

INFECTIOUS DISEASES

CHAPTER

9

LEARNING OBJECTIVES

After the completion of this chapter, you should be able to,

- ◆ Describe the sexually transmitted diseases such as syphilis, gonorrhoea and AIDS
- ◆ Explain the types, causes and pathogenesis of UTIs
- ◆ Elaborate the pathogenesis and types of pneumonia
- ◆ Summarize the life cycle of malarial parasite
- ◆ Outline the types and pathophysiology of tuberculosis and leprosy
- ◆ Discuss the different types of hepatitis.

1. SEXUALLY TRANSMITTED DISEASES

1.1 SYPHILIS

Introduction

Syphilis is a sexually transmitted disease caused by *Treponema pallidum* (Spirochaete) which is transmitted sexually. The organism is detected only by special stains like silver stain and also by dark field examination and immunofluorescence technique.

Routes of Transmission

1. Sexual intercourse which leads to lesions on pelvis, vulva, vagina and cervix.
2. Contact with a person having lesions on lips, tongue, fingers.
3. Blood transfusion.
4. Perinatal transmission (from infected mother to child through placenta).

Pathophysiology

1. **Primary Stage**
The chancre (red lesion) shows dense inflammatory infiltrate of lymphocytes, plasma cells and macrophages. Aggregation of plasma cells is seen around the blood vessels.
2. **Secondary Stage**
It is characterised by mucocutaneous lesions on oral cavity, palms and soles of the feet. In secondary stage of syphilis, infiltration of monocytes and neutrophils occurs but inflammation is less when compared to primary stage.

3. Tertiary Stage

It shows two types of lesions.

(a) Diffused Lesions

These are seen when spirochetes are spread all over the body. It mainly affects the cardiovascular system and central nervous system.

Cardiovascular Syphilis : Lesions develop in aorta, hence the aortic wall dilates and weakens. This results in aortic aneurysm (swelling of the aorta) and incompetence of aortic valves.

Neurosyphilis : Lesions affect the meninges of the brain (meningovascular syphilis), spinal cord (*tabes dorsalis*) and brain (general paresis).

(b) Gummatous Lesions

Gummas are localised, rubbery lesions with a central necrotic area. They are seen in liver, testes, bone and brain. Gummatous lesions have a central coagulated necrotic material surrounded by palisade and fibroblasts. The entire lesion is surrounded by mononuclear leucocytes and plasma cells.

Signs and Symptoms

1. Primary Stage

Chancre (red lesions) develops at the site of infection (anus and cervix). It is infectious and painless and heals on its own within 2-3 weeks. This stage is confined to the genitourinary tract.

2. Secondary Stage

Appears 2-10 weeks after the primary stage. Rashes develop on the arms and soles. The patient experiences fever, sore throat, generalized weakness, joint pains, arthritis and headache. Generalized skin eruptions are seen on the entire body. This stage is highly infective.

3. Tertiary Stage

This is seen after few years. Ulcerated lesions develop anywhere on the skin and any organ may be affected including those of cardiovascular system and nervous system.

1.2 GONORRHOEA

Introduction

Gonorrhoea is a sexually transmitted bacterial infection caused by *Neisseria gonorrhoea*, a Gram-negative diplococci which is transmitted sexually and infects the genital mucous membrane of both the sexes.

Pathophysiology

Neisseria is an intracellular pathogen. It binds to the epithelial cells of the host by pili. Adhesion leads to internalization of the bacteria which is mediated by another set of adhesive proteins. The bacteria secretes proteases that cleave IgA of the epithelial cell. It releases peptidoglycans and endotoxins which induce the release of TNF- α (tumour necrosis factor) from the host cells. TNF- α damages the epithelial cells and leads to multisystem failure.

Gonococcal lesions show exudative reaction, pus formation followed by formation of granulomas. Plasma cell infiltration and fibrosis is also seen.

Signs and Symptoms

1. It affects the cervix, urethra, rectum, anus and throat.
2. In females, the symptoms are,
 - (a) Changes in vaginal discharge (yellow or bloody)
 - (b) Bleeding associated with vaginal intercourse
 - (c) Pain or burning sensation during voiding (urination or defecation)
 - (d) Development of pelvic inflammatory disease (PID)
 - (e) Irritation and discharge from the anus
 - (f) Infection of fallopian tubes
 - (g) Chances of ectopic pregnancy.
3. In males, the symptoms are,
 - (a) Pus from the penis
 - (b) Yellow or white discharge from the penis
 - (c) Burning sensation during micturition
 - (d) Irritation and discharge from the anus
 - (e) Painful bowel movements with fresh blood accompanying the faeces
 - (f) Inflammation of the testicles and prostrate gland.

1.3 ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

This topic has already been discussed in Chapter-3.

2. URINARY TRACT INFECTIONS

Introduction

Urinary tract infection is defined as the presence of organisms in the urinary tract along with signs and symptoms of inflammation. It is also defined as the presence of at least 1 lakh bacteria per ml of urine. Normal bacterial count is 1000 per ml of urine. If the inflammatory conditions are confined to urethra and bladder, then it is known as lower urinary tract infection and if it involves the ureters and kidneys, then it is known as upper urinary tract infection.

Various urinary tract infections include,

1. *Ureteritis*
It is the inflammation of the ureters, mainly due to descending infection.
2. *Cystitis*
It is the inflammation of the urinary bladder, which is more common in females than in males. This is because females have shorter urethra and hence the microbes can easily enter into the bladder.
3. *Pyelitis*
It is the inflammation of the renal pelvis and calyces, which occurs due to bacteria (like *Escherichia coli*). It is more common in women than in men.
4. *Pyelonephritis*
Inflammation of the kidneys which impairs their function.

Types of UTIs

Urinary tract infections are of the following two types.

1. Acute Infection

Acute infection involves infection of the urinary bladder termed as *cystitis* and urethra known as *urethritis*. This condition or infection is collectively termed as *cysto-urethritis*.

Symptoms

- (a) Frequent micturition.
- (b) Dysuria (painful micturition).
- (c) Pain in the perineum (region between the anus and urethral opening), loin pain (loin is the region between thorax and pelvis), chills, fever and leucocytosis are seen when kidneys are also involved.
- (d) Pyuria (presence of pus cells in urine) and significant bacteriuria (presence of bacteria in urine).

- (e) Septicaemia occurs in pregnant women, in patients on immunosuppressants and those suffering from lymphoproliferative disorders.

If acute infections are not treated properly, then they may lead to recurrent and chronic infection (pyelonephritis).

2. Chronic Infection

Chronic infection involves infection of kidneys. It includes acute pyelonephritis and chronic pyelonephritis. Acute pyelonephritis involves acute infection of one or both kidneys along with lower urinary tract. The cause of chronic pyelonephritis is unclear as it may be due to an infection while in some cases it may occur due to other reasons also.

Symptoms

- Polyuria (production of large volumes of urine)
- Weight loss
- Anaemia and hypertension
- Pyuria
- Fever (of unknown origin), vomiting and vague abdominal pain are seen in infants and children.

Aetiology

- Causative organisms of urinary tract infections (UTI) are *E. coli*, *Pseudomonas aeruginosa*, *Streptococcus faecalis*, *Staphylococcus epidermis* and *Proteus mirabilis*.
- Organisms which cause UTI in hospitals are *E. coli*, *Streptococci* and *Klebsiella*.
- Sexual intercourse.
- Women who often change sexual partners.
- Sexually transmitted diseases like gonorrhoea causes urethritis.
- Having bubble bath, wearing tight fitting clothes or holding urine for long time can cause the microorganisms to enter into the bladder or kidneys and cause UTI.
- Risk factors for developing UTI include, pregnancy, diabetes, presence of tumour, stones or any foreign bodies in the urinary tract.

Pathogenesis

The microorganisms gain access into the urinary tract by different routes.

- By ascending pathway (urethra → urinary bladder → ureters → kidney), thus causing ascending infection.
- Through blood known as haematogenous or descending infection. It occurs in bacteraemic illness wherein the organisms (*Staphylococcus aureus*) affect the kidney.
- Through lymphatic route bacteria enters the rectum and then affects the kidneys by an unknown mechanism.

Pathogenesis of Ascending Infection

It is common in females (due to short urethra and secretion of premenopause hormones), diabetic patients, pregnant women and in persons suffering from obstruction in the urinary tract. It is also seen during instrumentation (catheterization).

The important steps involved in ascending infection are,

Step 1 : Colonization of Bacteria

The bacteria gains access into the urethra from the colon. Colonization of bacteria occurs in the urethra. This is facilitated by adhesion of bacteria (by pili) to the uroepithelial surface.

Step 2 : Transfer of Bacteria from Urethra to Urinary Bladder

The bacteria then enters the urinary bladder by moving against the flow of urine. This occurs during,

- Instrumentation (catheterisation or cystoscopy)
- Sexual intercourse
- Obstruction of urine outflow (due to which incomplete emptying of bladder occurs and the microorganisms multiply in the retained urine).

Step 3 : Establishment of Bacteria in the Bladder

From urinary bladder, the microorganisms enter the ureters. The opening of the ureters into the bladder is closed due to the contraction of bladder which occurs during micturition. This opening is known as vesico-ureteral orifice.

In some cases, vesico-ureteral orifice does not close completely during micturition, so urine enters the ureters from urinary bladder (urine flows in opposite direction) which is known as vesico-ureteral reflux (VUR). The microorganisms then enter the ureters and then the kidneys. This is called upper UTI. This results in pyelitis (inflammation of renal pelvis) and pyelonephritis (inflammation of the kidney and pelvis).

Pathological Changes

1. Acute Pyelonephritis

Gross Changes

The kidneys are enlarged, swollen and the cut surface shows yellow or white abscess with haemorrhagic lining.

Microscopic Changes

Patchy interstitial inflammation is seen with tubular destruction due to accumulation of neutrophils.

2. Chronic Pyelonephritis

It occurs due to repeated attacks of inflammation and scarring which leads to complete failure of the kidneys. Chronic pyelonephritis is of two types.

- Reflux nephropathy : It occurs due to vesico-ureteral reflux.
- Obstructive pyelonephritis : Due to obstruction of urine outflow at different levels.

Gross Changes

Kidneys shrink and get constricted. Weight of the kidneys also decreases and they weigh less than 100 gram (normal weight is 135 to 150 g). The surface of the kidney shows irregular scars.

Microscopic Changes

Inflammation is seen due to inflammatory infiltrate of lymphocytes, plasma cells and macrophages. Kidney tubules, renal pelvis and calyces show dilatation and inflammatory reaction.

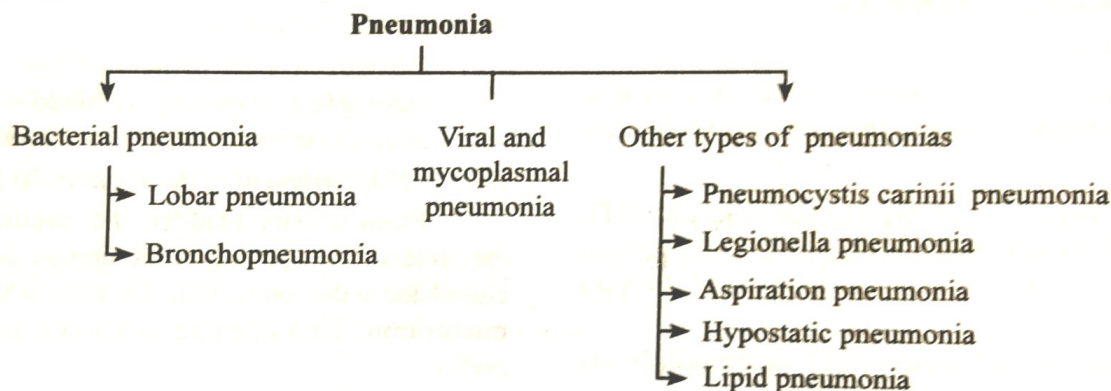
3. PNEUMONIA**Introduction**

Pneumonia is the sudden and intense onset of sensations of pain in chest accompanied by swelling, redness and loss of function of the lung parenchyma which may lead to a hardened appearance of the lungs.

There exists various means by which the lungs prevent microorganisms from entering.

1. The nasopharynx purifies the air before it reaches the lungs.
2. Cilia present along the lower respiratory passages entrap the microorganisms onto the mucus that lines the cilia and push the mucus towards the digestive tract.
3. Macrophages and immunoglobulins present in the alveoli engulf and digest the microorganisms.

When the above mentioned processes are unsuccessful, combined with a few risk factors, it would lead to pneumonia.

Types of Pneumonia**1. Bacterial Pneumonia**

As the name suggests, bacterial pneumonia is caused by infection of the lung parenchyma by bacteria. Depending on the causative agent and structural changes that occur, it can be further classified as lobar pneumonia and bronchopneumonia.

(a) Lobar Pneumonia

In lobar pneumonia, a section of the lobe or complete lobe/lobes of either one or both the lungs are infected by bacteria.

Aetiology

Lobar pneumonia is further classified into different types depending on the causative agents, which are as follows.

Table: Types of Lobar Pneumonia

Types	Causative agent	Remarks
Pneumococcal pneumonia	<i>Streptococcus pneumoniae</i>	This is usually community acquired and comprises of more than 90% of all lobar pneumonias.
Staphylococcal pneumonia	<i>Staphylococcus aureus</i>	In this case, microbes are carried to the lungs by blood or blood components from another site of infection.
Streptococcal pneumonia	β -hemolytic streptococci	Diabetics, extremely weak geriatrics and rarely pediatrics (whose have just recovered from measles or influenza) are affected.
Pneumonia caused by Gram-negative aerobic bacteria	(i) <i>Haemophilus influenzae</i> (ii) <i>Klebsiella pneumoniae</i> (iii) <i>Pseudomonas</i> (iv) <i>Proteus</i> (v) <i>Escherichia coli</i>	(i) These microorganisms rarely cause pneumonia. (ii) In children below the age of 3, <i>H. influenzae</i> frequently causes pneumonia after an episode of infection by viruses.

Structural Properties

Lobar pneumonia can be divided into the following phases depending on the pathological and structural changes that occur.

Table: Phases of Lobar Pneumonia

Stage	Overall structural changes	Histological changes
Stage of congestion: Initial phase (1-2 days)	A deep red colouration and an increase in the size and weight of the lobe is seen and a foamy red coloured liquid oozes on slitting the surface of the infected lobe.	❖ Capillaries in the walls of the alveoli contract and expand. ❖ Air spaces show the presence of liquid containing eosinophils which causes swelling.
Red hepatization: Early consolidation (2-4 days)	There is reddish colouration and solidification of the lobe that is infected and when the lobe is slit, the surface appears to be reddish-pink, devoid of air and moisture and grainy in texture.	❖ Air spaces show the presence of fibrin threads and are devoid of any liquid. ❖ There is a leakage of fluid from the RBCs and neutrophils.
Grey hepatization: Late consolidation (4-8 days)	There is increased rigidity and weight of the lobe that is infected and on slitting the surface appears to be powdery, devoid of moisture and smoky in appearance.	❖ There is thickening and multiplication of the threads composed of fibrin. ❖ A narrow area separates the liquid leaking from the cells of the septum.
Resolution : (8 days - 1 or 3 weeks)	Infected lobe becomes tender due to hydrolysis of the previously hardened fibrin strands and the surface appears to be smoky red or dirty brown in colour on sectioning and there is oozing of a foamy buttery mustard coloured fluid on compression.	❖ Spaces in the alveoli are majorly occupied by macrophages. ❖ Capillaries of the alveoli swell up.

Complications

Complications of lobar pneumonia include pleural effusion (accumulation of fluid in the pleural cavity), empyema (pus in the pleural cavity), lung abscess (collection of pus or necrotic tissue), metastatic infections (spread of a malignant tumour from its site of origin) and carnification (fibrosis of the septum of the alveoli).

Clinical Features

Symptoms include chills, fever, cough, fatigue, difficulty in breathing, increased heart rate, cyanosis (bluish discolouration of skin and mucous membrane due to lack of oxygen) and rapid breathing.

(b) *Bronchopneumonia*

In bronchopneumonia, there is solidification of certain areas of the lungs and the bacteria infects the bronchioles. It is also referred as lobular pneumonia.

Aetiology

Staphylococci, *Streptococci*, *Pneumococci*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Pseudomonas* and *Coliform* bacteria are the causative organisms.

Structural Properties

Certain regions of the lungs become hardened and appear rosy and smoky and on slicing appear powdery and devoid of moisture. Intense inflammation of the bronchioles and solidification of the septum of the alveoli by condensed capillaries is observed on histological examination.

Clinical Features

Symptoms include long-term weakness, withdrawal of contents of the stomach into the respiratory tract, infection of the upper part of the respiratory tract and sudden or intense inflammation of the bronchi.

Complications

Thickening and scarring of the bronchiole is seen. The rest of the complications are same as that of lobar pneumonia.

2. **Viral and Mycoplasmal Pneumonia**

Irregular inflammation (mainly of the interstitial tissues of the lungs) devoid of any leakage of fluid from the alveoli characterizes viral and mycoplasmal pneumoniae. They are also referred as primary atypical pneumonias or interstitial pneumonitis.

Aetiology

Causative organisms include *Mycoplasma pneumoniae*, influenza and parainfluenza viruses, adenoviruses, rhinoviruses, Coxsackie viruses, cytomegaloviruses, psittacosis, coxiella and predominantly, respiratory syncytial virus.

Structural Properties

Lungs become hardened, either completely or partially. An increase in the weight of the lobe may be seen. A foamy red stained fluid oozes on cutting the surface. Inflammation of the bronchioles, accompanied by the condensation of the walls of the alveoli may also be seen.

Clinical Features

Symptoms include fever, headache, pain in the muscles, cough without expectoration.

Complications

Complications include scarring and thickening of the interstitial cells of the lungs, infection by bacteria and indefinite destruction of the lungs.

3. **Other Types of Pneumonias**

Various other types of pneumonias include. *Pneumocystis carinii* pneumonia, legionella pneumonia, aspiration pneumonia, hypostatic pneumonia and lipid pneumonia.

Pathophysiology

The microbes reach the lungs via the following passages.

1. By inhaling the air containing microbes via mouth or nose.
 2. Withdrawal of microorganism containing fluid from the nasopharynx and oropharynx into the lungs.
 3. Microbes may spread from an infected area that is near the lungs.
 4. Microbes may be carried from a far off site of infection to the lungs by blood or its components.
- Pneumonia occurs in the following situations.

1. **Change in the Conscious State**

Substances present in the oropharynx may get withdrawn into the lungs causing the person to lose consciousness in certain situations like in case of toxicity of certain drugs, during epileptic attacks etc.

2. **Oppressed Cough**

Substances present in the stomach may get withdrawn into the lungs due to oppressed cough in certain situations like in disorders of the neuromuscular system, due to weakness associated with unhealthy diet etc.

3. **Dysfunctioning of the Mucociliary Mechanism**

Many factors like smoking, viral infections of the respiratory tract, inhaling gases which are harsh and old age lead to weakening of the defensive mechanism of the ciliated epithelium lined by mucus, thereby allowing the microbes to enter into the lung parenchyma.

4. **Dysfunctioning of the Macrophages Present in the Alveoli**

Several factors such as smoking, lack of oxygen, lack of blood, accumulation of fluid in the lungs, respiratory infections caused by viruses and malnourishment contribute to the loss of function of the macrophages present in the alveoli leading to pneumonia.

5. **Blockage of the Bronchi and Bronchioles**

There could be blockage of the bronchi or bronchioles due to the presence of a tumour, any foreign particles or due to fibrocystic diseases of the pancreas or due to chronic bronchitis, leading to improper clearance of the tract, resulting in pneumonia.

6. **Impaired Functioning of Leucocytes**

Defects in the granulocytes and lymphocytes including birth related and acquired deficiencies of the immune system like AIDS may increase the risk for pneumonia.

4. **TYPHOID**

Introduction

Typhoid fever is an acute disease or illness characterised by continuous fever for 3-4 days that increases by 1°C each day. It is also known as *enteric fever* as it mainly affects the intestine. The infection subsequently spreads to the reticuloendothelial system and then to different organs throughout the body.

Epidemiology

The disease is endemic in areas with poor environmental sanitation. It is prevalent in India, Pakistan, Egypt etc. According to the World Health Organization, typhoid is considered as a serious health problem. Typhoid incidence is highest in individuals between 5-19 years of age and in people who travel or often visit endemic areas.

Stages

Depending upon the severity of the infection, typhoid is divided into four stages with an incubation period of approximately one week for each stage.

1. **First Stage**

In this phase, patients are more likely to develop symptoms like fever as high as 40°C accompanied with bradycardia, headache, weakness, abdominal pain, malaise, cough, epistaxis (bloody nose), leukopenia, eosinophilia and lymphocytosis.

In this stage, the samples of blood tested for *Salmonella typhi* give positive result but the classical Widal test which detects *Salmonella* antibodies O and H gives negative.

2. Second Stage

If the treatment is not initiated in the first stage, then the patients are likely to enter the second stage during which they become very ill and experience life-threatening complications. This phase of illness is known as height of the disease.

The symptoms developed during this stage are continued fever accompanied with bradycardia, dicrotic pulse wave (pulse characterised by two peaks resulting in double pulsation or exaggeration of dicrotic wave), appearance of rash of flat rose coloured spots especially on chest and abdomen, extremely distended abdomen, either diarrhoea with characteristic smell or constipation, hepatosplenomegaly (enlarged liver and spleen), delirium and bronchi in lung bases.

3. Third Stage

During this stage, patients develop complications that can be fatal or nonfatal. These complications include intestinal haemorrhage and intestinal perforation, encephalitis, metastatic abscess, endocarditis, cholecystitis and osteitis.

By the end of this stage, fever starts decreasing gradually until the normal body temperature is attained.

Aetiology

Salmonella typhi, a rod shaped Gram-negative bacteria is the causative organism of typhoid fever. This bacteria is usually ingested from contaminated food and water and occasionally through direct contact with the infected person. Most of the people while travelling pick up this bacteria and further spread it to other people through faeco-oral or urino-oral route.

Pathophysiology

Salmonella typhi, after entering into the gastrointestinal tract, perforates through the intestinal wall and gets phagocytosed by macrophages. Further, it alters its own structure and resides within the macrophage. This protects them from destruction by human host defence mechanism. *Salmonella typhi* then grows and multiplies within the macrophage and reaches the reticuloendothelial system. After incubation period of about 14 days, it travels through lymphatic system and spreads the infection to spleen, liver and gall bladder.

Signs and Symptoms

Persons with typhoid fever usually show the following signs and symptoms.

1. Sustained low grade fever (39-40°C)
2. Non-bloody diarrhoea
3. Stomach pain and weakness
4. A rash of flat, rose-coloured spots.

5. TUBERCULOSIS

Introduction

Tuberculosis is a chronic granulomatous disease caused by *Mycobacterium tuberculosis* which is an acid-fast bacilli. It is resistant to intracellular killing, when it is ingested by phagocytes.

Tuberculosis is mainly a disease of the lungs (pulmonary tuberculosis), but once the bacteria are inside the lungs, they impair the immune system and escape into the blood and lymph to infect other organs. Hence, infection can spread from lungs to all the organs of the body via blood.

Types of Tuberculosis

1. Primary Tuberculosis

It is seen in persons who have not been infected previously. The organism enters the body through the lungs. Within an hour of reaching the lungs, the tubercle bacilli reach the draining lymph nodes at the hilum of the lungs and few organisms enter the systemic circulation.

Features

- (a) Increased resistance is seen.
- (b) T-cells (cellular immunity) prevent the spread of disease and the organisms remain inactive in the host.
- (c) Reactivation of tubercle bacilli leads to progressive primary tuberculosis or miliary tuberculosis.

Morphology

Granulomatous lesions formed may consist of central necrotic material of cheesy nature (central caseation necrosis) or lack central necrotic material. It is surrounded by epithelioid cells and Langhan's giant cell with multiple nuclei.

2. Secondary Tuberculosis

It is seen in persons who have been previously infected with primary lesions. It affects the apex of the lungs and other sites like tonsils, pharynx, larynx, small intestine and skin.

Features

- (a) Caseous necrosis rupture the blood vessels, thereby spreading the mycobacteria throughout the body.
- (b) Infection of the airway tract by mycobacteria.

Morphology

Lesions are located in the apex of one or both the lungs. The granuloma comprises epithelioid cells surrounded by fibroblasts, lymphocytes and Langhan's giant cells. Some necrosis (caseation) is present in the centre of the tubercles.

Pathophysiology

Tuberculosis is an infectious disease which occurs when a droplet nuclei containing tubercle bacilli is inhaled. Inhaled droplet nuclei quickly reaches the terminal bronchioles and alveoli of the lungs and thereby prevents the activation of defense mechanisms in the upper airways. Soon after the entry of bacilli into the lung, alveolar macrophages ingest them but fail to destroy them. Consequently, the bacilli start multiplying within the macrophages. As the bacilli proliferate, the macrophages present the bacilli as antigens to T-lymphocytes which in turn increase the concentration of degrading enzymes in macrophages and improve their ability to destroy the bacilli. Development of T-lymphocytes and macrophages capable of destroying and controlling the infection constitute the cell-mediated response.

When the pathogens inhaled are low and the host has an intact immune system, the containment (destruction) and control of bacilli results in the formation of a grey-white granulomatous lesion in lung called *Ghon's focus* (primary lung lesion). This Ghon's focus contains tubercle bacilli, macrophages and other immune cells. On the other hand, when large number of pathogens are inhaled and the host has a compromised immune system, the hypersensitivity reactions produced by the bacilli causes the Ghon's focus to undergo caseous (pasty, yellow and cheese-like) necrosis. The bacilli which are present within the Ghon's focus drain along the lymph channels and reach the lymph nodes of the affected lung and form further caseous granulomas. Ghon's focus and the granulomas that form in the lymph nodes are together called as *Ghon's complex*. Due to inflammatory and immune response, Ghon's complex undergoes healing. However if body's defense mechanisms fail, then primary infection develops into secondary tuberculosis.

Signs and Symptoms

A patient with active tuberculosis presents the following clinical manifestations.

1. Fatigue, fever, night sweats and loss of weight.
2. Cough which is initially nonproductive but is accompanied by purulent sputum in the later stages. The production of sputum is triggered by inflammation and tissue necrosis.
3. Patient, though rarely, may cough up blood in the sputum (haemoptysis).
4. Chest pain and hoarseness of the voice.

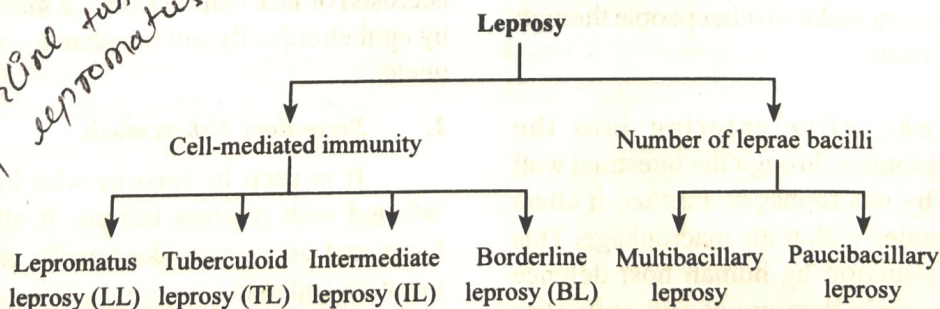
6. LEPROSY

Introduction

Leprosy is a slow progressing infection, also called Hansen's disease. Its causative agent is *Mycobacterium leprae*, a Gram-positive, rod-shaped intracellular bacilli. It first affects the skin causing lesions and then the peripheral nerves causing characteristic deformities.

Types of Leprosy

Borderline tuberculoid
B-99 septumatus



1. Based On Cell-Mediated Immunity

Lepromatous leprosy (LL) shows low resistance while tuberculoid leprosy (TL) shows high resistance. These two types are opposite to each other, one exhibiting minimal cell-mediated immunity and the other exhibiting strong immune reactions. As they represent the two poles of the immune system, they are called polar forms of leprosy.

(a) Lepromatous Leprosy (LL)

In this, a suppressed or low resistance is shown by the host to the bacilli and lepromin test gives negative results. As the immune system is unresponsive to the causative agent this type is also referred to as *anergic leprosy*. It progresses rapidly and affects the face, nose, eyes, ears and lymph nodes by forming typical symmetrical lesions.

These lesions are multiple, erythematous and contain characteristic macules (flat area with altered skin colour) and papules (small raised spots). This produces nodules on the skin that coalesce and cause *leonine facies* (typical facial expression). Nerves are affected later but not very severely. Minimal inflammation of the nerves occur that causes sensory disturbances like loss of sensation. The skin lesions cause hypoaesthesia (diminished sense of touch or loss of sensation) of the affected part.

In lepromatous type, lesions contain lepra cells (large collection of macrophages containing many bacilli). In advanced conditions, these macrophages are also seen in lymph nodes, spleen, liver and testes. Nephritis occurs commonly.

(b) *Tuberculoid Leprosy (TL)*

In this case, high resistance is shown by the host to the bacilli and lepromin test gives positive results. It progresses slowly forming few asymmetric lesions. The lesions are erythematous macules with depressed centres and raised hyperpigmented margins that show lack of sensation. These are less severe when compared to lesions of lepromatous type.

Neuronal effects are severe and observed at early stages. This leads to loss of sensation and degeneration of skin and muscle, causing impairment of the affected part. The lesions are granulomatous, hard and erode the basal layer of the epidermis. These lesions resemble those of tuberculosis and hence this type is called tuberculoid leprosy. Unlike lepromatous type, the tuberculoid lesions contain fewer bacteria.

(c) *Intermediate Leprosy (IL)*

In this, the lesions occur at an early stage and are not clear enough to be able to judge the type of disease. The lesions are flat and not well defined.

(d) *Borderline Leprosy (BL)*

In this, the host shows minimal immunity. It is an unstable condition where the mycobacterial multiplication is balanced by the host immunity. When left untreated, it advances to lepromatous leprosy. It is also known as *dimorphic leprosy*.

2. *Based on the Number of Lepae Bacilli*

(a) *Multibacillary Leprosy*

When the skin lesions are more than five, it is classified as multibacillary leprosy (containing abundant bacilli in the lesions). It is an infectious type of leprosy.

Lepromatous and borderline types come under this group. Cell-mediated immunity is largely diminished due to the production of interleukin-4 which blocks the immune response by suppressing IFN- α . It gives negative results for lepromin test.

(b) *Paucibacillary Leprosy*

When the skin lesions are less than five, it is classified as paucibacillary leprosy. Few bacilli are seen in the lesions and it is non-infectious. The tuberculoid and intermediate types come under this group. The host shows normal or partially diminished immunity and rapidly produces IFN- α responsible for immune response. It gives positive results for lepromin test.

Pathophysiology

Leprosy is a communicable disease. It is transmitted from an infected person to a healthy individual via the secretions of the upper respiratory tract like cough droplets that contain the leprae bacilli. The microorganism is taken up by the macrophages present in the alveoli of a healthy person. From there, they spread into the blood causing infection. The bacilli first infects the moist areas such as mouth, eyes, respiratory system and peripheral nerves and later spreads into the reticuloendothelial system (monocytes and macrophages that are responsible for immune response) affecting the liver, spleen, bone marrow and lymph nodes.

In chronic conditions, the person acquires secondary amyloidosis (infiltration of amyloid, a starch like substance into the liver, kidneys and spleen) and renal disease due to immunological disorders. In few cases, antibodies to *M.leprae* antigen are produced which form complexes. These complexes cause glomerulonephritis, erythema nodosum (tender swelling on the shins) and vasculitis (inflammation of walls of small blood vessels).

7. MALARIA

Introduction

Malaria is a blood-borne disease caused by the protozoan species of microorganisms which is transmitted by the bite of female anopheles mosquito to humans.

Aetiology

Causative organisms include *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium ovale* and *Plasmodium malariae*, which are carried by the female anopheles mosquitoes.

Life Cycle of Malarial Parasite

Life cycle of malarial parasite is divided into two stages,

1. Sexual cycle/sporogony (occurring in female anopheles mosquito)
2. Asexual cycle (occurring in man).

1. Sexual Cycle/Sporogony

- (a) When mosquito bites, it sucks the blood from an infected person thereby the gametocytes along with the blood enter into the mosquito.
- (b) In the body of the mosquito, fertilization of male and female gametocytes takes place which results in the formation of zygote.
- (c) Zygote develops into an oocyst or sporocyst or ookinete. This further undergoes several divisions and releases sporozoites which migrate into the salivary glands and remain there until they are released into the human body to continue their life cycle.

2. Asexual Cycle

When an infected mosquito bites a healthy individual, sporozoites present in the salivary glands are released into the blood stream. Asexual cycle gets initiated in man which is further divided into 4 stages.

(a) Pre-erythrocytic Stage

Sporozoites after their entry into the blood stream move into the parenchymal cells of liver within half-an-hour. They reside in the liver for a period of 10-14 days, where they undergo several divisions to form merozoites which get released at the end of this cycle.

(b) Erythrocytic Stage

Merozoites reach the RBC where they undergo several divisions to form intracellular motile parasites, the trophozoites.

(c) Exo-Erythrocytic Stage/Schizogony

Trophozoites formed in the RBC undergo mitosis and form schizonts, which on further division form several merozoites. This is termed as *schizogony*. Thus, released merozoites may either enter fresh RBC and initiate the erythrocytic stage or may enter liver, remain dormant (inactive) for a certain period (months or years) and get reactivated to start the exo-erythrocytic stage. Such dormant merozoites in the liver are termed *hypnozoites*.

Some of the merozoites undergo meiosis and get differentiated to form male and female gametocytes which enter into the mosquito (when it bites the infected person) and continue their life cycle.



When the female anopheles mosquito bites, about 8-15 malarial sporozoites are infused into the blood stream which then reach the liver cells and evolve into pre-erythrocytic schizonts by asexual means of reproduction. This is an asymptomatic phase. After 7-30 days, 30-40,000 merozoites are liberated into the blood circulation which then perforate the RBC, after fusing via receptors. Merozoites evolve into trophozoites and the schizonts liberate newer merozoites, which destroy the newly formed RBCs, causing fever. The RBCs disintegrate and release toxins which stimulate the macrophages to release cytokines, which lead to other symptoms. Amongst the four plasmodia, *P.falciparum* causes the most severe symptoms like parasitaemia (relating to multiple entry pathways of the plasmodia into erythrocytes), cytokine responses, impaired red cell deformability, sequestration (mature trophozoites fuse to the endothelial cells of small blood vessels) and resetting (infected and uninfected RBCs form a mass). These symptoms lead to low survival rates in humans and malaria is the 7th leading cause of death in humans in low income countries.

Symptoms include fever, chills, headache, nausea, vomiting, fatigue and cold.

The complications which might occur include coma, decreased blood glucose level, kidney dysfunction, intense anaemia, jaundice, swelling of lungs due to retention of fluid, haemoglobinuria (presence of free haemoglobin in the urine) and increased acidity of body fluids and tissues (acidosis).

8. DYSENTERY

Amoebic dysentery

Definition

Amoebic dysentery is an infection which mainly affects the large intestine leading to diarrhoea (frequent evacuation of bowel by passage of soft or liquid faeces), prolonged painful contraction of abdominal muscles, frequent sensation of the desire to defecate and presence of mucus in the faeces.

Aetiology

The causative organism, *Entamoeba histolytica*, when swallowed in its cyst form leads to amoebic dysentery. On reaching the small intestine, the wall of the cyst disintegrates and releases the microbe, which moves into the large intestine and destroys the mucosal epithelium and gives rise to flask shaped ulcers on reaching the submucosa.

Pathophysiology

The parasite releases an enzyme called histolysin which destroys the epithelial lining of the colon resulting in the formation of ulcers which upon microscopic observation exhibit RBCs, lymphocytes, tissue debris etc. The ulcers result in the formation of abscesses. These abscesses may later transform into bleeding ulcers.

Symptoms

Acidic stools containing mucus and blood, severe abdominal pain, flatulence, nausea, headache, fatigability and frequent passage of stools that show the presence of amoebae and RBCs.

Complications

The complications include formation of amoeboma (non-malignant tumour like inflammatory mass), creation of a hole in the intestines, leakage of blood, inflammation of the liver (amoebic hepatitis) and amoebic liver abscess (localized collection of pus and necrotic tissue, surrounded by inflamed and damaged tissues).

Bacillary Dysentery

Definition

Bacillary dysentery is an infection caused by the *Shigella* species of microorganisms leading to diarrhoea (frequent evacuation of bowel by passage of soft or liquid faeces), prolonged and painful contractions of the abdominal muscles, tenesmus (frequent sensation of the urge to defecate) and excretion of mucus in faeces.

Aetiology

The causative organisms belong to the *Shigella* species which include *S.dysenteriae*, *S.flexneri*, *S.boydii* and *S.sonnei*. The infection occurs via the faeco-oral route, by the common housefly and by consuming polluted food and water.

Pathophysiology

The mucosal cells of the intestine are destroyed by the microbes, which then divide intracellularly and eventually damage the host cells. They also release toxins like shiga toxin, which destroys the cells of the endothelium in the colon and glomeruli leading to inflammation of the colon causing bleeding and haemolytic-uraemic syndrome. They also release antigens which might lead to joint pains.

Symptoms

The symptoms include nausea, vomiting diarrhoea, pain in the stomach, fever, chills, rectal bleeding, loss of weight and anorexia (loss of appetite).

Complications

The complications include leakage of blood (haemorrhage), formation of holes in the intestine, pains in multiple joints and inflammation of the iris and ciliary bodies of the eye.

9. HEPATITIS

Hepatitis is defined as the inflammation of liver which results in damage to hepatocytes followed by their death.

Types and Aetiology of Hepatitis

1. Acute Hepatitis

Acute hepatitis is a milder form of hepatitis, caused by HAV, HBV and HCV. Drugs like isoniazid, halothane, aspirin etc., are commonly responsible for inducing hepatitis. Two types of acute hepatitis are discussed below.

(a) *Viral Hepatitis*

Viral hepatitis is the term used to describe the infection of liver caused by hepatotropic viruses. They generally lead to transient and innocuous hepatitis, causing acute inflammation of liver. Mainly six types of hepatotropic viruses have been discovered till date which have been discussed in the following table. A seventh type of hepatotropic virus known as hepatitis F virus (HFV) was discovered in early 1990s. However, presently its existence is not clearly understood and hence the scientific community no longer lists it under the category of viruses that causes hepatitis.

Table: Summary of Various Types of Viruses Causing Hepatitis

Type	Features	Mode of transmission	Severity and progression	Epidemiology	Prognosis
Hepatitis A: Hepatitis A virus (HAV)	- Single stranded RNA - Non-enveloped and linear shaped - Incubation period: 2-7 weeks.	Faeco-oral route	Mild disease. May progress to fulminant hepatitis.	Highest rate of incidence is in children between 5-14 years. Rate of incidence is less in females when compared to males by 20%.	It can be cured very well by treatment.
Hepatitis B: Hepatitis B virus (HBV)	- Single stranded or double stranded DNA - Double shelled and enveloped - Incubation period: 3-6 months.	- By blood transfusion - Through sexual contact - From mother to neonate during birth via vertical transmission.	It is usually mild but may occasionally turn severe and progress to chronic hepatitis.	Incidence of acute infection is more than chronic infection. 1-14% of chronic hepatitis is most likely to develop in neonates than in adults.	Prognosis worsens as the age progresses. Patients suffering from acute HBV infection recover in 1-2 months after the onset of jaundice.
Hepatitis C: Hepatitis C virus (HCV)	- Single stranded RNA - Linear or circular shaped with envelope - Incubation period: 20-90 days.	Commonly transmitted through blood.	It is moderately severe disease. Both acute and chronic types are found. Most of the cases become chronic. 85% of individuals with chronic hepatitis show progressive liver damage.	It occurs in all age groups, highest incidence being in individuals between 20-39 years of age.	Moderate prognosis for both chronic and acute infections of HCV.
Hepatitis D: Hepatitis D virus (HDV)	- Single stranded RNA similar to defective RNA plant virus - Circular shape. Envelope is present but its replication is defective - Incubation period: 30-50 days.	- By sexual contact - Through blood transfusion.	HDV is an incomplete virus i.e., it can cause infection only when individuals simultaneously get infected by HBV. HDV infection is usually mild but may occasionally become severe.	Highest prevalence is among people who are exposed percutaneously. It is an endemic disease in Mediterranean region.	Prognosis for acute infection is good but for chronic infections it is poor.
Hepatitis E: Hepatitis E virus (HEV)	- Single stranded RNA - Linear, icosahedral, non-enveloped - Incubation period: Average of 42 days.	Faeco-oral route	It is a very mild disease but may cause death in pregnant women.	It is an endemic disease in India, Asia, Middle East and some areas of Latin America.	Good prognosis prevails for HEV infection. Patients recover completely.
Hepatitis G: Hepatitis G virus (HGV)	- Single stranded RNA - Linear	- By blood transfusion - Through sexual contact	Persistent infection with HGV is very common.		

(b) *Drug-induced Hepatitis*

Drug-induced hepatitis which is a very rare condition, occurs due to adverse reactions of the drugs on liver. Generally, drug-induced hepatitis remains asymptomatic until liver gets destructed extensively.

2. *Chronic Hepatitis*

Hepatic disease that relapses for more than 6 months time period is known as chronic hepatitis. It is mostly accompanied with inflammation and necrosis. It mainly occurs when structural changes with hepatocyte damage take place leading to loss of normal liver architecture.

The major causes of chronic hepatitis are HBV and HCV accounting for more than 70-80% of cases. Other causes include drug induced adverse reactions, Wilson's disease and autoimmune chronic hepatitis.

Pathophysiology

1. *Hepatitis A (Infectious Hepatitis)*

The exact mechanism by which hepatitis A occurs is not established clearly. It may occur due to cytopathic or immunological hepatocyte damage.

2. *Hepatitis B (Serum Hepatitis)*

The mechanism by which hepatitis B develops is immunological hepatocyte destruction which is similar to that occurring with HAV.

3. *Hepatitis C (Non-A Non-B Hepatitis or Blood Borne Hepatitis)*

The mechanism by which HCV infection occurs is either direct or indirect immunological responses produced by the HCV. Direct mechanism involves accumulation of viral proteins or intact virus in the hepatocytes. In indirect immunological mechanism, the virus stimulates liver CD8⁺ lymphocytes via antigen independent pathway that activates CTL and initiates hepatocyte destruction.

4. *Hepatitis D (Delta Hepatitis)*

HDV causes hepatitis mainly via immune-mediated response. It is mainly caused by auto-antibodies associated with HDV.

5. *Hepatitis E and G*

Pathogenesis is not clearly described.

6. *Drug-induced Hepatitis*

The exact mechanism is not clearly established. It was assumed that adverse drug reactions lead to liver damage and eventually hepatitis.

Signs and Symptoms

1. *Hepatitis A*

About 2-8 weeks after infection, the symptoms that appear include malaise, anorexia, nausea, fatigue, diarrhoea and alteration of taste. These symptoms follow right-upper quadrant discomfort, dark urine and light coloured stools. Jaundice may follow soon after few days in a small percentage of patients. Fulminant hepatitis, if developed, may lead to liver failure or encephalopathy.

2. *Hepatitis B and C*

The symptoms of acute hepatitis are similar to those of hepatitis A.

The most common symptoms of chronic hepatitis include malaise, weakness, anorexia and weight loss. These symptoms turn more severe upon development of cirrhosis. Later the patient may also develop hepatic encephalopathy, jaundice, ascites, muscle wasting and oesophageal varices. Arthritis and urticaria are also seen sometimes.

Late or end stage symptoms are seen in 15-25% of chronic infection. These may include alterations in consciousness, liver failure and death.

3. *Drug-induced Hepatitis*

Common symptoms include nausea, fever, abdominal complaints, hepatomegaly, eosinophilia, arthralgias and jaundice. Patients with this type of hepatitis show variations in their serum aminotransferase levels.