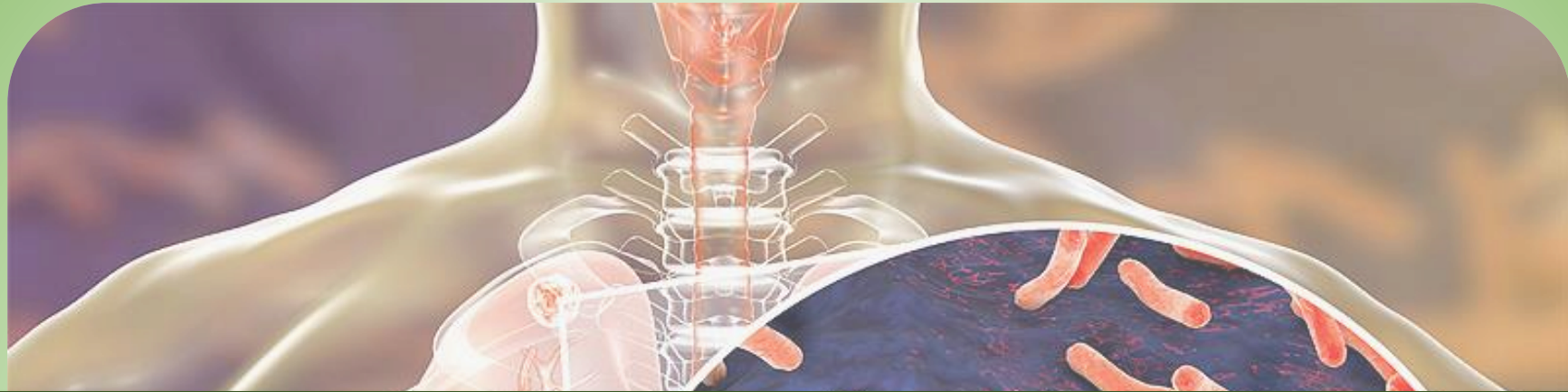
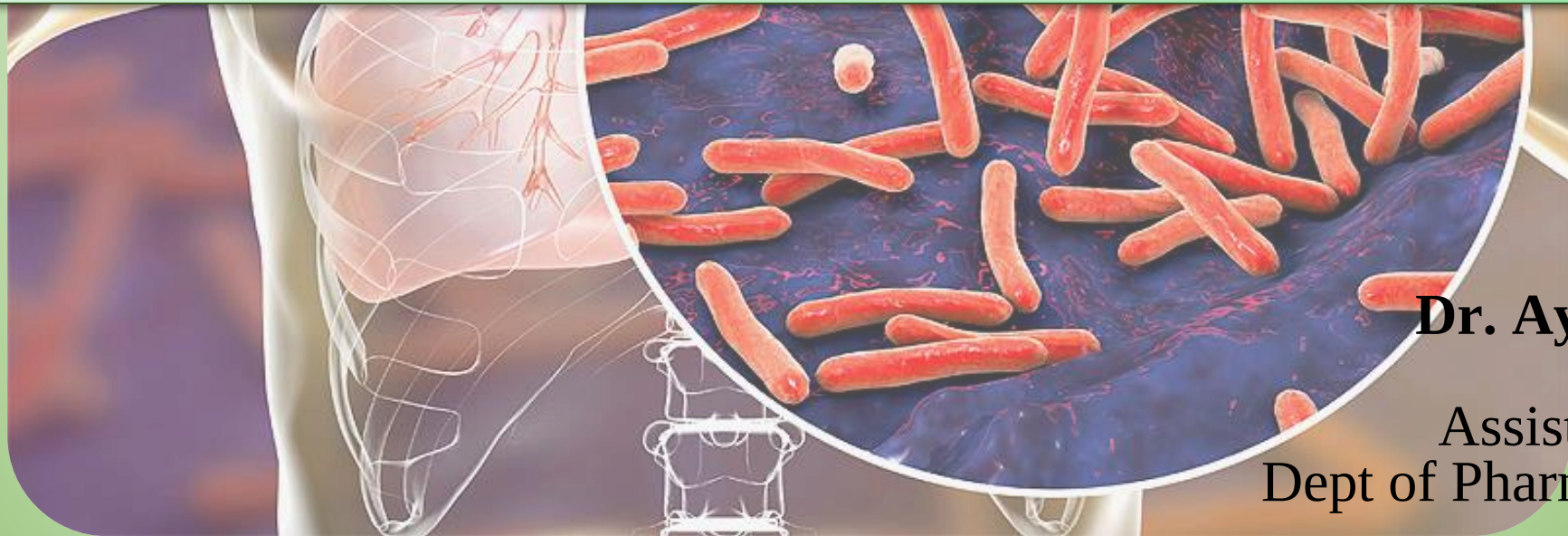




TUBERCULOSIS



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Tuberculosis (TB) is a chronic infectious disease caused by the acid-fast bacillus *Mycobacterium tuberculosis*.

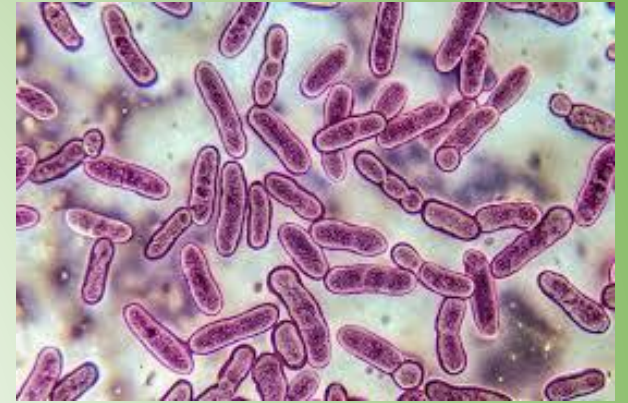
It most commonly affects the lungs, referred to as pulmonary tuberculosis, but can also involve other organs such as the central nervous system, lymphatic system, bones, joints, genitourinary tract, and bloodstream.

The disease is characterized by slow bacterial growth, granuloma formation, and progressive tissue destruction, and it spreads primarily through airborne droplet nuclei expelled by individuals with active pulmonary TB.



Etiology

- Caused by *Mycobacterium tuberculosis*, an aerobic, acid-fast bacillus.
- Infection occurs after inhalation of airborne droplet nuclei expelled by a person with active pulmonary TB.
- Droplets are produced during: Coughing, Sneezing, Talking, Singing, Any forced respiratory maneuver
- Droplet nuclei can remain suspended in air for several hours, increasing the chance of exposure.



Risk factors include

1. Living in overcrowded, enclosed, poorly ventilated spaces
2. Close contact with active TB cases
3. Health-care workers exposed to infectious patients
4. Individuals with weakened immunity

Pathogenesis of TB

latent *Mycobacterium tuberculosis* infection

Step	Process
1	Inhalation of droplet nuclei containing <i>M. tuberculosis</i> into the body.
2	Droplet nuclei settle in the bronchioles and alveoli of the lungs.
3	Initial Encounter/Infection (dependent on organism's virulence and alveolar macrophage microbicidal ability).
4	After 14 to 21 days, tubercle bacilli spread via the lymphatic and blood systems to other organs.
5	Organism replicates for 2 to 12 weeks until it reaches a specific number.
6	T cells secrete interferon gamma, interleukin-2, interleukin-10, and other cytokines.
7	Macrophages are activated to engulf and kill the tubercle bacilli, preventing further spread.
8	Patient develops cell-mediated immunity (detectable by a reaction to the tuberculin test).

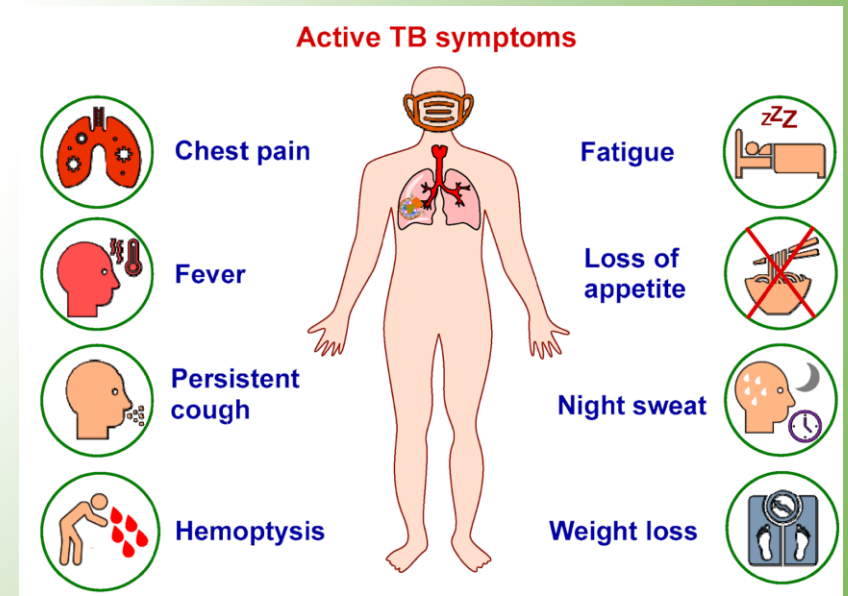
Active Disease (Tuberculosis)

- In most patients, TB occurs as a result of reactivation of a previously controlled latent infection, termed reactivation tuberculosis.
- The apices of the lungs are the most common sites for the reactivation of disease.

Clinical Manifestations

The following are the manifestations of Pulmonary TB:

1. Weight loss
2. Fatigue (Malaise)
3. Productive cough (usually lasting 3 weeks or longer)
4. Fever
5. Night sweats
6. Frank Hemoptysis
7. Chest Pain (often sharp pain with breathing/coughing)
8. Shortness of Breath (Dyspnea) (in more advanced cases)
9. Loss of Appetite (Anorexia)



Lab Investigations

1. Mantoux Test:

The Mantoux test is the preferred TB skin test.

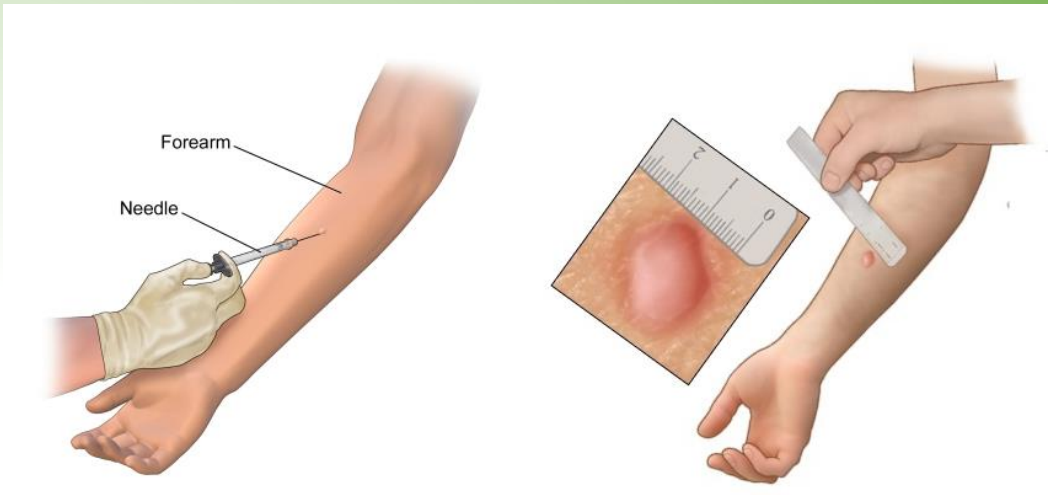
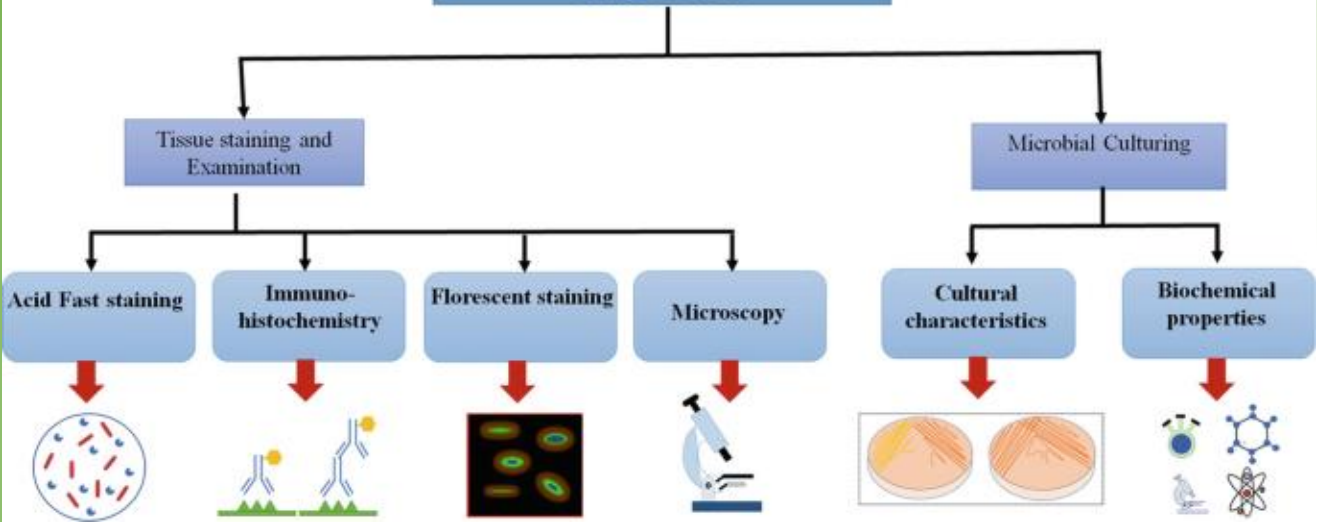
It uses tuberculin purified protein derivative.

The standard 5 tuberculin unit dose is placed intracutaneously volar aspect of the forearm with a 26-27-gauge needle. The injection should produce a small raised blanching wheal.

The area of induration("bump") is the endpoint.

2. **Acid-Fast Bacilli (AFB) Smear:** Rapid look for bacteria.
3. **Mycobacterial Culture:** Slow growth confirms TB.
4. **Nucleic Acid Amplification Tests (NAATs):** Fast molecular DNA detection.
5. **Drug Susceptibility Testing (DST):** Checks antibiotic resistance pattern.
6. **Chest X-ray (CXR):** Shows typical lung abnormalities.
7. **CT Scan:** Detailed lung injury imaging.

Histo-pathological Techniques for the diagnosis of TB



TUBERCULIN TEST

Mantoux reaction

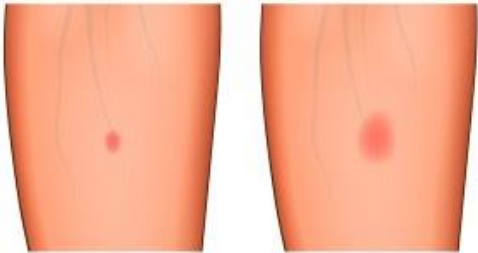
negative reaction



slight redness

or complete absence of tubercle

doubtful reaction



diameter of the tubercle of 2-4 mm
redness without tubercle

positive reaction

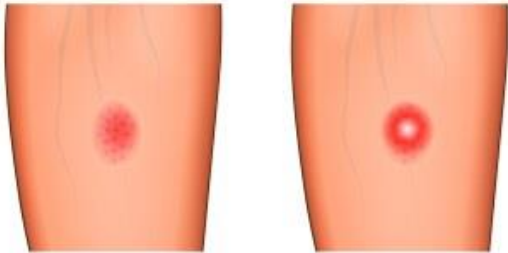


diameter 4-9 mm
weak reaction

diameter of 10-15 mm
average reaction

diameter more than 15 mm
strong reaction

hyperergic reaction



diameter over 17 mm

pustule

Management

Management includes both non-pharmacological and pharmacological management.

Pharmacological Treatment

Objectives of pharmacological therapy are:

1. To kill the extracellular tubercular bacilli living in lung cavities, which are metabolically active and divide continuously.
2. To sterilize and eliminate the bacilli that replicate less actively in acidic and anoxic closed lesions, and to kill semi-dormant bacilli living intracellularly in other host tissues.

Drugs Used for Treating Tuberculosis

First line drugs		Second line drugs	
Drugs	Dose	Drug	Dose
Isoniazid (H)	5 mg/kg(Max dose is 300 mg)	Ethionamide	15-20 mg/Kg
Rifampicin (R)	10 mg/kg(Max dose is 300 mg)	Cycloserine	10-15 mg/Kg
Ethambutol (E)	25 mg/kg	Kanamycin	15-30 mg/Kg
Pyrazinamide (Z)	15 mg/kg	Amikacin	15 mg/Kg
Streptomycin (S)	15 mg/kg	Levofloxacin	500-1000 mg
		Ofloxacin	200 mg bid

Treatment Regimens

- World Health Organization prescribes the following regimens based on the category of tuberculosis:

The current treatment for the complete elimination of active and dormant bacilli involves two phases:

- Initial phase: Three or more drugs (usually isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin) are used for two months, and allow a rapid killing of actively dividing bacteria, resulting in the negativization of sputum.
- Continuation phase: Fewer drugs (usually isoniazid and rifampicin) are used for 4 to 7 months, aimed at killing any remaining or dormant bacilli and preventing recurrence.

Category	Characteristic of TB cases	Initiative phase	Continuation phase
1	New sputum smear-positive seriously ill, sputum smear-negative seriously ill, extra-pulmonary	2(HRZE) 3	4(HR) 3
2	Release failure treatment after default others	2(SHREZ)3 1(HREZ)3	5(HRE) 3
3	Sputum smear-negative, not seriously ill, extra-pulmonary	2(HRZ) 3	4(HR) 3
4	Sputum smear-negative, not seriously ill, extra-pulmonary	Second line	

- 1, 2, 4, 5 are No. of months the treatment to be used.
- 3 is No.of days used in a week.

Counseling Points for TB Patients

Patients should be educated about the disease·

- Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* bacteria.
- It mainly spreads from person to person through inhalation of airborne droplets contaminated with TB pathogens.
- The infection primarily affects the lungs, but it can also involve other organs of the body (extrapulmonary TB).
- TB is a serious illness requiring a combination of medications for effective treatment.
- Common symptoms of TB include:
 1. Persistent cough lasting more than 2–3 weeks
 2. Fever lasting more than 7 days
 3. Shortness of breath
 4. Loss of appetite
 5. Sudden or unexplained weight loss
 6. Fatigue
 7. Night sweats
 8. Productive cough with sputum

About Medication

The patients should be counseled regarding specific medications and their side effects.

- **Rifampicin**: Rifampicin should be taken as advised by the doctor. Body fluids (tears, urine, and saliva) may turn orange colored after taking this medication. Please wear spectacles instead of soft contact lenses, as they may be permanently stained.
- **Isoniazid**: Ask patients to minimize alcohol consumption because it increases the chance of hepatitis. The patient must be asked to seek medical attention if signs of liver disorder, like persistent vomiting, anorexia, and jaundice, develop.
- **Pyrazinamide**: Advise the patient on how to take the medication. Patient must be asked to seek medical attention if signs of liver disorder, like persistent vomiting, anorexia, and jaundice.
- **Ethambutol**: Advise the patient about safe use of medication. The patient must also be told to get a routine vision test done, as ethambutol can cause blindness.

Recommended Lifestyle Modifications

The patient should be counseled regarding lifestyle changes, as TB spreads as a droplet infection.

1. Patient should be asked to cover the nose and mouth with a handkerchief while sneezing or coughing.
2. Patient should be advised to stay in well well-ventilated room where adequate sunlight and air circulation is there..
3. Patient should be advised to avoid close contact with children and the elderly who have a weak immune system.
4. Patient should be advised to dispose patient's sputum by burning or burying.

Prevention of Tuberculosis

1. Early detection and timely treatment of active TB cases to reduce the spread of infection.
2. BCG vaccination in infants and children to protect against severe forms of TB.
3. Avoid close contact with individuals who have untreated or infectious pulmonary TB.
4. Practice good respiratory hygiene, such as covering the mouth and nose during coughing or sneezing and using masks when needed.
5. Ensure proper ventilation in homes, workplaces, and hospitals; this helps reduce airborne transmission of TB bacteria.
6. Screen high-risk groups (healthcare workers, close contacts, and immunocompromised persons) using tests like TST or IGRA.

7. Follow airborne infection control measures in healthcare settings, including isolation rooms, N95 masks, and proper protective equipment.
8. Provide preventive therapy (e.g., isoniazid preventive therapy) for individuals with latent TB infection, especially in high-risk groups.
9. Encourage a healthy lifestyle with good nutrition, adequate sleep, and avoidance of smoking and alcohol to strengthen immunity.
10. Promote community awareness programs to educate the public about TB transmission, symptoms, and prevention.

HEPATITIS

Hepatitis is defined as inflammation of the liver caused by various strains of hepatitis virus infection (e.g, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E), or medications (e.g, Methyldopa or Isoniazid), or due to immunologic abnormalities (e.g, autoimmune hepatitis). Hepatitis can occur as an acute or chronic disease. Chronic disease is generally considered any disease or infection persisting for six months or longer. Hepatitis may be self-limiting (healing on its own) or can progress into fibrosis (scarring) and cirrhosis. Hepatitis may occur with limited or no symptoms, but it often can lead to jaundice, anorexia (poor appetite), and malaise.

According to the prognosis, Hepatitis may be classified into

Acute: Illness with a discrete date of onset with jaundice or increased serum aminotransferase concentration of > 2.5 times the upper limit of normal (35-40 IU/L).

Chronic: Inflammatory condition of the liver involving an ongoing hepatocellular necrosis for 6 months or more after the onset of acute illness.

Viral hepatitis is further classified into the following based on the type of hepatitis virus:•

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D
- Hepatitis E•
- Hepatitis G

Etiopathogenesis

Viral Hepatitis

- **Hepatitis A:** Hepatitis A infection is caused by Hepatitis A Virus (HAV) and is asymptomatic in approximately one-third of the patients. It spreads through the faeco-oral route and has an incubation period of 15-45 days. A month after the infection, patients typically experience the acute onset of symptoms that lasts for about 4 weeks. Patients with more severe symptoms have an increase in their serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin, which resolve over 4 to 6 months.
- **Hepatitis B:** Hepatitis B infection is caused by Hepatitis B Virus (HBV). It spreads through the parenteral route or by intimate contact with the infected person and has an incubation period of 30-180 days. Acute hepatitis occurs in others with progression to fulminant hepatitis in less than 1%. Acute hepatitis B is typically associated with high elevations in AST and ALT (more than a 100-fold increase over normal) and bilirubin (20-fold increase over normal).
- **Hepatitis C:** Hepatitis C infections are caused by Hepatitis C Virus (HCV). It spreads parenteral route or by close contact and has an incubation period of 20-90 days. Serum AST, ALT, and bilirubin increase in acute hepatitis C infection, but the increase tends not to be as high as in hepatitis B.
- **Hepatitis D:** Hepatitis D infections are caused by Hepatitis D Virus (HDV). It spreads by parenteral route or by close contact and has an incubation period of 30-50 days.
- **Hepatitis E:** Hepatitis E infections are caused by Hepatitis E Virus (HEV). It is water-borne and has an incubation period of 20-90 days.
- **Hepatitis G:** Hepatitis G infections are caused by Hepatitis G Virus (HGV). It spreads through the percutaneous route and has an incubation period of 14-35 days.

Drug-Induced Hepatitis

Several medicines have been reported to cause liver injury as an adverse drug reaction. Drugs that cause liver injury are Amitriptyline, Amiodarone, Hormonal Contraceptives, Ibuprofen, Isoniazid, Rifampicin, Pyrazinamide, Methotrexate, Methyldopa, Phenytoin, and Valproic acid.

Clinical Presentations

Viral Hepatitis

Hepatitis A is associated with the abrupt onset of symptoms, including.

- Fever
- Nausea
- Anorexia
- Diarrhea
- Fatigue
- Malaise
- Abdominal discomfort
- Dark urine
- Jaundice

The severity of illness appears to be age-dependent. In most cases, children have no symptoms, whereas adults usually experience symptoms and experience jaundice.

Hepatitis B and C: After the incubation period, patients who become symptomatic may develop nonspecific, flu-like symptoms such as malaise, fatigue, weakness, anorexia, nausea, vomiting, and pain in the right upper part of the abdomen. These symptoms start about a week before the jaundice develops. The onset of clinical symptoms is insidious and usually continues for a few weeks after the development of dark urine, jaundice, and elevated serum bilirubin values.

Chronic hepatitis: The most common symptoms of chronic hepatitis are fatigue, weakness, and malaise. Some patients experience tenderness in the right upper part of the abdomen, nausea, anorexia, and muscle or joint pain. Once cirrhosis develops, the fatigue, anorexia, weight loss, and weakness become more severe. Also, patients may develop ascites, jaundice, muscle wasting, hepatic encephalopathy, and esophageal varices. A small group of patients may develop extrahepatic symptoms of chronic viral hepatitis, such as arthritis and urticaria.

Drug-Induced hepatitis: The signs and symptoms of drug-induced hepatitis are highly variable and can present as acute or chronic disease. Patients may develop fever, rash, arthralgias, nausea, jaundice, abdominal complaints, lymphadenopathy, hepatomegaly, and eosinophilia. All patients have elevations in at least some liver tests (AST, ALT, alkaline phosphatase, and bilirubin). The magnitude of the elevations and the enzymes involved depend on the offending agent and the severity and stage of the liver damage.

Diagnosis

Viral Hepatitis

Hepatitis A: The diagnosis of acute hepatitis A cannot be made on clinical symptoms alone. Diagnosis is based on measurement of immunoglobulin M (IgM) antibodies to hepatitis A in the serum. Later, IgG antibodies to hepatitis A appear in the serum and protect against re-infection.

Hepatitis B: HBsAg can be measured in the serum 30 to 60 days after exposure to the hepatitis B virus. Antibodies against HBsAg develop in response to an infection with hepatitis B and provide long-term immunity. IgM antibodies against the hepatitis B core antigen also develop in response to an acute hepatitis B infection and persist for about 6 months. The IgM antibodies against the core antigen can be used as a marker for acute hepatitis B infection.

Hepatitis C: HCV infections can be diagnosed by the detection of antibodies against the HCV or HCV RNA in the patient's serum. Antibodies against hepatitis C can be measured 4 to 8 weeks after infection, but it depends on the assay. About 15% of patients who test positive for antibodies against hepatitis C will test negative for HCV RNA.

Drug-Induced Hepatitis

The diagnosis of drug-induced liver injury requires exclusion of other causes because the symptoms of drug-induced hepatitis can be quite similar to those of hepatitis from other origins. A comparison between the time course, frequency, and type of injury the patient is exhibiting and those that have been reported, helps determine the likelihood that a particular reaction is drug-induced.

Treatment

Non-pharmacological therapy: The development of end-stage liver disease and cirrhosis can be hastened in patients by alcohol consumption. So patients need to be counseled regarding the discontinuation of alcohol consumption.

Alternative therapies: Several clinical studies have reported positive results with silymarin (derived from the milk thistle plant), suggesting that it decreases complications and hastens recovery from hepatitis. Many studies were conducted evaluating the effects of medicinal herbs for the treatment of HCV infections. Only a few agents appear to show promising results in the treatment of hepatitis C, but due to limitations in the study design, it is not well known.

Pharmacotherapy

Viral Hepatitis

Hepatitis A- Pre-exposure Prophylaxis: The Centers for Disease Control currently recommends hepatitis A vaccination of persons over 2 years of age, travelling to areas with increased rates of hepatitis A. The inactivated hepatitis A vaccines should be administered into the deltoid muscle. The vaccine takes about 4 weeks to induce a protective immune response and lasts for at least 20 years.

Hepatitis A- Post-exposure Prophylaxis: Immune globulin prophylaxis for hepatitis A is recommended for patients with illegal sexual contact, sharing narcotic drugs with people infected with hepatitis A. Immune globulin more than 2 weeks after exposure is not recommended.

Hepatitis B- Pre-exposure Prophylaxis: Hepatitis B vaccine series is recommended in people at high risk for exposure to hepatitis B, such as infants born to infected mothers, infants/children of immigrants from areas with high rates of hepatitis B virus infection, persons sharing illegal drugs, health care and public safety workers, and patients on hemodialysis.

Hepatitis B- Post-exposure Prophylaxis: Hepatitis B immune globulin (HBIG) is produced from plasma that contains high titers of antibody against HBsAg. It is used to provide passive immunity against hepatitis B infection. Because HBIG provides only short-term protection against hepatitis B, the hepatitis B vaccine series or booster doses should also be given to these patients as appropriate. HBIG (0.06 m//kg for adults and children) should be administered through IM injection, preferably into the deltoid muscle or the anteroposterior aspect of the thigh, as soon after exposure to the hepatitis B virus.

The hepatitis B vaccine is a recombinant product in which common baker's yeast is used to produce a noninfectious subunit of HBsAg. The series of three IM injections (second and third doses are given 1 and 6 months, respectively, after the first dose) produces an adequate antibody response in adults and children. The deltoid muscle is the recommended location for injection for adults and children because injections into the buttocks produce a lower response rate. The anterolateral thigh muscle should be used for infants and neonates.

Chronic Hepatitis B

Interferon was the first approved agent used to treat chronic hepatitis B. Several types of interferons are commercially available, like interferon alpha-2a and α -2 b, interferon alfacon-1, interferon β -1a and β -1b, and interferon γ -1b. Interferon has antiviral and immune stimulatory properties and may be beneficial in treating viral hepatitis. Interferon α -2b at a dose of 5 million international units (IU) subcutaneously daily or 10 million IU three times weekly for 16 weeks for HBeAg-positive patients and 12 months for HBeAg-negative patients has been used to treat chronic hepatitis B infection with some success. Interferon treatment is associated with flu-like symptoms (fever, fatigue, headache, and myalgia) in some patients. Administering interferon at bedtime improves tolerability to this drug. Some patients also have photosensitivity reactions while on interferon and should be encouraged to use sunscreen and protective clothing.

Lamivudine, an antiviral drug, is an irreversible inhibitor of reverse transcriptase that blocks hepatitis B viral replication. Chronic hepatitis B treatment in HBeAg-positive patients with lamivudine 100 mg daily per oral results in loss of HBeAg, normalization of ALT, and histologic improvement. The greatest concern with lamivudine use is the high incidence of hepatitis B viral mutation and drug resistance. The most common adverse effects of lamivudine are headache, malaise, fatigue, nausea, vomiting, diarrhea, neuropathy, cough, congestion, and musculoskeletal pain. Dose adjustments must be made for patients with renal insufficiency.

Adefovir is an acyclic nucleotide analogue with antiviral activity against hepatitis B. In HBeAg-positive and HBeAg-negative patients, Adefovir 10 mg daily is used in the treatment of chronic hepatitis B. The most common adverse effects associated with adefovir are nausea, diarrhea, vomiting, dyspepsia, headache, and weakness. Pruritus and rash have also been reported.

Entecavir is a guanosine nucleoside analog with selective activity against the hepatitis B virus. Entecavir has been approved by the FDA at a dose of 0.5 mg orally once a day or in lamivudine-resistant patients at a dose of 1 mg orally once a day.

Hepatitis C

For those patients who have not previously been treated for hepatitis C and have chronic hepatitis C genotype 1, peginterferon (a-2a or a-2b) plus ribavirin 1,000 to 1,200 mg per day results in sustained viral response (SVR) and is superior to conventional interferon plus ribavirin treatment. For patients with genotypes 2 or 3, interferon (conventional or pegylated) plus a lower dose of ribavirin at 800 mg per day may result in sustained viral response in most patients. Ribavirin is highly teratogenic and embryotoxic, and therefore should not be used in women who are pregnant or in men whose female partners are pregnant. Major side effects of combination treatment include flu-like symptoms(headache, fever, fatigue, myalgia, nausea), hematologic side effects (anaemia, leukopenia, thrombocytopenia), and depression.

Drug-Induced Hepatitis

The most important step that can be taken in a suspected clinically significant drug-induced liver injury is discontinuation of the offending agent. Management of the liver injury should be supportive.

Patient Counseling in Hepatitis

- ***Knowledge about the disease and transmission:*** Patient must be provided information about Hepatitis disease and also made aware of strategies to be implemented to reduce its transmission to others.
- ***Fluid intake:*** Plenty of fluid must be taken by the patients, as less intake of fluid may lead to dehydration.
- ***Diet:*** Avoid a fatty and oil-rich diet as digestion is improper during the disease condition. Also, avoid intake of protein protein-rich diet as it may lead to accumulation of proteins, which may lead to complications like hepatic encephalopathy.
- ***Alcohol consumption:*** The development of end-stage liver disease and cirrhosis can be hastened in patients by ethanol consumption. Thus, it is very important to counsel patients about discontinuation of alcohol consumption.
- ***Risk reduction plans:*** Risk Reduction Plans are the tools to initiate discussions with patients about risk behaviors and are a sample of strategies that may reduce the risk. Avoiding Injecting Drug Use (IDU), illegal sexual contacts, tattooing/body piercing, and alcohol reduction are the risk reduction strategies to prevent exposure to infection.

Avoidance of hepatotoxic and nephrotoxic drugs•

- Hepatotoxic drugs like acetaminophen should be avoided as they may cause liver toxicity and also the drugs used for the treatment of hepatitis, like anti-viral drugs, must be used with caution in patients with kidney damage, as they may lead to nephrotoxicity.