

Microbiology Lecture 4

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PhD Medical Microbiology



Pathogenesis of bacterial disease

- **A pathogen:** is any a microorganism that capable of causing a disease.
 - Fortunately, only a minority of the vast multitude of microorganisms in nature are pathogenic.
 - Whereas, some organisms are highly virulent and cause disease in healthy individuals, even with a small inoculum,
 - Others, cause disease only in compromised individuals when their defenses are weak.
- The latter are called **opportunistic** organisms, as they take the opportunity offered by reduced host defences to cause disease. These opportunists are frequently members of the body's normal flora.



General aspects of infection

- **Virulence** is a quantitative measure of pathogenicity and is related to an organism's toxigenic potential and invasiveness.
- **Virulence** can be measured by the no. of microorganisms (M.O.) required to cause disease. **LD50** {50% lethal dose} no. of M.O. needed to kill half the hosts. While, **ID50** {50% infectious dose} no. of M.O. needed to cause infection in half the hosts.



Communicable diseases

- Infections are called 'communicable diseases' if they are spread from host to host.
 - Many, but not all, infections are communicable: Tuberculosis is communicable vs staphylococcal food poisoning is not.
 - If a disease is highly communicable, it is called a 'contagious disease' (e.g. chickenpox).
 - Depending on the degree of incidence and prevalence of an infectious disease in a community, it may be called an endemic, an epidemic or a pandemic infection.
 - An endemic infection is constantly present at a low level in a specific population (e.g. endemic malaria in some African countries).
 - An infection is an epidemic if it occurs much more frequently than usual (e.g. an epidemic of influenza in the winter).
 - An infection is a pandemic if it has a worldwide distribution (e.g. human immunodeficiency virus (HIV) infection).



Stages of infectious disease

➤ An acute infection generally progresses through four stages:

1. **The incubation period:** time between the acquisition of the organism or the toxin and the commencement of symptoms (this may vary from hours to days to weeks).
2. **The prodromal period:** non-specific symptoms such as fever, malaise and loss of appetite appear during this period.
3. **The acute specific illness:** the characteristic signs and symptoms of the disease are evident during this period.
4. **The recovery period:** the illness subsides and the patient returns to health during this final phase.



Stages of infectious disease

- **an inapparent or subclinical infection**, without overt symptoms, where the individual remains asymptomatic although infected with the organism.
- **chronic stages**, when infected, the body may not completely eliminate the pathogen after recovery and some individuals may become chronic carriers of the organism.



Determinants of bacterial pathogenicity

➤ The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.

1. **Transmission**, Most infections are acquired by transmission from external sources; i.e. they are exogenous in origin. Others are caused by members of the normal flora behaving as opportunist pathogens; i.e. they are endogenous in origin. Transmission can be by:

1. **inhalation** – the airborne route
2. **ingestion** – faecal contamination of food and water
3. **inoculation** – by sexual contact, contaminated needles, skin contact, blood transfusions or biting insects.



Determinants of bacterial pathogenicity

- The major steps are **transmission**, **adherence to host surfaces**, **invasiveness** and **toxigenicity**.

1. **Transmission.**

There are four important portals (or gates) of entry of pathogens:

1. Skin
2. Respiratory tract
3. Gastrointestinal tract
4. Genitourinary tract.



Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.

2. Adherence to host surfaces:

- Adherence is the first step in infection, Unless organisms **have the ability to stick or adhere** to host surfaces, they will be unable to cause infection.
- Some bacteria and fungi have specialized **structures or produce substances** that facilitate their attachment to the surface of human cells.
- These adherence mechanisms are critical for organisms that attach to mucous membranes; mutants that lack these mechanisms are often **non-pathogenic**.



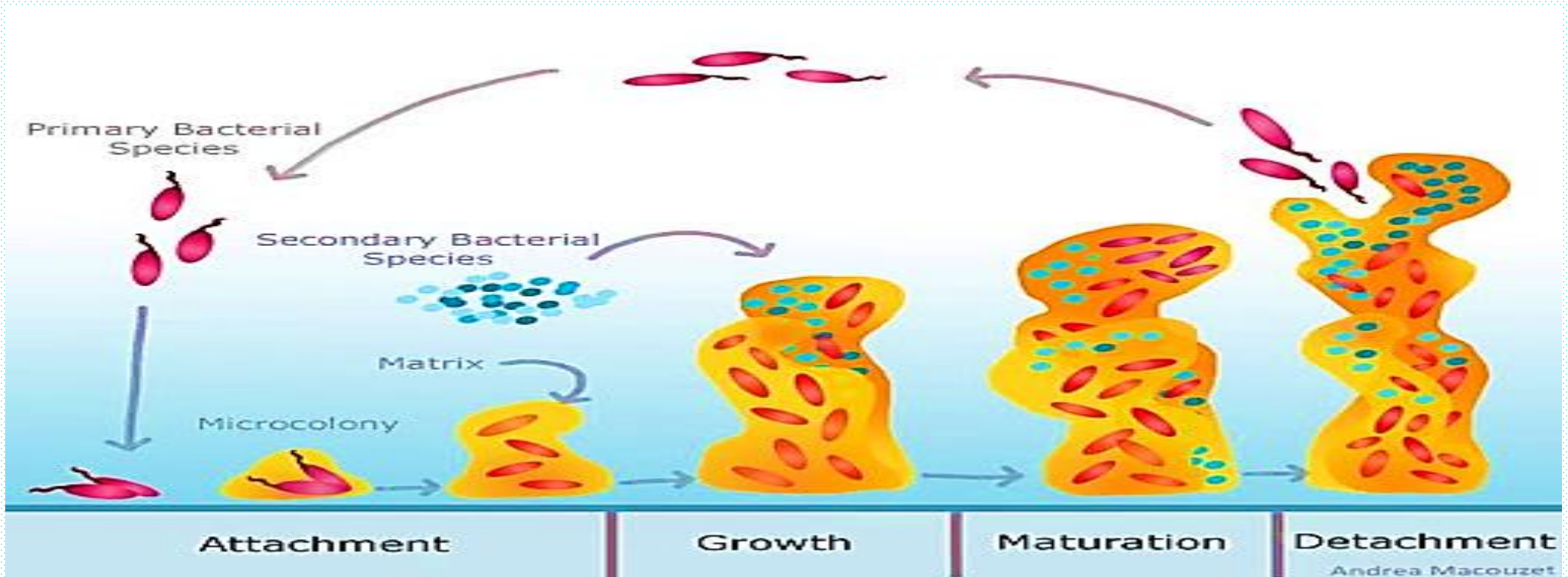
Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.

2. Adherence to host surfaces:

- **Biofilm formation:** Once the organisms adhere to a host surface they usually tend to aggregate and form intelligent communities of cells called **biofilms**.
- A **biofilm**; is defined as **an aggregate of interactive bacteria** attached to a **solid** surface (such as a denture prosthesis or an intravenous catheter) or to **each other, encased** in an **extracellular polysaccharide matrix**.
- **Dental plaque** on solid enamel surfaces is a classic example of a biofilm.





Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.
- 3. **Invasiveness:** Invasiveness of bacteria plays a critical role in pathogenesis; this property is dependent upon secreted bacterial enzymes. A few examples are:
 - **Collagenase and hyaluronidase:** degrade their respective intercellular substances, allowing easy spread of bacteria through tissues, and are especially important in skin infections caused by *Streptococcus pyogenes*.
 - **Coagulase:** produced by *Staphylococcus aureus*, accelerates the formation of a **fibrin clot** (from fibrinogen). It helps protect the organisms from **phagocytosis** by walling off the infected area and by coating the organisms with a fibrin layer.



Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.
- 3. **Invasiveness:** Invasiveness of bacteria plays a critical role in pathogenesis; this property is dependent upon secreted bacterial enzymes. A few examples are:
 - **Immunoglobulin A (IgA) protease** degrades protective IgA on mucosal surfaces, allowing organisms such as *N. gonorrhoeae*, *Haemophilus influenzae* and *Streptococcus pneumoniae* to adhere to mucous membranes.
 - **Leukocidins** can destroy both neutrophilic leukocytes and macrophages; the periodontopathic organism *Aggregatibacter actinomycetemcomitans* possesses this enzyme. The mutants that do not secrete the enzyme are less virulent.



Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.
- ❖ Other factors also contribute to invasiveness by interfering with the host defence mechanisms, especially phagocytosis:
 - The **polysaccharide capsule** of several common pathogens, such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, prevents the phagocyte from adhering to the bacteria.
 - The **cell wall proteins** of the Gram-positive cocci, such as the **M protein** are also antiphagocytic.



Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.
- ❖ Therefore, Bacterial infection may lead to two categories of inflammation: pyogenic (pus-producing) and granulomatous (granuloma-forming).:
 - **Pyogenic inflammation**, The neutrophils are the predominant cells in this type of inflammation *Streptococcus pyogenes*, *Staphylococcus aureus* and *Streptococcus pneumoniae* are the common pyogenic bacteria.
 - **Granulomatous inflammation**, Macrophages and T cells predominate in this type of inflammation. The most notable organism in this category is *Mycobacterium tuberculosis*.



Determinants of bacterial pathogenicity

- The major steps are **transmission, adherence to host surfaces, invasiveness** and **toxigenicity**.
- 4. **Toxigenicity:** Toxin production or toxigenicity is another major mediator of bacterial disease. Toxins are of two categories: **endotoxins** and **exotoxins**.:
 - **Endotoxins:** Endotoxins are the cell wall lipopolysaccharides of Gram negative bacteria (both cocci and bacilli) and are not actively released from the cell.
 - **Exotoxins:** Both Gram-positive and Gram-negative bacteria secrete exotoxins. An exotoxin can cause damage to the host by destroying cells or disrupting normal cellular metabolism.
 - **Bacterial exotoxins can be broadly categorized as:**
 1. **Neurotoxins** (action is mediated via neuronal pathways).
 2. **Enterotoxins** (act on the gut mucosa and cause gastrointestinal disturbances).
 3. **miscellaneous exotoxins (clostridia)**

