Microbiology

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Pathogenesis of bacterial infection

- Pathogenesis of bacterial infection
  - *Pathogenic Bacteria:* These are bacteria that can cause disease by possessing attributes that help them reach the host, persist within the host, replicate, and cause harm (disease) to the host.
  - *Characteristics of Pathogenic Bacteria:*
    - ✓ The traits that enable bacteria to cause disease are often referred to as virulence factors. These factors include:
      - Transmissibility
      - Adherence to host cells
      - Motility
      - Persistence
      - Invasion of host cells and tissues
      - Toxigenicity
      - Iron uptake mechanisms
      - Ability to evade or survive the host's immune system
      - Resistance to antimicrobials and disinfectants

- Transmission of Bacteria:
  - Bacteria can *adapt* to various environments, including external sources like soil, water, and organic matter, as well as internal environments such as insect vectors, animals, and humans.
  - Bacteria often *cause* asymptomatic or mild infections, promoting transmission from person to person rather than host death.
  - Clinical symptoms like diarrhea, cough, or genital discharge can *help spread* the bacteria.
  - Common *entry points* for bacteria include the respiratory, gastrointestinal, genital, and urinary tracts, as well as damaged mucous membranes and skin (e.g., cuts, burns)
  - Transmission by: contact, airborne, droplet, vector and vehicular (including food water and fomite transmission).
  - *Different between:*
    - ✓ *Airborne transmission*: can spread droplets of saliva and mucus by coughs and sneezes.
    - ✓ *Droplet transmission*: tiny particles, possibly produced by talking are suspended in the air for longer and travel further.

- Adhesion of Bacteria:
  - For successful infection, bacteria *must adhere* to tissue surfaces in the host. Without adhesion, they would be cleared away by mucus and other bodily fluids.
  - Bacteria have *specific* surface *molecules* that interact with host cells.
  - Many bacteria possess *pili* (long, rodlike appendages) or *fimbriae* (short, hairlike structures) that aid in adherence to host cell surfaces.

- Motility
  - Bacterial motility allows bacteria to *reach* the host, navigate within the host, and evade the immune system.
  - The bacterial *flagellum* is a complex molecular machine essential for pathogenesis, helping bacteria reach optimal sites, colonize, invade, maintain infection, and disperse post-infection.

- Invasion
  - Invasion occurs through tight junctions of epithelial surfaces or *internalization* into epithelial cells.

- This active process involves the pathogen interacting with host cells, often requiring actin polymerization. Once inside, bacteria can be transported to lysosomes, remain or multiply in the cytoplasm, escape the vesicles, or induce apoptosis in infected cells.

- Toxins/Exotoxins
  - *Exotoxins* are secreted actively (through contact or cell death), while *endotoxins* are part of the bacterial cell wall.
  - Exotoxins are the basis for some *vaccines*, known as toxoids.
  - Exotoxins consist of *two subunits*: A (responsible for toxic activity) and B (assists with attachment and internalization into cells).
  - Exotoxins *linked to* diarrheal diseases are often referred to as enterotoxins.

- Toxins/Endotoxins
  - *LPS* (Endotoxins) are components of the cell wall of gram-negative bacteria, released when the bacteria lyse.
  - Endotoxins are *heat-stable*.
  - In *response to LPS*: proinflammatory cytokines like IL-1 and TNF-α are released, and the complement and coagulation cascades are activated.
  - Clinical or *experimental effects* include:
    - ✓ Fever, leukopenia, and hypoglycemia
    - ✓ Hypotension, shock, and impaired organ perfusion (brain, heart, kidneys)
    - ✓ Intravascular coagulation and potential death from organ dysfunction.
  - Peptidoglycan from *gram-positive* bacteria can cause similar immune responses, though it is less potent than endotoxins.

- Secretion Systems:
  - *Bacterial secretion systems* are protein complexes on the cell membranes that facilitate the secretion of substances, particularly virulence factors (mainly proteins) used by pathogenic bacteria to invade host cells.
  - Secretion systems are *classified* based on their structure, composition, and activity.
  - <u>Key Types of Secretion Systems:</u>
    - ✓ *Type III* Secretion Pathway: A contact-dependent system activated upon host cell contact, injecting toxin proteins directly into host cells.
    - ✓ *Type I and IV* Secretion Systems: Found in both gram-negative and gram-positive bacteria.
    - ✓ *Type II, III, V, and VI* Secretion Systems: Specific to gram-negative bacteria.

- Iron Uptake Mechanisms:
  - Most iron in the mammalian body is bound to various proteins, and its availability is reduced during infection, both extracellularly and intracellularly.
  - Bacteria require iron for *growth*, and successful pathogens have evolved mechanisms to compete for iron in the host's iron-deprived environment.
  - One such mechanism is the production of *siderophores*, which are small, high-affinity iron-chelating compounds secreted by microorganisms (including bacteria and fungi) to scavenge iron from the host.

- Evasion of the Host Immune System:
  - Pathogenic bacteria have various mechanisms to *evade phagocytosis*, including capsule production and proteins like Protein A in Staphylococcus aureus, which binds antibodies in an inactive form.
  - Some bacteria produce *proteins* that *inhibit* complement activation, *reducing* immune signaling and opsonization, while others *prevent* phagolysosome fusion inside host cells.
  - Opsonization:is the process where substances like antibodies or activated complement components bind to bacteria, making them easier for phagocytes to engulf and destroy.
  - Pathogenic bacteria produce *enzymes* to degrade tissues and spread infection. For example, hyaluronidase

- Enzyme production
  - Pathogenic bacteria produce enzymes to degrade tissues and spread infection. E.g *Hyaluronidase and collagenase* are enzymes that hydrolyze hyaluronic acid and collagen respectively, constituents of the ground substance of connective tissue.
  - Bacteria produce *cytolysins* which directly kill cells usually by forming pores in their membranes (e.g. hemolysins, leukocidins).

- Pathogenicity Islands:
  - Pathogenicity islands are *discrete genetic units*, either chromosomal or extra-chromosomal, that encode genes aiding bacterial virulence.
  - These genes *include* those for adhesins, secretion systems (e.g., type III secretion system), toxins, invasins, capsule synthesis, and iron uptake systems.
  - These islands are typically *absent* in non-pathogenic bacteria.
  - Virulence genes within pathogenicity islands are often *activated by* environmental change, such as temperature changes.
  - Pathogenicity islands are commonly *located* on mobile genetic elements (e.g., plasmids, transposons), and their G-C content often differs from the rest of the bacterial genome

- Bacterial Communities / Biofilm and Pathogenesis:
  - *A biofilm* is a community of bacteria that are attached to a solid surface or to each other, encased in extracellular polymeric substances (EPS).
  - Bacteria within the biofilm produce EPS, which *consists* of extracellular polysaccharides, proteins, lipids, and DNA.
  - Biofilms can form on both *living* and *non-living surfaces*, and are commonly found in natural, industrial, and hospital environments.
  - Biofilms *contribute* to bacterial persistence on surfaces, *help evade* the immune response, and *increase* antimicrobial resistance and *dissemination*.

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