INFECTIOUS DISEASES

Pharmaceutical Microbiology

Second Year Pharm D.

Sunil Kardani
Department of Pharmacy
Sumandeep Vidyapeeth ,
Vadodara,Gujarat

Tuberculosis

Tuberculosis

Organ affected: Mainly Lungs, but can also affect brain, liver, kidney , spleen, intestine

Symptoms:

- Loss of appetite,
- weight loss,
- Fatigue,
- Night sweats,
- Persistent and worsening cough, may be with blood stain

Risk factor:

- contact with the active pulmonary TB patients.
- During coughing, sneezing, spiting, speaking and singing, there is an emission of thousand of droplets containing the pathogenic bacilli, which can transmit the disease to other

Tuberculosis

Causative agent: *Mycobacterium tuberculosis and*
Mycobacterium bovis, Mycobacteria

- *M. tuberculosis* is responsible for almost 90% of TB case worldwide.
- *M. tuberculosis* is a acid-fast bacilli, because it contains large amount of lipid and mycolic acid in its cell wall.
- So, when phagocytic cells engulf the *Mycobacterium tuberculosis,* it can not be destroyed in phagolysome because of this thick waxy mycolic acid capsule.
- *Mycobacterium Tuberculosis* can survive and multiply in phagocytic cell such as macrophages.
- *M. tuberculosis* also contain cord factor (trehalose dimycolate) which can disrupt the respiration of mitochondria in phagocytes and tissue cells.
- Therefore, *M. Tuberculosis* which contains cord factor are pathogenic and those which are lacking cord factor are not.

Tuberculosis

Pathogenesis:

- Disease begins when bacteria enters the air sac of the lungs, where they are rapidly ingested by macrophages, in which they will multiply.
- If left untreated, then cell-mediated immunity develops and T-lymphocytes migrates towards the bacilli in lung and then release the lymphokines.
- These lymphokine will attract more phagocytes at lung and will get accumulated.
- These will lead to formation of small, pearl-grey nodules made up of the bacilli, and layers of phagocyte and T-lymphocytes. This nodule, a type of granuloma, is known as **Tubercle.**
- In many instance, cell mediated immunity develops sufficiently and macrophage activating factor (MAF) activates the macrophages and which can arrest the growth of bacilli and suspend the tubercle expansion. So TB will remain subclinical and dormant bacilli may exist for lifetime unless it is eliminated by drug therapy

Tuberculosis

Pathogenesis :

- In 10 percent cases of untreated infection, cell-mediated immunity is not strong enough and hence can not inhibit the bacilli growth.
- Therefore, initial tubercle continue to develop and becomes larger. Within tubercle, macrophages and phagocytes begins to die and fuse with each other to form a amorphous cheese like mass (caseous necrosis).
- Even at this stage healing can occur known as calcification. But if infection progress then several tubercle coalesce to form an area of a dead tissue which is large enough to be detected by chest X-ray.
- As the area of dead tissue expands it erodes the wall of bronchus, thus bacilli begin to appear in sputum. If the blood vessels are eroded in the lungs then patient may cough the blood streaked sputum. Bacilli may migrate to other organs through blood and can cause the numerous secondary infection.
- Death may occur when a sound damage has occurred in lung and

Tuberculosis

Diagnosis:

1) Chest X-ray:

Mass of dead tissue in lungs can be visible in X-ray film

2) Tuberculin test (mantoux test):

Extract of a harmless protein isolated from M. tuberculosis, known as purified protein derivative, PPD, is administered 0.1 ml intradermally at forearm.

After 48 hrs site of injection is observed for induration i.e. swelling and hardening, which represent the positive test

3) Sputum analysis:

Detection of *M. tuberculosis* is a presumptive test for tuberculosis but for final confirmation isolation and identification of the acid fast bacilli is required. Microscopic Identification is done by acid-fast zheil-nelson staining method

Tuberculosis

Prevention:

Bacilllus Calmette-Guerin vaccine (BCG vaccine):

It's made up of live attenuated cells of *M. bovis.* Its given to the new born babies, o.1 ml intradermaly, once.

However, immunized person can give a false positive tuberculin test which can be misleading, hence vaccine is not used in the countries where the incidence of the TB is less i.e. US

Treatment:

Isoniazide, rifampicin, ethambutol and pyrazinamide are choice of medication in combination for period of many months or even more than a year because of the chronic nature of disease

Typhoid

Typhoid

Organ affected: Intestine

Symptoms:

- Rose spot on chest
- Continued fever
- Intestinal ulcer
- Inflammation of intestine
- Spleen enlargement

Risk factor:

- Unhygienic environment
- Consumption of the food contaminated by feces and urine of the infected persons
- Maintaining and following the hygiene condition is prime requirement for the prevention of disease

Typhoid

Causative agent:

- *Salmonella typhi* and *Salmonella paratyphi,* Facultative anaerobic gram-negative rod shape bacteria
- Over 2000 serovars of the salmonella exist, all of which are pathogenic for human and often for animals. These serovers can cause mainly three type of diseases i.e. typhoid, gastroentitis and septicemia, out of which typhoid occurs only in human and is caused by *S. typhi* and *S. paratypi* serovar.
- *Salmonella* bacteria are characterized by different combination of O-antigens and H-antigen. O-antigen is heat-stable outer membrane lipopolysaccharide, while H-antigen is heat-labile flagellar protein antigen.
- O-antigens are designated with numbers, i.e. 1 to 67, while H-antigen exhibits in two category, phase-I and phase-II. Phase-I H-antigen is designated with letters, a to z, and phase-II H-antigens are designated with numbers

Typhoid

Pathogenesis:

- Disease begins when bacteria reaches the small intestine, where they attach with the epithelium of the intestinal wall, penetrate this layer, multiply, and eventually reach to the blood stream.
- In blood, complement lyse the bacteria, which liberate the endotoxins responsible for the generalized symptom of the disease i.e. fever
- Bacteria also undergoes multiplication in the macrophages within blood. Some the bacterial cells pass from liver to gall bladder and bile ducts and are secreted in intestine where they establish secondary infection and may cause diarrhea

Typhoid

Diagnosis:

1) Widal test:

   It is an agglutination reaction in which typhoid bacilli is mixed with patient's serum which contains the antibody against typhoid bacilli, and hence will give the agglutination, indicating a positive test

2) Isolation and identification of organism from the blood sample after 1 to 2 weeks and from the stools samples after 2-3 weeks

Typhoid

Prevention:

- Live, oral Ty21a vaccine and the injectable Typhoid polysaccharide vaccine are the newly licensed typhoid vaccine.
- It is recommended for travellers to areas where typhoid is endemic.
- Boosters are recommended every five years for the oral vaccine and every two years for the injectable form.
- There exists an older, killed-whole-cell TAB vaccine that is still used in countries where the newer preparations are not available, but this vaccine is no longer recommended for use because it has a higher rate of side effects (mainly pain and inflammation at the site of the injection).

Typhoid

Treatment:

- Ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, amoxicillin and ciprofloxacin, is commonly used to treat typhoid.
- In case of resistance to above mentioned antibiotics, third generation cephalosporins is used i.e. ceftriaxone, cefotaxime or cefixime

Cholera

Cholera

- Cholera is disease of antiquity and has been the cause of suffering and death.
- In history, cholera has cause a series of six great pandemic between 1817 to 1923.
- since then, in twentieth century cholera is almost eradicated mainly because of the improved sanitation and hygiene living

Cholera

Organ affected: systemic circulation

Symptoms:

- Vomiting
- Profuse diarrhea leading to severe dehydration
- Loss of mineral
- Acidosis
- Hypovolemia and increased hemoconcentration

Risk factor:

- Consumption of the food and water contaminated by patient excreta
- Improved sanitization and hygiene condition is prime requirement for the prevention of disease

Cholera

Causative agent:

- *Vibrio cholera,* Facultative anaerobic gram-negative rod shape bacteria
- *V. cholera* serovers contains the somatic O-antigen.
- The strain that cause epidemic and pandemic cholera belongs to serovar O1. it is further divided into two biovars: “el tor”, which hemolytic, and “classical”, which is not hemolytic.

Cholera

Pathogenesis:

- *Vibrio cholera* cause the complications through the cholera enterotoxin
- Cholera toxin consists of one A subunit and five B subunit. B subunit is responsible for the attachment of the toxin to the epithelial cells of the small intestine.
- The A subunit then penetrate the cell membrane and is cleaved into the fragment $A_{1,}$ which cause the alteration of the regulatory protein which governs the activity of adenylate cyclase enzyme in the cell.
- This enzyme is catalysing the conversion of ATP to cAMP.
- now, this altered regulatory protein is permanently “turned on”, which cause the continuous and higher production of cAMP.
- Higher level of cAMP will cause the loss of the water and electrolyte by intestinal cells into the lumen of the intestine, i.e. severe diarrhea

Cholera

Pathogenesis:

- as a result condition may get severely worsen that, patient may loss 10 to 12 liters of fluid per day by diarrhea, leading to the number of complications like loss of minerals, hypovolemia, increased hemoconcentration, and acidosis which can be fatal.

Cholera

Diagnosis:

- Diagnosis of cholera includes the Isolation and identification of organism from the diarrheal samples of the patient
- Agglutination test can also be performed in which cholera cells are agglutinated by O1 antiserum

Prevention:

Cholera vaccine:

Cholera vaccine is made up of dead cells of *Vibrio cholera* . Unfortunately, it provides protection only in 50% of the cases and immunity last only for 3-6 months.

So, prevention is mainly dependent on improved sanitation

Cholera

Treatment:

- Doxycycline is the first-line treatment of cholera, but, given only in severe cholera
- Oral rehydration therapy (ORT) is usually enough for the recovery or sometimes intravenous rehydration ma be necessary in case of severe cholera

Malaria

Malaria

- Malaria is a disease since antiquity and is described as the single greatest killer of the human race.
- Globally, malaria is the one of the most infectious diseases of the humans, causing much morbidity and significant mortality.
- Each year approximately 300 millions people are getting infected with malaria out of which around 3 millions victims die of it

Malaria

Organ/body part affected: RBC

Symptoms:

- Paroxysm - a cyclical occurrence of sudden coldness followed by shivering and then fever and sweating, occurring every two days (tertian fever) in *P. vivax* and *P. ovale* infections, and every three days (quartan fever) for *P. malariae*. *P. falciparum*
- Anemia
- Enlarged spleen
- Weakness, muscle pain
- Sweating, headache
- In severe case, edema of brain and lungs and blockage of kidney activity

Risk factor:

- (female anopheles)Mosquito bite
- Stagnant still water which can be major breeding area of mosquito

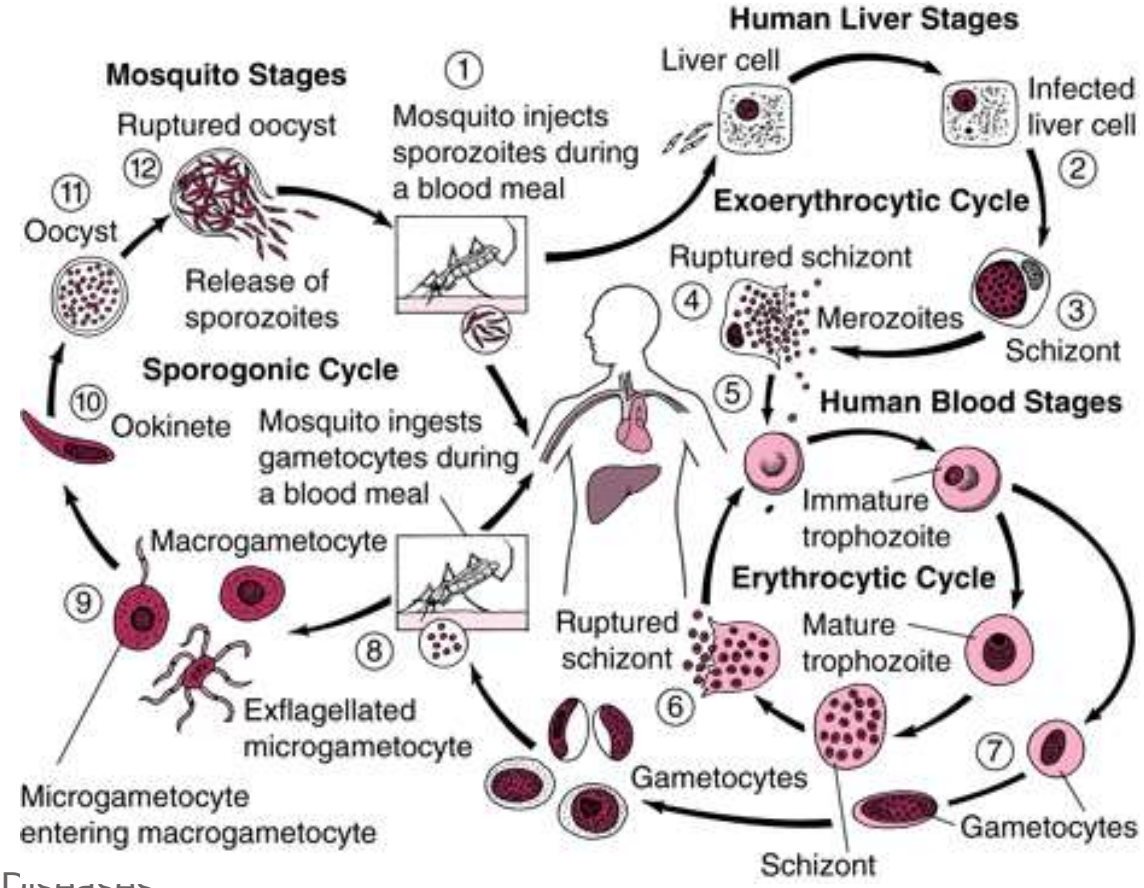
Malaria

Causative agent:

- Malaria is a protozoal disease which transmits through the arthropods, *anopheles* mosquito
- Malaria parasites belong to the genus *Plasmodium*. In humans, malaria is caused by *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax* and *P. knowlesi*.
- Among these, *P. falciparum* is the most threatening species, accounts for majority of malarial death.
- Among those infected, *P. falciparum* is the most common species identified (~75%) followed by *P. vivax* (~20%).

Malaria

Life cycle of malaria parasite



Malaria

Life cycle of malaria parasite:

- In the life cycle of *Plasmodium*, a female *Anopheles* mosquito (the definitive host) transmits a motile infective form (called the sporozoite) to a vertebrate host such as a human (the secondary host), thus acting as a transmission vector.
- A sporozoite travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue schizogony), producing thousands of merozoites.
- These infect new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that produce 8 to 24 new infective merozoites, at which point the cells burst and the infective cycle begins a new.
- Other merozoites develop into immature gametocytes, which are the precursors of male and female gametes.

Malaria

Life cycle of malaria parasite:

- When a fertilized mosquito bites an infected person, gametocytes are taken up with the blood and mature in the mosquito gut. The male and female gametocytes fuse and form a ookinete—a fertilized, motile zygote.
- Ookinetes develop into new sporozoites that migrate to the insect's salivary glands, ready to infect a new vertebrate host.
- The sporozoites are injected into the skin, in the saliva, when the mosquito takes a subsequent blood meal.
- Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar, and thus do not transmit the disease.
- The females of the *Anopheles* genus of mosquito prefer to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal.
- Malaria parasites can also be transmitted by blood transfusions, although this is rare.

Malaria

Pathogenesis:

- Disease starts when a infected female *Anopheles* mosquito bites a person, thus, injecting the sporozoites to the blood.
- During the life cycles, as described earlier, symptomatic phase occur when merozoites rupture the number of erythrocytes, causing the cold and shivering followed by the fever.
- Fever might be because of the pyrogens liberating from rupturing RBC
- Symptomatic phase usually last for 6 hr, followed by asymptomatic phase in which there is no sign of symptoms.
- After many such paroxysmal illness, spleen becomes enlarged and tender, eventually person become weak and exhausted and develop anemia.
- in case of *P. falciparum* symptomatic phase is more persistent and frequent, may cause edema of brain and lungs and blocking of kidney activity, abnormal posturing, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction),

Malaria

Diagnosis:

- Malaria can be diagnosed by demonstration of parasites in blood smear from patient
- Indirect immunofluorescent and indirect agglutination test can also be performed after two week of the infection, within which antibody level is sufficient to detect.

Prevention:

- Despite the efforts no efficient vaccine against malaria is developed yet.
- Prevention is mainly dependent on the elimination of the insect vector responsible for transmitting the disease, which can be done by destroying the mosquito breeding at larval and adult stage
- Using a mosquito net, mosquito repellent and insecticides is also important way of preventing the malaria

Malaria

Prevention:

Some antimalarial drugs are used as prophylactic purpose for the travelers to the malaria sensitive area. These includes…

- Chloroquine
- Mefloquine
- Doxycycline
- Atovaquone and proguanil hydrochloride

Malaria

Treatment:

- Artimisin is the first-line drug treatment for the treatment of malaria, but, to prevent the drug resistance it is given in combination with other drugs, that is known as a Artimisin – combination therapy or ACT.

  These additional drugs includes premaquine, mefloquine, amodiaquine, lumefentrine, or sulfadoxine/pyrimethamine,

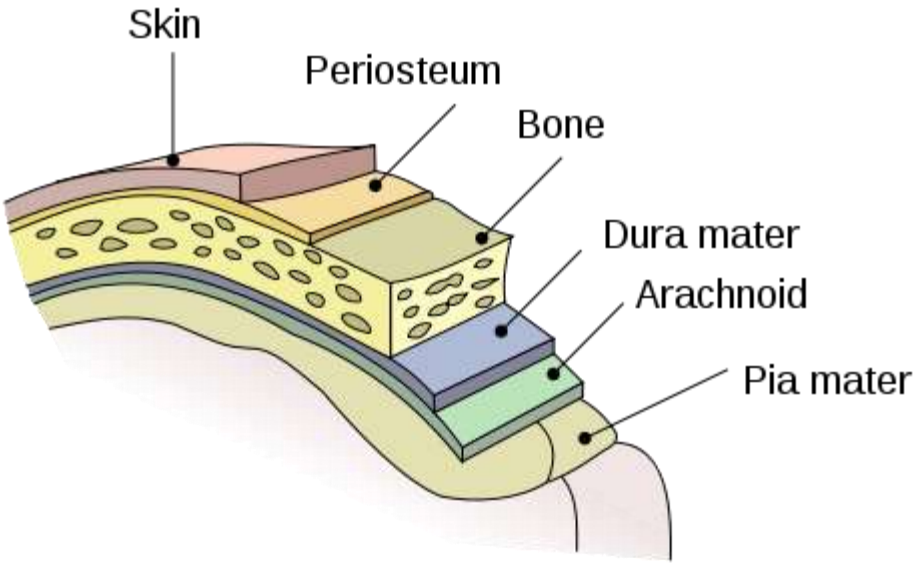
- Another combination therapy other than ACT include combination of dihydroartemisin and piperaquine
- In severe malaria artesunate is used intravenously

Meningitis

Meningitis

- **Meningitis** is an acute inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges.
- Meninges is made up of three layers, first and outer most dura mater, arachnoid and third inner most pia mater. Meninges together with CSF protects the CNS
- The inflammation may be caused by infection with viruses, bacteria, or other microorganisms, and less commonly by certain drugs.
- Meningitis can be life-threatening because of the inflammation's proximity to the brain and spinal cord; therefore, the condition is classified as a medical emergency.
- Meningitis mortality rate is very high, about 85% of the victims. Death can occur within the 24 hrs of the symptoms and hence immediate treatment is required

Meningitis



Meningitis

Organ/body part affected: Meninges

Symptoms:

- Excessive nasal secretion
- Sore throat
- Headache and neck stiffness associated with fever,
- Confusion or altered consciousness
- Vomiting
- Inability to tolerate light (photophobia) or loud noises (phonophobia)
- Skin rashes (sometimes)

Meningitis

Risk factor:

- Bacterial and viral meningitis are contagious; however, neither is as contagious as the common cold or flu.
- Both can be transmitted through droplets of respiratory secretions during close contact such as kissing, sneezing or coughing on someone, but cannot be spread by only breathing the air where a person with meningitis has been.

Meningitis

Causative agent:

Bacterial

- Premature babies and newborns: group *streptococci, Escherichia coli, Listeria monocytogenes*
- Children: ***Neisseria meningitidis*** **(meningococcus, aerobic gram negative capsulated diplococci)** and *Streptococcus pneumoniae, Haemophilus influenzae* type B
- Adults: *Neisseria meningitidis* and *Streptococcus pneumoniae*

Viral

- Viruses that cause meningitis include enteroviruses, herpes simplex virus type 2, varicella zoster virus (known for causing chickenpox and shingles), mumps virus, HIV.

Meningitis

Causative agent:

Fungal

- The most common fungal meningitis is cryptococcal meningitis due to *Cryptococcus neoformans*.

Non-infectious

- Spread of cancer to the meninges known as neoplastic meningitis
- Certain drugs can also cause meningitis, mainly non-steroidal anti-inflammatory drugs, antibiotics and intravenous immunoglobulins

Meningitis

Diagnosis:

Presumptive: demonstration of gram-negative diplococci in cerebrospinal fluid using a Gram-staining method

Confirmation: isolation of organism on pre-warmed plates of rich, blood containing medium

Meningitis

Prevention:

- MPSV(Meningococcal Polysaccharide Vaccine) and MCV Vaccine is given for the epidemic control of the meningococcal meningitis. It is made up of the purified capsular polysaccharides of serovars A and C; the serovar B capsular polysaccharides appears not to be highly immunogenic
- Routine vaccination against *Streptococcus pneumoniae* with the pneumococcal conjugate vaccine (PCV), which is active against seven common serotypes of this pathogen, significantly reduces the incidence of pneumococcal meningitis.
- HiB vaccine against *Haemophilus influenzae* type B, is routine childhood vaccination, as this bacterial species cause the meningitis mainly in children

Meningitis

Treatment:

Bacterial meningitis

- Third-generation cefalosporin such as cefotaxime or ceftriaxone.
- Chloramphenicol, either alone or in combination with ampicillin

Viral meningitis

- Aciclovir

Fungal meningitis

- amphotericin B and flucytosine

Hepatitis

Hepatitis

Organ/body part affected: Liver

- **Hepatitis** is a medical condition defined by the inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the liver
- Hepatitis is acute when it lasts less than six months and chronic when it persists longer. The condition can be self-limiting (healing on its own) or can progress to **fibrosis** (scarring), **cirrhosis** and may even **liver cancer** .
- Fibrosis is the formation of excess fibrous connective tissue in an organ or tissue in a reparative or reactive process.
- Cirrhosis is characterized by replacement of liver tissue by fibrosis (scar tissue) and regenerative nodules (lumps that occur due to attempted

Hepatitis

Symptoms:

- nonspecific flu-like symptoms:
  - Malaise,
  - Muscle and joint aches,
  - Fever, nausea or vomiting,
  - Diarrhea, and headache.
- Specific symptoms:
  - Profound loss of appetite,
  - Aversion to smoking among smokers,
  - Dark urine,
  - Yellowing of the eyes and skin (jaundice)
  - Abdominal discomfort,
  - Tender enlargement of the liver,
  - Enlarged lymph nodes (rare),
  - Enlargement of the spleen.

- A small proportion of people with acute hepatitis progress to acute liver failure, in which the liver is unable to remove harmful substances from the blood

Hepatitis

Risk factor:

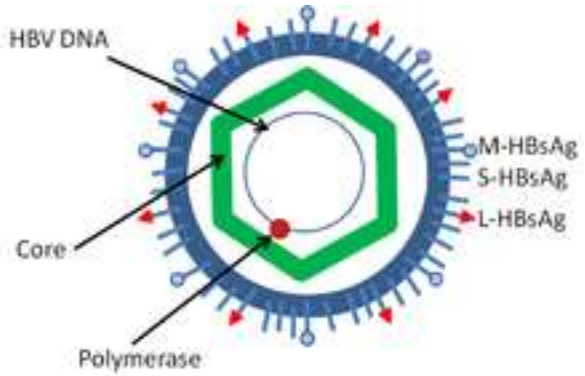
- **Hepatitis virus**, is main risk factor involved in hepatitis.
- Viruses most often transmitted sexually and transfusion of contaminated blood or blood product.
- The disease does not affect the sexual organs, but is highly contagious in its early stages, especially from sexual intimacy, and even kissing.
- Other risk factors include **autoimmune diseases** and ingestion of toxic substances; notably **alcohol,** and certain **medications**

Hepatitis

Causative agents:

Viral hepatitis

- The most common causes of viral hepatitis are the five unrelated hepatotropic viruses hepatitis A, hepatitis B, hepatitis C, hepatitis D (which requires hepatitis B to cause disease), and hepatitis E.
- **Hepatitis B virus** (species of the genus *Orthohepadnavirus*), is most common and threatening amongst other which causes between one and two million deaths per year.



Hepatitis

Pathogenesis:

The specific mechanism varies and depends on the underlying cause for the condition.

Viral hepatitis:

Presence of the virus in the liver cells causes the immune system to attack the liver, resulting in inflammation and impaired function.

Autoimmune hepatitis:

Immune system attacks the liver due to the autoimmune disease.

Hepatitis caused by alcoholism:

Fat deposits accumulate in the liver, resulting in fatty liver disease, also called steatohepatitis.

Hepatitis

Diagnosis:

- Diagnosis is made by assessing an individual's symptoms, physical exam, and medical history, in conjunction with blood tests, liver biopsy, and imaging.
- Blood testing includes **blood chemistry**, **liver enzymes** and **serology** testing.
- Abnormalities in blood chemistry and liver enzymes results may be indicative of certain etiologies or stages of hepatitis.
- These includes, Alanine transaminase (ALT), Aspartate transaminase (AST), Bilirubin, Alkaline phosphatase, Prothrombin time, Albumin, Gamma-glutamyl transpeptidase (GGT), Bile acids, and Lactate dehydrogenase.
- Serology test includes the detection of the HBsAg in a serum using specific antibody by RIA or ELISA

Hepatitis

Prevention:

Vaccines are available to prevent hepatitis A and B.

Hepatitis A vaccine:

- Immunity is achieved in 99-100% of persons receiving the two-dose inactivated virus vaccine.
- The hepatitis A vaccine is not approved for children under one year of age.

Hepatitis B vaccine:

- It's a recombinant vaccine made up of highly pure and isolated hepatitis B surface antigen, HBsAg.
- Its available since 1986 and have been incorporated into at least 177 national immunization programs for children.

Hepatitis

Prevention:

- Immunity is achieved in greater than 95% of children and young adults receiving the three-dose recombinant virus vaccine.
- Vaccination within 24 hours of birth can prevent transmission from an infected mother.
- The World Health Organization recommends vaccination of all children, particularly newborns in countries where hepatitis B is common to prevent transmission from the mother to child.

Hepatitis

Treatment:

- Acute hepatitis B infection does not usually require treatment and most adults clear the infection spontaneously.
- On the other hand, treatment of chronic infection may be necessary to reduce the risk of cirrhosis and liver cancer.
- Although none of the available drugs can clear the infection, they can stop the virus from replicating, thus minimizing liver damage.
- As of 2008, there are some antiviral drugs licensed for treatment of hepatitis. These include **Lamivudine, Adefovir, Tenofovir, Telbivudine And Entecavir**, and immune system modulators **Interferon alpha-2a**

HIV/AIDS

HIV

- **Human immunodeficiency virus infection / acquired immunodeficiency syndrome** (**HIV/AIDS**) is a disease of the human immune system caused by infection with human immunodeficiency virus (HIV).
- The term HIV/AIDS represents the entire range of disease caused by the human immunodeficiency virus from early infection to late stage symptoms.
- During the initial infection, a person may experience a brief period of flu-like symptoms. This is typically followed by a prolonged period without symptoms.
- As the illness progresses, it interferes more and more with the immune system, making the person much more likely to get infections, including opportunistic infections and tumors that do not usually affect people who have working immune systems.

HIV

- Without treatment, the average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype.
- AIDS was first recognized in 1981 and its cause—HIV infection—was identified in the early part of the decade (1984).
- Since its discovery, AIDS has caused an estimated 36 million deaths worldwide. As of 2012, approximately 35.3 million people are living with HIV globally.
- HIV/AIDS is considered a pandemic—a disease outbreak which is present over a large area and is actively spreading.

HIV

Symptoms:

Acute infection

- The initial period following the HIV infection is called acute HIV, In which many individuals develop a flu-like symptoms, 2–4 weeks post exposure while others have no significant symptoms.
- most common acute symptoms include fever, large tender lymph nodes, throat inflammation, a rash, headache, and/or sores of the mouth and genitals.
- Due to their nonspecific character, these symptoms are not often recognized as signs of HIV infection, and are often misdiagnosed as one of the many common infectious diseases with overlapping symptoms.

HIV

Symptoms:

Clinical latency/Chronic HIV

- Acute HIV is followed by a clinical latency or chronic HIV, which can last from about 03 years to over 20 years without treatment.
  - fever,
  - weight loss,
  - gastrointestinal problems,
  - muscle pains,
  - persistent generalized lymphadenopathy

HIV

Symptoms:

Acquired immunodeficiency syndrome

- Acquired immunodeficiency syndrome (AIDS) is defined in terms of either a $CD4^+$ T cell count below 200 cells/μL or the occurrence of specific diseases in association with an HIV infection.
- Without specific treatment, 50% of people infected with HIV develop AIDS within ten years.
- The most common initial conditions that alert to the presence of AIDS are pneumocystis pneumonia, cachexia, esophageal candidiasis and recurring respiratory tract infections.
- Opportunistic infections may be caused by bacteria, viruses, fungi and parasites that are normally controlled by the immune system.

HIV

Symptoms:

Acquired immunodeficiency syndrome

- People with AIDS have an increased risk of developing various viral induced cancers including Kaposi's sarcoma, Burkitt's lymphoma, primary central nervous system lymphoma, and cervical cancer.
- Additionally, people with AIDS frequently have systemic symptoms such as prolonged fevers, sweats (particularly at night), swollen lymph nodes, chills, weakness, weight loss and diarrhea.

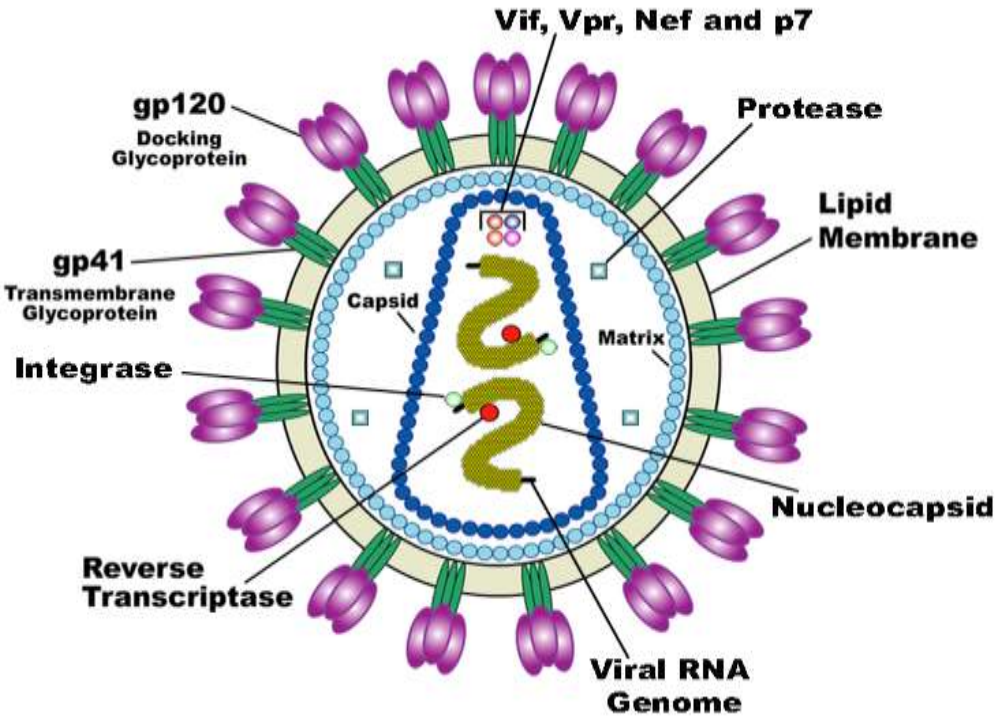
HIV

Risk factor/Transmission:

- Unprotected sexual contact
- Contaminated blood transfusions
- Contaminated hypodermic needles,
- HIV-positive mother to child during pregnancy and breastfeeding.
- However, some bodily fluids, such as feces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomit do not transmit HIV, unless these are contaminated with blood.

HIV

Causative agents:



HIV

Causative agents:

- HIV is a retrovirus, member of the genus *Lentivirus*, part of the family *Retroviridae*.
- Two types of HIV have been characterized: HIV-1 and HIV-2.
- HIV-1 is the virus that was originally discovered (and initially referred to also as HTLV-III). It is more virulent, more infective, and is the cause of the majority of HIV infections globally.
- The lower infectivity of HIV-2 as compared with HIV-1 is because of its relatively poor capacity for transmission, so, HIV-2 is largely confined to West Africa.

HIV

Pathogenesis:

- HIV are transmitted as single-stranded, enveloped RNA viruses. Upon entry into the target cell, the viral RNA genome is converted (reverse transcribed) into double-stranded DNA by a virally encoded reverse transcriptase that is transported along with the viral genome in the virus particle.
- The resulting viral DNA is then imported into the cell nucleus and integrated into the cellular DNA by a virally encoded integrase and host co-factors.
- Once integrated, the virus may become latent, allowing the virus and its host cell to avoid detection by the immune system. Alternatively, the virus may be transcribed, producing new RNA genomes and viral proteins that are packaged and released from the cell as new virus particles that begin the replication cycle anew.

HIV

Pathogenesis:

- After the virus enters the body there is a period of rapid viral replication, leading to an abundance of virus in the peripheral blood.
- During primary infection, the level of HIV may reach several million virus particles per milliliter of blood.
- During the acute phase, HIV-induced cell lysis and killing of infected cells by cytotoxic T cells accounts for $CD4^+$ T cell depletion, although apoptosis may also be a factor.
- During the chronic phase, gradual loss of the ability of the immune system to generate new CD4 cells appear to account for the slow decline in $CD4^+$ T cell numbers.
- Ultimately, HIV causes AIDS by depleting $CD4^+$ T cells. This weakens the immune system and allows opportunistic infections.
- T cells are essential to the immune response and without them, the body cannot fight infections or kill cancerous cells.

HIV

Diagnosis:

ELISA:

- antibody produced against the HIV, within the 3 to 12 weeks of the infection, can be detected by ELISA

CD4 count:

- CD4 level is an important parameter for the diagnosis of HIV. CDC have framed a classification system for HIV in 2008 as per following

  Stage 1: CD4 count ≥ 500 cells/µl and no AIDS defining conditions

  Stage 2: CD4 count 200 to 500 cells/µl and no AIDS defining conditions

  Stage 3: CD4 count ≤ 200 cells/µl or AIDS defining conditions

HIV RNA copies:

- Using a PCR, HIV RNA copies can be determined, and if found elevated, then can be concluded as positive HIV

HIV

Prevention:

- There is no effective vaccine against HIV as of today
- So, preventing the all possible mode of transmission of HIV is the only way to prevent the HIV infection, by …..
  - Using protection during sexual contact
  - Preventing the vertical transmission (mother to fetus)
  - Checking the sterility of blood, blood product, neddles etc. intravenous products

HIV

Treatment:

- Currently, there is no effective cure for HIV
- high active antiretroviral therapy (HAART) is the treatment for HIV, which slows progression of the disease rather than curing it.
- HAART is a combinations consisting of at least three medications belonging to at least two types of antiretroviral agents.
- Initially treatment is typically a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside analogue reverse transcriptase inhibitors (NRTIs). Typical NRTIs include: **zidovudine or tenofovir** and **lamivudine or emtricitabine**.
- Combinations of agents which include a protease inhibitors (PI) are used if the above regimen loses effectiveness.

Syphilis

Syphilis

- **Syphilis** is a sexually transmitted infection caused by the spirochete bacterium *Treponema pallidum* subspecies *pallidum*.
- The primary route of transmission is through sexual contact; it may also be transmitted from mother to fetus during pregnancy or at birth, resulting in congenital syphilis.
- Syphilis is thought to have infected 12 million additional people worldwide in 1999, with greater than 90% of cases in the developing world.
- After decreasing dramatically since the widespread availability of penicillin in the 1940s, rates of infection have increased since the turn of the millennium in many countries, often in combination with human immunodeficiency virus (HIV).

Syphilis

Symptoms:

Syphilis can present in one of four different stages: **primary, secondary, latent**, and **tertiary**, and may also occur **congenitally**.

Primary stage

- Primary syphilis is typically acquired by direct sexual contact with the infectious lesions of another person.
- Approximately 3 to 90 days after the initial exposure (average 21 days) a skin lesion, called a **chancre**, appears at the point of contact, mainly genitals in men and cervix in women.
- Chancre is a single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders between 0.3 and 3.0 cm in size.
- Occasionally, multiple lesions may be present when coinfected with HIV. Lesions may be painful or tender and may occur outside of the genitals.

Syphilis

Symptoms:

Secondary stage

- Secondary syphilis occurs approximately four to ten weeks after the primary infection and affects the skin, mucous membranes, and lymph nodes.
- There may be a symmetrical, reddish-pink, non-itchy rashes on the trunk and extremities, including the palms and soles.
- Other symptoms may include fever, sore throat, malaise, weight loss, hair loss, and headache.

Syphilis

Symptoms:

Latent stage

- Latent syphilis is defined as having serologic proof of infection, that means presence of syphilis specific antibody in blood.
- Latent stage is usually without symptoms of disease (asymptomatic), and not as contagious as early latent syphilis

Syphilis

Symptoms:

Tertiary stage

- It may be divided into three different forms: gummatous syphilis, late neurosyphilis, and cardiovascular syphilis. People with tertiary syphilis are not infectious.
- Gummatous syphilis or late benign syphilis usually occurs 1 to 46 years after the initial infection, with an average of 15 years. This stage is characterized by the formation of chronic **Gummas**, which are soft, tumor-like balls of inflammation which may vary considerably in size. They typically affect the skin, bone, and liver, but can occur anywhere.
- Neurosyphilis refers to an infection involving the central nervous system. Neurosyphilis typically occurs 4 to 25 years after the initial infection.
- Cardiovascular syphilis usually occurs 10–30 years after the initial infection. The most common complication is syphilitic aortitis

Syphilis

Causative agent:

- *Treponema pallidum* is a spiral-shaped, Gram-negative, highly mobile bacterium.
- It is unable to survive without a host for more than a few days. This is due to its small genome failing to encode the metabolic pathways necessary to make most of its macronutrients.
- It has a slow doubling time of greater than 30 hours

Transmission

- Syphilis is transmitted primarily by sexual contact or during pregnancy from a mother to her fetus; the spirochete is able to pass through intact mucous membranes or compromised skin. It is thus transmissible by kissing near a lesion, as well as all form of penetrative sex.
- Syphilis cannot be contracted through toilet seats, daily activities, hot tubs, or sharing eating utensils or clothing.

Syphilis

prevention:

- There is no effective vaccine against HIV as of today
- So, preventing the all possible mode of transmission of *Treponema pallisum* is the only way to prevent the HIV infection, by …..
  - Using protection during sexual contact
  - Preventing the vertical transmission (mother to fetus)

Syphilis

Diagnosis:

Syphilis is difficult to diagnose clinically early in its presentation. Confirmation is either via blood tests or direct visual inspection using microscopy.

Blood tests

- Generally nontreponemal test, venereal disease research laboratory (**VDRL**) and **rapid plasma reagin**, are used for the diagnosis.
- However, as these tests are occasionally false positives, hence, confirmation is required with a treponemal test, such as **treponemal pallidum particle agglutination (TPHA)** or **fluorescent treponemal antibody absorption test (FTA-Abs)**.

Direct testing

- **Dark field microscopy** of serous fluid from a chancre may be used to detect the *Treponema pallidum* spirochetes, as an immediate diagnosis.

Syphilis

Treatment:

- The first-choice treatment for uncomplicated syphilis remains a single dose of intramuscular **penicillin G** or a single dose of oral **azithromycin**.
- **Doxycycline** and **tetracycline** are alternative choices; however, due to the risk of birth defects these are not recommended for pregnant women.
- **Ceftriaxone**, a third-generation cephalosporin antibiotic is used in case of resistant infection

Gonorrhea

Gonorrhea

Symptoms:

- Half of women with gonorrhea are asymptomatic, whereas others have vaginal discharge, lower abdominal pain or pain with intercourse.
- Most infected men have symptoms such as urethritis (inflammation of urethra) associated with burning with urination and discharge from the penis.

Gonorrhea

Causative agent:

- Gonorrhea is caused by the bacterium *Neisseria gonorrhea*, which is Gram negative diplococci.
- The infection is transmitted from one person to another through unprotected sexual contact.
- A mother may transmit gonorrhea to her newborn during childbirth; when affecting the infant's eyes, it is referred to as ophthalmia neonatorum.
- It cannot be spread by toilets or bathrooms.

Gonorrhea

Diagnosis:

- **Gram staining** method is used for the demonstration of pink stained diplococci, suggesting the positive indication of gonorrhea.
- **Thayer-Martin culture media** is also used to grow the *Neisseria gonorrhea.* This media is selective media for the *Neisseria gonorrhea*, hence, only they can grow on this media.
- Now days **polymerase chain reaction (PCR)**-based testing methods are becoming more common for the diagnosis of Gonorrhea.

Gonorrhea

Prevention:

- Using a proper protection during a sexual contact is the only way to prevent the disease.

Treatment:

- **Ceftriaxone** in combination with either **azithromycin** or **doxycycline** given as a treatment of the gonorrhea.