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Medical Bacteriology (460 MIC)

lecture 1

Bacterial - Host Relationships

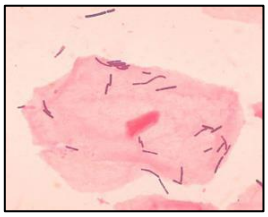
Bacterial - Host Relationships in Humans

Bacterial- Host relationships: Beneficial or harmful relationship between the host and the bacteria.

The association may take one of the three forms of symbiotic association:

1.Mutualism.

Both members of the association are **benefit**. For example, **lactic acid bacteria** live on the **vaginal** epithelium of a woman. The bacteria are provided habitat with a constant temperature and supply of nutrients (glycogen) in exchange for the production of lactic acid, which protects the vagina from colonization and disease caused by yeast and other harmful microbes.



Lactobacilli in association with a vaginal epithelial cell (CDC).

2. Commensalism.

No apparent benefit or harm to either member of the association. A problem with commensal relationships, as an example; ***Staphylococcus epidermidis***, a consistent inhabitant of the skin of humans. The bacteria produces lactic acid that protects the skin from colonization by harmful microbes that are less acid tolerant. But it has been suggested that other metabolites that are produced by the bacteria are an important cause of body odors (good or bad, depending on person).

Or

A Symbiotic relationship which **one member benefit, and the other is neither helped nor harmed.** For example: *E. coli* commonly found in the guts in human, where it gets important vitamins

3. Parasitism (Pathogenic).

Harmful

The bacteria is capable of causing **disease** to the host. This type of a symbiotic association may become pathogenic and damage to the host. Some pathogenic bacteria live as normal flora of humans while waiting for an opportunity to cause disease. Other non-indigenous pathogens generally always cause disease if they associate with a non-immune host.

Bacterial - Host interactions

The human is regularly in contact with bacteria but only a few of these are able to establish themselves within the host tissues.

When a bacteria tries to establish itself on its host, the host responds by assembling a series of defense mechanisms.

Resistance: ability of the host to prevent establishment of infection through defense mechanisms

Susceptibility: cannot prevent the infection establishment

The outcome of the host- bacteria relationship depends on a balance between the virulence of the bacteria and host defenses.

Bacterial Pathogenesis

Basic Terms describing aspects of pathogenesis

Pathogen: a microorganism (or virus) that is able to cause disease.

Pathogenicity the ability of microbe to initiate and cause disease in host.

Pathogenicity process decided by:

- Virulence factors of bacteria
- Infectious Dose (the number of bacteria required to cause disease).
- Route of entry into the body (if certain pathogen enter through the wrong portal, they will not be infectious- some infectious agents can enter by more than one portal, Such as: *Mycobacterium tuberculosis*)

Virulence: the degree of pathogenicity

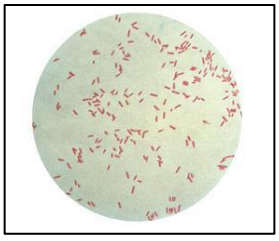
Producing ability of a microorganism as indicated by the severity of disease. Commonly ascertained by measuring the dosage required to caused specific degree of pathogenicity; one general standard is the **LD50 (lethal dose 50%)** = the number of bacteria (or bacterial products such as toxins) required to cause death or disease in 50% of the tested animal**.**

Opportunistic Bacteria: Normal flora that under normal condition cause no harm but can cause disease under certain condition.

- in a compromised host which would not occur in a healthy person.
- when transport from normal flora site (colonization) into sterile sites.
- Dysbacteriosis; microbial imbalance inside body (*the state in which the proportion of bacterial species and the number of normal flora colonization in certain site of a host present large- scale alteration*).

Examples of the normal flora can such as *Pseudomonas aeruginosa*, *Staphylococcus aureus,* and *E. coli* can cause an **opportunistic infection**.

When a member of the normal flora causes an infectious disease, it sometimes referred to as an **endogenous bacterial disease.**



P. aeruginosa, one of the **most common opportunistic pathogens** of humans. It causes urinary tract infections, respiratory system infections, dermatitis, bacteremia and a variety of systemic infections, particularly in immunosuppressed patients. CDC.

Obligate pathogens: There are some pathogens that do not associate with their host except in the case of disease. Some may rarely occur as normal flora.

Disease: any deviation or an abnormal condition of body function(s) or structure that is considered to be harmful to the affected individual (host) of any part, organ, or system of the body**.**

Invasiveness: is the ability of pathogen to enter the body and spread (invade) in the tissues. It includes mechanisms for

- **adherence factors such as pilli**
- **Capsules**
- **production of extracellular enzymes which facilitate invasion (**invasions) and **ability to overcome host defense mechanisms**.

Toxigenicity: the ability of pathogen to produce toxins causing a disease. Bacteria may contain two types of toxins (**exotoxins** and **endotoxins**).

Determinants of Virulence: Pathogenic bacteria are able to produce disease because they possess certain **structural** or **biochemical** or **genetic** traits (Virulence factors) that render bacteria to cause disease

- Some pathogens may rely on a **single determinant of virulence, such as toxin production**, to cause damage to their host. Bacteria such as ***Clostridium tetani*** **and** ***Corynebacterium diphtheriae***, are able to produce disease, the symptoms of which depend on a single genetic trait in the bacteria: the ability to produce a toxin.

- Other pathogens, such as ***S. aureus, Strep. pyogenes*** **and** ***P. aeruginosa,*** maintain a **large virulence determinants** and they are able to produce a **range of diseases** that affect different tissues in their host.

Infection: The process of colonization and / or invasion and multiplication of pathogen in the host with or without manifestation of disease.

Infectious process are complex and involve a series of shifting interactions between host and pathogen.

- **For the pathogen;**
  - depends on the ability to **evade or overcome host defenses**
  - **increase insufficient numbers**
  - **transmit to new host**

- **For the host,**
  - **having useful immune defenses.**
  - **Depends on susceptibility to infection.**

Sources of infectious diseases:

- Exogenous infections

- Patients
- Carriers (those in whom pathogens are present and may multiplying, but shows no sign of symptoms)
- Contaminated animals
- Endogenous infections

The Infectious Process

Pathogens must be able to accomplish the steps requirements for infection

1. Entry (getting in)

Sites of entry in human hosts include, the digestive tract; enter through eating- the respiratory tract; enter through inhaling- urogenital tract, the conjunctiva and Skin.

2. Colonization The first stage of bacterial infection

Establishment of the pathogen at the appropriate portal of entry (staying in)

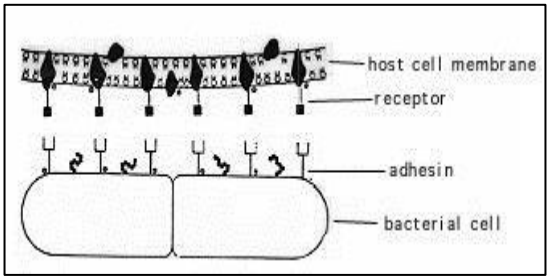
Pathogens usually colonize host tissues that are in contact with the external environment

Adhesion (Once bacteria in the body, it must adhere to host cells, usually epithelial cells by pilli, biofilm, surface proteins....etc.)

Bacterial adherence or attachment to tissue surface requires the participation of two factors: **Receptor** and **ligand.**

- **Receptors** are usually specific carbohydrate or peptide residues on the eukaryotic cell surface.
- **Bacterial ligand**, called also an **adhesion,** is a macromolecular component of the bacterial cell surface which interacts with the host cell receptor.

Adhesions and receptors usually interact in a complementary and specific fashion.



Specific adherence between host cell tissue and the bacterial surface.

•After establishment at a primary site of infection, they grow in the host and spread

•Infection can be **localized** (stand for the case that the bacteria remains confined to a specific tissue)

Or **systemic infection** (spread through tissues or via the lymphatic system to bloodstream).

•Bloodstream infection can be transient or persistent;

Bacteremia: transitory disease in which bacteria present in blood are usually cleared from vascular system with no harmful effects.

Bacteremia allows bacteria to spread widely.

Septicemia: disease in which the blood serves as a site of bacterial multiplication as well as allows bacteria to spread in the body.

3. Invasion

Most invasions are proteins (enzymes) that act locally to damage host cells and/or have the immediate effect of facilitating the growth and spread of the pathogen.

4. Immune Evasion Defeat the host defenses via bacterial virulence factors

5. Propagation Damage the host by bacterial toxins (*Toxic substances, both soluble and cell- associated, may be transported by blood and lymph and cause cytotoxic effects at tissue site remote from the original point of invasion or growth. Some bacterial toxins may also act at the site of colonization and play a role in invasion*).

6. Transmission Be transmissible

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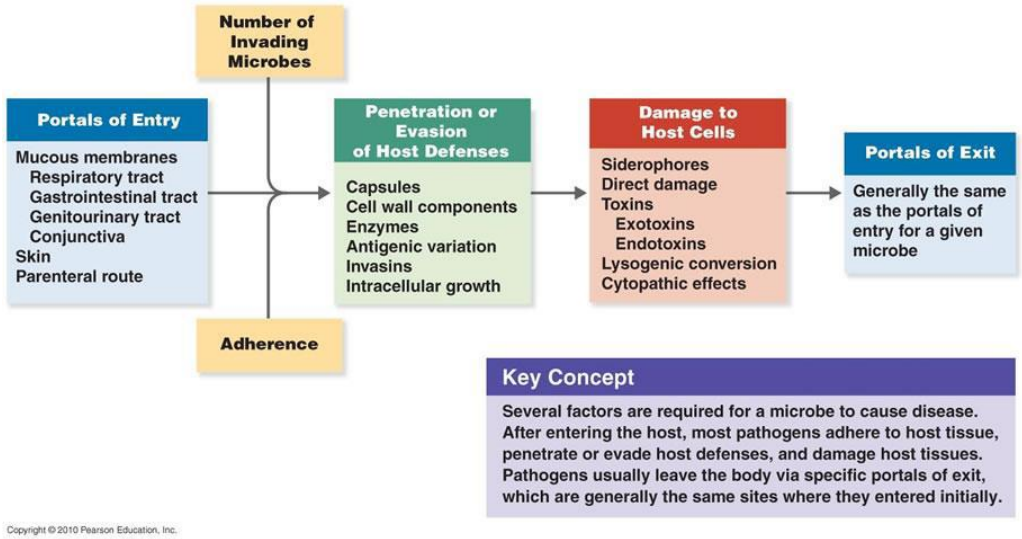
Terms used to describe Adherence factors in Host Bacteria interaction

Adhesion- Ligand	Surface macromolecule structure that binds bacteria to specific surface receptors.
Receptor	A complementary macromolecular binding site on a (eukaryotic) surface that binds specific adhesions or ligand
Lectin	Any protein that binds to a carbohydrate
Mucous	The mucopolysaccharide layer of glycosaminoglycan covering cell mucosal surfaces
Fimbriae	Filamentous proteins on the surface of bacterial cells that may behave as adhesions for specific adherence
S- layer	Proteins that form the outer cell envelope component of a broad spectrum of bacteria, enabling them to adhere to host cell membranes and environmental surfaces in order to colonize
Glycocalx	A layer of exopolysaccharide fibers on the surface of bacterial cells which may be involved in adherence to a surface. Sometimes a general term for a capsule
Capsule	A detectable layer of polysaccharide (rarely polypeptide) on the surface of a bacterial cell which may mediate specific or nonspecific attachment.
Lipopolysaccharide (LPS)	A distinct cell wall component of the outer membrane of Gram-negative bacteria- mediate specific adherence
Teichoic acids & lipoteichoic acids (LTA)	Cell wall components of Gram- positive bacteria that may involved in nonspecific or specific adherence

Mechanism of Microbial Pathogenic



Specific Adherence of Bacteria to Cell and Tissue Surfaces

Specific bacteria colonize specific tissues by one or another of mechanisms (**Tissue specificity**)

1- Tissue tropism: bacteria are known to have a preference to colonize certain tissues over others, host provides essential nutrients and growth factors for the bacteria, in addition to suitable oxygen, pH, and temperature for growth.

e.g. ***Strep. mutans*** is abundant in **teeth but does not occur on epithelial surfaces of the tongue**; the reverse is for ***Strep . salivarius*** which is attached in high numbers to **epithelial cells of the tongue but is absent in dental plaque.**

2- Specific Adherence: biochemical interaction between **(receptor and ligand)**

3- Species specificity: certain pathogenic infect only certain species of hosts, e.g. ***Niesseria gonorrhoeae*** infections are limited to humans; ***Strep. pyogenes*** infections occur only in humans.

Spreading Factors

"Spreading Factors" are family of bacteria enzymes that affect the physical properties of tissue matrices and intercellular spaces, thereby promoting the spread of the pathogen.

•**Hyaluronidase**. produced by **streptococci. staphylococci, and clostridia**. The enzyme attacks the ground substance of **connective tissue by depolymerizing hyaluronic acid.**

•**Collagenase.** Produced by ***Clostridium perfringens***. It breaks down **collagen, the framework of muscles,** which facilitates gas gangrene.

•**Neuraminidase.** Produced by intestinal pathogens such as ***Vibrio cholera*** and ***Shigella dysenteriae***. It degrades **neuraminic acid (also called sialic acid**), and intracellular cement of the epithelial cells of the intestinal mucosa.

•**Streptokinase & Staphylokinase.** produced by **streptococci and staphylococci . Kinase** enzymes **convert inactive plasminogen to plasmin which digests fibrin and prevents clotting of the blood.** The absence of fibrin allows more rapid diffusion of the infectious bacteria.

•**Leukocidin.** Produced by **Staphylococci & Streptococci** (Streptolycin); lyse **phagocytes and their granules.** They are also considered to be bacterial exotoxins.

•**Phospholipases.** Produced by ***C. perfringens*** (alpha toxin), hydrolyze phospholipids in cell membranes .

•**Lecithinase.** Produced by ***C. perfringens* ,** destroy **lecithin in cell membranes.**

•**Hemolysin.** Lyse **red blood cells**, produced by **Staphylococci, Streptococci and various Clostridia.**

•**Staphylococcal coagulase.** formed by ***S. aureus***, is a cell-associated and diffusible enzyme that **converts fibrinogen to fibrin which causes clotting**. Coagulase activity is almost always associated with pathogenic *S. aureus* and almost never associated with nonpathogenic *S. epidermidis,* which its role as a determinant of virulence.

•**Extracellular Digestive Enzymes** wide variety of extracellular enzymes including **proteases**, **lipases**, **nucleases**, etc., These enzymes have other functions related to bacterial **nutrition or metabolism**, but may aid in **invasion or pathogenesis** either directly or indirectly.

Review Questions

1- Definitions: Invasiveness, Toxigenesis , virulence, virulence factors, pathogenicity, LD50?

2- Compare between ligand & receptor- lipopolyscaccharide & Teichoic acid ?

3- What do you know about Tissue tropism with examples?

4- You studied different types of spreading factors, what they are, with examples?

5- How can you differ between pathogenic bacteria and non-pathogenic bacteria?

6- Some pathogens contains only one virulence factor, while other pathogens maintain large numbers of virulence factors. And each of them are able to produce disease. Give example of each of them?

7- Pathogenic must be able to accomplish the steps requirements for infection, what they are (in points) explain only second step?

8- What do you know about opportunistic pathogens, with give examples?

9- Give three examples of the forms of host bacterial relationships (only in points)?