

ANTI-ASTHMA AGENTS

1. **EPINEPHRINE (ADRENALINE)**	Refer Pg. 568		
2. **ISOPROTERENOL (ISOPRENALINE)**	Refer Pg. 568		
3. **ORCIPRENALINE** 20 mg TDS orally 0.5-1.0 ml IM	Similar to isoprenaline but lesser stimulant action on heart	Similar to Isoprenaline.	1. Bronchial asthma. 2. Bradyarrhythmias.
4. **BETA-2 STIMULANTS** **SALBUTAMOL** 100, 200, 400 µg inhalation 2-4 mg orally tds **SALMETEROL** 25 µg/puff 1-2 puffs BD **TERBUTALINE** 5 mg tds orally; 0.25 mg SC or 5 g/min IV **ISOETHARINE, FENOTEROL CARBUTEROL, IBUTEROL RIMITEROL, PIRBUTOL, RITODRINE**	Beta-2 stimulant. It is resistant to inactivation by COMT and has longer duration of action.	Nervousness, drowsiness, Weakness and tremors.	1. Bronchial asthma. 2. To delay delivery in premature labour. 3. Hyperkalemic periodic paralysis

Drug/Dose	Action	Side Effects	Uses
5. METHYL XANTHINE DERIVATIVES			
AMINOPHYLLINE 0.25 gm in 20 ml. 10% glucose I.V. **THEOPHYLLINE** 100,200,400 mg **ETOPHYLLINE-ETHYTENE DIAMINE**	1. Inhibits phosphodiesterase which increases local 3'5' cyclic AMP which stimulates beta-receptors in bronchial smooth muscles & relieves bronchospasm. 2. Peripheral vasodilator 3. Cardiac stimulant 4. Respiratory stimulant 5. Mild diuretic	1. Nausea, vomiting 2. Collapse and death 3. Convulsions and twitching of mouth	1. Bronchial asthma 2. Cardiac asthma 3. Diuretic 4. Cheyne's Stokes respiration 5. CO_2 narcosis 6. Respiratory stimulant 7. Cardiopulmonary resuscitation
6. EPHEDRINE HCI	Refer Pg. 569		
7. CORTICOSTEROIDS			
a) **SYSTEMIC CORTICOSTEROIDS: PREDNISOLONE BETAMETHASONE DEXAMETHASONE HYDROCORTISONE**	1. Inhibits phosphodiesterase 2. Reverses adenyl cyclase and ATPase abnormalities of leucocytes. 3. Exerts anti-inflammatory and stabilizing effect on cell membrane and lysozymes.	Refer Pg. 606	Refer Pg. 606
b) **BECLOMETHASONE DIPROPIONATE** 100 mg qds by inhalation. c) **BUDESONIDE** 100 µg BD puff d) **FLUTICASONE** 2000 µg/day	Inhaled steroid action. Anti-inflammatory and anti-allergic.	Candidiasis of mouth. (Always gargle after inhalation)	Bronchial asthma.
8. MAST CELL STABILISERS			
a) **DISODIUM CROMOGLYCATE** 5-20 mg capsules for inhalation.	Inhibits the degranulation of mast cells by stabilizing the membrane of mast cells and inhibiting the release of autocoids like SRS-A, serotonin, bradykinin.	Local irritation.	1. To prevent an acute episode of asthma 2. Allergic rhinitis 3. Other allergic disorders-food allergy, allergic alveolitis 4. Exercise-induced asthma 5. Ulcerative colitis 6. Aphthous stomatitis
b) **NEDROCROMIL SODIUM**	Same as above		
c) KETOTIFEN 1 mg B.D. 1 mg/5 ml syrup	Cromolyn analogue. Inhibits antigen induced release of chemical mediators especially histamine and SRS-A. Inhibits bronchial, nasal, ocular and dermal response to histamine. Interferes with eosinophil degranulation and chemotaxis and hence reduces inflammation	1. Drowsiness, dizziness, headache 2. Dry mouth, nausea vomiting 3. Increased appetite and weight gain 4. Thrombocytopenia with antidiabetic drug	1. Prophylaxis of childhood asthma 2. Allergic rhinitis 3. Allergic conjunctivitis 4. Allergic dermatitis 5. Desensitizer
9. **LEUKOTRIENE BLOCKERS**			
a) ZILUETON 800 mg OD **b) MONTELUCAST**	5-lipoxygenase inhibitor	Mild dyspepsia, headache, raised liver enzymes	1. Aspirin-induced asthma 2. Cold air-induced airway obstruction 3. Allergic rhinitis
10. **ANTI-CHOLINERGICS**			
a) IPRATROPIUM BROMIDE 40-80 µg, 1-2 puffs TDS **b) TIOTROPIUM BROMIDE** **c) OXYTROPIUM BROMIDE**	Atropine derivative	Similar to atropine	1. Smoker asthmatics 2. Chronic bronchitis, smokers 3. Perennial rhinitis, watery rhinorrhea

AGENTS FOR COUGH AND EXPECTORATION

Drug/Dose	Action	Side Effects	Uses
1. AMMONIUM EXPECTORANT 300 mg.	Stimulates the gastric reflex which increases respiratory tracts secretions, and produces less tenacious sputum which is easy to expectorate	1. Nausea, vomiting. 2. Metabolic acidosis.	Expectorant
2. **POTASSIUM IODIDE** 300mg. **POTASSIUM CITRATE** **VASICINE**	1. Acts reflexly as well as directly to increase the respiratory secretions. 2. Liquifies thick viscid sputum.	1. Iodism: Nasal catarrh, conjuntival swelling, edema of eyelids lacrimation, increased respiratory tract secretions, edema & ulcers of larynx, headache, skin rash 2. Hypothyroidism and goitre.	Expectorant
3. **CODEINE** 12mg in 4 ml.	Depresses respiratory centre	Constipation.	1. Analgesic 2. Antitussive
4. **DEXTROMETHORPHAN**	Same as codeine, but safer 10-20 mg TDS. Max 120 mg	Same as codeine, but safer	Same as codeine, but safer
5. **NOSCAPINE** 15-30 mg tds	1. Smooth muscle relaxant. 2. Bronchodilator. 3. Cough suppressant	Nausea	Antitussive
6. ACETYL CYSTEINE 10-20% solution direct instillation in tracheobronchial tree **CARBOCYSTEINE** METHYLCYSTEINE	Reduces viscosity of sputum.	1. Bronchospasm 2. Nausea, vomiting, stomatitis 3. Rhinorrhea, hemoptysis	To liquefy respiratory secretions
7. BROMHEXINE 8-16 mg tds orally or by inhalation.	Dissolves the mucopolysaccharide fibres, thus liquefies the sputum.	Insignificant	To liquefy respiratory secretions
8. **PANCREATIC DORNASE**	Degrades the DNA proteins and thus changes thick gelatinous sputum to thin milky material.	Allergy	To liquefy respiratory secretions

ANTI-ALLERGIC DRUGS

1. ANTI-HISTAMINICS A. DIPHENHYDRAMINE (DPH) 25-75 mg orally, 10 mg IM. B. PHENIRAMINE MALEATE (PN) 25-75 mg orally C. CHLORPHENIRAMINE MALEATE (CPN) 5.20 mg orally or IM. D. PROMETHAZINE (PM) 12.5-25 mg orally E. PROMETHAZINE (PMC) 25-75 mg orally. F. ANTAZOLINE (A) 50-100 mg	They inhibit the action of histamine releases on GI tract, uterus, blood vessels and salivation. They have no effect on bronchospasm, hypotension and gastric secretion.	1. CNS: Sedation, fatigue, lassitude, tinnitus, diplopia and euphoria. 2. Anti-cholinergic: Dryness of mouth, blurring of vision, tremors, impotence and retention of urine. 3. GI : Nausea, vomiting, epigastric distress. 4. Skin: Rash, photosensitivity. 5. Hemopoietic: Blood dyscrasias.	1. Allergic disease: Urticaria, hay fever, rhinorrhea, pruritus. 2. Hypnotic (DPH, PM) 3. In lytic cocktail (PM) to produce hypothermia. 4. Parkinsonism (DPH) 5. Motion sickness (PMC) 6. Cardiac arrhythmia (A, DPH) 7. Vertigo (PMC) 8. Drug-induced dystonias (extra-pyramidal reactions) (DPH, PM)
2. **ASTEMIZOLE** 10-30 mg once a day	Long acting H1 receptor antagonist without sedative effect	1. Dry mouth, abdominal pain, weight gain, increased appetite 2. Rash and eczema 3. CNS stimulation	Same as above
3. **LORATIDINE** 10 mg once a day orally	Similar to Astemizole	Similar to Astemizole. Can produce torsades de pointes, specially if co-prescribed with macrolides like Erythromycin	Same as above

Drug/Dose	Action	Side Effects	Uses
4. **TERFENADINE** 60 mg twice a day	Similar to Astemizole	Similar to Astemizole. Can produce torsades de pointes, specially if co-prescribed with-macrolides like Erythromycin	Same as above
5. **CETIRIZINE** 10 mg OD orally	Potent and highly selective H1-histamine receptor antagonist without anti-cholinergic and anti-serotoninergic actions	1. Headache, dizziness, drowsiness 2. GI discomfort	1. Allergic rhinitis 2. Urticaria
6. **FEXOFENADINE** 120-180 mg OD	Super-selective H1 blocker Anti-cytokine, anti-allergic.	Headache, nausea, fatigue	1. Allergic rhinitis 2. Allergic skin conditions 3. Urticaria

SEROTONINERGIC AGENTS

1. **CYPROHEPTADINE** 4-20 mg/day	1. It has anti-5 HT2, anti-histaminic, atropine-like anti-cholinergic, anti-tremor and anti-convulsant properties. 2. Directly stimulates hypothalamic appetite center 3. Stimulates hypothalamic CRH release 4. Suppresses aldosterone	1. Drowsiness, dizziness 2. Dry mouth 3. Mental confusion, headache, ataxia	1. Pruritus in allergic dermatitis, urticaria, etc. 2. Seasonal and perennial pollenosis. 3. To stimulate appetite 4. Post-gastrectomy dumping syndrome 5. Carcinoid syndrome 6. Rarely in refractory pituitary Cushing's disease 7. Rarely in refractory idiopathic aldosteronism
2. **KETANSERIN**	5 HT2 blocker		1. Vasospastic conditions like Raynaud's syndrome, peripheral vascular diseases 2. Bronchial asthma
3. **ONDANSETRON GRANISETRON**	5 HT3 blocker	Refer Pg. 610	Refer Pg.610
OTHER AGENTS ARE **KETOTIFEN, METHYSERGIDE, PIZOTIFEN, SUMATRIPTAN:**			Refer Pg. 571, 576

DRUGS IN CENTRAL NERVOUS SYSTEM DISEASES

OPIOIDS

1. **MORPHINE** 8-20 mg. orally 8-20 mg. S.C. or I.M.	Raises pain threshold & modifies emotional reaction to pain. Inhibits transmission of impulses across the pain pathways in CNS. In LVF, Morphine causes peripheral vasodilation causing shunting of blood from pulmonary to peripheral vasculature reducing cardiac work and pulmonary pressure.	1. Intolerance: Skin rash, anaphylaxis 2. Hypotension 3. Respiratory depression and bronchoconstriction 4. Urinary retention in elderly patients with prostate enlargement 5. Tolerance 6. Drug dependence 7. Constipation	1. Analgesic 2. Sedative and hypnotic 3. Preanesthetic medication 4. Antitussive 5. Severe diarrheas 6. L.V.F.

2. **PETHIDINE**
Same as morphine except for the following differences:

	Morphine	*Pethidine*
1. Source	Natural	Semisynthetic
2. Potency	1/10th	10 times
3. Pupils	Miosis	Mydriasis
4. Vomiting	Less	More
5. Antitussive	Marked	Not so
6. Heart rate	Bradycardia	Tachycardia
7. G.I. absorption	Erratic	Good
8. Dose	10-1 Smg.	50-100 mg.

Drug/Dose	Action	Side Effects	Uses
3. **ETHOHEPTAZINE** 75-150 mg TDS/QDS	Pethidine analogue	1. Nausea 2. Cholinergic	Pain and dysmenorrhea
3. **PENTAZOCIN** 60-120 mg. IV. I.M., S.C. or orally.	Similar to morphine	1. Respiratory depression. 2. Hallucinations and unpleasant dreams. 3. Pulmonary and systemic hypertension.	Potent analgesic with low addiction liability.
4. **TRAMADOL** 50-100 mg TDS/QDS 100 mg S.C., I.M. or I.V.	Weak agonist of all opioid receptors specially μ receptors	Similar to opioids	1. Moderate to severe pain 2. Post-operative pain
5. **BUPRINORPHINE** 0.2 mg tablets 0.3 mg/ml injection 0.2 - 0.4 mg sublingual every 8 hours; 0.3 to 0.6 mg I.M. or I.V. slowly every 6-8 hrs	Partial agonist at a opioid receptor	1. Dizziness 2. Sedation 3. Respiratory depression 4. Nausea, vomiting	Same as Morphine
6. **NALOXONE** 1 ml vial containing 0.4 mg/ml 0.8 - 2 mg every 2-3 min as bolus; maximum 10 mg	Pure antagonist of morphine at all receptors	1. Seizures 2. Pulmonary edema	Treatment of morphine toxicity
7. **NALORPHINE HYDROBROMIDE** 5-10 mg IM	Partial agonist of the nalorphine type	1. Nausea, vomiting, miosis, sweating, pallor etc. 2. Respiratory depression	1. Effective antidote to morphine and other opioid compounds overdose 2. Opioid de-addiction 3. With morphine, for opioid withdrawal syndrome
8. **NALTREXONE** 50 mg upto 350 mg/day	Long acting pure opioid antagonist	1. GI disturbance 2 Nervousness, insomnia, cramps 3. Thrombocytopenia, hepatotoxic	1. Heroin addiction 2. Opioid addiction 3. Deaddiction
9. **NEFOPAM** 30 mg BD/TDS or 20 mg I.M. BD	1. Analgesic via increasing monoaminergic function 2. Inhibits re-uptake of dopamine, nor-adrenaline and serotonin 3. No effect on opioid receptors, prostaglandins & therefore no anti-inflammatory or antipyretic effect	1. Nausea, vomiting 2. Insomnia/drowsiness 3. Sweating 4. Anti-cholinergic side effects	Pain killer

ANALGESICS AND ANTI-INFLAMMATORY DRUGS

NON-OPIOIDS

1. **SALICYLATES** ACETYL SALICYLIC ACID 300 mg - 1.0 gm. upto 4-5 gms/day orally. METHYL SALICYLATE 25% v/v in peanut oil.	Reduces the temperature by resetting the temperature regulating centre to normal when it is deranged. It blocks the pain centres in thalamus. It inhibits synthesis of prostaglandins & prevents sensitisation of pain receptors to histamine, bradykinin and 5 HT agent, mediators of pain and inflammation. It inhibits platelet aggreation by inhibiting ADP release from platelets & inhibiting the synthesis of prostaglandin endoperoxidase & thromboxane A2. A single dose may have this effect for 4-7 days.	1. Nausea, vomiting 2. Intolerance 3. Increases P.T. 4. Fatty infiltration of liver and kidneys 5. Salicylism: Headache, dizziness, vertigo, tinnitus, diminished hearing and vision 6. Respiratory depression 7. Acid-base imbalance: Respiratory alkalosis, metabolic acidosis.	1. Locally: Keratolytic, fungistatic and mild antiseptic 2. Analgesic 3. Anti-pyretic 4. Anti-rheumatic 5. Prevents platelet aggregation (low doses)

Drug/Dose	Action	Side Effects	Uses
2. **PARACETAMOL** 2-5 gm/day in divided doses	Similar analgesic and anti-pyretic actions as salicylates	1. Hemolytic anemia 2. Skin rash 3. Renal damage 4. Liver damage 5. Methemoglobinemia	Similar to salicylates, but more potent anti-pyretic without: 1. G.I. irritation or 2. Acid-base and electrolyte imbalance.
3. **PHENYLBUTAZONE** 200-400 mg/day.	Anti-inflammatory property more than salicylates or paracetamol, but less potent antipyretic or analgesic. Inhibits reabsorption of urea at proximal tubule thus causing uricosuria.	1. Nausea, vomiting, dyspepsia 2. Skin rashes and exfoliative dermatitis. 3. Aplastic anemia 4. Hepatitis, nephritis 5. Hypothyroidism 6. Precipitates C.C.F.	1. Gout. 2. Rheumatoid arthritis. 3. Osteoarthritis. 4. Ankylosing spondylitis.
4. **OXYPHENBUTAZONE** 100 mg TDS	It is a metabolic product of phenylbutazone.	Similar to it but lesser-gastric irritant.	Anti-inflammatory agent.
5. **INDOMETHACIN** 50-150 mg.	It inhibits prostaglandin synthesis and phosphodiesterase, thus increasing intra-cellular cyclic AMP. It also interferes with migration of leucocytes into the inflammatory site.Thus it is an antiinflammatory, analgesic and anti-pyretic agent.	1. Headache, giddiness, confusion, depression and blurred vision. 2. Nausea, vomiting, diarrhea. Peptic ulcer. 3. Skin rashes.	1. Gout 2. Osteoarthritis. 3. Rheumatoid arthritis. 4. Ankylosing spondylitis.
6. **IBUPROFEN** 200-400 mg TDS	Analgesic, anti-pyretic and anti-inflammatory properties similar to aspirin	Similar to aspirin but less potent	1. Acute gout 2. Rheumatoid arthritis 3. Ankylosing spondylitis 4. Osteoarthritis
7. **NAPROXEN** 250 mg BD	Same as Ibuprofen	Same as Ibuprofen	Same as Ibuprofen
8. **KETOPROFEN** 50 mg TDS	Same as Ibuprofen	Same as Ibuprofen	Same as Ibuprofen
9. **FENOPROFEN** 300-600 mg TDS	Same as Ibuprofen	Same as Ibuprofen	Same as Ibuprofen
10. **FLURBIPROFEN** 50 mg TDS	Same as Ibuprofen	Same as Ibuprofen	Same as Ibuprofen
11. **MEFENAMIC ACID** 250-500 mg TD	Similar to aspirin but much weaker analgesic	1. Gastric upset 2. Dizziness, headache 3. Skin rash 4. Hemolytic anemia	Chronic dull-aching pain
12. **ENFENAMIC ACID** 1.2-2.4 gm/day	Similar to Aspirin	Similar to Aspirin but less gastric upset.	Analgesic, antipyretic and anti-inflammatory agent.
13. **TOLMETIN**	Similar to Indomethacin	Similar to Indomethacin.	Similar to Indomethacin but less potent.
14. **PIROXICAM** 10-20 mg OD (analgesic) 20-40 mg OD (anti-inflammatory)	Similar to Aspirin	Similar to Aspirin but less G.I. upset	Similar to Aspirin
15. **TENOXICAM** 20mg - OD orally	Similar to Aspirin	Similar to Aspirin but less G.I. side-effects	Similar to Aspirin
16. **ALCOFENAC** 1 gm TDS	Similar to Piroxicam. but more potent	Similar to Aspirin	Similar to Aspirin
17. **DICLOFENAC** 50 mg twice a day orally	Similar to Alcofenac	Similar to Aspirin	Similar to Aspirin
18. **KETOROLAC** 10-20 mg TDS	It inhibits cyclo-oxygenase and the formation of prostaglandins. Is peripherally acting analgesic.	1. Renal toxicity 2. Hypersensitivity	Analgesic, but also has anti-pyretic and anti-inflammatory properties.

Drug/Dose	Action	Side Effects	Uses
19. **COX-2 INHIBITORS** **NIMESULIDE** 100 mg BD/TDS **MELOXICAM** 7.5-15 mg BD/TDS	1. Superselective cyclo-oxygenase type-II (Cox-2) blocker 2. Weak inhibitor of prostaglandins 3. Potent anti-inflammatory 4. Anti-histaminic 5. Inhibits superoxide anion formation 6. Inhibits release of TNF-α 7. Anti-cytokine	Lesser than other NSAIDS	1. Pain 2. Similar to other NSAIDS

DRUGS IN MIGRAINE

1. ERGOT ALKALOIDS a) ERGOTAMINETARTARATE (ET) - 1-2 mg; max. 6 mg/day or 12 mg/wk orally b) DIHYDROERGOTAMINE (DHE) - 1 mg S.C. c) ERGOMETRINE MALEATE (EM) - 0.5 mg I.V. d) METHYLERGOMETRINE (MM) - 0.25-0.5 mg orally or 0.2 mg S.C./I.M./I.V. e) METHYSERGIDE (MS) - 1-2 mg orallyTDS	1. Vascular: Potent vasoconstrictor directly (ET) or by alpha blockade (DHE). They also have 5 HT antagonistic activity with partial 5 HT1 agonistic action. 2. Oxytocic action on the uterus 3. Hyperperistalsis	1. Vascular: Thrombosis, gangrene 2. Nausea, vomiting 3. Intra-uterine fetal death (EM,MM) 4. Uterine rupture (EM,MM) 5. Retroperitoneal fibrosis (MS)	1. Acute attack of migraine (ET,DHE) 2. Migraine prophylaxis (MS) 3. Post-partum hemorrhage (EM,MM) 4. Uterine involution (EM) 5. Hypertension (Hydergine) 6. Orthostatic hypotension (oral DHE)
2. **SUMATRIPTAN** 6 mg S.C. or 100 mg orally	5 HT1 receptor agonist	1. Flushing, neck pain, dizziness, tingling 2. Can precipitate coronary ischemia 3. Allergy and rash	1. Acute attack of migraine 2. Status migrainosus 3. Cluster headache 4. Refractory headache
3. **FLUNARAZINE** 10 mg OD/BD	Piperazine calcium blocker. Cerebroselective action.	1. Depression 2. Extra-pyramidal 3. Rash	1. Prophylaxis of classical & common migraine. 2. Vertigo 3. Vestibular dysfunction 4. Peripheral vascular disease 5. Cerebrovascular disease 6. Adjuvant in refractory epilepsy
4. **PIZOTIFEN** 0.5- 2 mg OD at bedtime	1. Antihistaminic 2. 5 HT antagonist	1. Drowsiness 2. Weight gain 3. Urinary retention	1. Migraine prophylaxis 2. Prophylaxis of vascular headaches
5. **VERAPAMIL** 80 mg BD or 180 mg SR	Refer Pg. 560	Refer Pg. 560	Migraine prophylaxis

ALSO REFER ANALGESICS AND ANTI-INFLAMMATORY AGENTS

DRUGS IN GOUT AND ARTHRITIS

1. **COLCHICINE** 1 mg followed by 0.5 mg every 2 hours until pain is relieved or diarrhea. Max. dose 8 mg/day Prophylactic dose: 0.5 mg OD/BD	1. Inhibits microtubular function. Inhibits migration of granulocytes 3. Prevents production or release of glycoproteins by granulocytes 4. Prevents intra-articular release of cytokines by neutrophils in response to inflammation 5. Binds to tubulin, anti-mitotic action, and anti-fibroblastic.	1. Diarrhea 2. Anemia, leukopenia 3. Alopecia 4. Myopathy	1. Acute attack of gout 2. Prevention of gout 3. Primary biliary cirrhosis 4. Prevention of familial Mediterranean fever

Drug/Dose	Action	Side Effects	Uses
2. **ALLOPURINOL** 100-200 mg TDS	It inhibits xanthine oxidase and prevents the formation of uric acid from xanthine & hypoxanthine. It also increases the excretion of xanthine and hypoxanthine in urine	1. Nausea, vomiting, diarrhea 2. Allergy 3. Leucopenia 4. Hepatic damage 5. Hemosiderosis	1. Gout 2. Kala-azar 3. Secondary hyperuricemia specially with cancer chemotherapy
3. **PROBENECID** 0.5 gm OD-TDS	1. In low doses, decreases distal tubal secretion of uric acid 2. In high doses, increases excretion of uric acid by blocking tubular resorption (Uricosuric action)	1. Dyspepsia 2. Skin rash 3. Urate crystal nephropathy	1. Hyperuricemia 2. Gout prevention 3. In combination with penicillin, to increase duration of action
4. **GOLD SALTS SODIUM AUROTHIOMALATE** 10-25 mg I.M. weekly **AURONOFIN** 6 mg BD orally	Not known. It gets deposited in synovial macrophages, especially in activity inflamed joints	1. Dermatitis 2. Bone marrow depression 3. Kidney damage 4. Oral ulcers 5. Liver damage	Rheumatoid arthritis

ALSO REFER TO ANALGESICS AND ANTI-INFLAMMATORY AGENTS

ANTI-EPILEPTIC DRUGS

1. **DIPHENYLHYDANTOIN SODIUM** 100 mg tds; 4 mg - 8 mg/kg. **PHENACEMIDE** Analogue of phenyl hydantoin; Used in psychomotor epilepsy **METHOIN ETHOTOIN**	Inhibits the spread of seizure discharge in brain by decreasing intraneuronal sodium. It restores the balance between the excitatory glucamate pathway and inhibitory GABA pathway and causes anti-epileptic action	1. Intolerance: Rash 2. Gum hypertrophy 3. Cerebellar ataxia 4. Megaloblastic anemia 5. Nausea, vomiting 6. Aplastic anemia 7. Hirsutism 8. Osteomalacia 9. Facial coarsening	1. Grand mal epilepsy 2. Psychomotor and focal seizures 3. Cardiac arrhythmias 4. Trigeminal neuralgias 5. Diabetic neuropathy 6. Chorea Does not sedate the patient
2. **PHENOBARBITONE**	Refer Pg. 581 (Barbiturates)		
3. **PRIMIDONE** 125 mg qd sto 250 mg qds	Converted to phenobarbitone in body	1. Anorexia, nausea. 2. Drowsiness, headache, vertigo, ataxia. 3. Impotence, skin rash 4. Aplastic anemia	Grand mal psychomotor and myoclonic epilepsy.
4. **TROXIDONE** 250 mg qds	Raises the threshold of excitability of thalamic nuclei and thus prevents the spread of electrical activity to the thalamus.	1. Drowsiness and personality change. 2. Hemeralopia (blurring in bright light). 3. Skin rash, precipitates SLE 4. Agranulocytosis. 5. Hepatitis and Nephrosis	1. Useful selectively in Petitmal (aggravates grand mal). 2. Rarely in psychomotor epilepsy of abrupt onset.
5. **PARAMETHADIONE** 900 mg/day	Similar to troxidone but less toxic and less effective.		
6. **SUCCINIMIDES** 1. ETHOSUXIMIDE 1.0 gm 2. PHENSUXIMIDE 2.0 gm 3. METHSUXIMIDE 0.9 gm	Similar to troxidone	1. Anorexia, nausea, vomiting, hiccups 2. Drowsiness, dizziness 3. Leucopenia 4. Nephrotoxicity, skin rash	1. Petitmal 2. Myoclonic seizures
7. **DIAZEPAM** 10 mg I.V. or 5-10 mg tds orally. **CLOBAZAM** 10-20 mg total dose	Suppresses the spread of the seizure by raising seizure threshold. It, however, does not suppress the abnormal discharges of the focus.	1. Drowsiness. 2. Ataxia. 3. Respiratory depression 4. Hypotension. Tolerance develops for anti-epileptic action, hence it is used for status epilepticus only.	1. Petit mal, psychomotor and status epilepticus 2. Sedative & hypnotic 3. Muscle relaxant in tetanus 4. Preanesthetic medication 5. Alcohol withdrawal 6. Anxiety neurosis

Drug/Dose	Action	Side Effects	Uses
8. CARBAMAZEPINE 100 mgtds (max. dose 1200 mg.)	Similar to diphenylhydantoin.	1. Anorexia, nausea. 2. Ataxia, diplopia, dizziness, drowsiness. 3. Mental confusion 4. Skin rash 5. Bone-marrow depression 6. Obstructive jaundice 7. Peripheral neuritis	1. Grand mal and psychomotor seizures 2. Temporal lobe epilepsy 3. Trigeminal and glossopharyngeal neuralgias 4. Central diabetes insipidus 5. Lightning pains of tabes dorsalis 6. Diabetic neuropathy 7. Deafferentation pain 8. Psychiatric disorders: manic-depressive psychosis, drug resistant schizophrenia
9. NITRAZEPAM 5 - 40 mg. total dose	Similar to diazepam.	1. Lethargy 2. Ataxia	Petit mal, myoclonic seizures and hypsarrhythmia
10. CLONAZEPAM 0.5 mg tablets; 4-8 mg/day	Similar to diazepam.	1. Drowsiness 2. Ataxia, dyskinesias 3. Hyperexcitability 4. Hypotension	Petit mal and myoclonic seizures.
11. SODIUM VALPROATE 200 mg/day initially then 600-1600 mg/day	It acts by inhibiting GABA transaminase, thus increasing the concentration of GABA, an inhibitory transmitter in the CNS	1. Nausea, vomiting, diarrhea 2. Liver damage 3. Interferes with platelet aggregation. 4. Drowsiness 5. Weight gain 6. Loss and curling of hair 7. Teratogenic	Grand mal, petit mal, myoclonic and psychomotor epilepsy. It is less effective in partial seizures. It increases phenobarbital and decreases phenytoin blood levels on simultaneous administration
12. GABAPENTIN 900to 1800 mg/day in three divided doses	Increases release of GABA	Same as sodium valproate	Partial seizures resistant to other therapy.
13. TIAGABINE 4-12mg TDS	GABA reuptake inhibitor	Headache, dizziness, somnolence	Add-on drug for partial seizures with or without secondary generalisation
14. VIGABATRIN 500 mg; dose 1-3 g/day	GABA transaminase inhibitor, increases brain GABA	1. Weight gain 2. Drowsiness, diplopia 3. Depression, memory disturbances	Refractory epilepsy
15. LAMOTRIGINE 150- 500 mgBD	Blocks the influx of Sodium ions. Antagonist of NMDA glutamate receptor	1. Nausea, headache, ataxia 2. Skin rash 3. Steven Johnson syndrome	1. Partial and generalised secondary seizures 2. Lennox-Gestant syndrome
16. FELBAMATE 400mg, 600mg 2400 - 3600 mg/day	Dicarbamide derivative Exact Mechanism unknown	1. CNS: Insomnia, dizziness 2. Aplastic anemia 3. Liver failure 4. Weight loss, GI irritation	Partial seizures Lennox-Gastaut syndrome Refractory Epilepsy
17. SULTHIAME 100-600 mg/day	Sulphonamide derivative	1. Nausea, anorexia, weight loss 2. Apathy, ataxia, blurred vision 3. Photophobia, psychosis, paresthesia 4. Kidney damage	1. Temporal lobe epilepsy 2. Myoclonic epilepsy 3. Refractory grand mal epilepsy
18. TOPIRAMATE 300-600 mg/day	Blocks sodium channels through GABA	1. GI side effects 2. Same as newer anti-epileptics	Refractory epilepsy

MUSCLE RELAXANTS

Drug/Dose	Action	Side Effects	Uses
1. DIAZEPAM 2-10 mg tds orally	Centrally acting muscle relaxant	Refer Pg. 577	Refer Pg. 577
2. MEPHENESIN 1-2gm orally 0.5-1 gm I.V.	Acts on the entire neuraxis and causes muscle relaxation	1. Anorexia, nausea, vomiting 2. Dizziness, diplopia, nystagmus, ataxia 3. Respiratory depression 4. Hemolysis 5. Changeof hair colour	1. Myalgia 2. Arthralgia 3. Myositis 4. Spastic neurological disorders
3. BACLOFEN 5 mgTDS increased upto 80 mg/day	Acts on the pre-synaptic mechanisms and reduces the release of excitatory transmitter.	1. Drowsiness, lassitude, hallucination, depression 2. Blurred vision 3. GI disturbances	1. Relief of flexor spasm 2. Reduce tonic flexor dystonia of lower limbs in spinal spasticity 3. Refractory hiccups
4. DANTROLENE 25 mgTDS upto 300 mg/day.	It reduces the calcium release into the sarcoplasm and thus the muscle contraction is weakened.	1. Dizziness, drowsiness, fatigue and weakness 2. Diarrhea 3. Hepatotoxicity	1. Spasticity 2. Malignant hyperpyrexia 3. Neuroleptic malignant syndromes (NMS)
5. D-TUBOCURARINE 6-10 mg IV (1 ml = 3mg)	It combines with the receptors on the motor end-plate and thus blocks the action of acetylcholine by Competitive blockade	1. Hypoxia and respiratory paralysis 2. Hypotension 3. Esophageal ulceration due to paralysis of esophageal sphincter and regurgitation of gastric juice	Muscle relaxant
6. GALLAMINE 1 mg/kg IV	Similar to D-Tubocurarine	1. Respiratory paralysis 2. Hypotension, tachycardia and cardiac arrhythmias	Muscle relaxant
7. SUCCINYLCHOLINE 0.1-0.5 mg/kg IV	Acts as a partial agonist of acetylcholine	1. Cardiac arrest and ventricular arrhythmias 2. Respiratory failure 3. Muscle soreness	Muscle relaxant
8. ALCURONIUMCHLORIDE 0.04 - 0.08 mg/kg I.V. **ATRACURIUM, DOXACURIUM, MIVACURIUM, ROCURINIUM**	Same as D-Tubocurarine Does not release histamine Does not block ganglia	Same as D-Tubocurarine	Same as D-Tubocurarine
9. PANCURONIUM 0.04 - 0.08 mg//kg I.V.	Same as above	Same as above	More potent than D-Tubocurarine
10. VECURONIUM 80 - 100 µg/kg I.V.	Same as above	Same as above	Same as above
11. BOTULINIUM TOXIN TYPE A	Binds irreversible to cholinergic presynaptic sites	Uncommon and not serious	Spastic disorders like spasmodic torticollis, hemifacial spasm, blepharospasm, laryngospasm.

ANTI-PSYCHOTIC DRUGS

1. PHENOTHIAZINES CHLORPROMAZINE 10,25,50,100 mg. tablets. Dose: 100-1500 mg 25 mg/ml I.M. FLUPHENAZINE 2.5-10 mg orally (3-4 div.doses) PERPHENAZINE 12.5-50mg every 2-4 weeks	1. Reduces the incoming sensory stimuli by acting on brain-stem recticular formation. 2. Modifies the functions of the limbic system. 3. Causes chemical blockade of noradrenaline, dopamine and 5 HT, decreasing the sympathetic activity in hypothalamus.	1. Intolerance: Skin eruptions, visceral yellowish brown or purple pigmentation due to melanin or melanin-like substance 2. Anticholinergic effects 3. Thrombocytopenia and aplastic anemia 4. Intra-hepatic cholestasis. 5. CNS: Drowsiness, restlessness. Parkinsonism, hypothermia 6. Endocrine: Gynecomastia, weight gain, impotence, lactation & mental irregularities. Aggravation of diabetes mellitus.	1. Major Psychosis: Schizophrenia 2. Aggressive behavioral disorders in children. 3. Anti-emetic (depresses chemo-receptor trigger zone) 4. Anti-hiccup 5. To include hypothermia 6. Muscle relaxant in tetanus 7. Pre-anesthetic medication 8. Senile psychosis 9. Manic depressive psychosis NB: Potentiates analgesic drugs like morphine and phenobarbitone.

Drug/Dose	Action	Side Effects	Uses
2. RAUWALFIAALKALOIDS	Refer Pg. 565 (Reserpine)		
3. HALOPERIDOL 1.5 - 7.5 mg tds TRIFLUPERIDOL DROPERIDOL PENFLURIDOL	As phenothiazines.	Similar to phenothiazines but with less sedative and anti-cholinergic properties	1. Highly agitated and manic patients 2. Psychosis 3. Anxiety
4. PIMOZIDE 2-20 mg/day.	As phenothiazines	1. Drowsiness, extrapyramidal symptoms, tardive dyskinesias. 2. Skin rash 3. Glycosuria 4. Liver dysfunction	1. Psychosis 2. Anxiety 3. Behaviour disorders 4. Anorexia nervosa 5.Gilles de la Tourette syndrome 6. Malignant melanoma
5. MEPROBAMATE 400mg tds	1. Blocks inter-neuronal circuits 2. Inhibits variety of responses to hypothalamic stimulation. No effect on ANS.	1. Drowsiness, inco-ordination 2. Allergic reactions. 3. Blood dyscrasias 4. Tolerance and dependance	1. Anxiety 2. Neurosis Its advantage is that Parkinsonism does not occur and side-effects are mild.
6. CLOZAPINE 25 mg twice a day orally Maximum 200 to 250 mg OLANZAPINE 5-20 mg/day	Minimal interaction with Dopamine receptors. Less likely to produce extra-pyramidal effects. Interacts with presynaptic α2 adrenergic receptors and 5 HT receptors. Improves negative symptoms	Agranulocytosis (requires periodic monitoring of blood count). Other effects similar to phenothiazines	1. Refractory cases of schizophrenia and major psychosis 2. Chronic schizophrenia
7. RESPERIDONE 1-2 mg/day	Atypical anti-psychotic drug which blocks D2, 5HT, α2 and H1 receptors	1. Dyskinesias like akathisia 2. Lesser than others	1. Psychosis -typical & atypical 2. Schizophrenia

SEDATIVES / HYPNOTICS

1. CHLORDIAZEPOXIDE 10-30 mg/day	Exact mechanism is not known. It probably acts on the limbic system and the brain-stem reticular system. It probably also acts on the neurons containing GABA increasing the concentration of the latter. This may be responsible for muscle relaxant and anti-convulsant action	1. Drowsiness, lethargy 2. Allergic reactions 3. Blood dyscrasias 4. Tolerance 5. May produce bizarre reactions with MAOI, barbiturates, alcohol and amitriptyline.	1. Anxiety 2. Withdrawal of alcohol in alcoholics 3. Epilepsy 4. Pre-anesthetic medication
2. DIAZEPAM	Refer Pg. 577		
3. OXAZEPAM 15-60 mg/day orally	Similar to diazepam	Similar to diazepam	Similar to diazepam.
4. ALPRAZOLAM 0.25, 0.5 and 1.0 mg tablets 1-3 mg/day in divided doses	Similar to diazepam.	Similar to diazepam.	1. Similar to diazepam 2. Panic disorders 3. Phobias 4. Psychosomatic disorders 5. Withdrawal states
5. LORAZEPAM 1 to 4 mg orally at bedtime	Similar to Diazepam	Similar to Diazepam	Similar to Diazepam
6. NITRAZEPAM 5 to 10 mg orally	Similar to diazepam	Similar to diazepam	Infantile spasms or myoclonic jerks
7. BUSPIRONE 5-10 mg TDS	Acts mainly on the 5HT-1a receptors. Interacts with dopaminergic D2 receptors	Dizziness and Drowsiness	Anxioselective for anxiety state without sedative, hypnotic, muscle relaxant and anti-convulsant properties
8. FLUMEZANIL 0.1-0.2 mg I.V.	Blocks benzodiazepine receptors	1. Withdrawal syndrome 2. Contra-indicated in head injury	1. Hepatic encephalopathy 2. Antidote to benzodiazepine poisoning

Drug/Dose	Action	Side Effects	Uses
9. CHLORMETHIAZOLE 192mg	Thiazole derivative with sedative, hypnotic and anti-convulsant action	1. Tingling, numbness 2. Hypotension 3. Respiratory depression	1. Delirium tremens 2. Adjuvant with anesthetic agents like nitrous oxide 3. Refractory status epilepticus 4. Hypnotic in elderly
10. BARBITURATES **PHENOBARBITONE** 30 mg - 400 mg orally or I.M.	Barbiturates inhibit the neuronal uptake of GABA or may stimulate the release of GABA which depresses CNS. REM sleep is suppressed. Depresses respiration by abolishing neurogenic, chemical & hypoxic drive. It causes hypotension by: 1. Direct myocardial and VMC depression 2. Hypoxia 3. Sympathetic blockade	1. *Intolerance*: Nausea, vomiting 2. *Allergic*: Urticaria, angioedema. 3. Megaloblastic anemia 4. Tolerance habituation and addiction 5. Aggravates petit mal and may cause excitement and hyperactivity in old people and children 6. Precipitates acute porphyria. 7. During labour may depress fetal respiration	1. As a sedative and hypnotic 2. Anti-convulsant, Grand-mal 3. Anesthesia (Thiopental) and in prenesthetic medication. 4. Potentiation of action of analgesics like salicylates 5. In jaundice, to increase the enzyme conjugation of bilirubin
11. GLUTETHIMIDE 0.5-1.0 gm orally	It induces hypnosis without analgesics, anticonvulsant or antitussive action. It suppresses REM sleep	1. Mydriasis, paralytic ileus, dry-mouth 2. Respiratory depression 3. Hypotension 4. Tremors, spasticity and brisk jerks or peripheral neuropathy. Psychosis. 5. Addiction 6. Blood dyscrasias	Sedative and hypnotic
12. CHLORAL HYDRATE 0.5-2.0 gm orally	Facilitates sleep induction. Does not affect sleep maintenance	1. Nausea, vomiting, unpleasant taste 2. Pin-point pupils 3. Hepatic and renal damage.	Sedative and hypnotic which does not depress respiratory or cardiovascular system.
13. PARALDEHYDE 3-8 ml orally, 10 ml deep I.M.	Selective hypnotic action without analgesic action. It has a rapid anti-convulsant effect (in 10-15 minutes).	1. Gastric irritant. 2. Tissue damage and nerve injury on I.M. injection. 3. Imparts odour to breath 4. Decomposes in presence of heat & light to acetaldehyde which may lead to death	1. Sedative and hypnotic. 2. Anti-convulsant.
14. ZOPICLONE 7.5 - 15 mg at night	1. Cyclopyrrolone, activates GABA via benzodiazepine receptors. 2. Anti-anxiety, anti-convulsant and muscle relaxant action.	1. Metallic or bitter taste 2. Nausea, vomiting 3. Neuropsychiatric disturbances	1. All types of insomnia 2. Nocturnal awakening 3. Early awakening
15. TRICLOFOS 1 g (10 ml) at night 250 mg (2.5 ml) in children	Trichloroethanol ester	1. Rash 2. Nausea, vomiting 3. Neuropsychiatric disorders	1. Insomnia 2. Sedation 3. Restlessness 4. Refractory seizures 5. EEG premedication 6. In children, for recurrent colic, teething, fretfulness

ANTI-DEPRESSANTS

Drug/Dose	Action	Side Effects	Uses
1. MAO-INHIBITORS			
a. ISOCARBOXAZIDE 10-30 mg orally b. NIOLAMIDE 75-150 mg orally c. PHENELAZINE 45-60 mg orally d. TRANYLCYPROMINE 10-30 mg orally e. BROFAROAMINE f. MOCLOBEMIDE	MAO oxidizes nor-adrenaline, dopamine and 5 HT to its inactive compounds. MAOI leads to accumulation of these amines in brain leading to excitement and increased motor activity in depressed person in whom these amines are probably low.	1. Behavioral: Headache, disturbed sleep, excitement, activates latent psychosis 2. CNS: Tremors: ataxia and hyperreflexia 3. Hypertensive crisis: If given with amphetamine ephedrine, cheese (tyramine), broad beans (DOPA), yeast, yoghurt, buttermilk, meat extracts 4. ANS: Constipation impotence, dry mouth 5. Hepatocellular jaundice 6. Allergy	Antidepressant. Interaction with morphine, pethidine, barbiturates, anticholinergics, imipramine.
2. TRICYCLIC ANTIDEPRESSANTS			
a. IMPRAMINE HYDROCHLORIDE b. TRIMIPRAMINE c. DESPRIMINE d. AMITRIPTYLINE	Inhibit the re-absorption of nor-adrenaline on its storage site thus causing a local increase in active nor-adrenaline at the receptor sites.	1. Anticholinergic 2. Aggravates latent psychosis 3. Arrhythmias and hypotension 4. Allergy 5. Cholestasis	1. Anti-depressant 2. Nocturnal enuresis 3. Acute panic attacks 4. Migraine 5. Deafferentation pain
e. DOXEPIN 50-150 mg orally		6. Agranulocytosis	6. Bulimia nervosa 7. Diabetic neuropathy
3. MIANSERIN 10-30 mg t.d.s	It blocks the presynaptic alpha adrenoceptors and increases the turnover of brain nor-adrenaline. Unlike amitriptyline it does not prevent the peripheral re-uptake of noradrenaline	1. Drowsiness, ataxia and dizziness 2. Weight gain 3. Agranulocytosis 4. Patients may swing from depression to mania 5. May raise blood sugar concentration	Anti-depressant without anticholinergic and cardiotoxic effects. Similar to tricyclics.
4. TRAZODONE 100-200 mg TDS **BUPROPION** 200-300 mg	Heterocyclic antidepressant	1. Sedation 2. VPBs and postural hypotension	1. Severe depression 2. Insomnia
5. NOMIFENSINE MALEATE 50 mg three times a day up to 200 mg/day	It prevents the re-uptake of dopamine and noradrenaline. It has no effect on serotonin.	1. Drowsiness, dizziness 2. Tachycardia 3. Dry mouth 4. Hemolytic anemia 5. Patients may swing from depression to hypomania	1. Anti-depressant 2. Parkinsonism 3. To diagnose hyperprolactinemia
6. MIANSERIN 10-30 mg t.d.s	It blocks the presynaptic alpha adrenoceptors and increases the turnover of brain nor-adrenaline. Unlike amitriptyline it does not prevent the peripheral re-uptake of nor-adrenaline	1. Drowsiness, ataxia and dizziness 2. Weight gain 3. Agranulocytosis 4. Patients may swing from depression to mania 5. May raise blood sugar concentration	Anti-depressant without anticholinergic and cardiotoxic effects. Similar to tricyclics.
7. TRAZODONE 100-200 mg TDS **BUPROPION** 200-300 mg	Heterocyclic antidepressant	1. Sedation 2. VPBs and postural hypotension	1. Severe depression 2. Insomnia
8. NOMIFENSINE MALEATE 50 mg three times a day up to 200 mg/day	It prevents the re-uptake of dopamine and nor-adrenaline. It has no effect on serotonin.	1. Drowsiness, dizziness 2. Tachycardia 3. Dry mouth 4. Hemolytic anemia 5. Patients may swing from depression to hypomania	1. Anti-depressant 2. Parkinsonism 3. To diagnose hyperprolactinemia

Drug/Dose	Action	Side Effects	Uses
9. SELECTIVE SEROTONIN REUPTAKE INHIBITORS			
a) FLUOXETINE 20-40 mg twice a day b) SERTALINE 50-200 mg OD c) FLUVOXAMINE 50-200 mg d) PAROXETINE 10-50 mg e) ZIMELDINE f) CITALOPRAM	Selective serotonin reuptake inhibitor Lesser anti-cholinergic effects. Lesser sedation Lesser cardiovascular side effects	1. Urticaria, rashes 2. Anxiety, headache insomnia, agitation 3. Nausea, weight loss	1. Depression 2. Obsessive compulsive neurosis 3. Adjuvant in obesity 4. Sexual dysfunction
ANTI-PARKINSONISM DRUGS			
1. BENZHEXOL 2 mg daily upto 10-30 mg/day	Atropine-like action reduces seborrhea, sialorrhea, rigidity and tremors.	1. Confusion, delirium, hallucinations 2. Urinary retention 3. Blurred vision, glaucoma 4. Dry mouth, paralytic ileus	Parkinsonism even in the presence of cardiac lesion and hypertension.
2. CYCRIMINE CHLORIDE 5-10 mg but as high as 45 mg can be used	Similar to benzhexol	Similar to benzhexol, but lesser side-effects.	1. Parkinsonism. Along with phenothiazines to counter extrapyramidal effects.
3. DIPHENHYDRAMINE 100-200 mg.	Reduces rigidity, improves gait, muscle strength. Mood elevator	1. Drowsiness. 2. Giddiness.	1. Parkinsonism 2. Anti-histaminic
4. ORPHENADRINE 50 mg tds up to 120 mg. qds	Relieves akinesia and rigidity. Has mild euphoriant and anti-cholinergic effect.	1. Drowsiness, dizziness. 2. Blurred vision. 3. Gastric irritation. 4. Central excitation.	Parkinsonism.
5. AMANTIDINE 100 mg o.d. tob.d. Refer Pg. 599	1. Augments presynaptic synthesis and release of dopamine 2. Inhibits synaptic dopamine re-uptake	1. Anti-cholinergic effects 2. Convulsions. 3. Livedo reticularis	Modestly effective in relieving bradykinesia and rigidity. It loses its effect after a few months.
6. AMPHETAMINE 5 mg b.d. to tds	Reduces tremors and oculogyric crisis. It also elevates mood and increases muscle strength. Depletes noradrenaline and forms false neuro-transmitter p-hydroxy norephedrine.	1. Habituation and tolerance. 2. Agitation, headache, tremors, restlessness, anxiety, confusion. 3. Dry mouth, nausea, vomiting, anorexia, diarrhea.	1. Post-encephalitic, Parkinsonism. 2. Appetite suppressant 3. Narcolepsy.
7. LEVA-DOPA 3-6 gm daily (Gradually increased).	Increases dopamine content of the basal ganglia by being converted to dopamine. It improves akinesia, tremors, rigidity, seborrhea, sialorrhea, aphonia and memory. It makes the patient alert and interested in the surroundings.	1. On and off phenomenon 2. Anorexia, nausea, vomiting 3. Behavioural: Depression, agitation, confusion, restlessness, hallucinations, delusions and suicidal tendencies 4. Choreiform movements 5. Palpitation, tachycardia, arrhythmias, postural hypotension. Increased AV conduction.	Idiopathic and arteriosclerotic Parkinsonism responds well. Post-encephalitic, less well tolerated and drug induced does not respond at all.
8. CARBI-DOPA Tablets of 25 mg. carbi-dopa with 250 mg L-Dopa BENSERAZIDE Tablets combined with L-Dopa	Inhibits dopa decarboxylase which coverts L-dopa to dopamine in the GI tract, hence more L-dopa is available to cross blood-brain barrier and concentrate in basal ganglia. Since carbi-dopa does not cross blood-brain barrier it does not prevent L-Dopa Dopamine in CNS.	By itself carbi-dopa does not cause any side-effects. However it does not prevent the following side effects of L-dopa. 1. Orthostatic hypotension 2. Involuntary movements 3. Adverse mental effects	In Parkinsonism, used with L-dopa, it decreases the requirement of L-dopa with out affecting the therapeutic effect.

Drug/Dose	Action	Side Effects	Uses
9. BROMOCRYPTINE 2.5 mg b.d. up to 30 mg/day (gradually). (Other Dopamine agonistsare: PIRIBEDIL AND NORPROPYL APOMORPHINE LERGOTRILE, LYSURIDE AND PERGOLIDE)	Acts directly on adrenergic receptors in CNS like dopamine (Dopamine agonist).	1. Nausea, vomiting 2. Postural hypotension 3. Choreoathetosis 4. Agitation, confusion, irritability, hallucination and paranoid ideas	1. Parkinsonism 2. Acromegaly 3. Prolactinoma
10. SELEGINE 5 mgBD	It is a MAO-B inhibitor which inhibits Dopamine catabolism. It is an anti-oxidant which reduces nigrostriatal neuronal death.	None so far known	It is supposed to increase the life-expectancy and halt the progress of Parkinsonism.
11. TOLCAPONE	Inhibits COMT enzyme	Dyskinesia, diarrhea	Adjunct with L-Dopa
12. PIRIVEDIL 150 - 250mg Combination with L-Dopa	Dopamine agonist D2 - D3 receptors	Nausea, vomiting	1. Parkinsonism- early, especially tremor dominant 2. Cerebral aging

DRUGS IN STROKE

1. ANTI-PLATELET AGENTS

a) TICLOPIDINE 250-500 mg OD Action starts in 4 days is maximum by 11 days. After stopping the drug effect lasts for2 weeks	It inhibits platelet aggregation induced by ADP, collagen, adrenaline, thrombin and platelet activating factor. The effect on platelet function is irreversible for the life of the platelet.	1. G.I. disturbances: Nausea, vomiting, diarrhea, abdominal pain 2. Skin rash 3. Blood dyscrasias	1. TIA 2. Reversible ischemic neurological deficit & stroke 3. Unstable angina 4. Prevention of hemodialysis shunt closure 5. Diabetic angiopathy 6. Post Coronary Stent 7. Post CABG (Bypass surgery)
b) SULFINPYRAZONE 100-200mg TDS	Anti-inflammatory anti-platelet agent and uricosuric agent	1. Nausea, vomiting, aggravation of peptic ulcer 2. Skin rash 3. Bone-marrow depression	1. Anti-platelet agent 2. Gout
c) LOW DOSEASPIRIN 75- 150 mg OD	Refer Pg. 574	Refer Pg. 574	1. Anti-platelet agent 2. Pregnancy-induced hypertension
2. NIMODIPINE (30 mg) 2 cap 4 hourly	It is a calcium channel blocker with preferential activity on cerebral vessels. It causes arterial dilatation particularly in smaller vessels.	1. Hypotension 2. Nausea 3. Flushing palpitations 4. Rash 5. Headache	1. Ischaemic neurological diseases 2. Subarachnoid hemorrhage
3. PENTOXIFYLLINE 400-800 mg tds. IV 0.6 mg/kg/hr 1200 mg/24 hrs	1. Increases the flexibility of RBCs thereby easing their passage through the capillary microcirculation 2. Serum fibrinogen is reduced 3. Platelet aggregation inhibited	1. Nausea 2. Dizziness 3. Headache	To improve micro circulation as in coronary and cerebral insufficiency

DRUGS IN DEGENERATIVE BRAIN DISORDERS

1. PIRACETAM 800mg tds (in children 50 mg/kg)	It acts selectively on telencephalon by improving its associative function. It increases the energetic output of the brain cell and activates its neurophysiological potentialities especially in deficit conditions.	Not yet known.	1. Behavioural and psychotic problems in old age 2. Mental retardation in children.
2. TACRINE 160 mg/day DONEPEZIL	Anti-cholinesterase	1. Hepatotoxicity 2. Similar to other anti-cholinesterases	1. Alzheimer's disease 2. Dementias 3. Cognitive dysfunction

Drug/Dose	Action	Side Effects	Uses
3. RILUZOLE	Blocks release of glutamate	1. Asthenia, somnolence 2. Nausea, vertigo, hepatotoxicity	1. Motor neurone disease

ANTIBACTERIAL AGENTS

SULFONAMIDES

1. SULFONAMIDES a) SULFADIAZINE: 2-3 gm initial. 1 gm 4-6 hrly. later. b) SULFADIMIDINE: as above. c) SULFAMETHIZOLE 10-200 mg 4-6 hrly. d) SULFAMETHOXYPYRIDAZINE: 300 mg 12 hourly e) SULFAPHENAZOLE: 1 gm. initially, then 0.5 gm. 12 hrly. f) SULFAGUANIDINE: 3-6 gm 6 hrly. g) SALAZOPYRINE: 0.5-1.0 gm. h) MEFENIDE HYDROCHLORIDE: 2.5% with 1% Methyl cellulose cream. i) SULPHASUXAZOLE: 2 gm initially; 1 gm 4-6 hrly later j) SULPHAMETHOXALE: 2 gm initially; 1 gm 4-6 hrly later k) SILVER SULPHADIAZINE 1% cream l) SULPHACETAMIDE: 10 to 30% Ophthalmic solution	Due to structural similarity with PABA it competes with and probably substitutes the latter in bacterial metabolism. It inhibits folic acid synthetase which converts PABA to folic acid, resulting in folic acid deficiency and injury to bacterial cell. This injured cell can be easily phagocytosed. It is ineffective in presence of pus and tissue breakdown products which contain large amounts of PABA. Similarly, Procainamide, Procaine and Amethocaine which yield PABA, antagonise sulfonamides.	1. *Intolerance:* a) Serum sickness. b) Anaphylactoid reaction. c) Steven Johnson syndrome 2. *Urinary tract:* Renal colic and stones due to precipitation of the drug in tubules. 3. *Hemopoietic:* a) Agranulocytosis, aplastic anemia, thrombocytopenia. b) With G6PD deficiency- Intravascular hemolysis. c) In fetus and neonates- Kernicterus 4. *Miscellaneous:* a) Goitre and hypothyroidism b) Acute psychosis c) Peripheral neuritis d) Jaundice	1. Meningococcal meningitis. 2. Bacillary dysentery. 3. Urinary tract infection. 4. Chancroid. 5. Trachoma and inclusion conjunctivitis. 6. H. influenza meningitis 7. Intestinal sterilisation prior to surgery on colon. 8. Ulcerative colitis. 9. Resistant malaria, nocardiosis, toxoplasmosis. 10. Prophylaxis of bacillar dysentery, meningococcal meningitis To prevent infection of burns Ocular infection
2. CO-TRIMOXAZOLE (TRIMETHOPRIM 80 mg. with SULFAMETHOXAZOLE 400mg)2 BD	Trimethoprim inhibits dihydrofolate reductase necessary for conversion of dihydrofolate to tetrahydrofolate. Bacterial cell is 50,000 times more susceptible. Sulphonamides inhibit folic acid synthetase. This combination is therefore synergistic, sequential and bacteriocidal.	1. Nausea, vomiting 2. Skin rash 3. Anemia, leucopenia and thrombocytopenia 4. Megaloblastic anemia	1. Urinary infection with E. coli and Proteus 2. Typhoid, shigellosis, plague 3. Gonorrhea, chancroid 4. PCP prophylaxis in HIV pts 5. Bronchitis 6. Prostatitis
3. TRIMETHOPRIM 200 mg BD	Dihydrofolate reductase inhibitor of the bacterial cell.	Same as above	Same as above
4. NITROFURANS NITROFURANTOIN: 50-150mg. 6 hrly. (bacteriostatic). FURAZOLIDONE 100 mg. 6 hrly. (bactericidal). **NITROFURAZONE:** 0.02% solution. NIFUROXIME	Not Known. Probably inhibits reversibly the anaerobic steps of pyruvate metabolism.	1. Nausea, vomiting 2. Skin rashes 3. Hemolytic anemia with G6PD deficiency 4. Megaloblastic anemia 5. Antabuse-like reaction 6. Polyneuritis	1. Urinary tract infection (Nitrofurantoin) 2. Gastro-intestinal infections e.g. Giardiasis, bacillary dysentery 3. Vaginal infections: Trichomonas vaginitis
5. METHANAMINE 0.5 - 2.0 g QDS	Unknown	1. Nausea, vomiting 2. Urinary: dysuria, hematuria, albuminuria	Urinary tract infection

Drug/Dose	Action	Side Effects	Uses
QUINOLONES			
1. NALIDIXIC ACID 1 gm 6hrly	It interferes with the synthesis of DNA. 20% of the drug is present in active form in urine which is an adequate antibacterial concentration. Excretion of free drug is increased in alkaline urine.	1. Nausea, vomiting, diarrhea 2. Allergy, fever, rash, pruritus, eosinophilia, urticaria 3. CNS: Headache, malaise, drowsiness, myalgia, convulsions 4. Hemolytic anemia 5. Respiratory depression	Effective against gram-negative urinary tract infection, especially with E. coli, Proteus, Klebsiella, Aerobacter and occasionally Pseudomonas. *Contra-indicated in:* 1. Cerebral atherosclerosis, Parkinsonism, Convulsions. 2. Impaired hepatic and renal function.
2. NORFLOXACIN 400 mg BD for 7-10 days one hour before or two hours after food.	Similar to Nalidixic acid	1. Nausea vomiting, 2. Drowsiness, dizziness, light-headedness It loses its potency if combined with Nitrofurans or antacids but not Ranitidine/cimetidine	1. Urinary tract infection 2. Gonorrhea.
3. ENOXACIN - 200-400 mg BD CINOXACIN - 500 mg BD ACROSOXACIN - 300 mg OD	Similar to Norfloxacin	Similar to Norfloxacin	Gonorrhea, UTI
4. CIPROFLOXACIN 250-500 mg TDS orally or 200 mg IV 8-12 hourly x 10-14 days	It inhibits DNA gyrase	1. Cardiac arrhythmias 2. Oral candidiasis 3. Hallucination, dizziness 4. Interstitial nephritis	1. Effective against gram negative organisms including pseudomonas. 2. Bacterial gastroenteritis 3. Typhoid fever 4. Septicemia 5. Osteomyelitis 6. Pneumonias, chronic bronchitis 7. STDs, e.g. gonorrhea, chancroid 8. Tuberculosis, esp. drug-resistant strains
5. PEFLOXACIN 400mg BD x 10-14days	As above	As above	As above
6. OFLOXACIN 200mg ODx 10-14days	As above	As above	As above
7. LOMEFLOXACIN 400mg OD	As above	As above	As above
8. SPARFLOXACIN 200 mg OD	As above	As above	As above
9. CIPROTINI COMBINATION CIPROFLOXACIN 500 mg + TINIDAZOLE 600 mg 1 tablet BD for 5 days		Uses: 1. Mixed parasitic infections 2. Anaerobic bacterial infections 3. Diarrhea/dysentery secondary to mixed infections 4. Surgical and gynecological surgery prophylaxis 5. Sepsis due to mixed infections	
BETA-LACTAMS			
1. PENICILLIN *Na-K salt of Benzyl Penicillin*: 5 lakh units/ml. I.M./I.V. Procaine Penicillin Forte: 5-10 lakh units I.M. daily. *Benzathine Penicillin*: 2-4 mega units I.M. once every 3 weeks.	Interferes with the cell wall synthesis of gram-positive bacteria. This makes the cell membrane vulnerable to damage by solutes in the surrounding media. Cell walls of gram-negative bacilli are complex, hence very high concentrations of the drug are required to inhibit cell wall synthesis.	1. Anaphylaxis. 2. Serum sickness syndrome 3. Skin rashes, hemolytic anemia, hematuria, albuminuria. 4. Jarisch-Herxheimer reaction. 5. Superinfection. 6. Local pain, erythema, induration.	1. Pneumococcal, streptococcal, taphylococcal, meningococcal, gonococcal infections 2. Syphilis 3. Diphtheria, tetanus, anthrax, Cl. welchii, plague. 4. Actinomycosis, pasteurella, listeriosis 5. Prophylaxis of Rheumatic fever, Gonorrhea, Syphilis

Drug/Dose	Action	Side Effects	Uses
2. METHICILLIN 1. 1-2 gm. 2-6 hrly. I.M. 2. 0.5-1 gm, in 5-10 ml. of normal saline intra-pleural or intra-articular. NAFCILLIN	Two methoxy groups attached to the benzene ring of the side chain of methicillin prevents effective contact by Penicillinase, hence it is effective against Penicillin-resistant Staph. Action is like Penicillin.	1. Similar to Penicillin. 2. Bone marrow depression. 3. Nephropathy. 4. Thrombophlebitis. 5. Fulminating super-infection with gram-negative organisms.	Penicillin-resistant staphylococcal infection.
3. CLOXACILLIN 0.5-1 gm. 4-6 hrly. DICLOXACILLIN FLUCLOXACILLIN	5-10 times more potent than Methicillin.	Allergic reactions.	Penicillin-resistant staphylococcal infection.
4. AMPICILLIN 250-500 mg. 6 hrly. AMOXICILLIN Twice as potent as Ampicillin. TALAMPICILLIN PIVAMPICILLIN	As penicillin, but less active against gram-positive organisms and more sensitive against gram negative organisms. It is inactivated by Penicillinase, therefore not effective against Staphylococci resistant to benzyl penicillin.	Similar to Penicillin	1. Urinary tract infection. 2. Respiratory infection. 3. Meningitis. 4. Endocarditis. 5. Biliary and intestinal diseases.
5. CARBENICILLIN 1 gm. 6 hrly. I.M. or I.V. TICARCILLIN	Similar to Penicillin.	Similar to Penicillin.	Urinary tract infection and septicemia due to Proteus and Pseudomonas.
6. PIPERACILLIN 15-20g/day AZOCILLIN MEZLOCILLIN	Broad spectrum penicillin active against Pseudomonas aeruginosa	Similar to Penicillin.	Pseudomonas and other gram negative organisms Neonatal meningitis
7. MECILLINAM PIVMECILLINAM 1.2-2.4 g daily	Amidino-penicillin active against gram-negative pathogens except Pseudomonas	Similar to Penicillin.	Gram-negative infections and enteric fever
8. BETA-LACTAMASE INHIBITORS a) CLAVULANIC ACID i) With amoxycillin ii) With ticarcillin iii) With ampicillin b) SULBACTAM i) With ampicillin c) TAZOBACTAM i) With piperacillin	Active against beta-lactamase producing bacteria like Staphylococci, H. influenza, Neisseria, E. coli, Proteus, Klebsiella, M. catarrhalis, bacteroides	Similar to Penicillin.	Abscesses, carbuncles, osteomyelitis, furuncles sp. due to Staph. aureus
9. CEPHALOSPORINS A. First generation: Effective against gram-positive and gram-negative organisms except Proteus, Pseudomonas Serratia, Enterobacter and B. Fragilis a) CEPHELEXIN 250 mg qds orally b) CEPHADROXIL 250-500 mg. BD orally c) CEPHADRINE 250 mg q OS orally d) CEPHAZOLIN 1 gm BD IV e) CEPHALOTHIN 0.5 - 2.0 gm 6 hrly f) CEPHARIN 1-2 gm 6 hrly B. Second generation: Effective against Indole positive Proteus and H. influenza a) CEFACLOR 250-500 mg 8 hrly b) CEFAMANDOLE 1-2 gm 6 hrly c) CEFOXITIN 1-2 gm 8 hrly d) CEFUROXIME 250- 500 mg BD orally e) CEFONICID 1-2 gm 6 hrly f) CEFOTETAN 1-3 gm 12 hrly g) CEFORANIDE 1-3 gm 12 hrly	They act by inhibiting the bacterial cell wall synthesis. They are bactericidal.	1. Thrombophlebitis. 2. Anaphylaxis. Skin rash, fever and serum sickness. 3. Superinfection. 4. Liver and kidney damage. 5. Bleeding diathesis (Moxalactum).	1. Gram-positive infection resistant to penicillin (it is not effective in osteomyelitis because of poor penetration in the bones). 2. Urinary tract infection by resistant gram-negative organisms. 3. Fulminating septicemia including endocarditis.

Drug/Dose	Action	Side Effects	Uses
C. Third generation: Effective against gram-negative organisms including Pseudomonas a) CEFETOXIME 1 gm 6 hrly IV b) CEFTIZOXIME 1-2 g m 8 hrly c) CEFTRIAXONE 1-2 gm 12 hrly d) CEFTAZIDIME 1-2 gm 8 hrly e) CEFPERAZONE 1-2 gm 12 hrly f) CEFSULODIN 1-2 gm 12 hrly D. Fourth generation: Effective against Streptococci and methicillin-sensitive Staphylococci a) CEFEPIME 200 mg BD orally b) CEFPODOXIME 100/200 mg BD orally			
10. CARBAPENEM IMIPENEM Available in combination with CILASTATIN 500 to 750 mg by deep I.M. injection 8-12 hrly. OR by I.V. infusion in doses of 1-2 gm daily in 3-4 divided doses **MEROPENEM**	Beta lactam antibiotic which is bactericidal.	1. G.I. disturbance 2. Allergic reactions 3. Pseudomembranous colitis	Broad spectrum of anti-bacterial activity effective against pseudomonas, proteus, klebsiella enterobacteria and anaerobic organisms
11. MONOBACTAM AZTREONAM 1-2gm 8-12hrly	Monobactam inhibits transpeptidase on the bacterial cell wall; bactericidal	1. Very mild 2. No cross reactivity with penicillin or cephalosporin	1. Alternative to aminoglycosides in gram-negative septicemia 2. Neonatal gram-negative infection and sepsis 3. Patients allergic to penicillin or cephalosporins
12. OTHER RELATED ANTIBIOTICS			
A. VANCOMYCIN 500 mg 4-6 hourly IV or IM TEICOPLANIN	It acts by inhibiting the cell wall formation.	1. Flushing, hypotension and bronchospasm on rapid infusion 2. Interstitial nephritis. 3. Ototoxicity 4. Neutropenia	1. Gram-positive organisms 2. MRSA- infective endocarditis 3. Pseudomembranous colitis 4. Penicillin - allergic patients with serious infection
B. LINCOMYCIN 500 mgTDS CLINDAMYCIN 150 mg QDS	It inhibits the 50 S site on the bacterial ribosomal RNA	1. Pseudomembranous colitis 2. Nausea, Vomiting, Jaundice 3. Bone-marrow suppression 4. Fever, rash, arthritis.	1. B. fragilis infection 2. Malaria 3. Toxoplasmosis 4. Pneumocystis carinii
Other agents are: SODIUM FUSIDATE, BACITRACIN, MUPIROCIN			

MACROLIDES

1. ERYTHROMYCIN 1-2 gm/day.	Inhibits protein synthesis in bacterial cell. Binds to 50 s ribosomal subunit.	1. *Allergic reaction:* Fever, rash, urticaria and lymphadenopathy. 2. Nausea, vomiting, epigastric pain. 3. Cholestatic hepatitis.	1. Infective endocarditis, (4-6 gm) 2. Diphtheria carriers. 3. Prophylaxis of rheumatic fever, streptococcal infection 4. Allergy to penicillins 5. Upper RTI 6. Pneumonia, also atypical 7. Vaginitis (chlamydia) 8. Wound, burn infections, impetigo, eczema, acne.
2. ROXITHROMYCIN 150 mg B.D. x 5 days	As above	As above	1. As above 2. Active against Legionella, mycoplasma, H. influenza
3. AZITHROMYCIN 250 -500 mg OD x 3 days	As above	As above	As above
4. CLARITHROMYCIN 250-500 mg BD for 5-7 days	As above	As above	1. As above 2. Treatment of MAI (atypical mycobacteria) in AIDS

Drug/Dose	Action	Side Effects	Uses
5. SPIRAMYCIN 1-5 million IU BD	As above	As above	1. As above 2. Toxoplasmosis 3. Cryptosporidial/Isospora related AIDS diarrhea

Other agents are: OLEONDOMYCIN, TRIACETYLOLEANDOMYCIN

AMINOGLYCOSIDES

1. STREPTOMYCIN 0.75 gm/day IM x 3 months in TB. Streptomycin sulfate tablets 0.5-2.0 g m orally as intestinal antiseptic	1. Combines with ribosomes and interferes with m-RNA-ribosome combination, inducing it to manufacture peptide chains with wrong amino-acids, which destroys the bacterial cell. Binds to 50 s ribosomal subunit. 2. Inhibits enzymes involved in Krebs cycle and xanthine oxidase. It is bactericidal.	1. Injection abscess. 2. Anaphylaxis. 3. Ototoxicity(vestibular>cochlear)-Imbalance, tinnitus, vertigo 4. Nephrotoxicity 5. Circumoral paresthesia 6. Curarimimetic and aggravates myasthenia 7. Eosinophilia, rash 8. Drug fever 9. Drug resistance	1. Tuberculosis 2. Bacteremia and SBE 3. Plague 4. Brucellosis 5. Tularemia 6. Urinary tract infection 7. Respiratory tract infection 8. H. influenza meningitis 9. Intestinal anti-septic-gut sterilization 10. Chanchroid, granuloma inguinale
2. KANAMYCIN 0.5-1.5 gm/day for maximum 10 days.	Similar to streptomycin	As above. Damage more to cochlear than vestibular division of VIII nerve.	1. Septicemia and SBE with gram-negative organisms. 2. MDR-TB
3. GENTAMYCIN 80 mg. 8 hrly. I.M. 5 mg, intrathecally.	Similar to streptomycin but also effective against Pseudomonas aeruginosa.	1. As for streptomycin. 2. Dizziness.	Pneumonia, septicemia and meningitis due to Pseudomonas, Proteus, Klebsiella, Aerobacter, Staphylococcus Streptococcus, Salmonella etc.
4. TOBRAMYCIN 3-5 mg/kg IM in three divided doses	Similar to gentamycin	Similar to gentamycin but less nephrotoxic	Four times more active than gentamycin against Pseudomonas.
5. AMIKACIN 15 mg/kg/day in two divided doses I.M. or I.V.	Similar to gentamycin.	Similar to gentamycin.	1. Active against gentamycin-resistant Pseudomonas, E-coli, Proteus and Klebsiella. 2. Tuberculosis.
6. NETILMYCIN 3-6.5 mg/kg per day	It resembles Sisomycin. It is resistant to enzymatic lysis.	Similar to Amikacin	1. Gram-positive organisms 2. Pseudomonas
7. NEOMYCIN 1 gm 6 hrly orally	Too toxic for systemic absorption	Similar to streptomycin	1. Intestinal decontaminant used in hepatic failure & coma & colonic surgery 2. Local uses for skin & eye
8. FRAMYCETIN 0.5% ointment, cream or soln.	Similar to neomycin	Similar to neomycin	1. Staph. skin infections 2. Nasal carrier of Staph.
9. PAROMOMYCIN Loading dose 4 gm 2 gm QDS	Similar to neomycin	Similar to neomycin	1. Amebic dysentery 2. Gut sterilization- surgery & hepatic coma 3. Visceral leishmaniasis

Other agents are: COLISTIN, POLYMYXIN B, TYROTHRICIN, CYCLOSERINE AND SPECTINOMYCIN

TETRACYCLINES

1. TETRACYCLINES 1-2 gm/day orally. IM or IV.	1. Chelates calcium and magnesium. 2. Inhibits essential enzyme systems of the organisms. 3. Interferes with phosphorylation of glucose. 4. Suppresses the bacterial protein synthesis by interfering with transfer RNA. (Bacteriostatic).	1. Intolerance 2. Nausea, vomiting, diarrhea 3. Superinfection 4. Hepatic dysfunction 5. Fanconi-like syndrome 6. Permanent yellow staining of teeth 7. Benign intracranial hypertension in infants	1. Plague 2. Cholera 3. Bacillary dysentery 4. Amebic dysentery 5. Urinary tract infections 6. VD: Syphilis, Gonorrhea Chancroid, G. inguinale 7. Mycoplasma pneumonia 8. Chlamydia infections, LGV, Trachoma, Psittacosis

Drug/Dose	Action	Side Effects	Uses
	5. Binds to 30s ribosomal subunit	8. Bone: Reduce linear growth of bones in fetus. 9. Aggravate peptic ulcer in uremia by inhibiting ureas of gastric mucosa, which breaks urea to ammonia (latter serves to reduce (gastric acidity)	9. Rickettsial infections 10. Spirochetal: leptospirosis 11. Actinomycosis, Anthrax 12. Diagnostic test in Neoplasms: Tetracyclines given for 5 days, Malignant cells exhibit brilliant yellow fluorescence under UV light
2. DOXYCYCLINE 100 mgOD/BD	Similar to tetracyclines.	Similar to tetracyclines.	Similar to tetracyclines.

CHLORAMPHENICOL

1. CHLORAMPHENICOL 1-3gm/day. **THIAMPHENICOL** is the other analogue	Interferes with protein synthesis of bacteria.	1. Intolerance 2. Bone marrow depression 3. Superinfection 4. Liver damage 5. Grey baby syndrome-in neonates and infants 6. CNS: Peripheral neuritis, optic neuritis, cochlear damage, convulsions, depression, ophthalmoplegia	1. Typhoid fever 2. Urinary tract infection 3. H. influenza meningitis 4. Plague 5. Gram-negative septicemia and SBE

ANTI-TUBERCULOUS DRUGS

1. RIFAMPICIN 450 - 600 mg/day orally (10 mg/kg)	Macrocyclic antibiotic. Inhibits DNA-dependent RNA polymerase thus stopping the expression of bacterial genes. BACTERICIDAL.	1. Liverdamage 2. Influenza-like reaction 3. Intolerance: Fever, skin rash, diarrhea, leucopenia, eosinophilia, ataxia, dizziness 4. Orange-red colour to urine, feces, sputum It is metabolized in liver. Hence, in liver disease the concentration is raised.	Tuberculosis. Other uses: 1. Leprosy and ENL 2. Meningococcal carrier 3. Staphylococcal septicemia 4. Herpes zoster 5. H. influenza 6. Brucella 7. Mycetoma 8. Q fever 9. Legionella 10. Chlamydia
2. RIFABUTIN 150 mg/day	Semisynthetic rifamycin spiropip-endyl derivative Inhibits DNA-dependent RNA polymerase	1. GI 2. Fever, rash	1. MAIS 2. HIV-associated TB 3. MDR-TB
3. ISONICOTINIC ACID HYDRAZIDE (INH) 300 mg daily for 1 1/2-2years orally (5 mg/kg)	BACTERICIDAL 1. Inhibits phospholipid synthesis of bacterial cell membrane. 2. It causes intracellular or extracellular chelation of calcium ions which are essential for bacterial metabolism.	1. Peripheral neuritis 2. Psychosis 3. Optic neuritis 4. Intolerance: Fever, malaise jaundice, skin eruptions 5. Diffuse vasculitis, blood dyscrasias	Tuberculosis. It crosses the blood brain barrier (BBB) and placenta. It diffuses into macrophages and necrotic material. Along with cycloserine it may cause convulsions.
4. ETHAMBUTOL 25 mg/kg x 12 wks. 15 mg/kg x 1 1/2 yrs. at night	Not known. BACTERIOSTATIC. Acts mainly against rapidly growing organisms.	1. Optic nerve damage 2. Anaphylactic reaction 3. Nausea, vomiting 4. Confusion, headache	1st line supplemental agent-TB only Crosses BBB and is equally concentrated in CSF and plasma.
5. PYRAZINAMIDE 500-750 mg BD (25 mg/kg) or MORPHAZINAMIDE (more potent) 3 gm/day orally (500 mg tablet)	Not known. BACTERICIDAL.Nicotinamide analogue Acts in acidic environment also.	1. Toxic hepatitis on 7th day. 2. Hyperuricemia, gout, polyarthralgia 3. Skin rashes and photosensitivity. It may cause bright red-brown discoloration of skin.	Intensive chemotherapy regimen drug
6. **STREPTOMYCIN**	Refer Antibiotics Pg. 589	—	—

Drug/Dose	Action	Side Effects	Uses
7. CYCLOSERINE 1-2gm daily	Broad-spectrum antibiotic Inhibits the synthesis of the bacterial cell wall.	1. CNS: Weakness, tremors ataxia, convulsion, slurred speech, brisk jerks and ankle clonus. 2. Insomnia, psychosis.	Reserve second line agent
8. VIOMYCIN 1 gm twice a week I.M.	Complex polypeptide antibiotic	Similar to streptomycin	Inhibits 90% strains of MDR-TB
9. CAPREOMYCIN 1 gm I.M. x 2 months. then 1 gm twice a week	Complex polypeptide antibiotic	1. Psychosis 2. Seizures 3. Peripheral neuropathy 4. Headache, somnolence 5. Allergy	Drug resistant organisms may be sensitive to capreomycin but not vice versa. Second-line anti-TB drug.
10. AMIKACIN/KANAMYCIN 1-1.5 gm. I.M. x 60 days.	BATERICIDAL to extracellular organisms. Refer Pg. 589	Similar to streptomycin.	Not effective against viomycin resistant organisms.
11. THIACETAZONE AMITHIOZONE 150mg daily	Not known. BACTERIOSTATIC. V. cheap. Banned by WHO due to side-effects.	1. Anorexia, nausea, vomiting. 2. Skin rashes, Steven Johnson syndrome. 3. Bone-marrow, kidney and liver damage.	HIV-associated TB. It is also useful in Leprosy. It crosses BBB producing equal concentration in CSF and plasma inflammation.
12. PARA-AMINO SALICYLIC ACID (PAS) 12-15 gm/day orally. PAS granules 4 gm 8 hourly	Interferes with utilisation of para-amino benzoic acid by the mycobacterium. Sulfonamides also act in similar fashion, but are not useful because tubercle bacillus accommodates PAS or PABA but rejects sulfonamides.	1. GI: Anorexia, nausea, vomiting, diarrhea. 2. Intolerance: Fever, skin rash, lymphadenopathy. 3. Hemopoietic: Leucopenia, eosinophilia, ataxia. 4. Hepatic damage. 5. Acute renal failure. 6. Myxedema, Loeffler's syndrome	Low level of anti-TB activity. Reserve drug.
13. ETHIONAMIDE 200 mg b.d. up to 1 gm. daily.	Derivative of INH. Like INH and PZA it inhibits protein synthesis.	1. Nausea, vomiting, diarrhea, metallic taste 2. Toxic hepatitis 3. CNS: As INH 4. Skin rashes, alopecia 5. Pellagra-like syndrome 6. Hypothyroidism	1. Crosses BBB and achieves good CSF concentration, specially in MDR-TB 2. It is also useful in Leprosy. 3. Atypical mycobacteria
14. CLARITHROMYCIN 250-500 mg OD	Macrolide sp. in macrophages and excellent activity against atypical mycobacteria	Nausea, vomiting, bitter taste	Atypical mycobacteria
15. AZITHROMYCIN 250-500 mg OD	Same as Clarithromycin	Refer Pg. 591	MDRTB, atypical TB

ANTI-LEPROSY DRUGS

1. DAPSONE DIAMINODIPHENYL SULFONE (DDS) 25 mg/wk: 4 wks. 50 mg/wk: 4 wks. 100 mg/wk: to continue, orally for 3-10 years.	Similar to sulfonamides. Bacteriostatic Inhibits bacterial folic acid synthesis.	1. Allergy: Dermatitis, drug fever. 2. Nausea, vomiting. 3. Hemolytic anemia in G6PD deficiency patients. 4. Anemia, methaemoglobinemia, agranulocytosis, 5. Hepatitis, goitrogenesis. 6. Nephrotic syndrome	1. Leprosy: Improvement occurs within 4-8 months. Morphological Index (MI) becomes zero in 5 months (with Rifampicin, MI becomes zero in 5 weeks). 2. Dermatitis herpetiformis 3. Pneumocystis carinii 4. Malaria 5. Cutaneous leishmaniasis

Drug/Dose	Action	Side Effects	Uses
2. CLOFAZIMINE 50 mg-100 mg/day in Leprosy 100 mg t.d.s. in ENL	Slowly Bacteriostatic after 50 days It has anti-inflammatory action. Inhibits DNA binding.	1. Nausea, vomiting, abdominal pain, diarrhea. 2. Red discoloration of urine, stools, saliva and conjunctiva. 3. Cardiotoxic	1. Leprosy 2. Erythema Nodosum Leprosum (ENL) 3. Multi-drug resistant TB 4. Skin disease, Discoid lupus vitiligo, psoriasis, trophic ulcer, pyoderma gangrenosa. 5. Tuberculosis in AIDS patient 6. American leishmaniasis 7. Atypical mycobacteria

3. OTHER ANTI-LEPROSY AGENTS
RIFAMPICIN (600 mg once a month), ETHIONAMIDE (250 mg/day), THALIDOMIDE (ENL), MACROLIDES (Clarithromycin), MINOCYCLINE, QUINOLONES (Ofloxacin, Sparfloxacin, Pefloxacin)

ANTI-AMOEBIC DRUGS

1. DEHYDROEMETINE 30-60 mg. I.M. or SC daily at night for 10 days.	Causes degeneration of nucleus and reticulation of cytoplasm of the trophozoites which arrests its multiplication and leads to its phagocytosis. No action on cysts.	1. Local reaction; Pain, weakness of muscle. 2. GI disturbances: Nausea, vomiting, diarrhea. 3. CVS: Tachycardia, hypotension, myocarditis, pericarditis.	1. Amebiasis (Extra-intestinal) 2. Paragonimus westermani (lung fluke) infestations 3. Emetic 4. Fascioliasis 5. Giardiasis 6. Cutaneous leishmaniasis
2. QUINOLINE DERIVATIVES a. *DIIODOHYDROXYQUINOLINE* b. *IODOCHLORHYDROXYQUINOLINE* 1-2 gm/day x 20 days. 0.75 gm/day x 10 days	1. Interferes with the essential enzyme system of the parasite. 2. Halogenates its proteins.	1. Nausea, vomiting, diarrhea 2. Fever, chills, skin eruptions. 3. Headache, vertigo, S.M. O.N.	Diiodo is more useful in acute dysentery against trophozoites whereas Iodochlor is more useful in cyst passers. 1. Amoebiasis (Intestinal). 2. Moniliasis. 3. Trichomonas vaginitis.
3. CHLOROQUINE 500 mg b.d. x 2 days 250 mg b.d. x 19 days	Direct amoebicidal but completely absorbed from G.I. tract so it is not effective in intestinal, but only in extra-intestinal amoebiasis.	1. Nausea, vomiting. 2. Intolerance. 3. Eye blurring, diplopia, lenticular and subcapsular cataracts. Retinopathy. 4. T wave changes on ECG. 5. Ototoxicity. 6. Psychosis and convulsions.	1. Malaria 2. Amebiasis (Extra-intestinal). 3. Giardiasis 4. Rheumatoid arthritis 5. Discoid Lupus and SLE. 6. Infectious mononucleosis 7. Taeniasis 8. Clonorchis sinensis infestation 9. Lepra-reaction.
4. METRONIDAZOLE 800 mg t.d.s. for intestinal 400 mg t.d.s. for extraintestinal x 10 days.	Effective against trophozoites at all sites - intestinal and extra-intestinal.	1. Nausea, vomiting, diarrhea, metallic taste, abdominal pain 2. Headache, dizziness, vertigo, ataxia, urticaria, pruritus, flushing. 3. Antabuse like action	1. Giardiasis. 2. Trichomonas vaginitis. 3. Dracunculosis. 4. Ulcerative gingivitis. 5. Amoebiasis 6. Anaerobic infections
5. TINIDAZOLE 300-600 mg BDS x 3 days	As above	As above	As above
6. SECNIDAZOLE 500 gm tablets 2 gm once or 30 mg/kg for intestinal and 1.5 - 2.0 gm for 5 days in hepatic amoebiasis	It enters the micro-organism by diffusion and is reduced intracellularly. This forms cytotoxic products which disrupts the DNA structure and function.	Mild and Transient 1. Rash, urticaria 2. Anorexia, nausea, stomatitis glossitis and diarrhea 3. Headache and fatigue 4. Antabuse like effect with alcohol	1. Amebiasis 2. Trichomoniasis 3. Giardiasis 4. Cl. perfringens 5. Bacteroides fragilis
7. ORNIDAZOLE	Same as secnidazole	—	—
8. DILOXAMIDE FUROATE 500mg t.d.s. x 10 days	Potent direct amoebicidal, especially against cyst passers. No value in extra intestinal.	1. G.I. disturbances, flatulence. 2. Skin rashes	Amoebiasis, chronic carrier state (on cyst forms)

Drug/Dose	Action	Side Effects	Uses
9. TETRACYCLINES 1-2 gms/day x 10 days or PARAMOMYCIN 25 mg/kg x 10 days.	Intestinal bacteria manufacture certain metabolites and vitamins on which the protozoa thrives. Tetracyclines alter the bacterial flora creating a medium unfavorable for the growth of amebae.	Refer Pg. 589	The return of bacterial flora to pretreatment level often leads to a relapse. Hence it is useful only as an adjuvant.

DRUGS FOR KALA AZAR

1. UREA STIBAMINE 50-200 mg I.M. on alternate days x 4 wks.	Pentavalent compound reduced to trivalent one in the body. It acts only on leishmanial forms.	1. Nausea, vomiting, diarrhea, metallic taste. 2. Anaphylactic shock. 3. Muscular pain, jaundice, hematuria.	Kala-azar.
2. SODIUM ANTIMONY GLUCONATE 600 mg in 6 ml water I.M. or I.V. up to 120 ml. Each inj. on alternate day. A break of 10 days between 5th and 6th inj. **MEGLUMINE ANTIMONATE**	Similar to urea stibamine.	Similar to urea stibamine.	Kala-azar.
3. ETHYL STIBAMINE 100 to 300 mg. I.M. as 5% or 25% solution on alternate days up to 3-4 gm.	Similar to urea stibamine	Similar to urea stibamine	Kala-azar.
4. PENTAMIDINE ISETHIONATE / MESYLATE 250 mg I.V. x 10 days repeated after 14 days if required, up to 7.5 gm.	Not known. It acts by inhibition of DNA, RNA and phospholipid metabolism.	1. Hypotension. 2. Hypoglycemia. 3. Liver and kidney damage. 4. Headache, fever, rigors. 5. Peripheral neuropathy.	1. More potent and more toxic than antimony compounds in kala-azar. 2. Blastomycosis 3. Pneumocystis carinii pneumonia.

Other drugs: DIHYDROXY STILBAMIDINE, ALLOPURINOL (Refer Pg. 577), PAROMOMYCIN (Refer Pg. 589), AMPHOTERICIN B, STIBOPHEN

ANTI-MALARIAL DRUGS

1. QUININE QUININE BISULFATE OR HYDROCHLORIDE 300-600 mg/day orally. QUININE DIHYDROCHORIDE 300-600 mg I.M. or I.V.	1. Schizonticidal hence useful as malarial suppressant. 2. Quinidine-like action on the heart. 3. Analgesic, muscle relaxant. 4. Smooth muscle relaxant. 5. Curarimimetic on skeletal muscles.	1. Idiosynchrasies: Flushing, pruritus, bronchospasm, ITP, agranulocytosis 2. Cinchonism: Tinnitus nausea, headache, visual impairment, deafness, vertigo. 3. Backwater fever: Fever, hemoglobinuria and acute renal failure.	1. Malaria. 2. Myotonia congenita. 3. To prevent nocturnal muscle cramps 4. Diagnosis of myasthenia gravis which is aggravated by quinine 600 mg 2 hourly for 3 doses. 5. As a Sclerosing agent.
2. CHLOROQUINE 1 gm stat; 0.5 gm after 8 hrs. 0.5 gm x 2 days Dose : 1 tab = 250 (150 mg base); 4 tab stat followed by 2 tab; After 8 hours followed by 2 tabs; Daily on Day 2 & 3; Total dose (150 mg base)	Acts by inhibiting the incorporation of phosphatesinto the RNA and DNA of Plasmodium. It also has anti-inflammatory anti-histaminic, local anesthetic and myocardial depressant action.	Refer Pg. 592	Useful against erythrocytic from of P. falciparum and vivax and gametocytes of P. vivax. It has no effect on sporozoites and persistent tissue forms.
3. AMODIAQUINE 0.5-0.75 gm on first day 0.5 gm for 2 days.	Similar to Chloroquine	1. GI disturbances. 2. Headache. 3. Photosensitivity. 4. Agranulocytosis.	In malaria it is as effective as chloroquine in a single dose.
4. PRIMAQUINE 15 mg/day x 14 days	Probably acts by affecting the metabolic functions of the mitochondria of gametocytes. It is effective against gametocytes of all species.	1. Epigastric distress. 2. Intravascular hemolysis in G6 PD deficiency. 3. Anemia, leucopenia, methemoglobinemia.	Malaria. (it should not be combined with mepacrine or proguanil as they potentiate its toxicity).

Drug/Dose	Action	Side Effects	Uses
5. PROGUANIL 300-600 mg initially 300 mg daily x 5 days. **CHLORPROGUANIL** 200 mg once a week to be continued for 4 weeks after leaving Malarial area.	Prevents the reduction of folic-acid by the plasmodium which interferes with the nucleic acid synthesis causing arrest in erythrocytic schizony. It is schizonticidal to P. vivax and falciparum. It prevents development of gametes in the gut wall of mosquito.	Free from side effects in therapeutic doses. In large doses. 1. GI disturbances 2. Reduces gastric acidity 3. Depresses myocardium 4. Leucopenia. 5. Hematuria	Malaria.
6. CYCLOGUANIL 5 mg/kg I.M.	Protects against P. vivax and falciparum for 3 months or longer due to slow release of active moiety from repository	Similar to proguanil	Long acting anti-malarial. *Disadvantages:* 1. Development of resistant strains. 2. Secondary folic acid deficiency
7. MEFLOQUINE 15 mg/kg or 1 gm/day 250 mg once a wk and one week prior to and 4 weeks after leaving endemic area for prevention	It is unknown.	1. Nausea vomiting diarrhea 2. Dizziness, vertigo, restlessness confusion or seizures	Treatment and prophylaxis of malaria *Precautions* 1. Avoid in pregnancy/lactation 2. Avoid with betablockers 3. Quinine should be used with caution if mefloquine is used as prophylaxis
8. PYRIMETHAMINE Pyrimethamine 25 mg + sulfadoxine 1.5 gm OR 500 mg sulphamethopyrazine. *Acute attack* 50 mg. 1st day 25 mg x 2 days. *Causal Prophylaxis* 25 mg/week.	Similar to proguanil	1. Megaloblastic anemia due to folic acid deficiency. 2. Agranulocytosis.	1. Malaria. 2. Toxoplasmosis 25 mg x 30 days. 3. Polycythemia vera.
9. HALOFANTRINE (250 mg) 2 TDS x 1 day	Unknown mechanism.	Nausea, vomiting. Do not use in pts. receiving quinine, chloroquine or quinidine	Malaria: P.falciparum and P. vivax
10. QUINGHAOSU **ARTEMETHER:** Loading 3. 2 mg/kg IM followed by 1.6 mg/kg I.M for 3-5 days Total dose : 480 mg **ARTESUNATE:** IV : 2 mg/kg stat followed by 1 mg/kg IV every 12 hrs till oral treatment possible Oral dose: Day 1 : 100 mg BD Days 2-5 : 50 mg BD ARTETHER	1. Inhibition of protein synthesis in trophozoite phase 2. Membrane lysis of plasmodium	1. Bradycardia and first degree heart block 2. Decreases WBC reticulocytes 3. Increases transaminases 4. Neurotoxicity 5. Fever	1. Drug-resistant falciparum malaria 2. Severe complicated falciparum malaria

ANTI-HELMINTHIC AGENTS

1. NICLOSAMIDE 1 gm early morning on empty stomach repeated after 1 hr. Purge after 1/2-1 hr.	Vermicidal. Inhibits anaerobic phosphorylation of ADP by mitochondria of parasite.	No side effect except mild GI disturbances	1. Teniasis 2. H. nana 3. D. latum
2. MALE FERN (Oleoresin of Aspidium) Fat-free diet for 2 days Saline purgative the previous night. (1 ml in capsule) 3-6 ml 2 hrs later purge	Filicic acid in it, acts by paralysing the muscles of the parasites.	1. Nausea, vomiting, diarrhea 2. Headache, vertigo, tremors fits, hyperreflexia. 3. Optic atrophy, Xanthopsia 4. Respiratory depression. 5. Myocardial depression. 6. Increased unconjugated bilirubin 7. Renal tubular necrosis.	T. solium, saginatum and H. nana.

Drug/Dose	Action	Side Effects	Uses
3. DICHLOROPHEN 6 gm for adults. 3-4 gm. for children (1 tab = 500 mg.)	Directly kills the worms	1. Nausea, vomiting diarrhea. 2. Jaundice. 3. Urticaria.	Teniasis
4. PIPERAZINE CITRATE For ascariasis 5 gm. single dose (5 ml=750 mg).	Reduces the formation of succinate in the worm leading to flaccid paralysis of the worm. Patient easily expels the paralysed worm.	1. Nausea, vomiting, diarrhea. 2. Urticaria. 3. Cerebellar ataxia, vertigo, convulsions, blurred vision, paresthesia.	1. Ascariasis 2. Oxyuriasis (thread worm)
5. TETRAMISOLE 150 mg for adults 50 mg for children.	Paralyses the worm by inhibiting succinate production in it.	1. Nausea, vomiting, diarrhea, abdominal colic. 2. Giddiness and drowsiness	1. Ascariasis. 2. Ankylostomiasis.
6. BEPHENIUM HYDROXY NAPHTHOATE 5 gm for adults. 2.5 gm for children No food for 2 hrs. after the drug.	Produces contracture of the muscle of the parasite.	Nausea, vomiting, diarrhea.	1. Ascariasis. 2. Ankylostomiasis. 3. Trichostrongylus orientalis.
7. MEBENDAZOLE 100 mg b.d. x 3 days. 600 mg t.d.s. x 21 days in hydatid cyst.	It causes a selective and irreversible inhibition of glucose uptake in helminths resulting in their immobilisation and death.	Rarely abdominal discomfort and diarrhea. In higher doses 1. Arthralgia 2. Dizziness, headache	1. Ascariasis. 2. Ankylostomiasis. 3. Trichuris trichura. 4. Enterobius vermicularis. 5. Listeriosis 6. Tenia saginatum & solium. 7. Hydatid cyst.
8. ALBENDAZOLE 400 mg once only	Similar to Mebendazole	Similar to Mebendazole	1. Similar to Mebendazole 2. Cysticercosis
9. PRAZIQUANTEL 500 mg TDS for 15 days	Acts by causing vacuolation and degeneration of the worm	1. Abdominal discomfort 2. Fever, malaise 3. Headache, dizziness 4. Raised SGOT, SGPT	1. Neurocysticercosis 2. Other nematode infections
10. THIABENDAZOLE 25 mg/kg x 3 days.	Interferes with metabolic pathway essential for the worms.	1. Anorexia, nausea, vomiting, epigastric distress. 2. Drowsiness, dizziness. 3. Skin rash, pruritus.	1. Ascariasis. 2. Ankylostomiasis. 3. Thread worms. 4. Strongyloids. 5. Trichiniasis. 6. Trichuriasis.
11. PYRANTEL PAMOATE 11 mg/kg (250 mg/5 ml) 15 ml for adult.	1. Depolarising neuro-muscular blocking-agent. 2. Inhibits cholinesterase.	1. Anorexia, nausea, vomiting 2. Skin rash. 3. Headache, drowsiness. 4. Raised SGOT.	1. Ascariasis. 2. E. vermicularis infestation 3. Hookworms (Ankylostomiasis).
12. TETRACHLOR ETHYLENE Low fat diet for 2 days Saline purge 3 ml. drug next morning. After 2 hrs. purge.	Paralysis of Hook worms	1. Vertigo, unconsciousness 2. Collapse if severe anemia. 3. Jaundice.	Ankylostomiasis.
13. BITOSCANATE 200 mg on first day followed by 100 mg the next day.	Not known.	Nausea, vomiting.	Ankylostomiasis.
14. HEXYL RESORCINOL Fat-free meal on previous night. On empty stomach 1 gm. swallowed 2 hrs. later. saline purge. No food for 5 hrs. Repeat every 3-7 days for 3 courses.	Not known.	Irritant to skin and mucous membrane.	1. Ascariasis. 2. Ankylostomiasis. 3. Dwarf tapeworm. 4. Giant lung fluke. 5. Thread worm. 6. Whipworm. 7. Fish tapeworm. 8. Spermicide in contraceptive jelly.

Drug/Dose	Action	Side Effects	Uses
15. PYRIVINIUM PAMOATE 7.5 mg once in E. vermicularis 7.5 mg x 7 days in strongyloids	Inhibits cellular oxidation within the worms.	1. Nausea, vomiting. 2. Photosensitivity 3. Stains stools red.	1. E. vermicularis. 2. Strongyloids
16. LUCANTHONE 1 gm t.d.s. x 3 days.	Interferes with the production of eggs by the parasites and eventually leads to death of the adult worm.	1. Nausea, vomiting, diarrhea 2. Anxiety, depression, dizziness. 3. Yellow discoloration skin. 4. Hepatic or renal damage.	S. hematobium and S. mansoni.
17. HYCANTHONE 4 mg/kg orally x 4 days. 2-3 mg/kg I.M. x 4days.	Stimulates the uptake of 5 HT by non-neuronal tissue of the worm. It interferes with the laying of eggs, induces separation of paired worms and produces degenerative changes in the worms leading to death.	1. Nausea, vomiting. 2. Hepatotoxic. 3. Mutagenic. 4. Minimal ECG changes.	S. haematobium and S. mansoni.
18. METRIFONATE 7.5 mg/kg x 3 days.	Inhibits cholinesterase of S. haematobium	Plasma and RBC cholinesterases are depleted.	1. S. hematobium. 2. Ascariasis, whip-worms 3. Ankylostomiasis.
19. NIRIDAZOLE 25 mg/kg x 7 days.	Destroys the vitellogenic glands of the female in the liver. Destroys the testes in males. The male is immobilised in connective tissue.	1. Reversible T wave changes (ECG) 2. Agitation, confusion, convulsions, hallucinations 3. Hemolysis if G6PD deficiency 4. Nausea, anorexia.	1. S. japonicum and S. mansoni. 2. Guinea worm. 3. Amoebiasis. 4. Cutaneous leishmaniasis.
20. ANTIMONY COMPOUNDS Stibophen 1. 5 ml. I.M. on first day, 2.5 ml. next day. 5 ml. on 3rd day up to 75 ml. Stibocaptate 30-50 mg/kg up to 2.5 gm.	Destroys the larvae inside thova.	1. Hepatic damage. 2. Renal damage. 3. Arrhythmia.	1. S. haematobium. 2. Leishmaniasis.
21. DIETHYL CARBAMAZINE 100 mg t.d.s.x 21	Sensitises the microfilaria so that they become suceptible to phagocytosis and are fixed by the RE cells in liver sinusoids. Microfilaricidal.	1. Anorexia, nausea, vomiting 2. Allergic reactions. 3. Fever, headache 4. Pruritus with constitutional symptoms (Mazzotti reaction, seen with Onchocerciasis)	1. Lymphatic filariasis-Loa Loa, W. bancrofti, W. Malayi 2. Tropical eosinophilia. 3. Onchocerciasis and B. malayi 4. Visceral Larva migrians
22. IVERMECTIN 200 mcg/kg	GABA agonist which paralyses the parasite	1. Itching, fever, arthralgia 2. Headache, skin edema 3. Blindness	1. Onchocerciasis 2. Microfilariasis 3. Scabies
23. LEVAMISOLE 50 -150 mg OD	Succinate blocker, causes worm paralysis	1. Nausea, vomiting, abd. pain 2. Diarrhea, drowsiness	1. Ascariasis 2. Hookworms 3. Strongyloidosis 4. Immunostimulant in cancer
Round Worms	***Hook Worms***	***Thread Worms***	***Schistosomiasis***
1. Piperazine citrate 2. Mebendazole. 3. Bephenium hydroxynaphthoate 4. Tetramisole. 5. Hexylresorcinol. 6. Thiabendazole. 7. Diethylcarbamazine	1. Tetrachlorethylene. 2. Bitoscanate. 3. 4-Iodothymol. 4. Bephenium hydroxynaphthoate. 5. Thiabendazole. 6. Mebendazole. 7. Hexylresorcinol. 8. Pyrantel.	1. Piperazine citrate. 2. Pyrantel 3. Pyrvinium pamoate. 4. Thiabendazole. 5. Mebendazole. 6. Hexylresorcinol.	1. Lucanthone 2. Hycanthone. 3. Trivalent antimony 4. Metrifonate. 5. Dichlorovos. 6. Niridazole.

Drug/Dose	Action	Side Effects	Uses
Tapeworm	***Filariasis***	***Guinea worms***	
1. Male fern 2. Niclosamide. 3. Bithionol 4. Chloroquine. 5. Dichlorophen	1. Diethylcarbamazine. 2. Ivermectin 3. Amocarzine	1. Niridazole. 2. Metronidazole. 3. Mebendazole. 4. Thiabendazole. 5. Albendazole.	

ANTI-FUNGAL AGENTS

1. GRISEOFULVIN 500 mg/day in 4 divided doses	Acts as purine analogue and interferes with the nucleic acid synthesis. It disrupts the fungal spindle formation. It tightly binds keratin and make epidermis resistantto fungal infection.	1. Nausea, vomiting, diarrhea. 2. Photosensitivity. 3. CNS: Headache, paresthesis, vertigo, insomnia, blurring. peripheral neuritis. 4. Superinfection. 5. Others: Gynecomastia, pigmentation, proteinuria, antabuse-like action.	1. *Superficial fungal skin infections:* Teniasis capitis, barbae, corporis, cruris, pedis, manus 2. Onychomycosis
2. AMPHOTERICIN B 0.05 mg/kg in 5% glucose IV over 6-12 hrs. increased gradually to 1 mg/kg and given on alternate days 0.5 mg. Intrathecally. 3% Cream. ABLC (Amphotericin B Lipid Complex) ABCD (Amphotericin B Colloid Complex) Liposomal amphotericin	Combines with the cell-wall and interferes with the vital cellular processes like respiration and glucose utilization. Bacteriostatic or bactericidal.	1. Local irritation - Phlebitis. 2. Nausea, vomiting, diarrhea. 3. Anaphylaxis. 4. Vertigo, fits, myalgia, peripheral neuritis. 5. Hepatocellularfailure. 6. Anemia, thrombocytopenia. 7. Renal impairment. 8. Superinfection. 9. Hypokalemia, hypomagnesemia	1. Topical cream in Candidiasis. 2. Blastomycosis, Histoplasmosis, Cryptococciosis, Candidiasis, Sporotrichosis Aspergillosis, Chromatomycosis, Phycomycosis, Maduromycosis. 3. Kala Azar 4. ABLC in Refractory Aspergillosis
3. NYSTATIN 5 lakh units 8 hrly. orally	Similar to amphotericin B.	Nausea, vomiting, diarrhea.	1. Localised candidiasis 2. Monilial vaginitis.
4. KETOCONAZOLE 200-400 mg once a day with food.	It acts by interfering with ergosterol synthesis and various oxidative enzyme systems. It inhibits adrenal steroidogenesis	1. Pruritus 2. Headache, vomiting, ataxia. 3. Gynecomastia. 4. Reversible hepatotoxicity.	1. Coccidioidomycosis, paraco-ccidioidomycois, histoplasmosis, cryptococcosis & blastomycosis infection, systemically or locally in vagina, nail beds or mucocutaneous junction 2. Medical adenectomy: Treatment of hypercortisolism (Cushing's syndrome, metastatic breast carcinoma) 3. Anti-androgenic hence useful in virilisation, adrenogenital syndrome and carcinoma of prostate 4. Familial testotoxicosis
5. FLUCONAZOLE *Mucosal*: 50-100 mg/day then 200-400 mg OD *Maintenance to prevent relapse of cryptococcal Meningitis* : 100-200 mg/day *Prophylaxis of fungal infection*: 50-100 mg/day OD *I.V infusion*: 5-10 ml/min.	A synthetic triazole which acts by inhibiting ergosterol synthesis in the fungal cell wall	1. Nausea, vomiting 2. Abdominal distress 3. Diarrhea 4. Allergic skin rash 5. Headache 6. Flatulence 7. Abnormalities in liver enzymes	1. Cryptococcal meningitis 2. Mucosal & systemic candidiasis 3. Coccidioidal meningitis 4. Sporotrichosis 5. Histoplasmosis 6. Vaginal candidiasis 7. Prevention of fungal infection following cytotoxic chemotherapy
6. ITRACONAZOLE 100 mg, 200 mg BD, OD **SAPERACONAZOLE**	Same as fluconazole	Less toxic than ketoconazole	Same as above and Onychomycosis, Sporotrichosis

Drug/Dose	Action	Side Effects	Uses
7. TERBINAFINE 250mgOD	Acts on onchomycosis and ringworm	1. Gastrointestinal distress 2. Rash 3. Hepatitis 4. Pancytopenia	1. Onychomycosis 2. Ringworm
8. MICONAZOLE 200-1200 mg/day by slow IV drip	Same as ketoconazole. It acts by altering the cell membrane permeability.	1. Pruritus, rash, fever. 2. Anaphylactoid reaction. 3. Nausea, vomiting 4. Phlebitis. 5. VT & cardiac arrest	1. Same as ketoconazole. 2. Systemic candidiasis. With the availability of Ketoconazole, this drug is restricted to topical use.
9. FLUCYTOSINE 50-150 mg/kg 6 hourly	Flucytosine is converted within the fungal cells to fluorouracil, a metabolic antagonist that ultimately leads to inhibition of thymidylate synthetase. It has no action on the host cells.	1. GI disturbances. 2. Liver damage. 3. Bone-marrow damage. 4. Colitis 5. Allergic rash	1. Cryptococcal meningitis. 2. Systemic candidiasis. 3. Chromoblastomycosis

ANTI-VIRAL AGENTS

1. ACYCLOVIR 5-10 mg/kg IV 8 hourly. 3% topical ophthalmic ointment, in paraffin base	Viral thymidine kinase converts acyclovir to acycloguanosine monophosphate which is phosphorylated to triple phosphate, a potent inhibitor or viral DNA polymerase.	1. Phlebitis. 2. Light headedness, nausea, sweating and hypotension.	Useful for systemic, ophthalmic & mucocutaneous infection with 1. Herpes simplex virus 1 & 2 2. Varicella zoster virus. 3. Prophylactically in immunocompromised host.
2. FAMCYCLOVIR PENCYCLOVIR 8 hrly.	Inhibits viral DNA polymerase Spectrum:HSV-1,HSV-2,VZV, HBV	1. Headache 2. Nausea 3. Diarrhea	1. Herpes zoster 2. Recurrent genital herpes 3. Resistant hepatitis B infection
3. VALACYCLOVIR 800 mg five times a day I.V., oral, topical 1 gm POTDS	Prodrug of acyclovir	1. TTP 2. Hemolytic uremic syndrome	Same as acyclovir
4. GANGLICYCLOVIR 5 mg/kg IV 12 hrly. 5 mg/kg oral	Inhibits DNA polymerase Spectrum: HSV, VZV, CMV	Similar to Acyclovir	1. CMV infections: Retinitis, colitis, pneumonia, hepatitis, wasting 2. CMV prophylaxis in AIDS, post-bone marrow transplant
5. IDOXURIDINE 0.5% drops or ointment applied every 1-2 hrs.	It resembles thymidine and gets incorporated in viral and host DNA	Toxic, therefore not used except for topical use 1. Gastrointestinal ulceration 2. Bone-marrow depression	1. Topical treatment of shingles 2. Post-herpetic neuralgia 3. HSV keratitis
6. TRIFLURIDINE Topical	Pyrimidine nucleoside. Irreversible inhibition of thymidylate synthetase and to some extent DNA polymerase	Systemic toxicity	1. HSV keratitis 2. Drug-resistant HSV mucocutaneous infections
7. SORIVUDINE	Inhibits viral synthesis Spectrum: VZV, HSV-1, EBV	Toxic in high doses. Causes liver and testicular tumors in rodents.	1. Herpes zoster 2. Varicella infections
8. VIDARABINE 10-15 mg/kg/day I.V. 3% eye ointment	Purine analogue. It inhibits viral DNA polymerase.	1. Fluid overload 2. Anemia, leukopenia 3. Thrombocytopenia 4. Neurotoxicity	1. Herpes simplex 2. Varicella-zoster 3. HSV keratitis 4. Neonatal herpes simplex
9. RIBAVIRIN 200 mg 5 times a day or aerosol	It interferes with the formation of viral messenger RNA and inhibits DNA polymerase.	1. Mutagenic, Teratogenic, Carcinogenic. 2. Apthous ulcer 3. Hemopoietic toxicity, anemia 4. Cardiotoxic 5. Allergy	1. Hepatitis B, C,D, G as adjuvant with interferon 2. Herpes simplex 3. Influenza A and B 4. Parainfluenza 5. Respiratory syncytial virus 6. Lhasa fever 7. Congo-Crimean & Hanta virus hemorrhagic fever

Drug/Dose	Action	Side Effects	Uses
10. FOSCARNET	Inhibits viral DNA polymerase Spectrum:HSV, VZV, HIV, CMV	1. Nephrotoxic 2. Hypocalcemia 3. Hypomagnesemia 4. Hypo/ hyper phosphatemia	CMV retinitis in AIDS
11. CIDOFOVIR	CMV	Nephrotoxic	1. Drug-resistant CMV retinitis 2. CMV with AIDS
12. AMANTIDINE 100 mg BD	Interferes with viral uncoating.Inhibits ion channel function on M2 matrix protein on influenza virus	1. CNS: Dizziness, anxiety, insomnia, difficulty in concentration.	1. Influenza A prophylaxis & Rx 2. Early parkinsonism (Reserve drug)
13. INTERFERONS INTERFERON α(2A,2B,L,N3) 3 or 5 million on alt. days or daily depending on indication, protocol & combination used **INTERFERON β** **INTERFERON γ**	*INTERFERON α* has: 1. Antiviral, antitumor activity 2. Inhibits RNA & DNA viruses 3. Antiproliferative effect on normal and malignant cells 4. Suppresses antibody formation through effect on B lymphocytes 5. Inhibits onset of delayed hypersensitivity	1. Flu-like syndrome 2. Myelosuppression, coma, MI 3. Nausea, vomiting 4. Hyper tension and hypotension 5. Arrhythmias, seizures, confusion 6. Taste disturbances 7. Thyroid, lupus and hemolytic anemia	*INTERFERON α*: 1. Chronic hepatitis B,C,D and G: with or without antivirals like Ribavirin or Lamivudine 2. Condylomata acuminata 3. Kaposi's sarcoma 4. CML, hairy cell leukemia, NHL, multiple myeloma, renal cell carcinoma *INTERFERON β*: Multiple sclerosis *INTERFERON γ* Chronic granulomatous disease

ANTI-RETROVIRAL AGENTS FOR HIV INFECTION

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI)

1. **ZIDOVUDINE** (AZT, Azidothymidine) 300 mg BD *Monotherapy*: Only for prevention of maternal-fetal transmission of HIV *In combination:* 200 mg TDS or 300 mg BDS	Nucleoside analogue. Acts by incorporating itself into DNA of the virus, thereby stopping the replication process. The resulting DNA is incomplete and cannot create a new virus.	1. **Anemia** 2. Granulocytopenia 3. Cardiomyopathy 4. **Lactic acidosis** 5. Hepatomegaly with steatosis 6. Headache, nausea, fatigue, malaise	1. Patients with AIDS or ARC 2. Patients with HIV infection CD4 + counts < 500/uL and plasma viremia > 20000 copies of HIV RNA./ml 3. Prevention of maternal-fetal transmission of HIV
2 **DIDANOSINE** (ddI, 2'3' Dideoxyinosine) *In combination*: 200 mg BDS if wt > 60 kg 125 mg BDS if wt < 60 kg Taken on empty stomach	Nucleoside analogue Action same as Zidovudine	1. **Pancreatitis** 2. Peripheral neuropathy 3. Abnormal liver function tests 4. Lactic acidosis 5. Hepatomegaly with steatosis	Alone or in combination with AZT for treatment of HIV infection in patients with CD4 + counts < 500/uL
3. **ZALCITABINE** (ddC, 2' 3' dideoxycytidine) *In combination:* 0.75 mgTDS Not to be used with ddI or antacids	Nucleoside analogue Action same as Zidovudine	1. **Peripheral neuropathy** 2. Pancreatitis 3. Lactic acidosis 4. Hepatomegaly with steatosis 5. Oral ulcers	1. In combination with AZT for treatment of patients with CD4+ counts < 500/ul 2. As monotherapy for advanced disease that is progressing despite AZT or patients intolerant to AZT
4. **STAVUDINE** (d4T, 2'3' didehydro-3'-dideoxythymidine) *In combination :* 30 mg BDS	Nucleoside analogue Action same as Zidovudine	1. **Peripheral neuropathy** 2. **Pancreatitis** 3. Lipoatrophy 4. Lactic acidosis 5. Hepatic steatosis	1. Adults intolerant to approved therapies 2. Patients whose disease is progressing despite other therapies
5. **LAMIVUDINE** (3TC, 2'3' dideoxy-3'-thiacytidine) *Only in combination :* 150 mg BDS	Nucleoside analogue Action same as Zidovudine	1. **Peripheral neuropathy** 2. **Pancreatitis** 3. Hepatotoxicity	1. In combination with othernucleoside analogues fortreatment of HIV infection 2. Hepatitis B, C infection
6. **ABACAVIR** *In combination :* 300 mg BDS	Synthetic carbocyclic analogue of nucleoside guanosine	1. Hypersensitivity reaction (Can be fatal) 2. GI disturbances, headache, rash malaise, asthma, fatigue 3. Loss of appetitie	Same as Lamivudine

Drug/Dose	Action	Side Effects	Uses
7. **EMTRICITABINE (FTC)** *In combination:* 200 mg OD	Action similar to Lamivudine. Longer half-life.	Hepatotoxicity	Same as Lamivudine
8. **TENOFOVIR** *In combination:* 300 mg OD	**Nucleotide inhibitor**	1. Renal toxicity possible.	In combination for HIV-1 infection
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)			
1. **NEVIRAPINE** *Monotherapy:* Orally 200 mg OD for 14 days then 200 mg BDS *In combination:* 200 mg BDS	Stops HIV production by binding directly to reverse transcriptase and prevents conversion of RNA to DNA	1. **Skin rash** 2. **Hepatotoxicity**	In combination with nucleoside analogues for treatment of progressive HIV infection
2. **DELAVIRDINE** 400 mg TDS	Action similar to Nevirapine	1. Skin rash 2. Abnormal liver function test	Same as nevirapine
3. **EFAVIRENZ** 600 mg HS (at night) on empty stomach	Action similar to Nevirapine	1. Rash, dysphonia, drowsiness 2. **Abnormal dreams, depression** 3. Abnormal liver function test	Same as nevirapine Not to be used in first trimester of pregnancy
4. **ETAVIRINE**			
PROTEASE INHIBITORS (PI)			
1. **SAQUINAVIR MESYLATE** *In combination:* (taken within 2 hrs of full meal) 1000 mg + 100 mg ritonavir BDS	Acts on last stage of viral life cycle. Inhibits protease enzyme and prevents HIV-1 from being successfully assembled and released from the infected CD4+ T cell	1. Nausea 2. Diarrhea, headaches 3. Hyperglycemia 4. Fat redistribution, lipid abnormalities	In combination with other antiretroviral agents for treatment of HIV infection when warranted
2. **RITONAVIR** *In combination:* (taken with meals) 600 mg TDS	Protease inhibitor Action same as Saquinavir	1. Nausea, abdominal pain 2. May alter levels of other drugs, e.g. saquinavir 3. Fat redistribution, lipid abnormalities	In combination with other antiretroviral agents for treatment of HIV infection when warranted
3. **INDINAVIR SUFATE** *In combination:* 800 mg TDS (taken on empty stomach 1 hr before or 2 hrs after a meal)	Protease inhibitor Action same as Saquinavir	1. Nephrolithiasis 2. Indirect hyperbilirubinemia 3. Fat redistribution, lipid abnormalities 4. Lipid abnormalities	In combination with nucleoside analogues for treatment of HIV infection when warranted
4. **NELFINAVIR MESYLATE** *In combination:* (taken with meals) 750 mg TDS or 1250 mg BDS	Protease Inhibitor Action same as Saquinavir	1. Diarrhea, loose stools 2. Hyperglycemia 3. Fat redistribution, lipid abnormalities 4. May contain potential carcinogen	Pediatric and adult HIV infection when warranted Avoided in pregnancy
5. **AMPRENAVIR** *In combination:* 1200 mg BDS	Protease Inhibitor Action same as Saquinavir	1. Rash, nausea, vomiting, diarrhea 2. Lipid abnormalities, elevated LFT 3. Oral parasthesisa 4. Fat redistribution, lipid abnormalities	In combination with other antiretroviral agents for treatment of HIV infection
6. **ATAZANAVIR** *In combination:* 400 mg OD	Protease Inhibitor Action same as Saquinavir	1. Hyperbilirubinemia 2. PR prolongation, fat maldistribution , nausea, vomiting, hyperglycemia	In combination with other antiretroviral agents for treatment of HIV infection
7. **LOPINAVIR/RITONAVIR** *Fixed dose combination* 400 mg/100 mg BDS	Boosted Protease Inhibitor	1. Diarrhea 2. Hyperglycemia 3. Fat redistribution, lipid abnormalities	In combination with other antiretroviral agents for treatment of HIV infection

8. **FOSAMPRENAVIR, TIPRANAVIR, DARUNAVIR** are other protease inhibitors

Drug/Dose	Action	Side Effects	Uses
ENTRY (FUSION) INHIBITORS			
1. **ENFUVIRTIDE** *In combination:* 90 mg SC Inj. BDS	Interferes with binding of HIV to its receptor or co-receptor or with the process of fusion	1. Local injection skin reaction 2. Bacterial pneumonia rate increased 3. Hypersensitivity reactions	Patients with persistent viremia after treatment with other ARV agents
INTEGRASE INHIBITOR			
1. **RALTEGRAVIR** *In combination:* 400 mg BDS	Inhibits viral enzyme integrase. Active against HIV-1 and HIV-2	1. Nausea 2. Rash	Treatment-experienced patients
CCR5 ANTAGONIST			
1. **MARAVIROC** *In combination:* 150-600 mg BDS	CCR5 Antagonist	1. Abdominal pain, cough 2. Dizziness, musculoskeletal symptoms 3. Fever, cough, rash, URTI	Treatment-experienced patients
ALCOHOL			
1. **ETHYL ALCOHOL** Loading dose 0.6 g/kg 10 g/ hr infusion in methyl alcohol poisoning.	1. Systemic actions are toxic and not discussed here. 2. Local actions: irritant, germicidal, astringent, antiseptic, and cosmetic/cooling effect. 3. 1 gm of alcohol = 7.1 calories, but these are empty calories.	1. Acute alcoholism 2. Chronic alcoholism 3. Alcohol related systemic damage	1. *Systemic*: Methyl alcohol poisoning 2. *Local*: Symptomatic treatment for fever, antiseptic (70% conc), prevention of bed sores, wash out phenol 3. Local inj. to destroy ganglia e.g. trigeminal neuralgia 4. Percutaneous ethanol inj. as a sclerosant e.g. autonomously functioning solitary thyroid nodules.
2. **DISULFIRAM** 100-200 mg daily 800 mg on day 1 **CARBIMIDE**	1. Interferes with oxidation of acetaldehyde formed during alcohol metabolism 2. Inhibits dopamine beta-oxidase, thus depletes catecholamines	1. Nausea, vomiting 2. Metallic taste 3. Headache, drowsiness, cramps 4. Severe acetaldehyde reaction	Alcohol de addiction, should be given in hospital only.
3. **4-METHYLPYRAZOLE** 100 mg diluted in 250 ml of saline IV slowlyfor 45 mins.	Alcohol dehydrogenase inhibitor	Non-toxic	1. Methyl alcohol poisoning 2. Ethylene glycol poisoning
ANTI-MALIGNANCY AGENTS			
1. **CYCLOPHOSPHAMIDE** 50 mg. tablet. 100-200 mg powder in vial for injections I.M. or I.V. 2-3 mg/ kg. In combination therapy with other drugs 150 mg for 5 days every 15-30days for 6 courses.	1. Damages the nuclei of growing and multiplying cells. This affects hemopoietic system, epithelial tissues, germinal epithelium of the gonads and hair follicle. Latter causes alopecia. 2. It suppresses the antibody production and immune response.	1. Anorexia, nausea, vomiting 2. Bone marrow depression leading to anemia, leucopenia and thrombocytopenia 3. Depress spermatogenesis in males. Amenorrhea in females. 4. Fetal abnormalities if given during pregnancy. 5. Hemorrhagic cystitis.	1. Lymphomas and Hodgkin's disease. 2. Acute leukemias. 3. Bronchogenic carcinoma. 4. Multiple myeloma. 5. Ovarian carcinoma and seminomas. 6. Immunosuppressant as in steroid resistant nephrosis, transplantation, etc. 7. Mycosis fungoides.
2. **MELPHALAN** 2 mg tablets 4-6 mg for 3 weeks repeated after 1 month.	Similar to cyclophosphamide	1. Bone marrow depression 2. Nausea vomiting 3. Alopaecia. 4. Oral ulceration	Multiple myeloma
3. **CHLORAMBUCIL** 5-10 mg for 3 weeks.	Similar to cyclophosphamide but no alopecia or hemorrhagic cystitis	Similar to cyclophosphamide	Chronic lymphocytic leukemia

Drug/Dose	Action	Side Effects	Uses
4. BUSULFAN 2 mg tablets 5-10 mg for 3 wks. Dose adjusted on platelet count	Similar to cyclophosphamide	1. Pancytopenia. 2. Skin pigmentation & wasting resembling Addison's dis. 3. Pulmonary fibrosis. 4. Gynecomastia	Chronic myeloid leukemia.
5. METHOTREXATE 2.5-10 mg. orally or I.V. or intrathecally 10-30 mg for 5 days in choriocarcinoma.	Methotrexate competes with folic acid and binds folate reductase irreversibly restricting the production of Tetra-hydro folate which inhibits nucleic acid synthesis and consequently cell division. Such cells ultimately die.	1. Megaloblastic anemia. 2. Pancytopenia. 3. Intestinal ulcers diarrhea. 4. Alopecia. 5. Liver damage. 6. Dermatitis.	1. Acute leukemias. 2. Choriocarcinoma. 3. Soft tissue sarcoma. 4. Breast cancer. 5. Psoriasis. 6. Immunosuppressant. 7. Rheumatoid arthritis 8. Bronchial asthma
6. 6-MERCAPTOPURINE 50 mg tablets. In combination therapy 150 mg for 5days every 15-30 days for 6 such courses	Acts by interfering with the synthesis and inter-coversion of purines.	1. Bonemarrow depression. 2. Liver damage. 3. Intestinal ulcers. 4. Hyperuricemia and hyperuricosuria.	1. Acute leukemia. 2. Chronic myeloid leukemia. 3. Choriocarcinoma.
7. AZATHIOPRINE 2-3 mg/kg.	Similar to 6-mercaptopurine.	Similar to 6-mercaptopurine.	1. Immunosuppressant in organ transplant 2. Autoimmune diseases.
8. 6-THIOGUANINE	It is converted to 6-thioguanine ribose Phosphate which inhibits purine biosynthesis	1. Myelosuppression 2. Nausea 3. Hepatotoxicity	Acute myeloid leukemia.
9. 5-FLUOROURACIL 7.5 - 15 mg/kg	It inhibits DNA synthesis as well as forms fraudulent RNA	1. Myelosuppression 2. Alopecia 3. Stomatitis, nausea, vomiting diarrhea 4. Neurotoxicity	1. Breast cancer 2. Gastrointestinal adenocarcinoma 3. Carcinoma of cervix, bladder and prostate.
10. VINCA ALKALOIDS VINCRISTINE 1.4 mg/sq.m VINBLASTINE 0.1 mg/kg body wt.	Inhibits mitosis at metaphase.	1. Nausea, vomiting, constipation 2. Alopecia. 3. Neurotoxicity: Peripheral neurits, cranial nerve palsy, ataxia, tremors, mental depression, marrow depression (more with Vinblastine).	1. Acute lymphoblastic leukemia (vincristine). 2. Hodgkin's lymphoma (Vinblastine) 3. Choriocarcinoma (Vinblastine).
11. RUBIDOMYCIN 40 mg/m/day.I.V.	It acts by inhibiting DNA-dependent RNA synthesis.	1. Bone-marrow depression. 2. Allergic reaction. 3. Myocardial depressant.	Acute myeloblastic leukemia in combination with Vincristine and prednisolone.
12. ADRIAMYCIN 20-30 mg/day for 2-3 days.	Binds to DNA and inhibits DNA synthesis. Binds myocardial DNA which may cause cardiomyopathy.	1. Myelosuppression. 2. G.I. disturbances & stomatitis 3. Alopecia. 4. Cardiomyopathy.	1. Acute lymphoblastic leukemia. 2. Lymphoblastic lymphosarcoma.
13. BLEOMYCIN 10-20 units I.V. or I.M. or S.C. twice a week.	Causes DNA nicking. Inhibits DNA ligases important for DNA replication, recombination and repair.	1. Pneumonitis leading to pulmonary fibrosis. 2. Dermographic and scleroderma-like skin changes.	1. Epidermoid carcinoma of skin, respiratory & oral cavity & genito-urinary tract. 2. Lymphomas.
14. MITHRAMYCIN 25 ug/kg/day.I.V. for 1 day.	Interferes with RNA synthesis.	1. Myelosuppression. 2. Liver and kidney damage. 3. Bleeding due to suppresssion of clotting factors.	1. Embryonic cell carcinoma of testis 2. Hypercalcemia of malignancy 3. Paget's disease
15. o'-p DDD (Mitotane) 8-10 gm orally for4-8 wks. followed by 4 gm as maintenancedose.	It gets selectively concentrated in adrenal cortex and destroys it.	1. Anorexia, nausea, lethargy, drowsiness. 2. Addison's disease.	Malignant neoplasms of adrenal cortex.

Drug/Dose	Action	Side Effects	Uses
16. L-ASPARAGINASE 200 IU/kg daily for 28 days.	Deaminates asparagine to aspartic acid & depletes asparagine the host, depriving only the malignant cells of the essential metabolite.	1. Sensitisation 2. Pyrogenic reaction.	1. Lymphoblastic leukemia. 2. Reticulum cell sarcoma.
17. CYTOSINEARABINOSIDE 2-4 mg/kg IV for 2 days Maintenance dose 1 mg/kg/ week S.C.	Inhibits DNA polymerase, during the 'S' phase of the cell cycle. Suppresses humoral and cellular immunity.	1. Nausea, vomiting. 2. Bone marrow depression.	1. Acute myeloid leukemia. 2. Hodgkin's disease and lymphoma.
18. LOMUSTINE (CCNU) 120-130 mg/sq.m. Repeated every 6-8 weeks	Similar to carmustine	1. Myelosuppression 2. Nausea, vomiting	1. Hodgkin's disease 2. Non-Hodgkin's lymphoma 3. Neoplasms of brain,kidneys lung, stomach and colon.
19. CARMUSTINE (BCNU)	It acts by alkylation of DNA and other nucleoproteins and the carbamylation of lysine residues on proteins.	1. Myelosuppression 2. Nausea, vomiting 3. Pulmonary fibrosis 4. CNS toxicity.	1. Hodgkin's disease 2. Meningeal leukemia 3. Tumours of the brain
20. PROCARBAZINE 50-300 mg 2-3 times a day	It causes degradation of DNA and protein synthesis.	1. Myelosuppression 2. Nausea, vomiting, CNS toxicity 3. Hypertension with tyramine containing food due to MAO inhibition.	1. Hodgkin's disease 2. Oat cell carcinoma of lung
21. CISPLATIN 20-30 mg daily upto 150 mg I.V.	It binds to DNA, nuclear and cytoplasmic proteins.	1. Renal impairment 2. Nausea, vomiting 3. Anaphylaxis 4. Hearing loss for high frequency	1. Solid tumours 2. Testicular tumours 3. Ovarian carcinoma
22. PACLITAXEL 35 mg/sq.m.	Inhibits microtubule formation	1. Suppresses bone marrow 2. Myalgia 3. Cardiotoxicity	1. Ovarian and breast cancers 2. Lung, esophagus, head and neck cancers
23. ETOPOSIDE 50-100 mg/sq.m.	Plant glycoside which arrests cells in G2 phase	1. GI toxicity 2. Myelosuppression 3. Neuritis	1. Lymphomas, acute leukemias 2. Testicular & bladder cancers 3. Trophoblastic disease 4. Small cell lung cancer
24. FLUTAMIDE 250 mg TDS	Anti-androgen, anti-estrogen	GI toxicity, Mucositis, CNS disturbances	1. Advance CA prostate 2. Refractory hirsutism
25. HYDROXYUREA 30-80 mg/kg	DNA inhibitor; inhibits ribonucleoside diphosphate reductase.	1. Myelosuppression 2. Skin and GI disturbances 3. Neurological disturbances	1. CML, myeloma, P. vera 2. Thrombocytosis 3. Sickle cell anemia HIV/AIDS

HEMOPOIETIC DRUGS

1. HEPARIN	Refer Pg. 566		
2. PROTAMINE SULFATE (1% solution). 1 mg neutralises 100 units of heparin. It is given slowly I.V. not to exceed 50 mg over 10 minute.	Because it is a strongly basic compound it neutralises the acidic group in heparin thereby abolishing the anticoagulant activity.	Hypotension, dyspnea, bradycardia, flushing and feeling of warmth.	To neutralise the excess anticoagulant effect of heparin. Protamine sulfate itself has anticoagulant activity and hence its dose should not exceed 50 mg. over 10 mins.
3. COUMARIN-DERIVATIVES: BISHYDROXYCOUMARIN (WARFARIN) (5 mg. tablets) 10-20 mg. oral for 3 days followed by further dose depending on Prothrombin time and International Normalized Ratio (INR)	1. Suppress the formation of factors II, VII, IX and X from liver by blocking the utilisation of vitamin K due to structural similarity. 2. Uricosuric by interfering with the renal tubular reabsorption of urate.	1. Hemorrhage. 2. Allergic manifestations. 3. G.I. upset. 4. Alopecia.	Oral anti-coagulant action takes 2-3 days to occur and remains for 2-3 days after the drug is withdrawn.

Drug/Dose	Action	Side Effects	Uses
4. EPSILON AMINO CAPROIC ACID (EACA) 5 gm. initially followed by 1 gm. 1 hrly. I.V. till satisfactory response.	It blocks the activation of Plasminogen by competitive blockade and thus reduces the fibrinolytic activity.	1. Nasal stuffiness. 2. Abdominal discomfort, nausea, vomiting, diarrhea. 3. Skin rash. 4. Hypotension.	Excessive fibrinolysis as in abruptio placentae, post-partum hemorrhage, snakebite, etc.
5. APROTININ	Refer Pg. 566		
6. ORAL IRON Ferrous sulfate Ferrous fumerate Ferrous gluconate	Iron is required for the formation of hemoglobin.	1. G.I. disturbances, abdominal colic, nausea, vomiting, diarrhea, 2. Black teeth, black stools	1. Prophylactic in pregnancy, infancy menstruating women following gastrectomy, etc 2. Iron deficiency anemia.
7. PARENTAL IRON Iron dextran, Iron-carbohydrate complex. 50 mg/ml. of elemental iron I.M. 20 mg/ml of elemental iron I.V.	Same as above.	1. Local pain, inflammation and discoloration of skin. 2. Anaphylaxis, Headache fever, arthralgia, tachycardia, flushing, circulatory collapse and even death.	1. Failure to absorb oral iron. 2. Intolerance to oral iron. 3. Exhausted iron stones when daily iron loss exceeds the absorption of oral iron. 4. Severe iron deficiency anemia in late pregnancy. 5. Unreliable patient.
8. VITAMIN K 2.5 - 25 mg orally OR 0.5 - 1 mg SC or IM OR 0.5 - 25 mg IV (< 1 mg/min)	Vit. K is essential for blood coagulation (Biosynthesis of prothrombin, factors VII, IX and X) and protein C and Protein S.	1. Anaphylaxis following. I.V administration 2. Hemolytic anemia 3. Hyperbilirubinemia 4. Kernicterus	1. Adult Vit K deficiency (malabsorption syn., obstruction, jaundice, malnutrition) 2. Vit K deficiency in infants following acute diarrhea 3. Neonatal Vit K deficiency 4. Bleeding state during oral anticoagulant therapy.
9. ERYTHROPOIETIN 25-500 I.U./kg thrice a week	Glycoprotein hormone stimulates erythroid colony forming unit	1. Hypertension 2. Headache, confusion, seizures 3. Flu-like syndrome, rashes	1. Anemia of chronic renal failure 2. AZT-induced anemia in AIDS 3. Chemotherapy-induced anemia 4. Increase yield of autlogous blood transfusion
10. FILGRASTIM (G-CSF) 30 million I.U./min	Granulocyte Colony stimulating factor.	1. Transient hypotension 2. Dysuria, hyperuricemia 3. Transaminitis	1. Neutropenia
11. MOLGRAMOSTIM (GM-CSF) 5-10 mcg/kg/day	Granulocyte-macrophage colony stimulating factor	1. Mild and transient	1. Lymphomas 2. AML- post-chemotherapy 3. Adjuvant to cancer chemotherapy or gangciclovir 4. Myeloblastic syndromes 5. Aplastic anemia

Other drugs are: Cyanocobalamin and Folic acid (Refer Pg. 13)

CHELATING AGENTS

1. DIMERCAPROL (British Anti Lewisite) 300 mg/day I.M. SUCCIMER- Chemical analog of dimercaprol orally	SH groups of Dimercaprol bind the metals (As, Hg, Cu, Au, Bi, Ni)	1. Vomiting 2. Tachycardia, sweating, rise in BP 3. Inflammation of mucous membranes 4. Cramps	1. Poisoning due to arsenic, bismuth, mercury, nickel 2. Lead poisoning as adjuvant 3. Wilson's disease, copper poisoning: as an adjuvant to poisoning: as an adjuvant to penicillamine.
2. CALCIUM DISODIUM EDETATE 1 gm IV over 1 hr, b.d. for 3 to 5 days	Exchanges Calcium for metals like Pb, Zn, Mn, Cu, Cd. The complex is then excreted in urine.	1. Proximal tubular necrosis 2. Anaphylaxis 3. Acute febrile reaction	1. Lead poisoning 2. Poisoning with zinc, copper, iron, manganese & radioactive metals- plutonium etc. 3. Porphyria

Drug/Dose	Action	Side Effects	Uses
3. d-PENICILLAMINE 250 mg b.d. to q.i.d. 1 hr before or 2 hrs after meals ACETYL d-PENICILLAMINE 1 gm total dose t.d.s./q.i.d.	Chelates Cu, Hg, Pb, Zn.	1. Anorexia, nausea, loss of taste sensation 2. Rash 3. Renal toxicity 4. Bone marrow depression	1. Wilson's disease 2. Copper poisoning 3. Mercury, lead poisoning 4. Cystinuria and cystine stones, hemosiderosis 5. Rheumatoid arthritis and scleroderma 6. Primary biliary cirrhosis
4. DESFERRIOXAMINE 0.5-1 gm/day IM in iron overload DTPA and L1 are other iron chelators	Forms a stable complex with ferric iron. This is excreted in urine.	1. Allergic reactions 2. Cramps 3. Pain in abdomen 4. Fever 5. Dysuria	1. Iron overload: in patients who receive repeated blood transfusions, e.g thalassemia 2. Hemachromatosis 3. Acute iron toxicity
5. TRIENTINE 400-800 mg t.d.s before meals	Similar to d-penicillamine	Similar to d-penicillamine, but less toxic	Wilson's disease

DRUGS IN ENDOCRINE DISORDERS

1. BROMOCRYPTINE 2.5-20 mg/day Max. 30 mg/day	1. It inhibits prolactin secretion at pituitary level. 2. It slows dopamine turnover. 3. It is a potent dopaminergic agonist acting at several sites in CNS.	1. Nausea, vomiting, constipation. 2. Dizziness and mood changes. 3. Postural hypotension. 4. Digital vasospasm. 5. Alcohol intolerance. 6. Dyskinesias	1. Suppression of lactation 2. Hyperprolactinemia/ galactorhhea 3. Hypogonadism 4. Acromegaly 5. Parkinsonism *Potential uses:* 1. Carcinoma of breast dependant on growth hormone and prolactin 2. Mania and depression. 3. Hypertension 4. Portasystemic encephalopathy 5. Cushing's disease, Nelson's syndrome and Conn's syndrome.
2. CLOMIPHENE CITRATE 50 mg from day 5 for 5 days	Ovulation inducer. Inhibits negative feedback mechanism which suppresses release of GNRH.	1. Rare, Abd. pain, bloating, blurred vision, multiple pregnancies.	1. Anovulatory infertility 2. Male infertility
3. OCTREOTRIDE 0.05 - 0.1 mg S.C. BD	Synthetic analogue of somatostatin Growth hormone inhibitor	1. Veryfew 2. Local pain, GI	1. Acromegaly 2. Gut endocrine tumors 3. Hematemesis 4. After pancreatic surgery
4. GROWTH HORMONE 4, 12, 16, 36 IU 0.1 IU/kg/day SC at night	Somatropin stimulates growth esp. in children with GH deficiency. Anabolic action.	1. Veryfew 2. Unmasks hypothyroidism 3. Lipo-atrophy 4. Urticaria	1. Short stature due to GHD 2. Short stature due to CRF, Turner's synd. & other secondary causes 3. Catabolic states like burns, critical care 4. Pan-hypopituitarism; aging; andropause (male menopause) 5. Adult GHD
5. DESMOPRESSIN 2-4 mcg/day SC/IV BD Nasal spray 20-40 mcg/day **TERLIPRESSIN** 1 - 2 mg IV **VASOPRESSIN** 5-20 IU SC/IV	Vasopressin analogue which acts on V2 receptor linked adenyl cyclase system on the collecting tubule.	1. Water intoxication 2. Dilutional hyponatremia 3. Nausea, headache, nasal congestion, epistaxis 4. Vasopressin is cardiotoxic	1. Cranial diabetes insipidus 2. Pituitary neurosurgery 3. Nocturnal anuresis 4. Renal function testing 5. Hemophilia A, von Willebrand's disease 6. Bleeding esophageal varices

Drug/Dose	Action	Side Effects	Uses
6. THYROID TABLETS Thyroxine 25, 50, 100, 200 mcg tablets 3-5 mcg/kg body wt.	1. Calorigenic action 2. Growth 3. Metabolic action a) Anabolic b) Increases glucose absorption and utilisation c) Enhances cholesterol synthesis by liver and increases its biliary excretion 4. Cardiac: Stimulates the rate & force of contraction of myocardium	1. Diarrhea 2. Weight loss 3. Palpitations, angina 4. Tremors, hyperkinesia 5. Irritability	1. Substitution therapy for myxedema and cretinism 2. Non-toxic TSH dependent goitre, because thyroxine inhibits TSH 3. Thyroid carcinomas 4. Thyroid Suppression test 5. Therapeutic test of hypothyroidism 6. Along with anti-thyroid drug to treat thyrotoxicosis of pregnancy & exophthalmos of hyperthyroidism. 7. Block replacement regimen.
7. THIOAMIDES Propylthiouracil Up to 600 mg.qds. Methimazole 5-20 mg/day Carbimazole 30-60 mg. initially, 5-20 mg. later.	They inhibit the organic binding of iodine, both iodination of tyrosine as well as coupling of Iodotyrosines.	1. Allergic: Skin rash fever arthralgia, lymphadenopathy 2. Blood: Leucopenia, agranulocytosis, thrombocytopenia 3. Liver damage 4. Alopecia	1. Hyperthyroidism 2. To induce hypothyroid state in conditions like severe angina or intractable cardiac failure.
8. IODIDES Sodium or Potassium 6-10 mg/day.	The exact mechanism is not known. It rapidly shuts off the release of thyroid hormone which gets stored in the colloid material of thyroid.	1. Iodism: Skin rash, rhinorhea, lacrimation, salivation. 2. Goitre and myxedema. 3. Precipitate thyrotoxicosis.	1. Pre-operative in thyroid surgery to reduce vascularity. 2. To control hyperthyroidism rapidly e.g. CCF.
9. RADIOACTIVE IODINE 5-10 ug. on empty stomach.	Radio-active iodine emits gamma and beta rays. Beta rays destroy thyroid follicles and produce fibrosis.	1. Hypothyroidism. 2. Genetic damage. 3. Thyroid carcinoma. 4. Damage to fetal thyroid if given during pregnancy.	Hyperthyroidism. The effect becomes apparent by 3-4 wks. and is maximum after 3-4 months.
10. GLUCOCORTICOIDS (Corticosteroids) Prednisolone 5 mg tablets 5-160 mg/day. Hydrocortisone 100 mg. 6 hrly. Triamcinolone 10 mg. Intra-articular, 40 mg. I.M. 3 mg. tablets up to 12 tablets/day Betamethasone 0.5 mg tablet up to 12 tab/day Dexamethasone 0.5 mg 1 tablet up to 12 tablets/day. 4 mg 6 hrly. I.M. or I.V.	1. *Metabolic*: Anti-anabolic, causes gluconeogenesis and mobilises peripheral fat depots. It antagonises Vitamin D in the gut. It interferes with the development of cartilage and inhibits linear growth. 2. *Fluid Electrolyte*: It has a feeble salt retaining and potassium wasting effect. It is needed for the excretion of water. 3. Anti-inflammatory actions are due to: a) Blocking capillary permeability. b) Maintaining cell membrane integrity. c) Stabilization of lysosomal membranes. 4. Immunological: Corticosteroids. a) Cause lysis of T cells and suppress cell-mediated immunity. b) Inhibit the phagocytosis of antigens and their intracellular digestion.	1. G.I. Gastritis, gastric hemorrhage, peptic ulcer perforation and pancreatitis 2. *CNS*: Acute psychosis aggravation of epilepsy. 3. *CVS*: Hypertension. 4. *Kidney*: Hypokalemic alkalosis. 5. *Musculo-Skeletal*: Myopathy and osteoporosis 6. *Growth*: Linear growth retarded. 7. *Immunity and Inflammation*: It suppresses immunity and inflammation and may mask serious infections. T.B. often spreads and there may be super-infection with fungi. 8. *Metabolic*: Hyperlipidemia. 9. *Miscellaneous*: Delays wound healing. Hirsutism and alopecia. Hypercoagulability of blood. Thromboembolic complication.	1. *Addison's hypopituitarism* 2. *Life threatening emergencies* e.g. Anaphylactic shock, status asthmaticus, hypoglycemia 3. *Immunosuppressive* e.g. Rheumatoid arthritis, rheumatic fever, chronic active hepatitis, collagen diseases, acute rejection of homograft. 4. *To reduce inflammatory edema* (Bell's palsy, Guillain Barre syndrome, heart block) 5. *To suppress pituitary ACTH* as in adrenocortical hyperplasia 6. *Local application*: iridocyclitis, phlyctenular conjunctivitis, eczema 7. Intra-articular in osteoarthritis painful fascial nodules 8. *To reduce raised intracranial tension* in cerebral edema (only dexamethasone useful) 9. *Diagnostic Tests:* a) Dexamethasone Suppression test for Cushing's disease b) Cortisone test: hypercalcemia c) Stress GTC for prediabetes d) To distinguish intra-and extra hepatic cholestasis.

Drug/Dose	Action	Side Effects	Uses
11. ESTROGEN & ITS DERIVATIVES CONGUGATED ESTROGENS 0.625 mg OD ETHNYL ESTRADIOL 0.01, 0.02, 0.05 mg, E2GEL TRANSDERMAL THERAPEUTIC SYSTEM ESTRADIOL 0.025, 0.05, 0.1 mg/day ESTRIOL 1 mg, 2 mg 17-β ESTRADIOL 3 mg per 5 gm gel ESTRADIOL VALERATE 10 mg/ml	1. Major estrogen in premenopausal women 2. Addition of 17-a-ethyl gp enhances oral activity 3. Promotes endometrial growth thickening, stratification & cornification of vagina 4. Inhibits anterior pituitary 5. Capillary dilation, fluid retention 6. Protein anabolism 7. Contraception	1. Endometrial hyperplasia and malignancy 2. Ca breast 3. Thrombosis 4. Hypertension 5. Nausea, vomiting 6. Fluid retention, wt.gain, increased appetite 7. Depression 8. Decreased libido, impotence 9. Fungal infection	1. Hormone replacement therapy 2. Menopause 3. Oral contraception 4. Endometriosis 5. Dysfunctional uterine bleeding 6. Carcinoma breast, prostate 7. Osteoporosis 8. Atrophic vaginitis
12. PROGESTERONE and PROGESTROGENS NATURAL MICRONISED PROGESTONE 100 mg capsl HYDROXYPROGESTONE CAPROATE 250-500 mg IM weekly MEDROXYPROGESTERONE ACETATE 5-10 mg daily 5-10 days orally 150 mg depot every 12 weeks DYDROGESTHONE 10 mg BDS/TDS ALLYLOESTENOL 5-10 mg OD NORETHISTERONE 5-20 mg ORALLY	1. Progesterone prepares uterus for receiving the fertilised ovum & suppresses uterine motility. 2. Can inhibit ovulation, prolonged uterotrophic effects, stimulates luteal action 3. Some androgenic & anabolic effects but no estrogenic effects.	1. GI disturbances 2. Acne, breast discomfort 3. Fluid retention, edema, weight gain 4. Rash, depression 5. Hepatotoxic 6. Virilisation 7. Thromboembolism 8. Ectopic pregnancy	1. Premenopausal syndrome 2. Anovulation- amenorrhea 3. Benign mastopathy 4. Menopause 5. Threatened, habitual abortion 6. Luteal phase defects 7. Mild to moderate endometriosis 8. Contraception 9. DUB, Menorrhagia, Metropathia hemorrhagica 10. Dysmenorrhagia
13. TESTOSTERONE & ITS DERIVATIVES TESTOSTERONE DEPOT 100, 250 mg IM 3-weekly DIHYDROTESTOSTERONE GEL 2.5 gm MESTRALONE 25 mgTDS	Male sex hormone	1. Water, Na and K retention 2. Anabolic 3. Virilisation 4. CNS effects 5. Stunting of growth	1. Hypogonadism 2. Impotence 3. Gynecomastia 4. Delayed puberty 5. Controversial: aging, eunuchoidism, sexual frigidity, aplastic anemia, menorrhagia, metropathia hemorrhagica.
14. DANAZOL 200-800 mg OD/BDS	Attenuated androgen which suppresses pituitary-ovarian axis. Releases FSH & LH- Endometrium atrophies	1. Edema, weight gain 2. Sweating, acne, hirsutism, rash, flushing 3. Virilisation 4. CNS, GI disturbances	1. Endometriosis 2. Infertility 3. Fibrocystic breast disease 4. Precocious puberty 5. Endometrium atrophy 6. Gynecomastia/Mastalgia 7. Menorrhagia

DRUGS FOR DIABETES

1. INSULINS (Before food) *a)* PLAIN INSULIN *b)* PROTAMINE ZINC INSULIN (PZI) *c)* NPH INSULIN *d)* LENTE INSULIN (3 parts semilente and 7 parts ultralente). e) *ULTRALENTE INSULIN* f) INSULIN ANALOGUE Lispro, Aspart (short acting). Glargine, Detemir (Long-Acting). The insulins are purified bovine, purified porcine and human insulins (manufactured by recombinant DNA technology)	1. Liver: Insulin decreases glycolysis and gluconeogenesis and stimulates fatty acid synthesis. 2. Fatty tissue : It is anti-lipolytic on low dose and lipogenetic on high dose. 3. Skeletal Muscle: Stimulates glucose transport and glycogen synthesis. It inhibits lipolysis and proteolysis.	1. Hypoglycemia 2. Allergy 3. Lipodystrophy 4. Presbyopia 5. Neuropathy 6. Obesity 7. Insulin edema 8. Insulin resistance	1. Diabetes mellitus a) Insulin dependant (Type I) b) Type II uncontrolled with drugs (Drug failure) c) Pregnancy/gestational DM d) Perioperative/stress/infection e) Complications: Ketoacidosis, infections,coma, trauma f) MRDM (maturity related DM) 2. Glucose insulin drip for hyperkalemia 3. Glucose insulin drip during cardiac surgery 4. Insulin Tolerance Test to diagnose hypopituitarism. 5. Schizophrenia. Insulin shock 6. Hollander's test: Following vagotomy to test for achlorhydria.

Drug/Dose	Action	Side Effects	Uses
2. GLUCAGON 0.5 mg (IU) SC/IM/IV	Hyperglycemic pancreatic hormone	Nausea, vomiting, hypertension, hypersensitivity.	1. Hyperglycemia 2. Diagnostic aid in GI radiology
3. SULFONYLUREAS (Before food) a. Tolbutamide 0.5-1 gm.TDS b. Chlorpropamide 0.25-0.5 gm TDS c. Glibenclamide 5-20 mg OD or BDS d. Glipizide 5-20 mg OD or BDS e. GLICAZIDE 40-80 mgTDS f. GLIMPERIDE 1-2 mg OD	1. Stimulate the release and synthesis of insulin. 2. Prolonged use stimulates the proliferation of islet cells. 3. Inhibits gluconeogenesis and glycolysis.	1. Allergic reaction: Skin rash, leucopenia, aplastic anemia. 2. Goitre. 3. Potentiates action of ADH. 4. Cholestatic jaundice. 5. Increased risk of mortality from cardiovascular deaths.	1. Maturity onset diabetics who are without complication and with FBS less than 300 mg%. 2. Diabetes insipidus (Chlorpropamide). 3. Diagnosis of insulinomas and diabetes.
4. BIGUANIDES (after food) a. Phenoformin : 25 mg. tablets up to 8 tablets per day. b. Metformin: 500 mg tablets upto 8 tablets per day. 850 mg BD	1. Stimulate the peripheral utilisation of glucose. 2. Correct insulin insensitivity of muscles. 3. Interferes with glucose absorption. 4. Inhibits insulin degradation.	1. Bitter metallic taste, nausea, vomiting, abdominal discomfort. 2. Lethargy, weakness, wt. loss. 3. Anaphylactic reaction. 4. Lactic acidosis. 5. Decreases hepatic glycogen, inhibits lipogenesis and increases fibrinolytic activity of plasma.	1. Obese, type II diabetes 2. Adjuvant in juvenile diabetics who have marked fluctuations of glucose levels. Biguanides help to smoothen the control of blood sugar by insulin. 3. Insulin resistance 4. Polycystic ovarian syndrome
5. ALPHA GLUCOSIDASE INHIBITORS **ACARBOSE** 50 to 100 mg given with each meal **VAGLIBOSE, MIGITOL**	Alpha glucosidase inhibitor. Interferes with absorption of glucose from the gut.	1. Flatulence and abdominal bloating 2. Transient transaminitis	1. NIDDM 2. IGT 3. Adjuvant to insulin in type I
6. GLITAZONES (INSULIN SENSITISERS) **TROGLITAZONE (banned)** **ROSIGLITAZONE** 2, 4, 8 mg **PIOGLITAZONE** given with meal	Activates PPAR-γ (perioxime proliferation activated receptor)	1. Hepatotoxicity 2. Hypoglycemia 3. GI Intolerance	1. Insulin resistance 2. Type 2 DM 3. Polycystic ovarian syndrome
7. **MEGLITINIDES** **REPAGLINIDE** 0.5, 1, 2 mg **NATEGLINIDE** given with meal	Non-sulyphonyl urea, acts on a special receptor on the beta cell	1. Hypoglycemia 2. Headache	1. Adjuvant in Type 2 DM 2. Diabetics with erratic eating habits (dose only with meal) 3. Fasting states 4. Chronic renal insufficiency
8. **INCRETINS**			
1. **INCRETIN MIMETICS** a. Exenatide: 5-10 mcg SC twice a day, 1 hour before meals b. LIRAGLUTIDE: 1.2-1.8MG SC once a day	Long Acting GLP 1 Agonist	1. Nausea, vomiting, stomach discomfort 2. Headache 3. Hyperglycemia 4. Pancreatitis, Nesidioblastosis (rare)	Type 2 DM: Monotherapy as initial treatment or Combination therapy
2. **INCRETIN ENHANCERS (DPP IV INHIBITORS)** a. Vildagliptin, 50mg twice a day Sitagliptin, 100 - 200 mg per day	Dipeptidyl peptidase (DPP) IV Inhibitors	1. Nausea 2. Headache 3. Hypersensitivity and Skin Reactions	Type 2 DM: Monotherapy as initial treatment or Combination therapy

LIPID LOWERING AGENTS

1. **STATINS** **LOVASTATIN** 5-20 mg OD **SIMVASTATIN** 5-20 mg OD **CEREVASTATIN** 200,300 mcg **PRAVASTATIN,** **ATORVASTATIN** 5,10,20mg	HMG- CoA reductase inhibitors which is a rate limiting step in the lipid metabolism.	1. Flatulence, nausea, heart burn 2. Rhabdomyolysis, renal failure 3. Myopathy, myalgia, rash 4. Transaminitis	1. Hypercholesterolemia 2. Combined hypercholesterolemia with mild hypertriglyceridemia.

Drug/Dose	Action	Side Effects	Uses
2. FIBRATES **GEMFIBROZIL** 300, 600 mg BD or TDS **BEZAFIBRATE** 200-400 mg TDS **FENOFIBRATE** micronised	It reduces VLDL, LDL production in the liver.	Increases the risk of gall stones.	1. Type III, IV and V hyperlipidemias. 2. Hypertriglyceridemia
3. CLOFIBRATE 2-3 gm/day.	It inhibits the hepatic synthesis of cholesterol and transfer of triglycerides from the liver to the plasma.	1. Nausea, diarrhea,weight gain. 2. Allergy 3. SGOT may rise 4. Displaces drugs like tolbutamide & coumarin derivatives from their plasma binding sites & hence the dose of these drugs must be reduced.	1. To reduce plasma lipid. 2. Atherosclerotic arterial disease. 3. Angina.
4. PROBUCOL	Lowers both LDL and HDL cholesterol.	1. Diarrhea 2. Prolonged QT, 3. Liver damage.	Type III, IV and V hyperlipidemias.

GASTRO-INTESTINAL DRUGS

1. ALUMINIUM HYDROXIDE Al (OH)3 4-8 ml. hrly. orally.	1. Al (OH)3 combines with HCl in stomach forming AlCl3 and H2O; thus neutralizing acid. 2. It has astringent and demulcent properties, by which it forms a protective coating over ulcer.	1. Constipation. 2. It prevents absorption of phosphates which may rarely lead to osteomalacia. 3. It interferes with the absorption of tetracyclines, corticosteroids, iron, anticholinergic drugs, etc.	1. Non-systemic antacid astrigent and demulcent. 2. To prevent phosphate reabsorption as in chronic renal failure or phosphatic renal calculi. 3. To control bile salt diarrhea 4. To treat ectopic calcification.
2. MAGNESIUM TRISILICATE 2-4 gm/day	Similar to Aliminium hydroxide	Diarrhea	1. Antacid 2. Cathartic
3. SODIUM BICARBONATE $NaHCO_3$ 2 gm. 2 hrly.	1. NaHCO3 combines with HCl in stomach to from NaCl 2. Eructations due to CO_2 liberated during neutralisation gives a sense of abdominal discomfort. This is carminative action.	1. Systemic alkalosis. 2. Retention of sodium. 3. Rarely it may precipitate peptic perforation in a patient with gastric ulcer due to distension caused by liberated CO_2.	1. Systemic antacid. 2. Metabolic acidosis. 3. To render urine alkaline in urinary tract infections or to prevent precipitation of sulfonamides or uric acid. 4. Locally: Antipruritic lotion. for mouth or eye wash, douche, enema, and to loosen wax in the ears.
4. CARBENOXOLONE 50-100 mg TDS for 48 weeks.	Exact mechanism not known. 1. It probably acts by stimulating mucus secretion. 2. It also stimulates collagen activity and epithelisation at the base of the ulcer.	1. Water and sodium retention which may precipitate cardiac failure and hypertension. 2. Hypokalemia. 3. Headache. 4. Heart-burn.	1. Peptic ulcer. 2. Aphthous ulcer (Lozenges containing 5 mg).
5. H2-RECEPTOR ANTAGONISTS **CIMETIDINE** 1000 mg/day **RANITIDINE** 300 mg/day **FAMOTIDINE** 40 mg/day **ROXATIDINE ACETATE** 75 mg BDS x 8 weeks Reduce to 75 mg on alt. days if Cr clearance 20-50 ml/min.	1. Abolishes histamine stimulated gastric and acid secretion and flushing 2. Inhibits gastric H2 receptors, this reduces basal, 24 hours and nocturnal acid secretion as well as Pepsin 2. Has mucosal protective action	1. Blood dyscrasias. 2. Skin rash 3. Hepatotoxicity 4. Gynecomastia. 5. VPBs, AV block 6. Decreased libido 7. Leucopenia	1. Peptic ulcer. 2. Esophagitis 3. Stress ulcers 4. Zollinger Ellison syndrome 5. Gastro-oesophageal reflux N.B. Has no anti-androgen action. Does not interfere with hepatic drug metabolism.
6. PROTON PUMP INHIBITORS **OMEPRAZOLE** 20 mg daily up to 600 mg for 4-8 weeks **LANZOPRAZOLE** 30 mg OD **PANTOPRAZOLE**	It causes irreversible inactivation of H-K-ATpase. This prevents the exchange of K with H and thus reduces the secretion of H and increases pH in stomach.	Reduced acidity in stomach may predispose the person to enteric infections.	1. Duodenal and gastric ulcer 2. Zollinger Ellison syndrome 3. Reflux esophagitis. 4. Mastocytosis 5. Multiple endocrine neoplasia

Drug/Dose	Action	Side Effects	Uses
8. PIRENZEPINE 50 mg BDS	Competitive muscarinic acetylcholine antagonist.	1. Dry mouth, constipation 2. Headache, mental confusion 3. Blurring of vision	Peptic ulcer
9. BISMUTH COLLOIDS 120 mg 4 times a day	Colloidal bismuth are salts of subcitrate, subnitrate, subsalicylate or subgallate. They do not neutralise the acid but by its action on *H.pylori* reduces peptic ulcer relapses.	Generally well tolerated. Long term side effects are encephalopathy, osteodystrophy and darkening of the oral cavities.	Peptic ulcer
10. SUCRALFATE 1 gm Q.I.D.	It forms a protective layer over the ulcer and prevents the action of acid on the ulcer.	1. GI: Constipation flatulence, nausea, vomiting, indigestion, dry mouth. 2. Skin rash 3. CNS: Dizziness, insomnia, vertigo.	1. Peptic ulcer 2. To prevent GI bleed in a critically ill patient.
11. ONDANSETRON 8mg BDS or TDS orally or I.V. **GRANISTERONE**	It is a 5 HT antagonist used to prevent vomiting induced by chemotherapy.	1. GI : Diarrhea 2. Skin : Rashes 3. Miscellaneous: Headache, blurred vision, hypokalemia, anaphylactoid reaction.	It is given before starting chemotherapy especially cisplatin.
12. CASTOR OIL 4-16ml.	It is hydrolysed in small intestine by pancreatic lipase to glycerol and ricinoleic acid. Latter produces purgation.	1. Gripping pain. 2. Fluid loss. 3. Peculiar odour and nauseating after-taste.	Irritant cathartic
13. PHENOLPHTHALEIN 50-300 mg. at bed-time.	Mechanism of action is not known. It acts on large bowel after 6-8 hrs. and produces soft stools.	1. It stains urine and faeces red. 2. Allergy-Pink or deep purple muscular rashes.	Cathartic.
14. BISACODYL 5 mg orally on 100 mg. per rectally.	Exact mechanism of action is not known. It acts mainly on large bowel.	Non-toxic	Cathartic. Suppository acts within 15-60 minutes.
15. OSMOTIC CATHARTIC $MgSO_4$ (Epsom Salt) 2-16 gm. Milk of magnesia 15 ml. Na-d22SO_4 (Glauber's salt) 2-16 gm.	They are retained in the G.I. tract where they hold considerable water, increasing the intestinal bulk, which acts as a mechanical stimulus increasing the intestinal motor activity and evacuation.	They are non-toxic. In certain conditions they may cause untoward effect, e.g. in kidney failure Mg may be absorbed and cause CNS depression whilst sodium may worsen existing cardiac failure.	Saline cathartic.
16. BULK CATHARTICS Agar 4-40 gm. Isapgol 5-15 gm.	They absorb water and swell-up increasing the indigestible residue & provide mechanical stimulus for evacuation.	Very rarely intestinal obstruction.	1. Cathartic. 2. In obesity to increase satiety 3. In diarrhea, because they help to pass formed stools.
17. LIQUID PARAFFIN 8-30 ml.	Given orally, it is not absorbed and exerts a softening and lubricating effect on faeces.	Non-toxic, Rarely it causes: 1. Impaired absorption of fat soluble vitamins A, D and K. 2. Lipoid pneumonia.	Lubricant cathartic.
18. BISMUTH KAOLIN 0.6-2 gm. Bismuth 15-60 gm. Kaolin.	Bismuth salts have astringent protective & absorbent effect. Kaolin acts as an absorbent of bacterial toxins.	Not-toxic.	Anti-diarrheal.
19. DIPHENOXYLATE ATROPINE 5 mg. diphenoxylate 0.20 mg. atropine	Inhibit intestinal motility. Hence they reduce "intestinal hurry".	Paralytic ileus.	Anti-diarrheal.
20. DIMETHYPOLY SILOXANE 40 mg tablets TDS	Acts as a defoaming agent thus allowing easy escape of gases from GI tract.	Non-toxic.	Flatulence, bloating and distension.

Drug/Dose	Action	Side Effects	Uses
21. LOPERAMIDE 4 mg initially followed by 2 mg after each loose stool up to 16 mg in 24 hrs.	It interacts with the acetyl choline release at the nerve endings and intra-mural ganglia causing sustained inhibition of peristaltic activity.	1. Dry mouth. 2. Nausea. 3. Drowsiness.	Acute and chronic diarrhea.
22. METOCLOPRAMIDE 10 mg TDS orally 10 mg I.M.	Increases the resting tone of the gastroesophageal sphincter and stimulates co-ordinated gastric movements to speed up gastric emptying. It blocks dopaminergic receptors.	1. Extra-pyramidal reactions, usually transient and disappear within 24 hrs. on stopping the drug. 2. Gynecomastia Galactorrhea 3. Diarrhea, dizziness, skin rash	1. Functional GI disorders 2. Vomiting. 3. Non-Ulcer dyspepsia 4. Pre-anesthetic medication 5. Persistent hiccough 6. Gastroparesis due to diabetes, scleroderma, etc.
23. DOMPERIDONE 10 mg three to four time s a day before food.	Antagonises the inhibitory effects of dopamine and enhances gastric motility. This enhances gastric emptying and prevents vomiting.	1. Dry mouth, thirst, diarrhea 2. Galactorrhea & gynecomastia 3. Skin rash 4. Headache.	Similar to Metoclopramide. Extra-pyramidal reactions do not occur as it does not cross the blood brain barrier.
24. CISAPRIDE 10-40 mg/day 15 min before meals.	Acts at the myenteric plexus of the gut causing increased release of acetylcholine. It increases gastric and intestinal motility and lowers esophageal pressure.	Mild, related to GI tract. No endocrine or extra-pyramidal effects.	1. Delayed gastric emptying 2. Non-ulcerdyspepsia 3. Reflux esophagitis 4. Chronic constipation
25. BILE SALTS CDCA 10-15 mg/kg/day URSODEOXYCHOLIC ACID 13-15 mg/kg/day.	Choleretic agents; therefore dissolve gall stones.	1. Diarrhea 2. Hepatotoxicity	1. Medical dissolution of gall stones, sp. cholesterol & radiolucent stones 2. Primary biliary cirrhosis
ELECTROLYTES			
1. POTASSIUM IV (2 meq/ml): only given in a drip.	Hyperkalemia: cardiac arrhythmias neuromuscular effects.	1. Hypokalemia: Diabetic ketoacidosis, severe diarrhea hypokalemic periodic paralysis 2. Forced alkaline diuresis: barbiturate poisoning 3. Glucose-potassium-insulin drip for MI 4. With IV fluids 5. Paralytic ileus	
Oral (syrup)		1. With non potassium-sparing diuretics 2. With digoxin therapy 3. Mild hypokalaemia	
2. SODIUM BICARBONATE IV: available as 7.5% w/v $NaHCO_3$ (given diluted as it is hyperosmolar)	1. Alkalosis: Respiratory depression hypocalcemia 2. Thrombophlebitis 3. Sodium overload 4. Cerebral edema	1. Correction of acidosis 2. Hyperkalemia 3. Cardiopulmonary resuscitation	
As lavage fluid		1. Bladder washes 2. Auricular lavage 3. Bronchial lavage	
3. CALCIUM IV: calcium gluconate 10% (= 4meq potassium)	1. Cardiac arrhythmias 2. Hypotonia 3. Necrosis if it gets extravasated.	1. Severe hypocalcemia: hypoparathyroidism, Vit.D deficiency, alkalosis 2. Hyperkalemia 3. Cardiac arrest in diastole 4. Every 4th bottle of blood transfusion	
Oral		1. Mild hypocalcemia 2. Growing children 3. Pregnancy, lactation 4. Postmenopausal women 5. Patients on steroids, anticonvulsant therapy 6. As an Antacid (e.g. $CaCO_3$)	

PLASMA EXPANDERS

Drug/Dose	Action	Side Effects	Uses
1. **DEXTRAN** Dextran-150 Dextran-70 Dextran-40	1. Cheaper than other plasma expanders. 2. Action lasts for 24 hours 3. Dextran-40 decreases RBC sludging and improves microcirculation 4. Can be stored for many years.	1. May interfere with blood grouping and cross matching 2. Can cause hypersensitivity 3. Can disturb coagulation and plateletfunction.	1. Uses as substitutes for plasma: e.g. burns hypovolemic shock, endotoxic shock, extensive trauma 2. Temporary replacement for blood loss.
2. **Degraded gelatin** (Hemaccel)	1. Does not interfere with blood grouping and cross matching 2. Hypersensitivity is rare.	1. More expensive	Same as above. Can be used for priming heart-lung machines and dialysis machines.

NORMAL HEMATOLOGICAL VALUES IN SI UNITS

[Mean - 2 SD to Mean + 2 SD (95% range)]

	Parameter	*Normal Range*	*SI Units*
1.	Red cell count	***Males*** 4. 5 - 6. 5	X10 ^{12}/litre
		Females 3 . 8 - 5. 6	X10 ^{12}/litre
2.	Hemoglobin (Hb)	***Males*** 13. 0 - 17. 0	g/dl
		Females 11 . 5 - 15 . 0	g/dl
3.	PCV (Hematocrit)	***Males*** 0. 40 - 0. 52	litres/litre
		Females 0. 36 - 0. 48	litres/litre
4.	Erythrocyte sedimentation rate (ESR)	***Males*** 0 - 15	mm in 1 hour
	(Wintrobe's method)	***Females*** 0 - 20	mm in 1 hour
5.	Mean corpuscular volume (MCV)	78 - 95	Femtolitres (fl)
6.	Mean corpuscular Hb (MCH)	27 - 32	Picograms (pg)
7.	Mean corpuscular Hb concentration (MCHC)	30 - 35	g/dl
8.	White cell count (TLC)	4.0 - 11.0	X 10 ^{9}/litre.
9.	**Differential White cell count (DLC)**		
	Neutrophils	40 - 80	%
	Lymphocytes	20 - 40	%
	Monocytes	2 - 10	%
	Eosinophils	1 - 6	%
	Basophils	0 - 2	%
10.	Platelet count	150 - 400	X 10 ^{9}/litre.
11.	Clotting time	5 - 11	Mins
12.	Bleeding time (Ivy's Method)	2 - 7	Mins
	Bleeding time (Duke's Method)	2 - 5	Mins
13.	Prothrombin time	11 - 16	Secs.
14.	Partial thromboplastin time (Activated)	30 - 40	Secs.
15.	Thrombin time	12 - 16	Secs.
16.	Total blood volume	60 - 80	ml/kg.
17.	Red cell diameter	6.7 - 7.7	microns
18.	Reticulocytes	0.2 - 2.0	%
19.	Red cell life span	90 - 150	days
20.	Osmotic fragility at 20 ± C, pH 7.4: Hemolysis begins at 0.46% and is complete at 0.34% NaCl solution		

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