The Respiratory System

DISORDERS OF THE LUNGS

The most important diseases of the respiratory system?

-- Collapse of the alveoli (**atelectasis**) and pneumothorax

- Circulatory disturbances, such as **pulmonary edema** and chronic passive congestion, and adult respiratory distress syndrome

- Infections such as rhinitis, laryngitis, **bronchitis**, and pneumonia

-- Immunologically mediated diseases, such as asthma

- Environmentally induced diseases, such as pneumoconioses, asbestosis, and silicosis

- **Tumors**

Atelectasis.

Refers to incomplete expansion of the lungs or the collapse of previously inflated lung substance. It is a pathologic condition that produces areas of relatively airless pulmonary parenchyma.

Severe atelectasis significantly reduces oxygenation and predisposes to infection.

Acquired atelectasis is generally encountered in adults and may be divided into the following categories:

- **Obstruction (or resorption) atelectasis**:-

Results from complete obstruction of an airway. It is most often found in bronchial asthma, chronic bronchitis, and with aspiration of foreign bodies; bronchial neoplasms may also cause it.

- **Compression atelectasis:-**

Ensues whenever the pleural cavity is partially (or completely) filled by fluid exudate, tumor, blood, or air (pneumothorax) or, in the case of tension

pneumothorax, when the entry of air into the pleural cavity causes pulmonary collapse. It is most commonly found in patients with cardiac failure

- Patchy atelectasis:-

Develops when there is loss of pulmonary surfactant, as in neonatal and adult respiratory distress syndrome.

- **Contraction atelectasis**:-

Occurs when local or generalized fibrotic changes in the lung or pleura prevent full expansion of the lung.

Chronic obstructive pulmonary disease (COPD).

The term **COPD** includes a group of conditions that share one major symptom—dyspnea—and are accompanied by chronic or recurrent obstruction to airflow within the lung.

The most frequent causes of death in patients with COPD.

- Respiratory insufficiency causing severe hypoxia, respiratory acidosis, and coma

-Right-sided heart failure

- Massive collapse of the lungs secondary to pneumothorax from ruptured bullae.

Chronic bronchitis:-

Is defined clinically as persistent cough with sputum production for at least3 months of the year, in at least 2 consecutive years.

Clinically there are several forms of chronic bronchitis:

- **Simple chronic bronchitis**: Patients experience a productive cough but have no evidence of airflow obstruction.

- **Chronic asthmatic bronchitis**: Some patients may demonstrate severe dyspnea and wheezing in association with inhaled irritants or during respiratory infections due to hyperreactive airways.
- **Chronic obstructive bronchitis**: Some patients, especially heavy smokers, develop chronic airflow obstruction, usually accompanied by emphysema.

The factors important for the pathogenesis of chronic bronchitis:.

- Chronic irritation by inhaled substances (cigarette smoking).
- Infections.

DISEASES OF VASCULAR ORIGIN

Pulmonary embolism

Pulmonary embolism (PE) is the occlusion of a pulmonary artery, most commonly by thromboemboli originating in the systemic veins. The condition accounts for 1% of all hospital deaths, but this rises to 30% in patients with severe burns or trauma.

The vast majority of cases are caused by emboli arising from thrombosis of the deep leg veins (calf, popliteal, femoral and iliac veins). The consequences of PE are pulmonary hypertension and infarction of the lung.

Non-thrombotic emboli

These are rare, but include:

• fat, following a bone fracture
• amniotic fluid during labour
• air (after trauma or surgery)
• decompression sickness, e.g. in deep sea divers (‘the bends’ or Caisson disease). Rapid decompression releases nitrogen bubbles, which cause

problems in the CNS and bones and can produce functional obstruction of the pulmonary vessels

• foreign bodies

• tumour embolism—renal or bronchial cell carcinoma.

Etiologic agents have been known to promote lung cancers?

- Tobacco smoking

- Industrial hazards

○ All types of radiation may be carcinogenic, such as an atomic bomb blast and uranium

○ The risk is increased with exposure to asbestos (particularly in smokers) and among people who work with nickel, chromates, coal, mustard gas, arsenic, beryllium, and iron, as well as newspaper workers .

- Air pollution

The main histologic types of bronchogenic carcinomas.

- **Squamous cell (epidermoid) carcinoma**: Composed of groups of squamous cells, often with central keratinization.

- **Adenocarcinoma**: Composed of glands lined by mucin producing columnar cells. A variant of peripheral adenocarcinoma lining the alveolar spaces is called bronchioloalveolar carcinoma.

- **Small cell carcinoma**: Composed of ‘‘small blue cells’’ that have some neuroendocrine feature, recognizable by electron microscopy or immunohistochemistry

- Large cell carcinoma: Composed of anaplastic undifferentiated cells growing without any distinct pattern.

Glomerular Diseases

Definition and Classification

It is convenient to classify glomerular diseases into 2 broad groups:

I. *Primary glomerulonephritis* in which the glomeruli are the predominant site of involvement.

II. *Secondary glomerular diseases* include certain systemic and hereditary diseases which secondarily affect the glomeruli.

Clinical Manifestations

The clinical presentation of glomerular disease is quite variable but in general four features—proteinuria, haematuria, hypertension and disturbed excretory function.

A number of clinical syndromes are recognised in glomerular diseases. The following are six major glomerular syndromes commonly found in different glomerular diseases:

I. Acute Nephritic Syndrome: This is the acute onset of haematuria, proteinuria, hypertension, oedema and oliguria .

II. Nephrotic Syndrome: Nephrotic syndrome is a constellation of features in different diseases having varying pathogenesis; it is characterised by findings of massive proteinuria, hypoalbuminaemia, oedema, hyperlipidaemia, lipiduria, and hypercoagulability.

III. Acute Renal Failure: Acute renal failure (ARF) is characterised by rapid decline in renal function.

IV. Chronic Renal Failure: These cases have advanced renal impairment progressing over years and is detected by significant proteinuria, haematuria, hypertension and azotaemia.

V. Asymptomatic Proteinuria: Presence of proteinuria unexpectedly in a patient may be unrelated to renal disease (e.g. exercise- induced, extreme lordosis and orthostatic proteinuria).

VI. Asymptomatic Haematuria: Asymptomatic microscopic haematuria is common in children and young adolescents and has many diverse causes such as diseases of the glomerulus, renal interstitium, calyceal system, ureter, bladder, prostate, urethra, and underlying bleeding disorder, congenital abnormalities of the kidneys or neoplasia.

IgA Nephropathy *(Synonyms: Berger's Disease, IgA GN)*

IgA nephropathy is emerging as the most common form of glomerulopathy worldwide and its incidence has been rising.

Etiopathogenesis: The etiology of IgA nephropathy remains unclear:

i) It is idiopathic in most cases.

ii) Seen as part of Henoch-Schonlein purpura.

iii) Association with chronic inflammation in various body systems (e.g. chronic liver disease, inflammatory bowel disease, interstitial pneumonitis, leprosy, dermatitis herpetiformis, uveitis, ankylosing spondylitis, Sjögren's syndrome, monoclonal IgA gammopathy).

Pathogenesis of IgA nephropathy is explained on the basis of following mechanisms:

i) IgA nephropathy has been considered to arise from *entrapment* of these complexes in the mesangium.

ii) Activation of *alternate complement pathway.*

iii) *Increased mucosal secretion of IgA.*

iv) HLA-B35 association *genetically-determined* abnormality.

Clinical Features: The disease is common in children and young adults. The clinical picture is usually characterised by recurrent bouts of haematuria that are often precipitated by mucosal infections.

Tumours of Kidney

Both benign and malignant tumors occur in the kidney, the latter being more common. These may arise from *renal tubules* (adenoma, adenocarcinoma), *embryonic tissue* (mesoblastic nephroma, Wilms' tumor), *mesenchymal tissue* (angiomyolipoma, medullary interstitial tumor) and from the *epithelium of the renal pelvis* (urothelial carcinoma).

Benign Tumours

Cortical Adenoma

Cortical tubular adenomas are more common than other benign renal neoplasms.

Oncocytoma

Oncocytoma is a benign epithelial tumour arising from collecting ducts.

Other Benign Tumours

Angiomyolipoma is a hamartoma of the kidney that contains differentiated tissue element derived from blood vessels, smooth muscle and fat.

Mesoblastic nephroma is a congenital benign tumour.

Multicystic nephroma is another uncommon tumour of early infancy.

Medullary interstitial cell tumour is a tiny nodule in the medulla composed of fibroblast-like cells in hyalinised stroma.

Juxtaglomerular tumour or reninoma is a rare tumour of renal cortex consisting of sheets of epithelioid cells with many small blood vessels.

Malignant Tumours

Adenocarcinoma of Kidney

It is now known that the renal cell carcinoma (RCC) is an adenocarcinoma arising from tubular epithelium.

Etiology and Pathogenesis: Various etiologic factors implicated in the etiology of RCC are as follows:

1. Tobacco.

2. Genetic factors.

3. Cystic diseases of the kidneys.

4. Other risk factors.

Wilms' Tumour *(Synonym: Nephroblastoma)*

Nephroblastoma or Wilms' tumour is an embryonic tumour derived from primitive renal epithelial and mesenchymal components. It is the most common abdominal malignant tumour of young children,

Etiology and Pathogenesis: Wilms' tumour has following etiologic associations:

1. A defect in *chromosome 11p13*
2. Monozygotic *twins*
3. Association of Wilms' tumour with some *other congenital anomalies*
4. A few *other malignancies* are known to have higher incidence of Wilms' tumour.

Benign and malignant tumors in the oral soft tissues

Number of tumour-like lesions and premalignant lesions are encountered in the oral soft tissues such as

A. Tumour-like lesions

Fibrous growths. Fibrous growths of the oral soft tissues are very common. These are not true tumours (unlike intraoral fibroma and papilloma), but are instead inflammatory or irritative in origin.

Pyogenic granuloma. This is an elevated, bright red swelling of variable size occurring on the lips, tongue, buccal mucosa and gingiva. It is a vasoproliferative inflammatory lesion. *Pregnancy tumour* is a variant of pyogenic granuloma.

Mucocele. Also called mucous cyst or retention cyst, it is a cystic dilatation of the mucous glands of the oral mucosa. The cyst often ruptures on distension and incites inflammatory reaction due to mucous extravasation

Dermoid cyst. This tumour-like mass in the floor of the mouth represents a developmental malformation. The cyst is lined by stratified squamous epithelium. The cyst wall contains sebaceous glands, sweat glands, hair follicles and other mature tissues.

B. Benign tumours

Squamous papilloma. Papilloma can occur anywhere in the mouth and has the usual papillary or finger-like projections.

Haemangioma. Haemangioma can occur anywhere in the mouth; when it occurs on the tongue it may cause macroglossia. It is most commonly capillary type, although cavernous and mixed types may also occur.

Lymphangioma. Lymphangioma may develop most commonly on the tongue producing macroglossia; on the lips producing
macrocheilia, and on the cheek. *Cystic hygroma* is a special variety of lymphangioma occurring in children on the lateral side of neck.

Fibroma. Although most common benign oral mucous membrane mass is fibroma appearing as a discrete superficial pedunculated mass, it appears to be nonneoplastic in nature. It probably arises as a response physical trauma.

Fibromatosis gingivae. This is a fibrous overgrowth of unknown etiology involving the entire gingiva. Sometimes the fibrous overgrowth is so much that the teeth are covered by fibrous tissue.

Tumours of minor salivary glands. Minor salivary glands present in the oral cavity may sometimes be the site of origin of salivary tumours similar to those seen in the major salivary glands. Pleomorphic adenoma is a common example.

Granular cell tumour. Earlier called as granular cell myoblastoma, it is benign tumour which now by electron microscopic studies is known to be mesenchymal in origin than odontogenic. The most common location is the tongue but may occur in any other location on the oral cavity. It occurs exclusively in females.

Malignant tumours

Squamous Cell (Epidermoid) Carcinoma

There is a definite male preponderance. It can occur anywhere in the mouth but certain sites are more commonly involved. These sites, in descending order of frequency, are: the lips (more commonly lower), tongue, anterior floor of mouth, buccal mucosa in the region of alveolar lingual sulcus, and palate

Hematemesis of esophageal origin

Massive haematemesis (vomiting of blood) may occur due to vascular lesions in the esophagus. These lesions are as under:

1. Esophageal varices. Esophageal varices are tortuous, dilated and engorged esophageal veins, seen along the longitudinal axis of esophagus.

They occur as a result of elevated pressure in the portal venous system, most commonly in cirrhosis of the liver. Less common causes are: portal vein thrombosis, hepatic vein thrombosis (Budd- Chiari syndrome) and pylephlebitis.

2. Mallory-weiss syndrome. In this condition, there is lacerations of mucosa at the gastro-esophageal junction following minor trauma such as by vomiting, retching or vigorous coughing.

3. Rupture of the esophagus. Rupture of the esophagus may occur following trauma, during esophagoscopy, indirect injury (e.g. due to sudden acceleration and deceleration of the body) and spontaneous rupture (e.g. after overeating, extensive aerophagy etc).

4. Other causes

i) Bursting of aortic aneurysm into the lumen of esophagus

ii) Vascular erosion by malignant growth in the vicinity

iii) Hiatus hernia

iv) Esophageal cancer

v) Purpuras

vi) Haemophilia.

Carcinoma of esophagus

The tumour occurs more commonly in men over 50 years of age. Prognosis is dismal: with standard methods of therapy (surgical resection and/or irradiation), 70% of the patients die within one year of diagnosis. Five-year survival rate is 5-10%.

Etiology. Although exact etiology of carcinoma of the esophagus is not known, a number of conditions and factors have been implicated as under:

1. Diet and personal habits:

i) Heavy smoking

ii) Alcohol consumption

iii) Intake of foods contaminated with fungus

iv) Nutritional deficiency of vitamins and trace elements.

2. Esophageal disorders:

i) Esophagitis (especially Barrett's esophagus in adenocarcinoma)

ii) Achalasia

iii) Hiatus hernia

iv) Diverticula

v) Plummer-Vinson syndrome.

3. Other factors:

i) *Race*—more common in the Chinese and Japanese than in Western races; more frequent in blacks than whites.

ii) *Family history*—association with tylosis (keratosis palmaris et plantaris).

iii) *Genetic factors*—predisposition with coeliac disease, epidermolysis bullosa, tylosis.

iv) *HPV infection*—is the recent addition in etiologic factors.

Morphologic features. Carcinoma of the esophagus is mainly of 2 types—squamous cell (epidermoid) and adenocarcinoma.

Squamous cell (Epidermoid) carcinoma. Squamous cell or epidermoid carcinoma comprises 90% of primary esophageal cancers. The disease occurs in 6th to 7th decades of life and is more common in men than women. The sites of predilection are the three areas of esophageal constrictions. Half of the squamous cell carcinomas of esophagus occur in the middle third, followed by lower third, and the upper third of esophagus in that order of frequency.

Adenocarcinoma. Adenocarcinoma of the esophagus constitutes less than 10% of primary esophageal cancer. It occurs predominantly in men in their

4th to 5th decades. The common locations are lower and middle third of the esophagus. These tumours have a strong and definite association with Barrett's esophagus in which there are foci of gastric or intestinal type of epithelium.

Inflammatory Conditions.

The two important inflammatory conditions of the stomach are **gastritis** and **peptic ulcer**. Rarely, stomach may be involved in tuberculosis, sarcoidosis and Crohn's disease.

Gastritis

The term 'gastritis' is commonly employed for any clinical condition with upper abdominal discomfort like indigestion or dyspepsia in which the specific clinical signs and radiological abnormalities are absent.

A simple classification of various types of gastritis is presented

Acute Gastritis

Acute gastritis is a transient acute inflammatory involvement of the stomach, mainly mucosa.

Etiopathogenesis. A variety of etiologic agents have been implicated in the causation of acute gastritis. **<u>These are as follows:</u>**

1. Diet and personal habits:

Highly spiced food, Excessive alcohol consumption , Malnutrition, Heavy smoking.

2. Infections:

Bacterial infections ; Helicobacter pylori, diphtheria, salmonellosis, pneumonia, staphylococcal food poisoning.

Viral infections ; viral hepatitis, influenza, infectious mononucleosis.

3. Drugs:

Intake of drugs like non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, cortisone, preparations of iron, chemotherapeutic agents.

4. Chemical and physical agents:

Intake of corrosive chemicals such as caustic soda, phenol, lysol

Gastric irradiation, Freezing.

5. Severe stress:

Emotional factors like shock, anger. Extensive burn. Trauma, Surgery.

Chronic Gastritis

Chronic gastritis is the commonest histological change observed in biopsies from the stomach. The condition occurs more frequently with advancing age; average age for symptomatic chronic gastritis being 45 years which corresponds well with the age incidence of gastric ulcer.

Peptic Ulcers

Peptic ulcers are the areas of degeneration and necrosis of gastrointestinal mucosa exposed to acid-peptic secretions. Though they can occur at any level of the alimentary tract that is exposed to hydrochloric acid and pepsin, they occur most commonly (98-99%) in either the duodenum or the stomach in the ratio of 4:1. Each of the two main types may be acute or chronic.

Acute Peptic (Stress) Ulcers

Acute peptic ulcers or stress ulcers are multiple, small mucosal erosions, seen most commonly in the stomach but occasionally involving the duodenum.

Etiology. These ulcers occur following severe stress. The causes are as follows:

1- Psychological stress

2- Physiological stress as in the following:

Shock, Severe trauma, Septicaemia , Extensive burns , Drug intake (e.g. aspirin, steroids, butazolidine, indomethacin), Local irritants (e.g. alcohol, smoking, coffee etc).

Chronic Peptic Ulcers (Gastric and Duodenal Ulcers)

chronic peptic ulcers would mean gastric and duodenal ulcers, the two major forms of ‘peptic ulcer disease’ of the upper GI tract in which the acid-pepsin secretions are implicated in their pathogenesis.

Etiology.

1. Helicobacter pylori gastritis

2. NSAIDs-induced mucosal injury.

3. Acid-pepsin secretions.

4. Gastritis. Some degree of gastritis is always present in the region of gastric ulcer, though it is not clear whether it is the cause or the effect of ulcer.

5. Other local irritants.

6. Dietary factors. Nutritional deficiencies have been regarded as etiologic factors in peptic ulcers e.g. occurrence of gastric ulcer in poor socioeconomic strata, higher incidence of duodenal ulcer in parts of South India.

7. Psychological factors.

8. Genetic factors. People with blood group O appear to be more prone to develop peptic ulcers than those with other blood groups.

9. Hormonal factors. Secretion of certain hormones by tumours is

associated with peptic ulceration e.g. elaboration of gastrin by islet-cell tumour in Zollinger-Ellison syndrome, endocrine secretions in hyperplasia and adenomas of parathyroid glands.

10. Miscellaneous. Duodenal ulcers have been observed to occur in association with various other conditions such as alcoholic cirrhosis, chronic renal failure, hyperparathyroidism, chronic obstructive pulmonary disease, and chronic pancreatitis.

Malignant Tumours

Gastric Carcinoma

Carcinoma of the stomach comprises more than 90% of all gastric malignancies and is the leading cause of cancer-related deaths in countries where its incidence is high.

Etiology.

1. H. pylori infection. H. pylori infection of the stomach is an important risk factor for the development of gastric cancer.

2. Dietary factors.

3. Geographical factors.

4. Racial factors.

5. Genetic factors.

6. Pre-malignant changes in the gastric mucosa.

Accordingly, gastric carcinomas are broadly classified into 2 main groups:

I. **Early gastric carcinoma (EGC).**

EGC is the term used to describe cancer limited to the mucosa and submucosa.

II. Advanced gastric carcinoma:-

Advanced gastric carcinoma has following 5 patterns:

1) Ulcerative carcinoma . This is the most common pattern. The tumour appears as a flat, infiltrating and ulcerative growth with irregular necrotic base and raised margin.

2) Fungating (polypoid) carcinoma .

The second common pattern is a cauliflower growth projecting into the lumen, similar to what is commonly seen in the large intestine. It is seen more often in the fundus. The tumour undergoes necrosis and infection commonly.

3) Scirrhous carcinoma (Linitis plastica) .

In this pattern, the stomach wall is thickened due to extensive desmoplasia giving the appearance as 'leather-bottle stomach' or 'linitis plastica'.

4) Colloid (Mucoid) carcinoma .

This pattern is usually seen in the fundus. The tumour grows like masses having gelatinous appearance due to secretion of large quantities of mucus.

5) Ulcer-cancer .

Ulcer-cancers are adenocarcinomas without any specific features.

Inflammatory Bowel Disease

(Crohn's Disease and Ulcerative Colitis)

Definition The term inflammatory bowel disease (IBD) is commonly used to include 2 idiopathic bowel diseases having many similarities but the conditions usually have distinctive morphological appearance.

1. Crohn's disease or regional enteritis is an idiopathic chronic ulcerative IBD, characterized by transmural, non-caseating granulomatous

inflammation, affecting most commonly the segment of terminal ileum and/ or colon, though any part of the gastrointestinal tract may be involved.

2. Ulcerative colitis is an idiopathic form of acute and chronic ulceroinflammatory colitis affecting chiefly the mucosa and submucosa of the rectum and descending colon, though sometimes it may involve the entire length of the large bowel.

Both these disorders primarily affect the bowel but may have systemic involvement in the form of polyarthritis, uveitis, ankylosing spondylitis, skin lesions and hepatic involvement. Both diseases can occur at any age but are more frequent in 2nd and 3rd decades of life. Females are affected slightly more often.

Etiopathogenesis The exact etiology of IBD remains unknown. However, multiple factors are implicated which can be considered under the following 3 groups:

1. Genetic factors. Genetic factors are implicated in the etiopathogenesis of IBD.

2. Immunologic factors. Defective immunologic regulation in IBD has been shown to play significant role in the pathogenesis of IBD.

3. Exogenous factors. several exogenous and environmental factors has been assigned:

i) Microbial factors, ii) Psychosocial factors, iii) Smoking and iv) Oral contraceptives.

Malabsorption Syndrome

Definition and Classification

The malabsorption syndrome (MAS) is characterized by impaired intestinal absorption of nutrients especially of fat; some other substances carbohydrates, vitamins and minerals. MAS is subdivided into 2 broad groups:

Primary MAS, which is due to primary deficiency of the absorptive mucosal surface and of the associated enzymes.

Secondary MAS, in which mucosal changes result secondary to other factors such as diseases, surgery, trauma and drugs.

Clinical Features

1. Steatorrhea (pale, bulky, foul-smelling stools)
2. Chronic diarrhea
3. Abdominal distension
4. Barborygmi and flatulence
5. Anorexia
6. Weight loss
7. Muscle wasting
8. Dehydration
9. Hypotension
10. Specific malnutrition and vitamin deficiencies depending upon the cause.

<u>Investigations</u>

I. Laboratory Tests:

1. Tests for fat malabsorption:

i) Faecal analysis for fat content

ii) Microscopic analysis for faecal fat

iii) Blood lipid levels after a fatty meal

iv) Tests based on absorption of radioactive-labelled fat.

2. Tests for protein malabsorption:

i) Bile acid malabsorption

ii) Radioactive-labelled glycine breath test.

iii) Prothrombin time (vitamin K deficiency)

iv) Secretin and other pancreatic tests.

3. Tests for carbohydrate malabsorption:

i) D-xylose tolerance test

ii) Lactose tolerance test

iii) Hydrogen breath test

iv) Bile acid breath test

4. Vitamin B12, malabsorption:

i) Schilling test.

II. Intestinal Mucosal Biopsy:

Mucosal biopsy of small intestine is essential for making the diagnosis of MAS and also evaluation of a patient on follow-up. The availability of endoscopes has enabled easy viewing of affected mucosa directly and taking mucosal biopsy under vision; this has largely replaced the earlier peroral Crosby-Kugler capsule biopsy of small intestine.

Haemorrhoids (Piles)

Haemorrhoids or piles are the varicosities of the haemorrhoidal veins. They are called *'internal piles'* if dilatation is of superior haemorrhoidal plexus covered over by mucous membrane, and *'external piles'* if they involve inferior haemorrhoidal plexus covered over by the skin. They commonly

result from increased venous pressure. The possible causes include the following:

1. Portal hypertension
2. Chronic constipation and straining at stool
3. Cardiac failure
4. Venous stasis of pregnancy
5. Hereditary predisposition
6. Tumours of the rectum.

Hepatic Failure

hepatic failure may develop from severe acute and fulminant liver injury with massive necrosis of liver cells *(acute hepatic failure),* or from advanced chronic liver disease *(chronic hepatic failure).*

Etiology. It includes following:

Acute (fulminant) hepatic failure occurs most frequently in *acute viral hepatitis*. Other causes are hepatotoxic drug reactions (e.g. anaesthetic agents, nonsteroidal anti-inflammatory drugs, anti-depressants), carbon tetrachloride poisoning, acute alcoholic hepatitis, mushroom poisoning and pregnancy complicated with eclampsia.

Chronic hepatic failure is most often due to *cirrhosis*. Other causes include chronic active hepatitis, chronic cholestasis (cholestatic jaundice) and Wilson's disease.

Cirrhosis

It represents the irreversible end-stage of several diffuse diseases causing hepatocellular injury and is characterised by the following 4 features:

1. It involves the entire liver.
2. The normal lobular architecture of hepatic parenchyma is disorganised.

3. There is formation of nodules separated from one another by irregular bands of fibrosis.

4. It occurs following hepatocellular necrosis of varying etiology so that there are alternate areas of necrosis and regenerative nodules.

Classification

Cirrhosis can be classified on the basis of morphology and etiology

A. Morphologic classification. There are 3 morphologic types of cirrhosis—micronodular, macronodular and mixed. Each of these forms may have an active and inactive form.

1. Micronodular cirrhosis. In micronodular cirrhosis, the nodules are usually regular and small, *less than 3 mm* in diameter.

2. Macronodular cirrhosis. In this type, the nodules are of variable size and are generally *larger than 3 mm* in diameter. The pattern of involvement is more irregular than in micronodular cirrhosis.

3. Mixed cirrhosis. In mixed type, some parts of the liver show micronodular appearance while other parts show macronodular pattern.

B. Etiologic classification.

Based on the etiologic agent for cirrhosis.

Hepatic tumours and tumour-like lesions

Metastatic tumours are much more common than primary tumors and tumour-like lesions.

Malignant hepatic tumours

Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) or liver cell carcinoma, also termed as hematoma, is the most common primary malignant tumour of the liver. The tumour shows marked geographic variations in incidence which is closely related to HBV and HCV infection in the region.

Hepatoblastoma (Embryoma)

Hepatoblastoma is a rare malignant tumour arising from primitive hepatic parenchymal cells. It presents before the age of 2 years as
progressive abdominal distension with anorexia, failure to thrive, fever and jaundice.

Cholecystitis

Acute Cholecystitis

In many ways, acute cholecystitis is similar to acute appendicitis. The condition usually begins with obstruction, followed by infection
later.

Chronic Cholecystitis

Chronic cholecystitis is the commonest type of clinical gallbladder disease. There is almost constant association of chronic cholecystitis with cholelithiasis.

Etiopathogenesis. The association of chronic cholecystitis with mixed and combined gallstones is virtually always present. However, it is not known what initiates the inflammatory response in the gallbladder wall.

Tumours of biliary system

Malignant tumours

Carcinoma of the Gallbladder

Primary carcinoma of the gallbladder is more prevalent than other cancers of the extrahepatic biliary tract. Like cholelithiasis and cholecystitis.

Carcinoma of Extrahepatic Bile Ducts and Ampulla of Vater

This is an infrequent neoplasm but is more common than the rare benign tumours of the biliary tract. Unlike other diseases of the biliary passages, it is more common in males with peak incidence in 6th decade of life.

Etiology. There is no association between bile duct carcinoma and gallstones. Bile duct cancers are associated with a number of other conditions such as ulcerative colitis, sclerosing cholangitis, parasitic infestations of the bile ducts with *Fasciola hepatica* (liver fluke), *Ascaris lumbricoides* and *Clonorchis sinensis.*

Pancreatitis

Acute Pancreatitis

Acute pancreatitis is an acute inflammation of the pancreas presenting clinically with ‘acute abdomen’. The severe form of the disease associated with macroscopic haemorrhages and fat necrosis in and around the pancreas is termed *acute haemorrhagic pancreatitis* or *acute pancreatic necrosis.* The condition occurs in adults between the age of 40 and 70 years and is commoner in females than in males.

Etiology. The two leading causes associated with acute pancreatitis are *alcoholism* and *cholelithiasis,* both of which are implicated in more than80% of cases.

Complications. A patient of acute pancreatitis who survives may develop a variety of systemic and local complications.

Systemic complications:

1. Chemical and bacterial peritonitis.
2. Endotoxic shock.
3. Acute renal failure.

Local sequelae:

1. Pancreatic abscess.
2. Pancreatic pseudocyst.
3. Duodenal obstruction.

Chronic Pancreatitis

Chronic pancreatitis or *chronic relapsing pancreatitis* is the progressive destruction of the pancreas due to repeated mild and subclinical attacks of acute pancreatitis. Weight loss and jaundice are often associated. Later manifestations include associated diabetes mellitus and steatorrhoea.

Etiology. Most cases of chronic pancreatitis are caused by the same factors as for acute pancreatitis. Thus, most commonly, chronic pancreatitis is related to *chronic alcoholism* with protein-rich diet, and less often to *biliary tract disease. Familial hereditary pancreatitis,* though uncommon, is more frequently chronic than the acute form.

Carcinoma of Pancreas

Pancreatic cancer is the term used for cancer of the exocrine pancreas. It is one of the common cancers, particularly in the Western countries and Japan. It is commoner in males than in females and the incidence Japan. It is

commoner in males than in females and the incidence increases progressively after the age of 50 years.

Etiology. Following factors have been implicated in its etiology:

1. Smoking
2. Diet and obesity
3. Chemical carcinogens
4. Diabetes mellitus
5. Chronic pancreatitis
6. *H. pylori* infection
7. Genetic factors.

Prostatitis

Acute Prostatitis

Acute focal or diffuse suppurative inflammation of the prostate is not uncommon. It occurs most commonly due to ascent of bacteria
from the urethra, less often by descent from the upper urinary tract or bladder, and occasionally by lymphogenous or haematogenous spread from a distant focus of infection. The infection may occur spontaneously or may be a complication of urethral manipulation such as by catheterisation, cystoscopy, urethral dilatation and surgical procedures on the prostate. The common pathogens are those which cause UTI, most frequently *E. coli,* and others such as *Klebsiella, Proteus, Pseudomonas, Enterobacter,* gonococci, staphylococci and streptococci.

Chronic Prostatitis

Chronic prostatitis is more common and foci of chronic inflammation are frequently present in the prostate of men above 40 years of age.

Chronic prostatitis is of 2 types:

Chronic bacterial prostatitis is caused in much the same way and by the same organisms as the acute prostatitis. It is generally a consequence of recurrent UTI.

Chronic abacterial prostatitis is more common. There is no history of recurrent UTI and culture of urine and prostatic secretions is always negative, though leucocytosis is demonstrable in prostatic secretions.

Granulomatous Prostatitis

Granulomatous prostatitis is a variety of chronic prostatitis, probably caused by leakage of prostatic secretions into the tissue, or could be of autoimmune origin.

Carcinoma of Prostate

Cancer of the prostate is the second most common form of cancer in males, followed in frequency by lung cancer. It is a disease of men above the age of 50 years and its prevalence increases with increasing age so that more than 50% of men 80 years old have asymptomatic (latent) carcinoma of the prostate. Thus, it is common to classify carcinoma of the prostate into the following 4 types:

1. Latent carcinoma
2. Incidental carcinoma
3. Occult carcinoma

4. Clinical carcinoma

Etiology. The cause of prostatic cancer remains obscure. However, a few factors have been suspected. These are as under:

1. Endocrinologic factors. Androgens are considered essential for development and maintenance of prostatic epithelium.

2. Racial and geographic influences. There are some racial and geographic differences in the incidence of prostatic cancer.

3. Environmental influences. Some common environmental factors and carcinogens have been identified with high risk to development of prostatic cancer. These include high dietary fat, and exposure to polycyclic aromatic hydrocarbons. Flavonoids, antioxidants and selenium may reduce the risk.

4. Nodular hyperplasia. Though nodular prostatic hyperplasia has been suggested by some as precursor for development of prostatic cancer, it is considered unlikely. Approximately 15-20% of nodular hyperplastic prostates harbour carcinoma.

5. Heredity. The possibility of genetic basis of prostatic cancer has been suggested by the observations of familial clustering and 2-fold higher frequency in first-degree relatives.

Spread. It may spread by following routes:

Direct spread. Direct extension of the tumour occurs into the prostatic capsule and beyond.

Metastases. Distant spread occurs by both lymphatic and haematogenous routes. Haematogenous spread leads most often to characteristic osteoblastic *osseous metastases,* especially to pelvis, and lumbar spine; other sites of metastases are lungs, kidneys, breast and brain. The route of bloodborne metastases may be retrograde spread by prostatic venous plexus or via systemic circulation.

Clinical Features. By the time symptoms appear, the carcinoma of prostate is usually palpable on rectal examination as a hard and nodular gland fixed to the surrounding tissues. In such symptomatic cases, clinical features are: urinary obstruction with dysuria, frequency, retention of urine, haematuria, and in 10% of cases pain in the back due to skeletal metastases.
Two serum *tumour markers* employed commonly for diagnosis and monitoring the prognosis of prostatic carcinoma are as under:

Prostatic acid phosphatase (PAP) is secreted by prostatic epithelium. Elevation of serum level of PAP is found in cases of prostatic cancer which have extended beyond the capsule or have metastasised.
Prostate-specific antigen (PSA) can be detected by immunohistochemical method in the malignant prostatic epithelium as well as estimated in the serum.

Testicular tumours

Testicular tumours are the cause of about 1% of all cancer deaths. They have *trimodal* age distribution—a peak during infancy, another during late adolescence and early adulthood, and a third peak after 60 years of age.

Etiologic factors

Exact etiology of testicular germ cell tumours is unknown, but the following factors have been implicated:

1. Cryptorchidism. 30-50 times greater
2. Other developmental disorders e.g. dysgenetic gonads
3. Genetic factors: High incidence in first-degree family members, twins.
4. Other factors

i) Orchitis

ii) Trauma

iii) Carcinogens

Clinical features and diagnosis

The usual presenting clinical symptoms of testicular tumours are gradual gonadal enlargement and a dragging sensation in the testis.

Spread. Testicular tumours may spread by both lymphatic and haematogenous routes:

Tumour markers. Two tumour markers widely used in the diagnosis, staging and monitoring the follow-up of patients with testicular tumours are:

hCG is synthesised by placental syncytio-trophoblast such as in various non-seminomatous germ cell tumours of the testis (e.g. in choriocarcinoma, yolk sac tumour and embryonal carcinoma).

AFP is normally synthesised by the foetal liver cells, yolk sac and foetal gut. Its levels are elevated in testicular tumours associated with yolk sac components.

Germ Cell Tumours

Germ cell tumours comprise approximately 95% of all testicular tumours and are more frequent before the age of 45 years

Classic Seminoma

Seminoma is the commonest malignant tumour of the testis and corresponds to dysgerminoma in the female.

Spermatocytic Seminoma

It is an uncommon tumour having an incidence of about 5% of all germ cell tumours. Spermatocytic seminoma usually occurs in older patients, generally in 6th decade of life.

Embryonal Carcinoma

Pure embryonal carcinoma constitutes 30% of germ cell tumours but areas of embryonal carcinoma are present in 40% of germ cell tumours.

Yolk Sac Tumour

(Synonyms: Endodermal Sinus Tumour, Orchioblastoma, Infantile Embryonal Carcinoma)

This characteristic tumour is the most common testicular tumour of infants and young children up to the age of 4 years.

Choriocarcinoma

Pure choriocarcinoma is a highly malignant tumour composed of elements consisting of syncytiotrophoblast and cytotrophoblast.

Teratoma

Teratomas are complex tumours composed of tissues derived from more than one of the three germ cell layers—endoderm, mesoderm and ectoderm. Testicular teratomas are more common in infants and children and constitute about 40% of testicular tumours in infants.

Cervicitis

Some degree of cervical inflammation is present in virtually all multiparous women and some nulliparous women. The normal intact ectocervical stratified epithelium is usually more resistant to infection whereas the endocervical columnar epithelium bears the brunt of the initial inflammation. Cervicitis may be specific or nonspecific, acute or chronic. *Specific cervicitis* may be caused by tuberculosis, syphilis, granuloma inguinale, lymphogranuloma venereum, chlamydia and chancroid.

Acute cervicitis. Acute cervicitis is usually associated with puerperium or gonococcal infection. Other causes are primary chancre and infection with herpes simplex.

Chronic cervicitis. The most common organisms responsible for chronic cervicitis are the normal mixed vaginal flora that includes streptococci, enterococci (e.g. *E. coli*) and staphylococci. Other infecting organisms include gonococci, *Trichomonas vaginalis, Candida albicans* and herpes simplex. Factors predisposing to chronic cervicitis are sexual intercourse, trauma of childbirth, instrumentation and excess or deficiency of oestrogen.

Tumours

Cervical Polyps

Cervical polyps are localised benign proliferations of endocervical mucosa though they may protrude through the external os. They are found in 2-5% of adult women and produce irregular vaginal spotting.

Microglandular hyperplasia

Microglandular hyperplasia is a benign condition of the cervix in which there is closely packed proliferation of endocervical glands without intervening stroma. The condition is caused by progestrin stimulation such as during pregnancy, postpartum period and in women taking oral contraceptives.

Endometritis and Myometritis

Myometritis is seen less frequently than endometritis and occurs in continuation with endometrial infections. Endometritis and myometritis may be acute or chronic.

Acute form generally results from 3 types of causes—puerperal (following full-term delivery, abortion and retained products of conception), intrauterine

contraceptive device (IUCD), and extension of gonorrheal infection from the cervix and vagina.

Chronic form is more common and occurs by the same causes which result in acute phase. In addition, *tuberculous endometritis* is an example of specific chronic inflammation, uncommon in the Western countries but not so uncommon in developing countries.

Endometriosis

Endometriosis refers to the presence of endometrial glands and stroma in abnormal locations outside the uterus. Endometriosis and adenomyosis are closely interlinked, so much so that some gynaecologists have termed adenomyosis as *endometriosis interna* and the other category termed as *endometriosis externa* for similar appearance at the extrauterine sites. The chief locations where the abnormal endometrial development may occur are as follows (in descending order of frequency): ovaries, uterine ligaments, rectovaginal septum, pelvic peritoneum, laparotomy scars, and infrequently in the umbilicus, vagina, vulva, appendix and hernial sacs.

Tumours of endometrium and myometrium

Endometrial Polyps

‘Uterine polyp’ is clinical term used for a polypoid growth projecting into the uterine lumen and may be composed of benign lesions (e.g. endometrial or mucous polyp, leiomyomatous polyp and placental polyp), or malignant polypoid tumours (e.g. endometrial carcinoma, choriocarcinoma and sarcoma).

Endometrial Carcinoma

Carcinoma of the endometrium, commonly called uterine cancer, is the most common pelvic malignancy in females in the United States and Eastern Europe but is uncommon in Asia where cervical cancer continues to be the leading cancer in women. It is primarily a disease of postmenopausal women, the peak incidence at onset being 6th to 7th decades of life and is uncommon below the age of 40 years.

Etiopathogenesis. The exact etiology of endometrial cancer remains unknown. However, a few factors associated with increased frequency of its development are chronic unopposed oestrogen excess, obesity, diabetes, hypertension and nulliparous state.

Leiomyoma

Leiomyomas or fibromyomas, commonly called *fibroids* by the gynaecologists, are the most common uterine tumours of smooth muscle origin, often admixed with variable amount of fibrous tissue component. About20% of women above the age of 30 years harbour uterine myomas of varying size. Vast majority of them are benign and cause no symptoms.

Leiomyosarcoma

Leiomyosarcoma is an uncommon malignant tumour as compared to its rather common benign counterpart. The incidence of malignancy in preexisting leiomyoma is less than 0.5% but primary uterine sarcoma is less common than that which arises in the leiomyoma.

Fibrocystic change

Fibrocystic change is the most common benign breast condition producing vague ‘lumpy’ breast rather than palpable lump in the breast. Its incidence has been reported to range from 10-20% in adult women, most often between 3rd and 5th decades of life, with dramatic decline in its incidence after menopause suggesting the role of oestrogen in its pathogenesis. It was previously termed *fibrocystic disease* but is currently considered as an exaggerated physiologic phenomena and not a disease.

As such, fibrocystic change of the female breast is a histologic entity characterised by following features:

i) Cystic dilatation of terminal ducts.

ii) Relative increase in inter- and intralobular fibrous tissue.

iii) Variable degree of epithelial proliferation in the terminal ducts.

It is important to identify the spectrum of histologic features by core needle biopsy or cytologic findings by FNAC in fibrocystic changes since only some subset of changes has an increased risk of development of breast cancer. Presently, the spectrum of histologic changes are divided into two clinicopathologically relevant groups:

A. Non-proliferative Fibrocystic Changes:

Simple Fibrocystic Change

Simple fibrocystic change most commonly includes 2 features formation of cysts of varying size, and increase in fibrous stroma.

B. Proliferative Fibrocystic Changes;

Epithelial hyperplasia and Sclerosing adenosis

Proliferative fibrocystic change in the breasts includes 2 entities: epithelial hyperplasia and sclerosing adenosis.

Epithelial hyperplasia. Epithelial hyperplasia is defined as increase in the layers of epithelial cells over the basement membrane to three or more layers

in the ducts *(ductal hyperplasia)* or lobules *(lobular hyperplasia).* The latter condition, lobular hyperplasia, must be distinguished from adenosis in which there is increase in the number of ductules or acini without any change in the number or type of cells lining them.

Carcinoma of the breast

Cancer of the breast is among the commonest of human cancers throughout the world. Its incidence varies in different countries but is particularly high in developed countries.

General features and classification

Cancer of the breast occurs more often in left breast than the right and is bilateral in about 4% cases.

Carcinoma of the breast arises from the ductal epithelium in 90% cases while the remaining 10% originate from the lobular epithelium. For variable period of time, the tumour cells remain confined within the ducts or period of time, the tumour cells remain confined within the ducts or lobules (non-invasive carcinoma) before they invade the breast stroma (invasive carcinoma). While only 2 types of *non-invasive carcinoma* .

A. Non-invasive *(In situ)* Breast carcinoma

Intraductal Carcinoma

Carcinoma *in situ* confined within the larger mammary ducts is called intraductal carcinoma.

Lobular Carcinoma *in Situ*

Lobular carcinoma *in situ* is not a palpable or grossly visible tumour. Patients of *in situ* lobular carcinoma treated with excisional biopsy alone

B. Invasive breast carcinoma

Infiltrating (Invasive) Duct Carcinoma-NOS

Infiltrating duct carcinoma-NOS *(not otherwise specified)* is the classic breast cancer and is the most common histologic pattern
accounting for70% cases of breast cancer.

Infiltrating (Invasive) Lobular Carcinoma

Invasive lobular carcinoma comprises about 5% of all breast cancers.

Medullary Carcinoma

Medullary carcinoma is a variant of ductal carcinoma and comprises about1% of all breast cancers.

Colloid (Mucinous) Carcinoma

This is an uncommon pattern of breast cancer occurring more frequently in older women and is slow-growing. Colloid carcinoma has better prognosis than the usual infiltrating duct carcinoma.

Other Morphologic Forms

A few other morphologic forms of invasive breast carcinoma having clinical significance have been recognised:

Papillary carcinoma. It is a rare variety of infiltrating duct carcinoma in which the stromal invasiodn is in the form of papillary structures.

C. Paget's disease of the nipple

Paget's disease of the nipple is an eczematoid lesion of the nipple, often associated with an invasive or non-invasive ductal carcinoma of the underlying breast.

Non-infectious inflammatory dermatoses

1. Dermatitis (Eczema). The pathologic term dermatitis is synonymous with the clinical term eczema. Both refer to inflammatory response to avariety of agents acting on the skin from outside or from within the body such as

chemicals and drugs, hypersensitivity to various antigens and haptens etc. Accordingly, clinical types such as contact dermatitis, atopic dermatitis, drug-induced dermatitis, photo-eczematous dermatitis and primary irritant dermatitis are described. intercellular oedema) that may lead to formation of intraepidermal vesicles or bullae. The vesicles and bullae as well as the oedematous epidermis are permeated by acute inflammatory cells. The upper dermis shows congested blood vessels and mononuclear inflammatory cell infiltrate, especially around the small blood vessels.

Subacute dermatitis may follow acute dermatitis. Spongiosis and vesicles are smaller than in acute dermatitis. The epidermis shows moderate acanthosis and varying degree of parakeratosis in the horny layer with formation of surface crusts containing degenerated leucocytes, bacteria and fibrin. The dermis contains perivascular mononuclear infiltrate. The classical example of subacute dermatitis is *nummular dermatitis.*

Chronic dermatitis shows hyperkeratosis, parakeratosis and acanthosis with elongation of the rete ridges and broadened dermal papillae. Vesicles are absent but slight spongiosis may be present. The upper dermis shows perivascular chronic inflammatory infiltrate and fibrosis

Scaling dermatoses

1. Psoriasis. Psoriasis is a chronic inflammatory dermatosis that affects about 2% of the population. It usually appears first between the age of 15 and 30 years. The lesions are characterised by brownish-red papules and plaques which are sharply demarcated and are covered with fine, silvery white scales. As the scales are removed by gentle scrapping, fine bleeding points appear termed *Auspitz sign.*

Tumours and tumour-like lesions may arise from different components of the skin such as surface epidermis, epidermal appendages and dermal tissues. Each of these tissues may give rise to benign and malignant tumours as well as tumour-like lesions.

Malignant Tumours

1. Squamous cell carcinoma. Squamous cell carcinoma may arise on any part of the skin and mucous membranes lined by squamous epithelium but is more likely to occur on sun-exposed parts in older people.

2. Basal cell carcinoma (Rodent ulcer). Typically, the basal cell carcinoma is a locally invasive, slow-growing tumour of middle-aged that rarely metastasises. It occurs exclusively on hairy skin, the most common location (90%) being the face, usually above a line from the lobe of the ear to the corner of the mouth. Basal cell carcinoma is seen more frequently in white-skinned people and in those who have prolonged exposure to strong sunlight like in those living in Australia and New Zealand.

3.Metatypical carcinoma (Basosquamous cell carcinoma).

Metatypical or basosquamous cell carcinoma is the term used for a tumour in which the cell type and arrangement of cells cause difficulty in deciding between basal cell carcinoma and squamous cell carcinoma.

Bone tumours

Bone tumours may be primary or metastatic. Since histogenesis of some bone tumours is obscure, the WHO has recommended a widely accepted classification of primary bone tumours based on both histogenesis and histologic criteria. The diagnosis of any bone lesion is established by a combination of clinical, radiological and pathological examination, supplemented by biochemical and haematological investigations wherever

necessary. These include: serum levels of calcium, phosphorus, alkaline phosphatase and acid phosphatase. Specific investigations like plasma and urinary proteins and the bone marrow examination in case of myeloma, urinary catecholamines in metastatic neuroblastoma and haematologic profile in lymphoma and leukaemic involvement of the bone, are of considerable help.

Bone-forming (Osteoblastic) Tumours

Bone-forming or osteoblastic group of bone tumours are characterised by the common property of synthesis of osteoid or bone, or both, directly by the tumour cells (osteogenesis).

Osteoma

An osteoma is a rare benign, slow-growing lesion, regarded by some as a hamartoma rather than a true neoplasm. Osteoma is almost exclusively restricted to flat bones of the skull and face.

Osteoid osteoma and osteoblastoma

Osteoid osteoma and osteoblastoma (or giant osteoid osteoma) are closely related benign tumours occurring in children and young adults. Osteoid osteoma is more common than osteoblastoma.

Osteoid osteoma is small (usually less than 1 cm) and painful tumour, located in the cortex of a long bone.

Osteoblastoma is larger in size (usually more than1 cm), painless, located in the medulla, commonly in the vertebrae,ribs, ilium and long bones, and there is absence of reactive boneformation.

Osteosarcoma

Osteosarcoma or osteogenic sarcoma is the most common primary malignant tumour of the bone. osteosarcomas are classified into 2 main categories: central (medullary) and surface (parosteal and perosteal).

Chondrosarcoma

Chondrosarcoma is a malignant tumour of chondroblasts.

Hyperpituitarism

A. Hyperfunction of Anterior Pituitary

Three common syndromes of adenohypophyseal hyperfunction are: gigantism and acromegaly, hyperprolactinaemia and Cushing's syndrome.

Gigantism and acromegaly: Both these clinical syndromes result from sustained excess of growth hormone (GH), most commonly by somatotroph (GH-secreting) adenoma.

Hyperprolactinaemia: Hyperprolactinaemia is the excessive production of prolactin (PRL), most commonly by lactotroph (PRL-secreting) adenoma, also called prolactinoma.

Cushing's syndrome: Pituitary-dependent Cushing's syndrome results from ACTH excess. Most frequently, it is caused by corticotroph (ACTH secreting) adenoma.

B. Hyperfunction of Posterior Pituitary and Hypothalamus

Lesions of posterior pituitary and hypothalamus are uncommon. Two of the syndromes associated with hyperfunction of the posterior pituitary and hypothalamus are: inappropriate release of ADH and precocious puberty.

Precocious puberty: A tumour in the region of hypothalamus or the pineal gland may result in premature release of gonadotropins causing the onset of pubertal changes prior to the age of 9 years.

Pituitary tumours

Tumours of the anterior pituitary are more common than those of the posterior pituitary and hypothalamus. The most common of the anterior pituitary tumours are adenomas; primary and metastatic carcinomas being rare. Craniopharyngioma and granular cell tumour (choristoma) are the other benign pituitary tumours found occasionally.

All pituitary tumours, whether benign or malignant, cause symptoms by following 2 ways:

1. Pressure effects
2. Hormonal effects.

Pituitary Adenomas

Adenomas are the most common pituitary tumours. They are conventionally classified according to their H & E staining characteristics of granules into acidophil, basophil and chromophobe adenomas.

Thyroiditis

Inflammation of the thyroid, thyroiditis, is more often due to non-infectious causes and is classified on the basis of onset and duration of disease into acute, subacute and chronic as under:

I. Acute thyroiditis:

1. Bacterial infection e.g. *Staphylococcus*, *Streptococcus*.
2. Fungal infection e.g. *Aspergillus*, *Histoplasma*, *Pneumocystis*.
3. Radiation injury

II. Subacute thyroiditis:

1. Subacute granulomatous thyroiditis (de Quervain's thyroiditis, giant cell thyroiditis, viral thyroiditis)
2. Subacute lymphocytic (postpartum, silent) thyroiditis
3. Tuberculous thyroiditis

III. Chronic thyroiditis:

1. Autoimmune thyroiditis (Hashimoto's thyroiditis or chronic lymphocytic thyroiditis)
2. Riedel's thyroiditis (or invasive fibrous thyroiditis).

Hashimoto's (Autoimmune, Chronic Lymphocytic) thyroiditis

Hashimoto's thyroiditis, also called diffuse lymphocytic thyroiditis, struma lymphomatosa or goitrous autoimmune thyroiditis, is characterised by 3 principal features:

1. Diffuse goitrous enlargement of the thyroid.
2. Lymphocytic infiltration of the thyroid gland.
3. Occurrence of thyroid autoantibodies.

Hashimoto's thyroiditis occurs more frequently between the age of 30 and 50 years and shows an approximately ten-fold preponderance among females. Though rare in children, about half the cases of adolescent goitre are owing to autoimmune thyroiditis. Hashimoto's thyroiditis is the most common cause of *goitrous hypothyroidism* in regions.

Thyroid tumours

Follicular adenoma

Follicular adenoma is the most common benign thyroid tumour occurring more frequently in adult women

Thyroid cancer

Carcinoma of the thyroid gland has 4 major morphologic types with distinctly different clinical behaviour and variable prevalence. These are: papillary, follicular, medullary and undifferentiated (anaplastic) carcinoma;

Etiopathogenesis. Most important risk factor implicated in the etiology of thyroid cancer is external radiation, and to some extent there is role of TSH receptors and iodine excess, while pathogenesis of thyroid cancer is explained on genetic alterations.

1. External radiation. The single most important environmental factor associated with increased risk of developing thyroid carcinoma after many years of exposure to external radiation of high dose.

2. Iodine excess and TSH. In regions where endemic goitre is widespread, addition of iodine to diet has resulted in increase in incidence of papillary cancer.

3. Genetic basis. Familial clustering of thyroid cancer has been observed, especially in medullary carcinoma. Molecular studies reveal that thyroid carcinoma is a multistep process involving genetic alterations but distinct mutations

Papillary Thyroid Carcinoma

Papillary carcinoma is the most common type of thyroid carcinoma, It can occur at all ages including children and young adults but the incidence is higher with advancing age. The tumour is found about three times more frequently in females than in males.

Follicular Thyroid Carcinoma

Follicular carcinoma is the other common type of thyroid cancer

Medullary Thyroid Carcinoma

Medullary carcinoma is a less frequent type derived from parafollicular or Ccells present in the thyroid and comprises about 5% of thyroid carcinomas. It is equally common in men and women.

Anaplastic Carcinoma

Undifferentiated or anaplastic carcinoma of the thyroid comprises less than5% of all thyroid cancers and is one of the most malignant tumour in humans. The tumour is predominantly found in old age (7th-8th decades) and is slightly more common in females than in males

A large number of pathogens comprising various kinds of bacteria, fungi, viruses, rickettsiae and parasites can cause infections of the nervous system. The micro-organisms may gain entry into the nervous system by one of the following routes:

1. Via blood stream
2. Direct implantation

3. Local extension

4. Along nerve.

In general, resultant lesions are in the form of either diffuse inflammation of the meninges (meningitis) and of brain parenchyma (encephalitis), or combination of both (meningoencephalitis). In addition, other inflammatory lesions of CNS include: brain abscess, epidural abscess, subdural empyema, septic thromboembolism of dural sinuses and encephalomyelitis.

Meningitis

Meningitis is inflammatory involvement of the meninges. Meningitis may involve the dura called *pachymeningitis,* or the leptomeninges (pia-arachnoid) termed *leptomeningitis.* The latter is far more common, and unless otherwise specified, meningitis would mean leptomeningitis. Pachymeningitis is invariably an extension of the inflammation from chronic suppurative otitis media or from fracture of the skull. An *extradural abscess* may form by suppuration between the bone and dura. Further spread of infection may penetrate the dura and form a *subdural abscess.* Other effects of pachymeningitis are localised or generalised leptomeningitis and *cerebral abscess.* Infectious meningitis is broadly classified into 3 types: acute pyogenic, acute lymphocytic (viral, aseptic) and chronic (bacterial or fungal)

Encephalitis

Parenchymal infection of brain is termed encephalitis. Encephalitis may be the result of bacterial, viral, fungal and protozoal infections.

Bacterial Encephalitis

Bacterial infection of the brain substance is usually secondary to involvement of the meninges rather than a primary bacterial parenchymal infection. This results in bacterial cerebritis that progresses to form *brain abscess.* However, *tuberculosis* and *neurosyphilis* are the two primary bacterial involvements of the brain parenchyma.

Viral Encephalitis

Most viral infections of the CNS are the end-result of preceding infection in other tissues and organs. Most of the viruses reach the nervous system via blood stream before which they enter the body by various routes e.g. infection of the skin and mucous membrane (in herpes simplex and herpes zoster- varicella), by the alimentary tract (in enteroviruses including polio virus), by arthropod bite (in arbovirus), by transplacental infection (in cytomegalovirus), and through body fluids in AIDS (in HIV infection). Rabies virus travels along the peripheral nerves to reach the CNS. Herpes zoster-varicella is a distinct primary disease (chickenpox) but the virus remains latent for a long time before it gets reactivated to cause severe hyperalgesia and pain along the distribution of nerve related to acutely inflamed posterior root ganglia (herpes zoster).

Cerebrovascular diseases

Cerebrovascular diseases are all those diseases in which one or more of the blood vessels of the brain are involved in the pathologic processes. Various pathologic processes commonly implicated in cerebrovascular diseases are:

thrombosis, embolism, rupture of a vessel, hypoxia, hypertensive arteriolosclerosis, atherosclerosis, arteritis, trauma, aneurysm and developmental malformations. These processes can result in 2 main types of parenchymal diseases of the brain:

A. Ischaemic brain damage:

a) Generalised reduction in blood flow resulting in *global hypoxic-ischaemic encephalopathy*

b) Local vascular obstruction causing *infarcts.*

B. Intracranial haemorrhage:

a) Haemorrhage in the brain parenchyma *(intracerebral haemorrhage)*

b) Haemorrhage in the subarachnoid space *(subarachnoid haemorrhage).*

The *stroke syndrome* is the cardinal feature of cerebrovascular disease. The term stroke is used for sudden and dramatic development of focal neurologic deficit, varying from trivial neurologic disorder to hemiplegia and coma.