www.FirstRanker.com

PATHOGENESIS OF BACTERIAL INFECTIONS

Definition

- It is the process / mechanism by which a pathogen can produce the disease in a normal healthy person.

Types of Pathogens

- A microorganism is pathogenic if it is capable of producing a disease in an immuno- competent person.

- True Pathogens
  a) Highly Pathogens
  b) Less Pathogens

- Opportunistic Pathogens
  - Causes disease rarely in immunocompetents but causes serious disease in immunocompromised patents, although they are part of the normal body flora.
  - Reduced host defense causes the disease.

Important Terminologies

- Normal Flora:
  - These organisms are permanent residents of the body and vary in types according to the anatomic site.

- Colonization:
  - Refers to the presence of new oragnsims i.e neither member of the normal flora nor the cause of symptoms. It becomes difficult at times to distinguish between a pathogen and colonizer specially the specimens obtained from respiratory tract e.g throat cultures and sputum cultures.

- Virulence:
  - defined as quantitative measure of pathogenicity, and is measured by minimum number of bacteria to cause the disease.

- LD 50:
  - Number of organisms required to kill 50% hosts.

- ID 50:
  - Number of organisms required to cause infection in 50% of host population.

- Organisms with lower LD 50 are more virulent than higher ID 50, as fewer bacteria are required to cause death or disease.

- Infectious dose varies among organisms.
- Shigella (ID 50 less than 100) and Salmonella (100,000) cause diarrhea by producing infection in GIT.

- **Virulence factor:** Infectious dose of bacteria depends upon virulence factor i.e. whether a bactria has :
  - Pilli
  - Toxin
  - Capsule
  - Stomach acid (non specific host defense)

- **Parasite:** Bacteria that are human pathogens are called parasites.
  - Obligate intracellular parasites e.g. Chlamydia and Richettsia.
  - Intracellular parasites e.g. Mycobacterium tuberculosis.
  - Protozoa and helminths.

Why patients get sick

- There is a balance of power between the bacteria and the host.
- When balance between the organisms and the host shifts in favor of organisms, the patient starts getting the disease.
- Number and virulence of organisms determines the severity of the disease.
- Greater the no. of organisms, greater is the likelihood of getting the disease.

- Specific virulence factors:
  - It determines what disease a bacteria can cause e.g. E.coli has the capacity to produce non bloody diarrhea / bloody diarrhea.

- Immunity:
  - Is the body's immune defense against microbes.
    - Innate immunity
    - Acquired immunity (antibody mediated and cell mediated)

- Immunocompromised patients:
  - It is the important cause of host defense reduction.
    - Genetic Immunodeficiencies e.g. agammaglobulinemia
    - AIDS
    - Diabetes
    - Drug induced immunosupperession (organ transplant)
    - Autoimmune disease
    - Cancer Patients
    - Longer use of steriods

Types of Bacterial Infections

- Non communicable.
- Communicable, spreads from host to host via airborne, droplets and coughing e.g. TB
- Contagious , Highly communicable.
- Asymptomatic / inapparent.
- Latent , reactivation of growth organisms.
- Chronic carriers, the organisms continue to grow with or without producing the symptoms in the host.

Epidemiological Classification of Bacterial Infections

- **Endemic:**
  - Infection at persistently low level in specific geographical area.
- **Epidemic:**
  - Higher than the usual.
- **Pandemic:**
  - Spreads rapidly over large population area and is considered emergency which requires immediate remedial measures to control it.

Stages of Pathogensis

Transmission

- Means how the organism transmits the disease to the body cells:
  - Human to human.
  - Non human to human (fomites, animals, soil and water).
  - Normal flora can become pathogenic at times but the infection is mostly acquired from the external sources.

- Respiratory and GIT passage is the mode of excretion of bacteria e.g. faecal contamination of food and water, airborn droplets.

- Other modes include

1. Sexual contacts.
2. Urine contacts.
3. Skin contacts.
4. Blood transfusion.
5. Contaminated needles.
6. IV drug abusers by sharing needles.
7. Insect bites.
8. transmission by Tics (Lymes disease, rocky mountain spotted fever, relapsing fever, tularemia).

- Bacteria, virus and other microbes can be transmitted via vertical transmission (mother to child).
  - Across the placenta
  - Birth canal
  - Breast milk
- Transmitted via horizontal transmission (person to person).

- Four important portals of entry:
  - Respiratory tract
  - GIT
  - Skin
  - Genital
- Bacterial diseases can be transmitted via food and insects.
- Animals can also act as reservoir or vector.

Adherence to Cell Surface

- Certain bacteria have specialized structures called Pili or produce substances like capsule, glycocalyces which allow the bacteria to adhere to the human cell surface.
- Bacteria which do not have this capacity cannot produce the disease and are called non pathogenic.
- Pili of Neisseria gonorrhoeae & E.coli produce urinary tract infection (UTI).

- Glycocalyces are present in staph. epidermidis and certain viridans streptococci. These infect heart valves.
- Production of biofilm is initiated after the attachment of bacteria to the cell surface.
- Biofilm is polysacchride and protein in nature which infects the foreign bodies e.g prothesis, used in the human body.

- Biofilm is a powerful weapon of bacteria which protects it against antibiotics and host immune defense.
- Persistence of pseudomonas species in cysticfibrosis is facilitated due to biofilm formation.
- Some stains of E.coli and salmonella have special surface proteins called curli, which helps in binding of bacteria to endothelium.

- Curli also interacts with serum proteins such as factor 12 and helps in thrombus formation leading to DIC.

Invasion, inflammation & Intracellular Survival

- Bacteria causes disease by one of the 3 mechanisms:
  1. Invasion of the tissue, followed by inflammation.
  2. Toxin production.
  3. Immunopathogenesis.
- Enzymes secreted by invasive bacteria play role in producing the disease.

- These are :
  - Collegenase & Hyaluronidase, these enzymes degrade collegen and hyaluronic acid allowing the bacteria to spread through subcutaneous tissue e.g streptococcus pyogenese.
  - Coagulase, it accelerates the formation of fibrin clot e.g staphylococcus aureus.
  - Immunoglobulin A (IgA) protease, it degrades IgA allowing the organism to adhere to the mucousmembrane e.g N. gonorrhae, Haemophilus influenzae, strept. Pneumonae.

- Leucocidine, it destroys neutrophilic leukocytes and macrophaeges.

- Virulence factor:
  - It is most important antiphagocitic factor in the capsule external to the cell wall e.g strept. pneumoniae and N. memingitidis. It is a poly sacchride capsule which prevents the phagocytes from adhering to the bacteria.

- Second antiphagocytic factor is cell wall proteins of gram positive cocci, M proteins in streptococcus group A & protein A in staph. aureus.

Toxin Production

- It is the second major mechanism for disease production.
- **Exotoxins**:
  - They are produced by gram positive and gram negative bacteria, polypeptide in nature, secreted by certain bacteria which alter specific cell functions resulting in production of disease symptoms. The toxin is produced by the bacteria itself.
  - Exotoxins are amongst most toxic substances known e.g fatal dose of tetnus toxin for human disease is estimated to be less than 1 micro gram.

- Exotoxins are antigenic and induce antibodies called antitoxins. Exotoxins can be modified as toxoides e.g tetnus toxoide.
- It has two subunits A & B. A subunit is active while B subunit binds to the cell membrane and mediates the entry of unit A into the cell.
- Exotoxins have different mechanisms of action and different targets within the cell, hence cause a variety of diseases.

- Several exotoxins are enzymes that attach ADP ribose to the cell component. Some exotoxins act by proteolytic cleavage of the cell component, while others act as superantigens causing over production of cytokines.

- **Endotoxins**:
  - These are lipopolysacchride in nature, located in the outer membrane of the cell wall of gram negative bacteria.

- Lipid A is the toxic component of lipopolysacchride (LPS) which induces over production of cytokines e.g TNF, IL1, nitric oxide, causing symptoms of septic shock.
- LPS also activates blood components and formation of thrombus leading to start of coagulation cascade finally to DIC.

- Endotoxins are poorly antigenic and do not produce antitoxins.

Immunopathegenis

- In rheumatic fever and glomerulonephritis, it is not the organism itself which causes the disease but it is the immune response to the presence of oraganisms.
- Antibodies against M proteins cross react with joint, heart and brain tissue.
- Inflammation occurs resulting in arthritis, carditis and chorea.

Stages of infectious diseases

1. Incubation period
2. Prodromal period
3. Specific illness period
4. Recovery period
5. Chronic carriers
6. Latent stage
7. Sub clinical stage.

Types of inflammation

- Bacteria can cause two types of inflammation
  1. Pyogenic inflammation, pus producing, neutrophils prominent e.g gram positive and gram negative cocci.
  2. Granulomatous inflammation, macrophages and T cells are predominant e.g mycobacterium tuberculosis.
     - Phagocytosis by macrophages kills most of the bacteria but some survive and grow within the macrophages in the granuloma.

- Intracellular pathogens cause granulomatous leisions e.g Mycobacterium, legionella, brucella, listeria.