Unit-V

INFECTIOUS DISEASES:

* **Meningitis:** Meningitis is inflammatory involvement of the meninges.

- Meningitis may involve the dura mater c/a pachymeningitis, or the leptomeninges (pia-arachnoid) termed as leptomeningitis.
- **Classification of meningitis:** Infectious meningitis is broadly classified into 3 types:
  1) Acute pyogenic meningitis
  2) Acute lymphocytic meningitis
  3) Chronic meningitis

1) **Acute pyogenic meningitis / Acute purulent meningitis:** It is the acute infection of the pia-arachnoid and of the CSF enclosed in the subarachnoid space.
   - **Gross anatomy:** Pus accumulates in the subarachanoid space. So, that normally clear CSF becomes turbid or frankly purulent.
   - **Morphology:** There is presence of numerous polymorphonuclear neutrophils in the subarachanoid space as well as in the meninges, particularly around the blood vessels. There are Gram-staining microbes.
   - **Causative agent:** Escherichia coli, Haemophilus influenzae, Neisseria meningitis, Streptococcus pneumoniae.
   - **Clinical features:** Fever, severe headache, vomiting, coma, occasionally convulsions and stiffness of the neck on forward bending.

2) **Acute lymphocytic meningitis:** It is a viral or aseptic meningitis, especially common in children and young adults.
   - **Causative agents:** viruses such as enteroviruses, mumps, ECHO viruses, herpes simplex virus-2 and HIV etc.
   - **Gross anatomy:** Some cases show swelling of the brain while others show no distinctive change.
   - **Morphology:** There is mild lymphocytic infilterate in the leptomeninges.
   - **Clinical features:** Viral meningitis has a benign and self-limiting clinical course of short duration and is invariably followed by complete recovery without the life-threatening complications of bacterial meningitis.

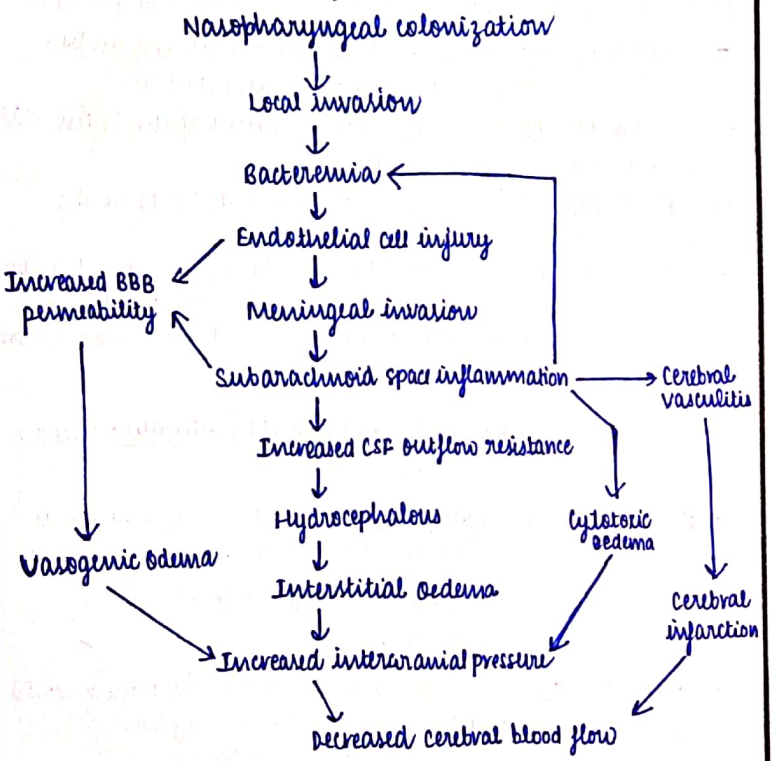
3) **Chronic (tuberculous and cryptococcal) meningitis:** There are 2 types of chronic meningitis:

   A) **Tuberculous meningitis:** It occurs in children and adults through haematogenous spread of infection from tuberculosis.

   B) **Cryptococcal meningitis:** It develops particularly in immunocompromised persons.

   - **Gross anatomy:** The subarachnoid space contains thick exudate in tuberculous meningitis. The exudate in cryptococcal meningitis is scanty, translucent and gelatinous.
   - **Morphology:** Tuberculous meningitis shows exudate of acute and chronic inflammatory cells, and granulomas with or without caseation necrosis and giant cells. Cryptococcal meningitis is characterised by infilteration by lymphocytes, plasma cells, an occasional granuloma and abundant characteristic capsulated cryptococci.

• **Pathophysiology of meningitis:**



* **Leprosy:** Leprosy or Hansen's disease, is a chronic non-fatal infectious disease.

• It mainly affects the cooler parts of the body such as the skin, mouth, respiratory tract, eye, peripheral nerves, superficial lymph nodes and testis. In leprosy, the earliest and main involvement is of the skin and nerves.

• **Causative agent:** The disease is caused by **Mycobacterium leprae**.

• **Classification:** Traditionally, 2 main forms of leprosy are distinguished:

A) Lepromatous type representing low resistance.

B) Tuberculoid type representing high resistance.

• **Sign and symptoms:**

I.) **Amyloidosis:** Formation of amyloid protein.

II.) **Peripheral neuritis:** It is the inflammation of peripheral nerve leads to blindness.

III.) **Skin lesions:**

a) **Macules** (It is the flat area less than 1cm of skin discolouration).

b) **Papules** (It is circumscribed elevated solid lesions).

c) **Nodules** (They are small fluid-filled or solid lump under the skin as in an organ).

IV.) **Lepra reaction:** It is an episode of acute inflammation in pre-existing lesion of the leprosy. It is of 2 types:

a) **Type I:** Reversal reaction

b) **Type II:** Erythema nodosum leprosum [characterized by

cutaneous nodules, fever, iridocyclitis (inflammation in iris and ciliary body), synovitis (inflammation in synovial membrane) and lymph node involvement, vasculitis (inflammation in blood vessels), panniculitis (group of disease characterized by inflammation of subcutaneous adipose tissue, weight loss, fatigue and skin nodules)].

- **Pathophysiology of leprosy:**

M. Lepraе enters the body (skin, nose etc).
↓ attack
peripheral nerve
↓
Binds to Schwann cells of axon
↓
Demyelination of nerve
↓
Loss of axonal conductance
↓
Deformity (loss of pain, temperature, touch and sensation).

- **Difference b/w lepromatous and tuberculoid leprosy:**

Features	Lepromatous leprosy	Tuberculoid leprosy
1.) Skin lesions	Symmetrical, multiple, hypopigmented, or erythematous, or maculopapular, or nodular lesions (leonine facies).	Assymetrical, single or a few lesions, well-defined, hypopigmented and erythematous, macular lesions.
2.) Nerve involvement	present but late and sensory disturbance is less severe.	present with distinct sensory disturbance
3.) Histopathology	Collection of foamy macrophages or lepra cells in the dermis separated from epidermis by a 'clear zone', lymphocytes absent or a few only.	Hard tubercle similar to granulomatous lesion, eroding the basal layer of epidermis; no clear zone, lymphocytes plenty.
4.) Bacteriology	Lepra cells highly positive for lepra bacilli seen as 'globi' or 'Cigarettes-in pack' appearance (multibacillary type).	Lepra bacilli few, seen in destroyed nerves as granular or beaded forms (paucibacillary type).
5.) Complications	Type 2 reactional leprosy (ENL) may occur.	Neurologic damage causing sensory loss and paralysis may occur
6.) Immunity	Suppressed (low resistance).	Good immune response (high resistance).
7.) Lepromin test	Negative	Positive
8.) Prognosis	Progressive disease, bad prognosis.	Milder disease, better prognosis.

- **Mode of transmission:** Leprosy is a slow communicable disease and the incubation period b/w first exposure and appearance of signs of disease varies from 2 to 20 years (average about 3 years).

The infection may be transmitted by following routes: (28)

A) Direct contact with untreated leprosy patients.
B) Materno-foetal transmission across the placenta.
C) Transmission from milk of leprosy affected mother to infant.

* **Typhoid**: It is an intestinal infection.

- **Causative agent**: Typhoid is caused by the bacilli *Salmonella typhi*.
- **Route of transmission**: Typhoid is transmitted by faeco-oral route.

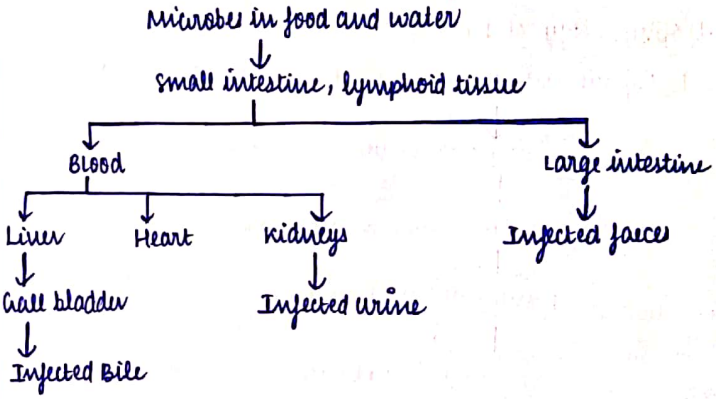


Fig: The route of microbes excretion in typhoid fever

- **Pathology**: Typhoid bacilli are ingested through contaminated food or water. During the initial asymptomatic incubation period of about 2 weeks, the bacilli invade the lymphoid follicles and Payer's patches (aggregated lymph follicle) of the small intestine and proliferate.
and ulcer is followed by bleeding.
- **Clinical symptoms:**
  - **From 1 to 7 days**: Typhoid fever alongwith headache, pain in the limbs, splenomegaly (↑ size of spleen), red spots on the skin

especially of the Chest and back of the human body, cough and bleeding of nose (epistaxis), pulse is weak and unexpected rise in body temperature (Diarrhoea and vomiting are noticed in children).

At the end of first week rashes appears on the abdomen.

- From the next 7 to 10 days: Yellow colour of spleen, At this time constipation is followed by diarrhoea, bronchitis, Deriliium (belief in non-existence circumstances), pneumonial (infection in alveali), meningitis (inflammation in brain covering layer), Typhoid Cholecystitis (inflammation in gall bladder).

- At 14 days: Toxaemia (bacterial toxicity in the blood), Myocarditis (inflammation of myocardium), Nephritis (inflammation in nephron), acute peritonitis (inflammation in peritoneum), chronic infection of gall bladder

- Diagnostic test for typhoid: Typhoid is diagnosed by the widal test.

- Pathophysiology of typhoid:

Predisposing factors:
- Age
- immuno-compromised
- medical history
- Geographical area

Etiology:
Ingestion of foods or fluids contaminated with S. typhi bacteria.

Precipitating Factors:
- Poor hand hygiene
- Eating food from outside.
- Unboiled / unpurified drinking water.

↓

Bacteria enter the stomach and survive a pH as low as 1.5.

↓

Bacteria invade the peyer's patches of the small intestinal wall (incubation period is first 7 to 14 days after ingestion).

↓

Enters bloodstream via lymphatics (peyer's patches)

↓

Inject toxin known as the effector proteins into the intestinal cells. → Symptoms: Abdominal cramps.

↓

Bacteria induced macrophage apoptosis, breaking out into the bloodstream and cause systemic infection.

↓

TYPHOID FEVER → Symptoms:
- High fever & chills.
- Rashes made up of flat, rose colored spots.
- Fatigue / weakness
- Body malaise
- Headache

↓

- Intestinal haemorrhage
- Typhoid psychosis
- Sepsis

* **Urinary tract infections:** UTI is an infection of any part of urinary system i.e., kidneys, ureters, bladder and urethra. Most infections involves the lower urinary tract- the bladder and the urethra.

- **Causative agents:** It is caused by Escherichia coli, chlamydia, mycoplasma etc.
- **Types of UTI:** If is of 3 types:

A) **Cystitis:** A urinary bladder infection. It includes low fever, pressure and cramping in the abdomen and lower back.

B) **Urethritis:** A urethra infection.

C) **Pyelonephritis:** It is a kidney infection. It may be severe. The symptoms are upper back and side pain, high fever, shaking chills, fatigue and mental changes.

- Womens are at greater risk of developing a UTI than are men. Among adults aged 20 to 50 years, UTI are about 50 times more common in women.
  - In females in this age group, most UTIs are cystitis or pyelonephritis.
  - In ♂ of the same age, most UTIs are urethritis or prostatitis.

- **Risk factors for UTIs:**

1) Sexual intercourse especially if more frequent, intense and with multiple or new partner.
2) Diabetes
3) Blocked flow of urine
4) Kidney stone
5) Pregnancy
6) Immobility for a long period.
7) use of spermicides.
8) Heavy use of antibiotics which can distrupt the natural flow of bowel and urinary tract.
9) Problem in emptying the bladder completely.
10) Poor personal hygiene.
11) Long lastening kidney infection can cause permanent damage and some sudden kidney infection can be life threatening particularly if the bacteria enters the blood stream. i.e., septicemia. They can also increase the risk of women delivering infants that are premature have a low birth weight.

- **Symptoms:** Strong and frequent urge of urination, muscle and abdominal pain.

Part of urinary tract infected	Sign and symptoms
• Kidney (acute pyelonephritis)	- Upper back and side (flank) pain. - High fever - Shaking and chills - Nausea - Vomiting
• Urinary bladder (cystitis)	- Pelvic pressure - Lower abdomen discomfort - Frequent, painful urination - Blood in urine and strong smelling urine
• Urethra (urethritis)	- Burning sensation during urination. - Discharge.

• Pathophysiology of urinary tract infection (UTI):

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Adhesion of uropathogenic E.Coli to renal parenchyma

↓

Effect of bacterial lipopolysaccharides (endotoxin release) with complement activation

- ← Release of cytokines (interleukin-6, interleukin-8 etc)
- → Intravascular neutrophil aggregation

↓

Chemotaxis of neutrophils

↓

Phagocytosis of bacteria

- ← Bacterial killing
- ← Release of toxic enzymes (lysozymes)
- ← Respiratory burst releasing superoxide (oxygen radicals)

↓

Renal tubular cells death (release of toxic inflammatory agents)

↓

Interstitial inflammation

↓

Renal scar

Intravascular neutrophil aggregation → Capillary obstruction → Renal ischemia → Reperfusion → Respiratory burst releasing superoxide (oxygen radicals)

*Tuberculosis:

• Tuberculosis is a communicable granulomatous disease. The tissue response to causative agent, Mycobacterium tuberculosis are presents classical example of chronic granulomatous inflammation in humans.

• Etiologic agents/causative agents: Tubercle bacillus (TB) or Koch's bacillus or Mycobacterium tuberculosis cause tuberculosis in human beings. In cow TB is caused by Mycobacterium bovis.

• Symptoms: Chronic cough with blood, tinged sputum, fever, night sweat, weight loss.

• Special characteristics: It is a chronic inflammatory disease due to formation of granuloma.

∵ GRANULOMA: It is defined as circumscribed, tiny lesions, about 1mm in diameter, composed predominantly of collection of modified macrophages called epithelioid cells, and rimmed at the periphery by lymphoid cells.

-The word "granuloma" is derived from "granule" meaning circumscribed granule-like lesion, and "-oma" which is a suffix commonly used for true tumours but here it indicates a localised inflammatory mass or collection of macrophages.

-Evolution of granuloma: Formation of granuloma is a type IV hypersensitivity reaction. It is a protective defense reaction by the host but eventually causes tissue destruction bcoz of persistence of the poorly digestible.

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The sequence in evolution of granuloma is schematically shown in given flow chart:

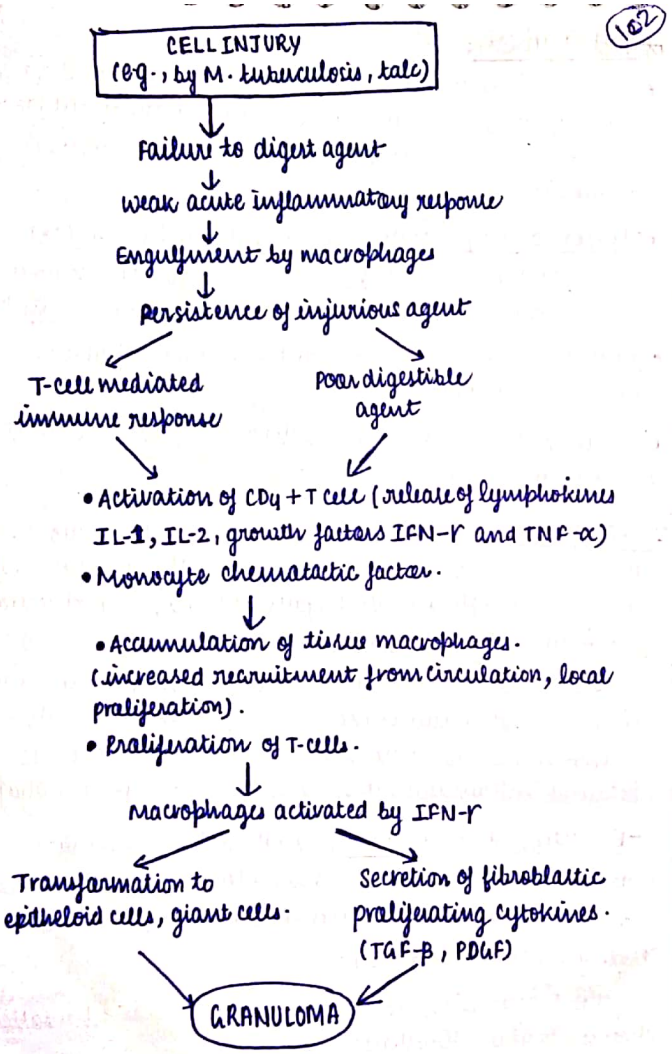


Fig: Pathogenesis of granuloma. (IL = Interleukin; IFN = Interferon; TNF = Tumour necrosis factor; TGF = transforming growth factor; PDGF = platelet-derived growth factor; CD = cluster of differentiation).

- Composition of granuloma: In general, a granuloma has the following structural composition:

1) Epitheloid cells: These are so c/a bcoz of their epithelial-cell like appearence. They are modified macrophages/ histocytes which are somewhat elongated cells having slipper-shaped and lightly stained nucleus.

2) Multi-nucleated giant cells: Multi-nucleated giant cells are formed by fusion of adjacent epitheloid cells and may have 20 or more nuclei. These nuclei may be arranged at the periphery like the horse-shoe or as a ring, or may be clustered at the 2 poles (Langhan's giant cells), or they may be present centrally (foreign body giant cells).

3) Lymphoid cells: As a cell-mediated immune reaction to antigen, the host response by lymphocytes (predominantly T-cells) is integral to composition of a granuloma. Plasma cells indicative of accelerated humoral immune response are ⊕nt in some types of granuloma. These cells are defined by absence of antigen specific B and T-cells receptors bcoz of lack of recombination activating gene.

4) Necrosis: Necrosis may be a feature of some granulomatous conditions e.g., central caseation necrosis in TB, so c/a bcoz of its dry cheese-like appearence.

5) **Fibrosis:** Fibrosis is a feature of healing of proliferating fibroblast at the periphery of granuloma.

**Note: Tubercle bacillus or Mycobacterium tuberculosis is the acid fast bacilli.

- **Spread of tuberculosis:** The disease spreads in the body by various routes:
  1) Local spread
  2) Lymphatic spread
  3) Haematogenous spread.

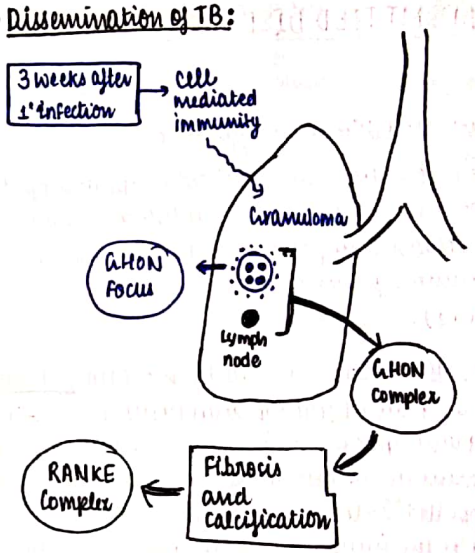
- **Pathophysiology of tuberculosis:**

M. tuberculosis infection
↓
Acquired immune response
↓

Delayed-type Hypersensitivity	Cellular immune response	Humoral immune response
↓	↓	↓
Skin induration after MTB antigens intradermal injection.	Memory T-cells, cytokine-chemokine expression upon stimulation with MTB antigen.	Immunoglobin expression towards MTB antigens.

∴ MTB = M. tuberculosis bacterium.

- **Dissemination of TB:**



Immune system compromised (due to AIDS or ageing)
↓
Spreads to upper lobes (oxigenation maximum)
↓
Memory T-cells releases cytokines
↓
Caseous necrosis
↓
CAVITATES
↓
TB spreads.

- **Transmission of tuberculosis:** Human being acquire infection with Tubercle bacilli by one of the following routes.
  1) Inhalation of organism ⊕nt in fresh cough droplet or dried sputum from an open case of TB.
  2) Ingestion of organism leads to development of tonsil or intestinal tuberculosis.
  3) Inoculation of organism into the skin may rarely occurs from infected post-mortum tissue.
  4) Transplacental route (from mother to child) results in development of con-genital TB in the foetus from infected mother and it is rare mode of transmission.

SEXUALLY TRANSMITTED DISEASES:

* AIDS: Acquired Immunodeficiency Syndrome

This syndrome is a condition characterized by the development of life threatening multiple opportunistic infection and uncommon form of malignant neoplasm in patient with severe depression of T-cell mediated immune system caused by HIV (Human immunodeficiency virus).

• **Etiologic/causative agent:** AIDs is caused by an RNA (retrovirus) virus called Human immunodeficiency virus (HIV). HIV produces the enzyme reverse transcriptase inside the cells of infected person. This enzyme transforms viral RNA to DNA and this new DNA is c/a provirus is incorporated into the host cell DNA. These cell then produces the new copies of the virus that infect other cells, when infected cells divide, copies of provirus are integrated into the DNA of daughter cells, spreading the disease within the body.

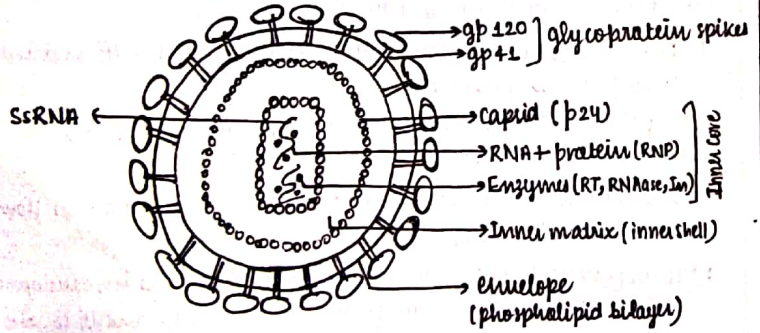


Fig: structure of retrovirus (eg. HIV)

- HIV contains 8 core proteins mainly p24, 2 strands of genomic RNA and RNA transcriptase enzyme.
- The core is covered by a double layer of lipid membrane derived from the outer membrane of the infected host cell during budding process of virus. The membrane is decorated with 2 enveloped glycoproteins (gp 120 and gp 41). Besides various other genes, 3 important gene codes for the respective components of virion:
  a.) **gag:** (group antigen for core protein)
  b.) **pol:** (polymerase enzyme for reverse transcriptase)
  c.) **env:** (for envelope protein).
- HIV has an affinity for cells having a protein receptor c/a CD_4 in their membrane including T-cells, monocytes and B-cells, macrophages in the GIT and neuron, neuroglial cells in the brain.

• **Major abnormalities in immune system in AIDs:**

1.) **T-cell abnormalities:**
- Lymphopenia (abnormal reduction in WBC (lymphocytes) in blood)
- CD_4 + T-cell depletion.
- CD_8 + T cell lymphocytosis
- Reversal of $CD_4 : CD_8$ cell ratio.
- Led production of cytokines by CD_4 + T cells.
- Led antibody dependent cellular cytotoxicity by CD_8 + T cells.

2.) **B-cell abnormalities:**
- Not infected, no viral damage
- Hypergamaglobulinaemia
- circulating immune complexes.

- ↓ed immunoglobulin production.

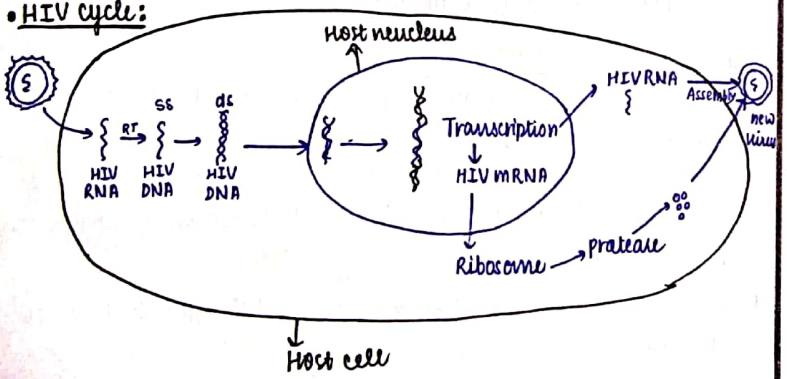
3.) **NK cell abnormalities:**
- Not infected, no viral damage.
- Depressed number, impaired function.
- Increased iNKRs, decreased cytotoxicity.

4.) **Monocyte-macrophage cell abnormalities:**
- No destruction.
- ↓ed chemotaxis
- Decreased phagocytosis
- ↓ed HLA class II expression
- ↓ed antigen presentation.

• **Symptoms:** Fever, chill, skin rashes, headache, weight loss, Anxiety and depression, nausea, diarrhoea.

• **Incubation period:** 7 to 10 years.

• **HIV cycle:**



Exposure of infected body fluids
↓
Infection with HIV (retrovirus)
↓
HIV invades nucleus of helper T-lymphocytes (CD_4 surface antigen)
↓
HIV replicates
↓
Destruction of lymphocytes
- helper T-cells → ↓ Immune suppression → Fever, Fatigue, weight loss; TB, pneumocystis, opportunistic infection
- HIV released from cell

→ AIDS.

Fig: pathophysiology of AIDs

• **Route of transmission:**
1.) Sexual contact with infected person
2.) Contaminated needle used.
3.) When drug user share needle.
4.) An infected mother to her child.
5.) Across the placenta before birth.
6.) From the breast milk.

* **Syphilis:** Syphilis is a venereal (sexually-transmitted) disease caused by spirochetes, Treponema pallidum, characterized by episodes of active disease interrupted by periods of latency.

- **Causative agents:** It is caused by the Treponema pallidum.
- **Stages of acquired syphilis:** Acquired syphilis is divided into 3 stages depending upon the period after which the lesions appear and the type of lesions:

I.) **Primary syphilis:** Typical lesions of primary syphilis is Chancre (painless open sore at the point of contact) which appears on genitals or extra-genital sites in 2 to 4 weeks after exposure to infection.

The later sign and symptoms such as skin rashes, mucosal ulceration of mouth and genital tract, fever, pain in joints and muscles.

II.) **Secondary syphilis:** (Systemic infection)

Inadequately treated patients of 1° syphilis develops the mucocutaneous lesions and painless lymphoadenopathy in 2 to 3 months after the exposure.

III.) **Tertiary syphilis:** Organ degeneration appears. Cardiovascular syphilis (involves thoracic aorta) and Neurosyphilis (meningo-vascular syphilis) occurs.

As motor areas become damaged extensively, victim may be unable to control urine and bowel movement. Damage to the cerebral cortex produces memory loss for a short period (dementia) & personality changes that ranges from irritability to hallucinations, still birth (not born alive) in case of congenital transmission.

T. pallidum infection
↓
1° syphilis
(Chancre and regional lymphoadenopathy)
↓
2° syphilis
(Disseminated rash, generalised lymphoadenopathy)
↓
Latent syphilis
(Recurrance of 2° syphilis symptoms)

72% → No further complications.

28% → Tertiary syphilis (cardiovascular syphilis, Neurosyphilis).

Fig; Pathogenesis of syphilis

- **Mode of transmission:**

A.) Sexual transmission is the most common route of infection and results in lesions on glans penis, vulva, vagina, cervix and rectum.

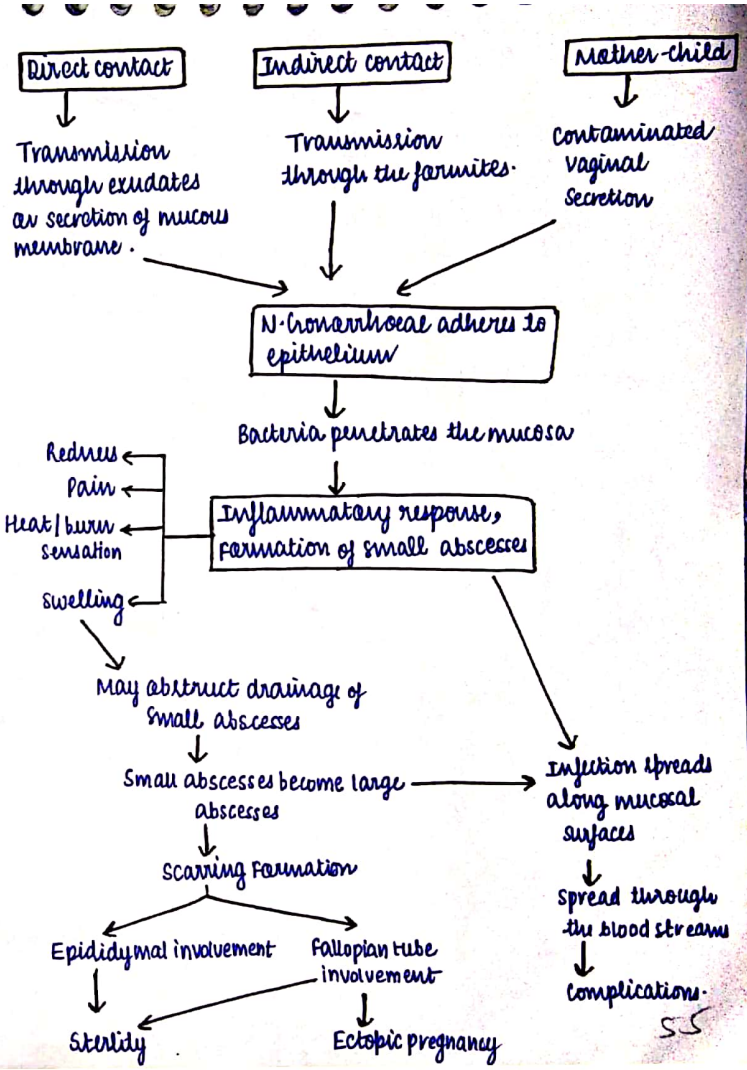
B.) Intimate person-to-person contact with lesions on lips, tongues/fingers.

C.) Transfusion of infected blood.

D.) Materno-foetal transmission in con-genital syphilis if mother is infected.

* **Gonorrhoea:** It is also k/n as clap. In US, 1 to 2 million new cases of gonorrhoea appear each year, most among the individual aged b/w 15 to 29 years. (107)

- **Causative agents:** This is caused by the bacterium Neisseria gonorrhoeae, which infects the mucosa of the reproductive and urinary tract.
- **Mode of transmission:** Discharge from infected mucus membranes are the source of transmission of the bacteria either during sexual contact or during the passage of new born via birth canal.
- In males, suppurative urethritis occurs and the infection may spread to the prostate gland, epididymis and testis. In females, the infection may spread from vulvar glands, vagina and cervix to the body of the uterus, uterine tubes, ovaries and peritoneum.
- Healing by fibrosis in the female may obstruct the uterine tubes, leading to infertility. In males it may cause the urethral stricture (morbid contraction of urethra).
- Non-venereal transmission of gonorrhoea may cause neonatal opthalmia in babies born to infected mothers. The eyes becomes infected as the babies passes through the birth canal.
- **Pathophysiology of gonorrhoea:**



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