

UNIT 3

MICROBIAL PATHOGENICITY

Infectious Disease

The ability of the organism to cause disease is called microbial pathogenicity. The pathogenic effect of one organism differ from other organism. For example: HIV causes AIDS, *Salmonella typhi* causes typhoid.

Types of pathogen

There are 2 types of bacterial pathogen

- Opportunistic pathogen
- Primary pathogen.

Opportunistic pathogen

When the host immune system is in impaired condition it becomes pathogen and cause disease. Eg. Candidiasis → *Candida albicans*.

Primary Pathogen

It causes disease in healthy individual who has intact immunological defense.

Eg: Dysentery → *Shigella dysenteriae*

Virulence

The organism has the ability to cause disease in relation to resistance to host. It has been classified into 2 strain,

- A virulent strain
- Virulent strain

Avirulent Strain

It does not cause disease because it lacks some antigenic property.

Virulent strain

Which induces disease to human. Eg: Smooth capsule of *Streptococcus pneumonia* induces infection to human whereas rough strain *Streptococcus pneumonia* does not cause any infection.

Invasiveness

Organism invades the host cell, tissue and spreads throughout the body. Eg: Pyogenic infection caused by *Streptococcus pyogenes*.

Toxigenicity

The ability of the micro organism to produce toxin that contributes the development of disease. Eg: Exotoxin produced by *Conjnebacterium diptheriae*, Enterotoxin produced by *Vibrio cholera*, Endotoxin produced by: *Neisseriae* species

Types of infection**Establishment of Infections**

Most cell factor: Most possess are receptor and organism efficiently bind with help of Flagella and pili.

Microbial factor: Organism posses pili and fibrae with that it binds to the host cell and facilitate the infection.

Penetration

Organism attaches to the epithelial cell of mucosal coated



Enter submucosal region



And spreads the infection to other parts of body

Multiplication or Colonization

Organism multiplies in the host cell by absorbing the host nutrition.



Resisting phagocytosis



By releasing enzymes like coagulases, nucleases, proteases and capsule.

Toxigenicity

The ability of the pathogen to produce a compound called toxin which are either protein or LPS that produce specific harmful effects to the host. It has been classified into 2 types.

Endotoxin, Exotoxin

Exotoxin: These are the toxin which are secreted outside the bacterial cell. It has been classified into 3 sub types.

- i) Cytotoxin
- ii) Neurotoxin
- iii) Enterotoxin

Cytotoxin is produced by *Corynebacterium diphtheriae* Neurotoxin is produced by *Clostridium botulinum*. Enterotoxin by *Vibrio cholera*

Endotoxin

These are lipopolysaccharide present in the outer membrane of gram negative bacterial cell wall. The organism lysis its cell and releases the toxin inside the medium. Eg. Endotoxin produced by *Neisseriae* species.

Bacteria, virus and fungi as potential pathogens

Potential pathogens are one that has the ability to cause disease to the human beings and animals by producing various toxins, enzymes and other antigen property. All bacteria, viruses, fungi and parasites are potential pathogens which causes infection in gastro intestinal, respiratory tract and urogenital tract.

Virus

Viruses are obligate intracellular parasites which has the property of multiplying inside the host cell.

Mechanism of viral injury

Viruses can directly damage host cell by entering and replicating at the host expenses.

Mechanism of bacterial injury

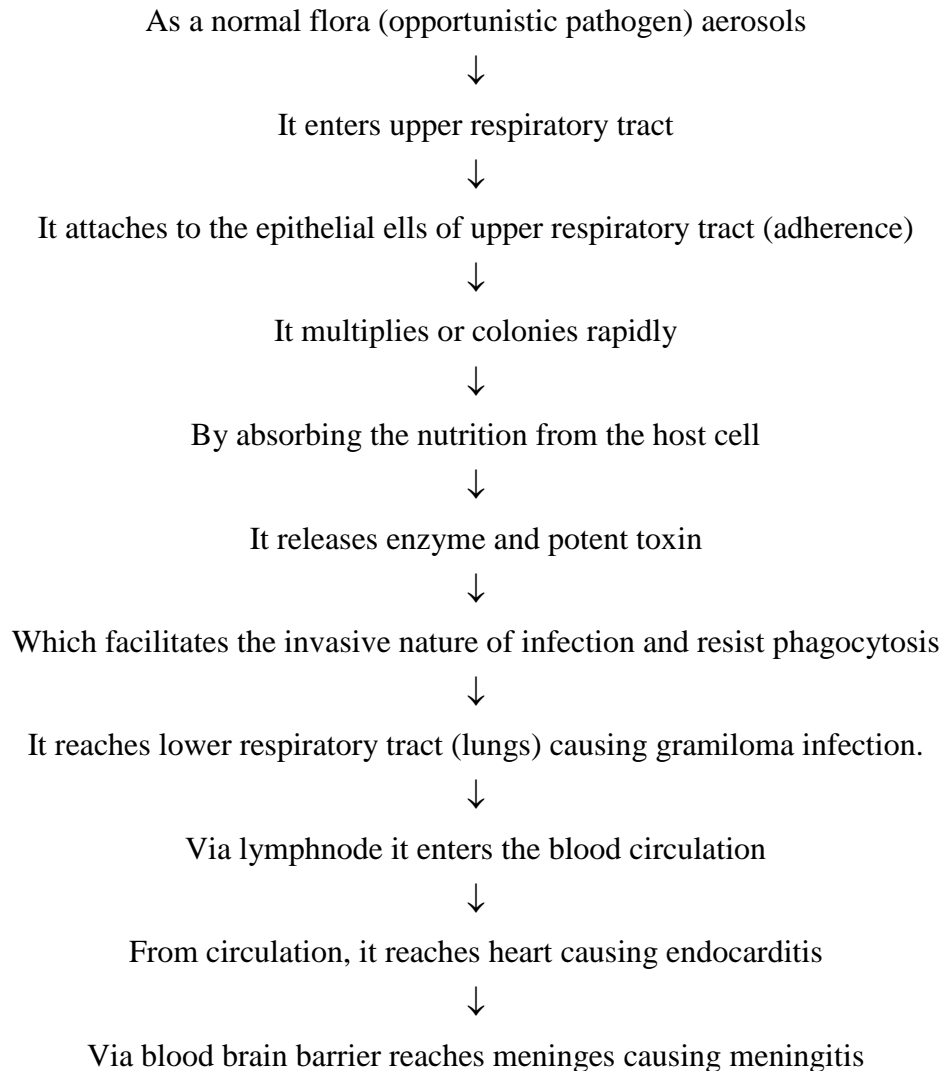
The bacterial damage to host tissue depends on the ability of the bacteria to adhere to the host cell, invade cells and tissue to deliver toxin. Pathogenic bacteria have virulence gene that encodes protein and facilitates the infection.

Mechanism of fungal injury

Candida albicans is normal flora of skin, and cavity, gastro intestinal tract etc.

Entry of organism to the host





Clinical symptoms

- Oral thrush
- Candida oerophagitis
- Cutaneous candidiasis
- Lymphadenopathy
- Endocarditis (inf of heart)
- Meningitis

Mechanism of development of resistance

The virulent of the particular strain is not constant, it may undergo spontaneous or induced chain. The virulent strain may spontaneously change into divirulent strain, virulent strain may spontaneously change into virulent strain. This occurs due to mutation, transformation and conjugation. This mechanism is called development of resistance by microorganism. Eg: Organism develops resistance by various factor.

Antiphagocytosis

Organism resist phagocytosis by producing capsule, pili, fimbriae and flagella.

Inhibitors

Some intracellular parasites secrete inhibitors of lysosomal enzyme or even prevent the fusion of lysosome with phagosome. Eg: Mycobacterium tuberculosis.

Salmonella typhi fails to stimulate the O₂ dependent killing during phagocytosis.

Staphylococcus aureus inhibits phagocytosis by producing catalase enzyme which blocks oxygenic radical formation.

Antigenic heterogeneity

Variation in antigenic structure.

- Salmonella species have more than 2000 serotypes.
- E. coli possess somatic 'o' antigen and flagella 'h' ag. Which is of 100 serotype.
- Streptococcus pyogenes possess 'M' protein which shares some common epitope between human myocardial self ag.
- Some viruses like influenza, HIV maintain the virulent state without yielding to the host defense system by constantly changing the surface antigen.

Antigenic shift

Antigenic shift is the small change in the surface ag.

Antigenic drift is the drastic alteration in this surface ag.

The reason for antigenic drift and shift are due to mutation. This strategy helps microbes to escape host defense and remain in virulent state.

Development of resistance towards antibiotics by microbes

Antimicrobial resistance: Organism develop resistance by new environmental condition. Some organism like *Staphylococcus aureus* produce *Penicillinase* enzyme which are resistant to penicillin antibiotic. Organism shows resistance to the penicillin antibiotic by converting penicillin into penicillonic acid. Some organism shows resistance by exposing them to high osmosis pressure so it loses its cell wall and resist antibiotic.

Competitive between organism and antibiotic for a essential metabolic analog eg. Sulphanamide.

Cell membrane is altered in such a way that the drug cannot penetrate the cell membrane due to permeability defect. Eg. Polymixin B.

- Alteration in the target site.
- Modification of essential metabolic pathway.
- Drug inactivation mechanism by the production of microbial enzyme.
- Some organism shows resistant to the antibiotic by lapsing into dormant site.

Some micro organism shows resistance to antibiotic such as tetracycline which is plasmid encoded protein, which pumps out the drug out of the cell. Due to decreased permeability, change in shape of receptor or alter in receptor the drug cannot enter the bacterial cell and micro organisms shows resistance towards the particular antibiotics.

Transmission of Drug resistance

Some organisms the resistance gene is transmitted by conjugation process. The isolates of antibiotic sensitive and antibiotic resistance is isolated from the patient suffering from enteric fever. The resistance gene were transferred from *E. coli* which was found in intestinal tract. This factor might be transferred from *E. coli* to *Sphigella dystenriae* which causes enteric fever infection. The resistance is transferred from the resistance factor (R. plasmid) present in *E. coli*.

E. coli is a donor and the recipient are Salmonella, Shigella, Klebsiella (staining).

Bacterial infection

Staphylococcus aureus

Gram positive cocci in clusters, non motile, non capsulated, non spring, aerobic in nature.

Cultural characteristics

S. aureus is cultivated by following medium

- Nutrient agar
- Blood agar
- Manitol salt agar

Virulence produced by *Staphylococcus aureus*

Enzymes

- Coagulase
- Lipase

- Staphylokinase
- DNase
- Hyaluronidases

Toxins

- Alpha toxin
- Beta toxin
- Gamma toxin
- Delta toxin
- Enterotoxin
- Exoflotative toxin
- Toxic shock syndrome I

Antigenic structure

It posses

- Peptidoglycan layer
- Tericholoric acid
- Protein A

Mode of Transmission

- Direct contact
- Aerosol
- Contaminated food and water

Pathogenicity

Enterotoxin

Enterotoxin is responsible to course food poisoning. It consists of 6 sub units. A, B, C₁, C₂, D, E. Among all these subunit type A is responsible to cause food poisoning in human beings.

Exoflotatie toxin

It consists of 2 sub units ETA and ETB.

ETA: is heat stable and chromosomal mediated.

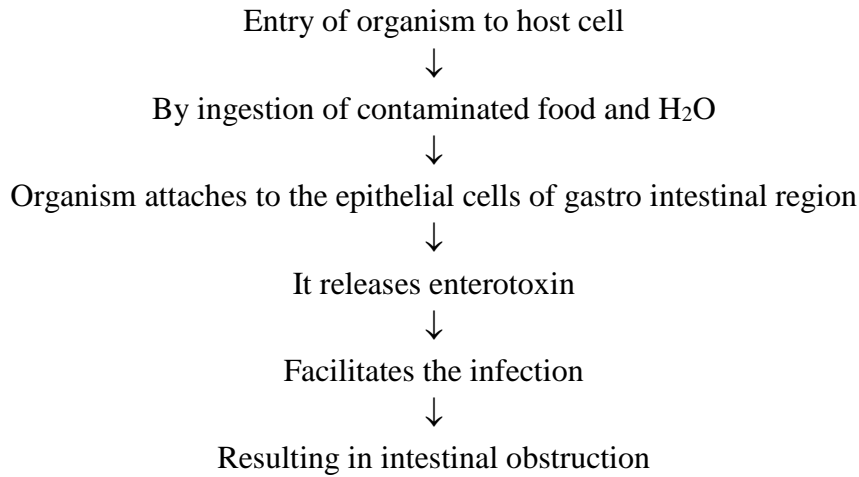
ETB: is heat labile and plasmid mediated

Toxic shock syndrome I

This toxin stimulates the interleukin 1 and induces fever.

Mechanism of toxin action

Enterotoxin



Clinical symptoms

- Abdominal pain
- Nausea
- Vomitting
- Diarrhoea

Streptococcus

Streptococcus pyogenes

Morphology

- Gram positive cocci in chains
- Non motile
- Non capculated
- Non sporing
- Aerobic

Cultivation

This organism can be cultivated by using blood agar. It produces β haemolysis pattern.

Virulence factor produced by Streptococcus pyogenes

- Peptidoglycan layers
- Group specific carbohydrate
- Lipoteichoic acid
- Pili
- M.T.R. → Protein
- 'M' protein → major virulence factors causing infection in humans.

Toxins

- Haemolysin → Streptolysin 'O' → 'O₂' labile immunogenic
Streptolysin 'S' → 'O₂' stable non immunogenic
- Erythrogenic toxin responsible for causing scarlet fever.
- Streptodornase hydrolysis DNA
- Hyaluronidase Hyaluronic acid connective tissue
- Streptokinase Lysis of fibrin clot by activating plasma precursor

Pathogenicity

i) Respiratory infection

Sour throat is a common infection of streptococcus which leads to tonsillitis, pharyngitis, followed by inflammation in the middle ear called OTITIS MEDIA and SINUSITIS.

Clinical symptoms

- Cervical lymphadenopathy
- Red patches in mucous membrane
- High fever.

ii) Skin and sub cutaneous infection

ii) Genital infection: It causes infection in endometritis

Symptoms

- Puerperal fever (fever with chill)

Systemic infection

It causes infective endocarditis

Post streptococcal sequelae

- Rheumatic fever
- Acute glomerular nephritic (ag-ab complex in nephron)

Biochemical test

- Catalase – positive
- Coagulase – negative
- DNase – Negative
- Manitol fermentation – Negative

Treatment

- Penicillin
- Erythromycin
- Oxacillin
- Cephalexin

Plaque

Causitive agent – *Yersinia pestis*

Morphology

- Stained with giemia staining
- Capsulateed
- Non sporinig, non motile
- Facultative anaerobic

Cultivation

Organism can be cultivated by

- Nutrient agar
- Blood agar

Antigenic structure

- It consists of heat labile protein envelop antigen (fraction I)
- Fraction I inhibits phagocytosis
- Two Ag Vandw → Present together potent protein

Toxins

- **Plaque toxin:** It possess both characteristics of both exo and endotoxin.
- It is thermo labile in nature

Enzymes

- Coagulase
- Bacteriocin

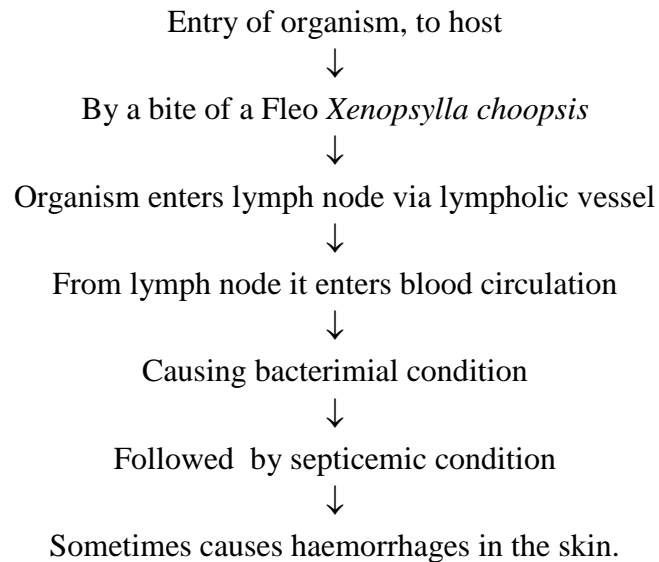
Mode of Transmission

Zoonotic disease transmitted through rodents.

Pathogenicity

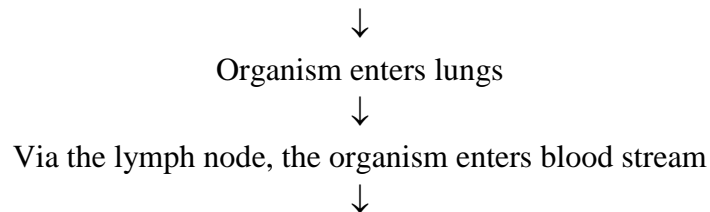
It causes three forms of infection in human beings.

- Bubonic plague
- Pneumonic plague
- Septicemic plague



Pneumonic plague

If may occur due to droplets every of organism to the host via aerosols.



From blood circulation, it reaches vital organs.



In Lungs it causes thrombopneumonia

Bubonic plague

It involves the infection of cervical, axillary in inguinal lymph node involvement.

Septicemic plague

This may occur as the primary infection or as a complication of bubonic or pneumonic plague.

Clinical Symptoms

- Lymphadenopathy
- Bacteremia
- Septicemia
- Pneumonia
- Haemorrhage
- Haematopysis – Blood in sputum

Bio Chemical Test

- Glucose
 - Maltose
 - Manitol
- } Sugar fermentation test
- Catalase – Positive
 - Oxidase – Negative

Molecular study

Polymerase chain reaction – ELISA

Treatment

- Streptomycin
- Tetracyclin
- Gentamycin

Syphilis

Causative agent : Treponema palladium / Spirochetes (spiral in shape)

Morphology

- Activity motile
- Presence of Endoflagella
- Exhibits gliding motility
- Micro aerophilic (O_2 – survival)
- Delicate spirochete with tapering ends

Cultivation

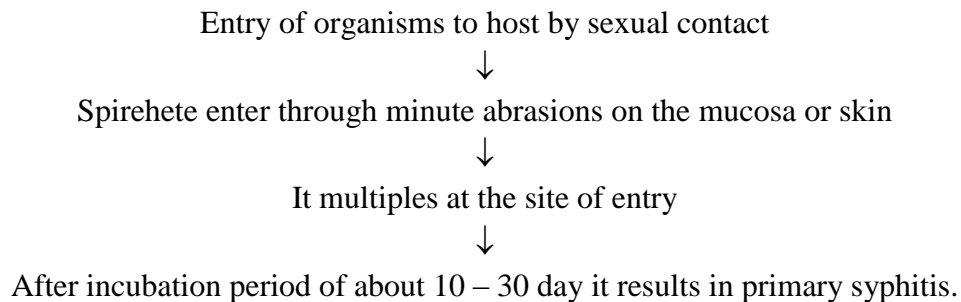
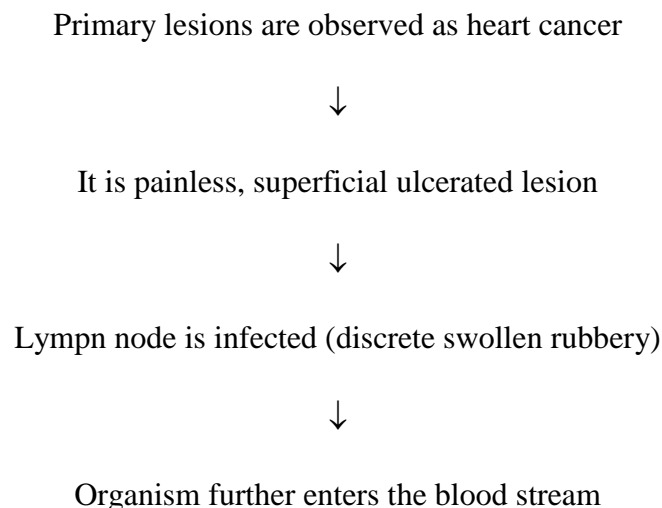
Organism can be cultivated by animal inoculation method using Rabbits.

Antigenic structure

It possess complex antigenic structure. It has antigen known as cardiozipin antigen. This antigen shares common epitope with OX HEART.

Mode and transmission

Sexual intercourse / venereal disease (STD)

Pathogenicity**Primary syphilis**



Chancre invariably heals in about 10 – 40 days without treatment



Leaving a thick scar

Secondary synthesis

Popular skin rashes, mucous patches (oropharynoc), condylomata. Patients are more infections during secondary syphitis due to abundant lesion. Further secondary lesion disappears.

As period between 2^o and 3^o syphilis it is known as LATENT SYMPHILIS.

Tertiary Syphilis

Cardiovascular lesion, meningo vascular manifestation, neurological manifestation (paralysis).

Lab Diagnosis

Specimen - Exudates

- Serum sample

WET MOUNT EXAMINATION

- Wassermann 'C' fixation test
- Kahn flocculation test
- Venereal disease research laboratory (VDRL)
- Rapid plasma regain test (RPF)
- *Treponema pallidum* immobilization test (Tp I)
- *Treponema pallidum* fluorescent antibody absorbent test (FTA-ABS)
- *Treponema pallidum* haemagglutination test (TPHA)

Treatment

- Penicillin
- Ceflaxone

Clostridial infection

Clostridial infection is caused mainly by 3 organisms.

- *Clostridium tetani* which causes Tetanus
- *Clostridium botulinum* which cause food poisoning (botulism)
- *Clostridium perfringens* which cause gas gangrene

Morphology

- Terminal spore produced by *Clostridium tetani*
- Subterminal spore *C. perfringens*
- Central spore by *C. botulinum*

Gram negative bacilli, non capsulated, actively motile, spore bearer, strict anaerobic

Cultivation

The organism can be grown by using a medium called Robertson cooked meat media.

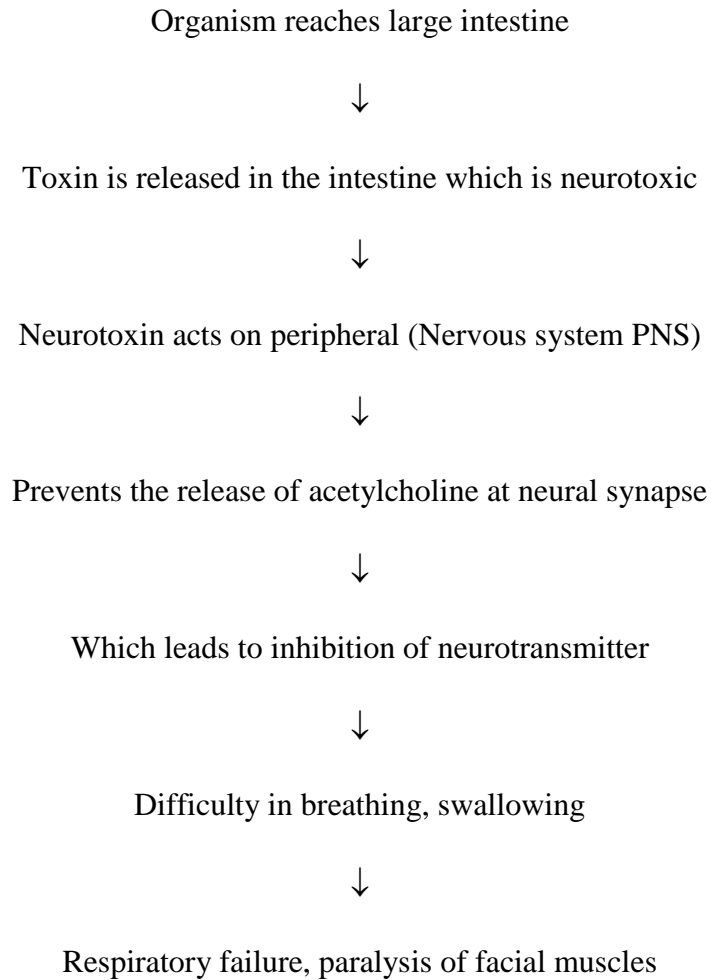
i) *Clostridium botulinum* pathogenicity

Entry of organism to host

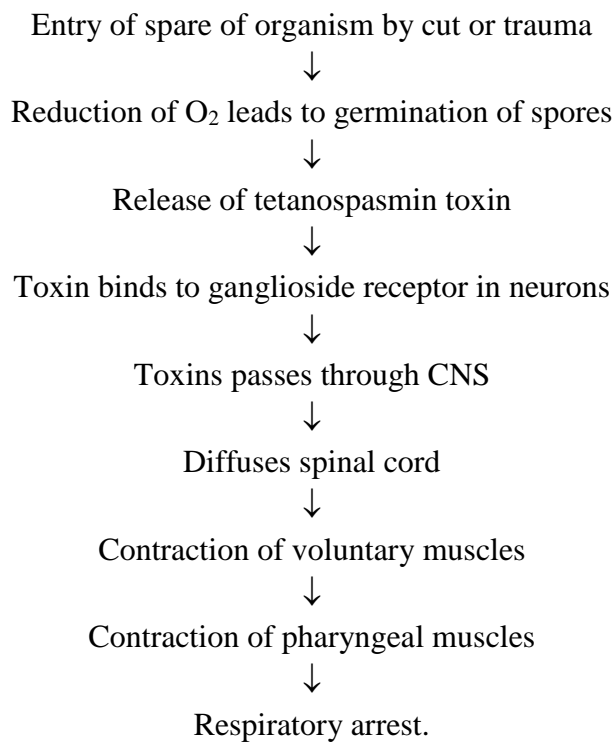


By ingestion of contaminated food

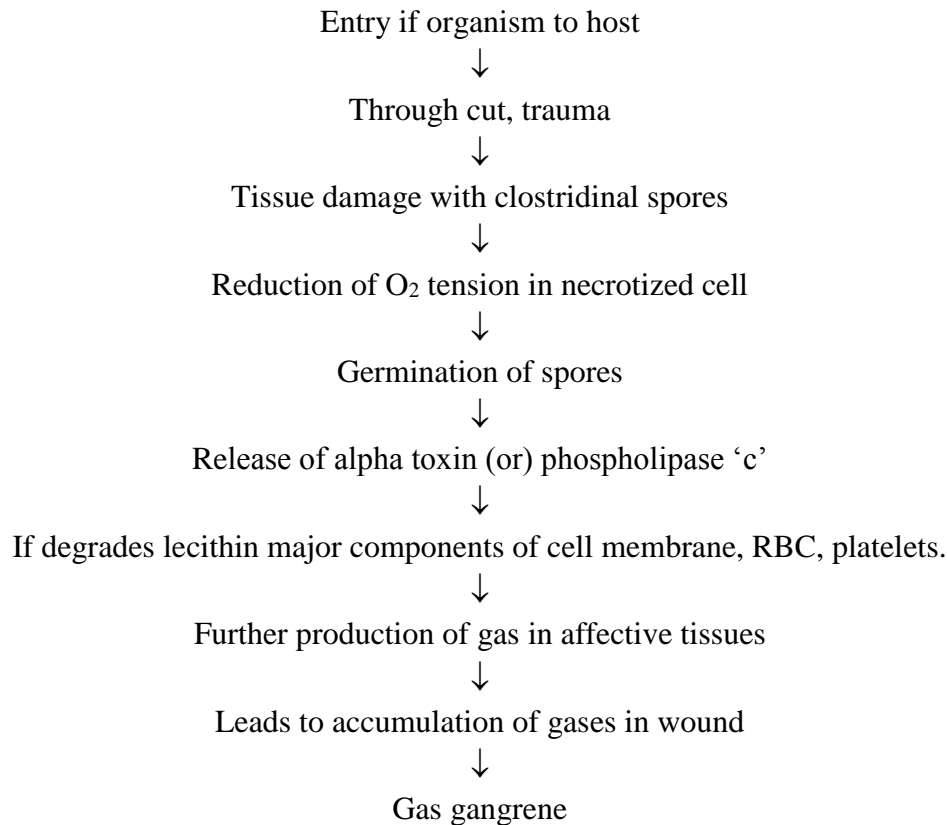




ii) Clostridium tetany Pathogenicity



iii) Clostridium perfringens Pathogenicity



Clinical symptoms

- Fever
- Lymphadenopathy
- Cellulitis
- Necrotis
- Ischemia

Treatment

- Penicillin, erythromycin, entamycin, ampicillin.

Influenza virus belongs to the family ORTHOMYXO VIRIDAE. Influenza is an acute infectious disease of respiratory tract which occurs in epidemic and pandemic

Morphology

- Influenza is single standard RNA genome
- It is a enveloped virus.
- This virus encode protein which include haemagglutine and neuraminidase. The spikes are projected from envelop.
- It possess RNA dependent RNA polymerase enzyme.

Haemagglutinin

- It contains trimer of glycoprotein sub unit.
- Each subunit consists of 2 polypeptide chains HA₁ and HA₂.
- It facilitates the attachment of the virus to respiratory epithelial cell.
- It undergoes antigen changes from antigenic drift and antigenic shift.

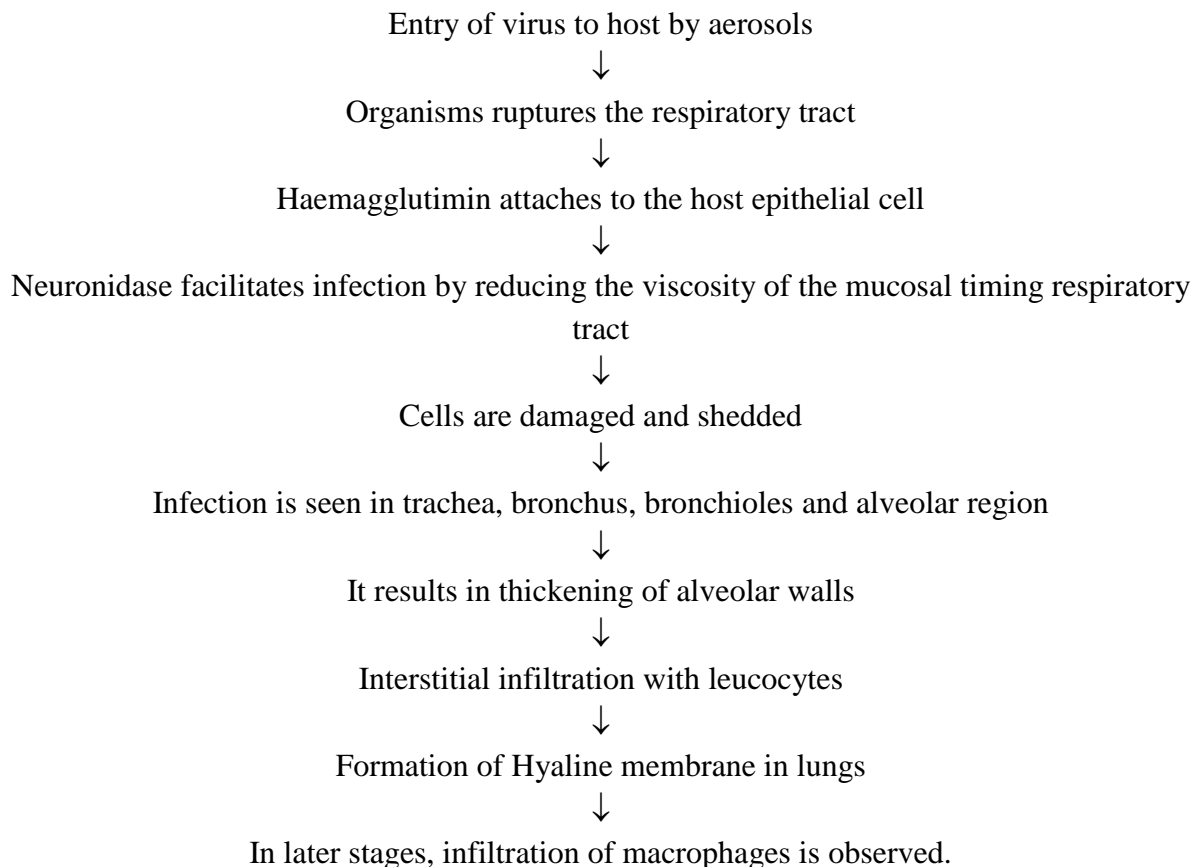
Neuraminidase

- It is the 2nd glycoprotein spike like structure on the surface of influenza. It is mushroom shaped, it contains box which destroys receptor on the host cell.
- This enzyme cleaves the bond between the viral gene agglutinin and the cell receptor

Cultivation

- The virus can be grown by using monkey kidney cell line.

Pathogenicity



Clinical symptoms

- Productive cough
- Nasal discharge

- Fever
- Headache
- Pneumonia

Lab Diagnosis

- Throat swab
- Asopharyngeal swab
- Serological test
- Complement fixation test
- Immunoflourescent test

Treatment

- Rimatadine
- Amantadine

Fungal Infections

i) Determatophytoses

They are the most common type of cutaneous fungal infection seen in man and animals affecting skin, hair and nails, They are caused by a group o fungi which have the capacity to invade the keratinized tissue of skin and its appendages and these are collectively known as dermatophytes.

Causative agent

- Trichophyton species – skin, nail, hsit
- Microsporum species – skin, hair
- Epidermatophyton species – skin, nail.

Clinical features

It produces ring worm like infection or Tinea infection.

- i) Tinea capitis (scalp)
- ii) Tinea corporis
- iii) Junea imbricate
- iv) T. gladiatorium
- v) T. facial
- vi) T. cruris
- vii) T. mannum
- viii) T. pedis
- ix) T. ungulum

x) T. barbae

Tinea capitis: This is the infection of the shaft and scalp region.

Tinea corporis: This infection is seen globrous skin of body and the infection may extend to scalp, groin or beard.

Tinea imbricata: These are concentric ring of scaling which spreads out peripherally as Hanuman (or Indian Ring worm).

Tinea gladiatorium: It is a converging infection in Wrestler. It is found in athletics due to playing jsnoy

Tinea faciei: This is dermatophytic infection, skin or face and the infection extends to beard.

Tinea cruris: It is the dermatophytic infection of groin mostly present in men. It involves in the perinanal area and may spread to thigh. In female infection is seen in obese women.

Tinea mannum: This is the infection of the skin of palm of hand.

Tinea pedis: This is the infection of the foot, toes and interdigital web spaces.

Tinea unguum: It is the dermatophytic infection of nail plate and mostly seen in adult.

Tinea barbae: This is the ring worm infection of beard and mustache areas of the face, it is called barbers MCH.

Lab diagnosis

Specimen: Skin, nail, hair,

- KOH mount
- Lactophenol cotton blue staining.

Treatment

- Imidazole
- Amphotercin B
- White man ointment

Mycetoma

It is chronic localized granuloatize infection skin and subcutaneous tissue. This infection is caused by *Actinomadhura machurae*, *Nocardia cavivae*. This disease was 1st reported in Madhurai, so called Madura mycosis or Madura foot.

Made of Transmission

Entry of fungal spores by picking of rose thorn which contains fungal spore



Spore enters the intact skin through deep penetrating wound



Spores start germinating which leads to the formation of hyphae growth



Adjacent cell damage which induces inflammatory reaction.



Formation of pus and fibrin deposit in the infected area



Swelling occurs which is commonly called tumefaction



Tumefaction is due to abscess formation



Abscess formation produces a tunnel known as sinus tract



Sinus tract reaches the superficial structure where the pus is released.



The pus are commonly called sulphur granules which contains fungal mass.

Treatment

- Keto conazole

Aspergillosis

Systemic fungal infection seen in immunocompromise or immunocompetent species. It causes primary pulmonary infection. It is ubiquitous in nature. Aspergillus produces a toxin – AFLA toxin which is responsible to cause food poisoning.

Mode of transmission

Through aerosols.

Pathogenicity

Entry of spores through aerosols



It enters upper respiratory tract and reaches bronchial and pulmonary alveoli



Since the size of the spore is less, the spore will easily get phagocytosed



In case of immunocompromised patient, the spores resist and start germinating



Which leads to aspergilloma.

Clinical features

Pulmonary Aspergillosis

It is classified into 3 types

- Allergic Aspergillosis – Asthma, Pulmonary eosinophilia, increased concentration of IgE. It causes allergic bronchopulmonary aspergillosis.
- Aspergilloma – compact mass of fungal mycelia are often surrounded by dense fibrous wall called fungal ball or aspergilloma. Aspergilloma is 8 – 10 cm in diameter.
- Invasive aspergillosis – it causes chronic granulomatous diseases.

Treatment

- Itraconazole

- Amphotericin B

iv) **Candidiasis**

Candidiasis is an opportunistic infection caused by *Candida albicans*

Candidiasis is the common fungal disease found in human affecting mucosa, skin, nail and other organs of the body.

Morphology

Budding yeast cell

Antigenic and Virulent properties of *Candida albicans*

- It produces cytoplasmic and cell wall antigen
- The virulence factors are
- Toxin – eg. Endotoxin
- Enzyme – Proteases, phospholipases, esterases.
- **Adhesion Property** – They adhere to endothelial and epithelial cells of host cell receptors.
- **Complement receptor** – It inhibits phagocytosis by binding to the complement protein.
- **Phenotypic switching**

Predisposing factor:

- Immune compromise patient
- Immuno suppressed patient
- Diabetic patients.

Pathogenicity

Refer microbial pathogenicity, in fungal as a potential pathogen.

Clinical symptoms

- Oral candidiasis
- Alimentary candidiasis
- Vulvo vaginitis
- Ocular candidiasis
- Mucocutaneous candidiasis
- Cutaneous candidiasis
- Pulmonary candidiasis

Lab diagnosis

- Gram staining
- Germ tube test position
- Sugar assimilation test
- Sugar fermentation test
- Serological test – ELISA

Treatment

- Canazole
- Amphotericin B

Protozoan Disease: Helminth

- i) Filariasis: Causative agent – *Wuchereria bancrofti*

Morphology

- Adult worm
- Microfilaria

Adult Worm

- Minute
- Whitish Thread like
- Filiariform in shape
- Both anterior and posterior end are trapping.

Microfilaria

- First stage larva
- Covered of hyaline sheath

Third stage larva

Infection form of filarial worm elongated.

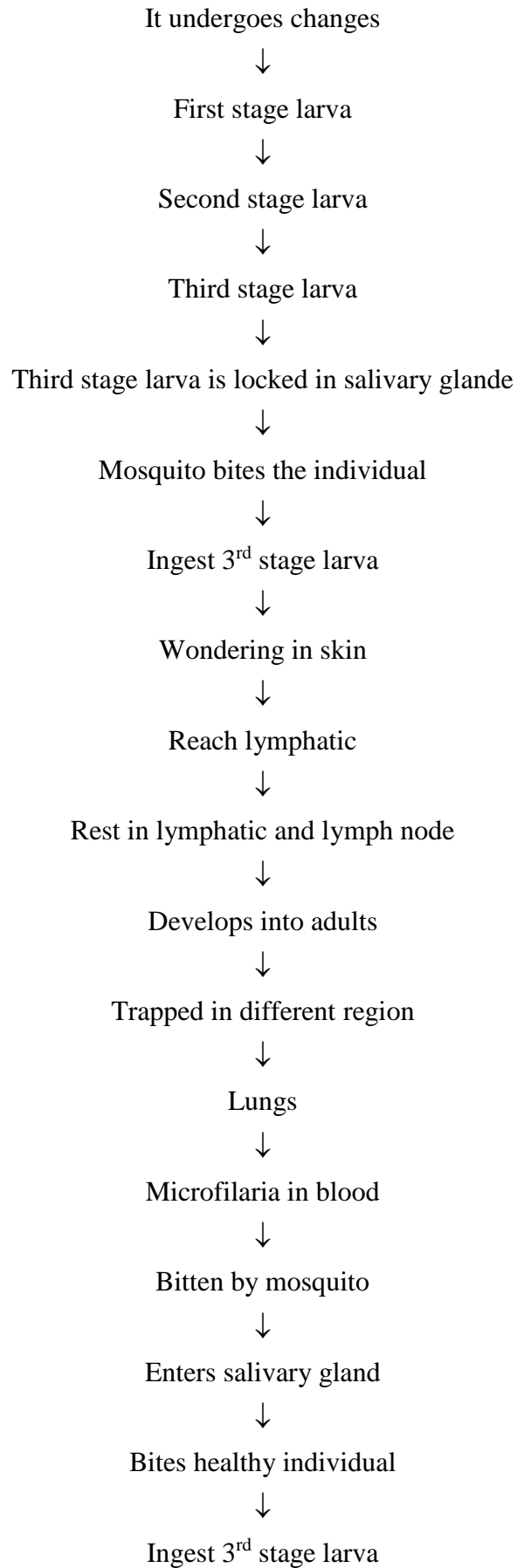
Life Cycle

Mosquito bites the human suffering from filariasis



Microfilaria reaches intestine of mosquito





Clinical Features

i) Lymphatic filariasis

- Dilation of lymphatic vessel
- Infection of lymphatic vessel
- Obstruction of lymph node
- Lymph adenopathy

ii) Filarial funiculitis

- Inflammation in the sperm cord

iii) Orchitis

- Characteristic by oedematous testis

iv) Hydrocele

- Hydrocele fluid typically consist of blood clot, fibrin cholesterol crystals and ca particles

Lab Diagnosis

Specimen – peripheral blood smear



Giemsa or leishman staining

Observation

- Observation of 3rd stage larva or microfilaria
- Serological diagnosis – ELISA

Treatment

- Diethyl carbamazin

Amoebiasis

- Causative agent : Entamoeba histolytica
- Habitat – Large Intestine

Morphology

- It occurs in 3 stage

- Trophozoite
- Precyst
- Cyst

Trophozoite

- Invasive form of the parasite
- Actively motile
- Infects large intestine

Precyst

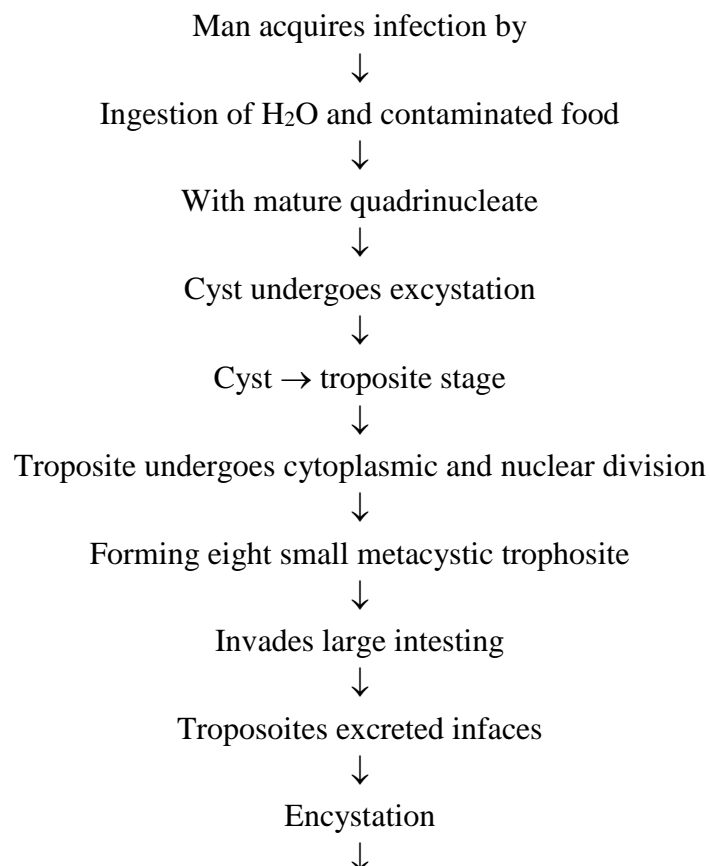
- Stage between trophozoite and cyst
- Oval in shape

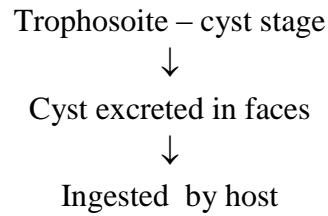
Cyst

- Infective stage of parasite
- Mature cyst contains 4 nuclei

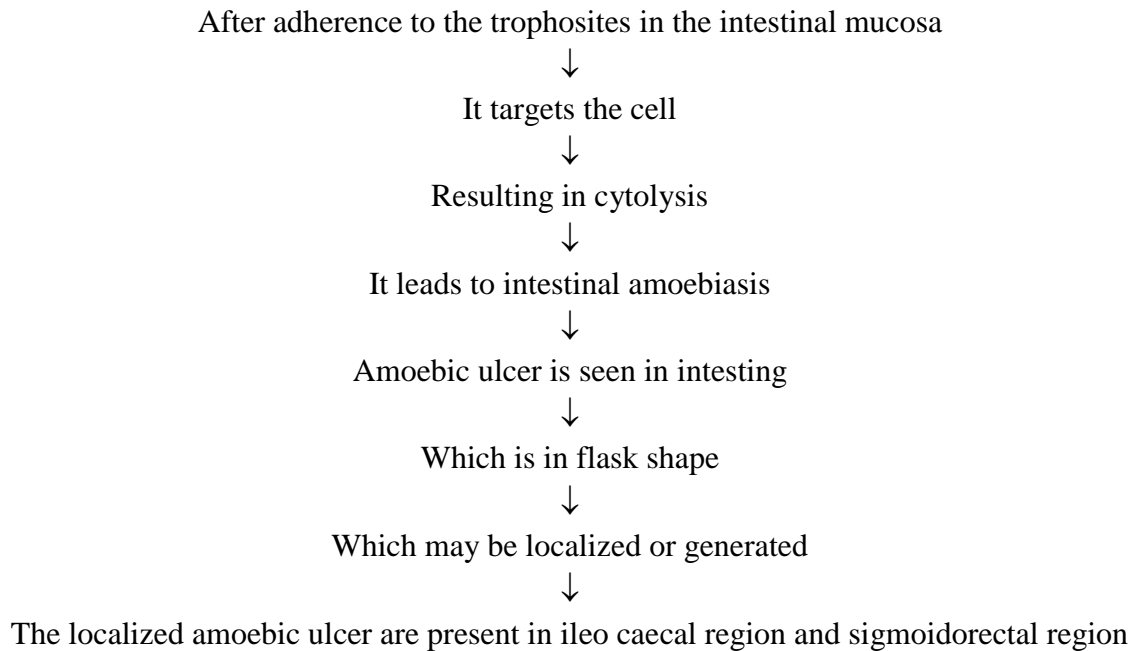
Mode of transmission – Contaminated food and H₂O.

Life cycle





Pathogenicity



Clinical symptoms

- Acute intestinal amoebiasis
- Chronic intestinal amoebiasis
- Extra intestinal amoebiasis
- Pulmonary amoebiasis
- Cerebral amoebiasis
- Hepatic amoebiasis
-

Lab Diagnosis

- Specimen – stool
- Saline mount
- Iodine mount
- Concentration flotation method
- Concentration segmentation method
- Serological diagnosis – Elisa

Treatment

- Metionidazole