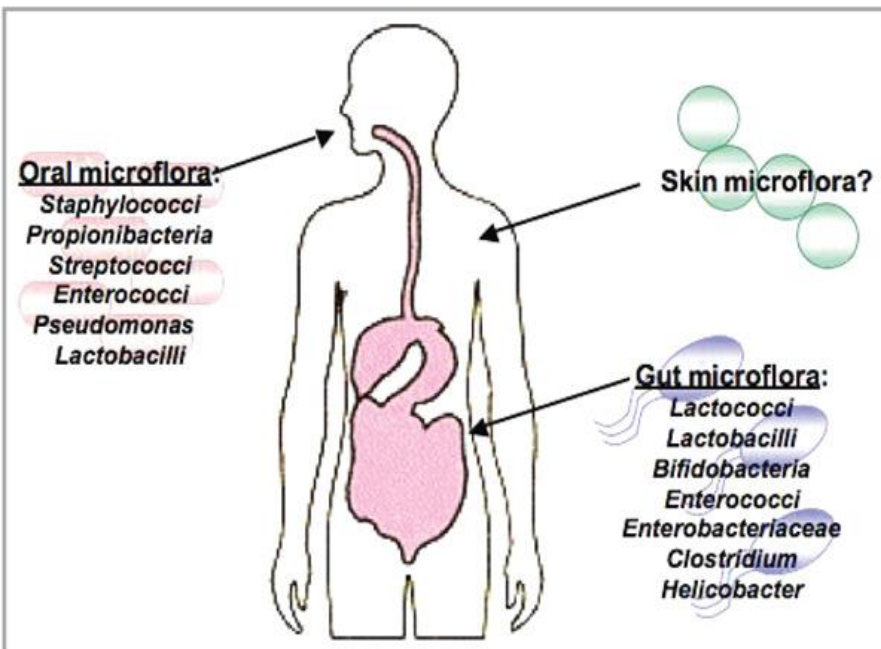
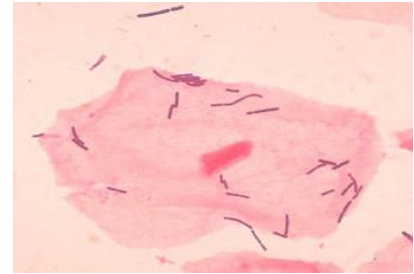


# Medical bacteriology: lecture 1

## 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:
  1. **Mutualism.** Both members of the association **benefit**. For humans, **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).
  - **3. Parasitism (Pathogenicity).** 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.

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



# Bacterial - Host interactions

- The human host is regularly in contact with microorganisms 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 the resistance of the host**

# Bacterial Pathogenesis

## Basic Terms describing aspects of pathogenesis

- **Pathogen:** is a microorganism (or virus) that is able to produce disease.
- **Pathogenicity** is the ability of a microorganism to cause disease in another organism. Pathogenicity may be a manifestation of a host-parasite interaction.
- In humans, some of the normal bacterial flora (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*) are **potential pathogens** that live in a commensal or parasitic relationship without producing disease. They do not cause disease in their host unless they have an opportunity brought on by some compromise or weakness in the host's immunity. Furthermore, the bacteria are in a position to be transmitted from one host to another, giving them additional opportunities to colonize or infect.
- There are some pathogens that do not associate with their host except in the case of disease. These bacteria may be thought of as **obligate pathogens**, even though some may rarely occur as normal flora.
- **Opportunistic Pathogens** Bacteria which cause a disease in a compromised host which typically would not occur in a healthy (non compromised) host are acting as **opportunistic pathogens**. A member of the normal flora can such as *S. aureus* or *E. coli* can cause an **opportunistic infection**, but so can an environmental organism such as *Pseudomonas aeruginosa*.
- An agent capable of causing a disease only when transport from normal flora site into sterile sites.
- When a member of the normal flora causes an infectious disease, it sometimes referred to as an **endogenous bacterial disease**. Classic opportunistic infections in humans are dental caries and periodontal disease caused by normal flora of the oral cavity.

# Basic terms describing aspects of pathogenesis

- **Disease:** an abnormal condition of body function(s) or structure that is considered to be harmful to the affected individual (host); any deviation from or interruption of the normal structure or function of any part, organ, or system of the body.
- **Infectious Dose:** number of pathogenic organism required to cause disease in a given host.
- **Invasiveness:** is the ability of pathogen to invade tissues. It includes mechanisms for **colonization (adherence and initial multiplication), production of extracellular substances which facilitate invasion (invasions) and ability to overcome host defense mechanisms.**
- **Toxigenicity:** the ability of pathogen to produce a toxin causing a disease. Bacteria may contain two types of toxins ( **exotoxins** and **endotoxins**).
- **Non-pathogens:** a microbe that does not cause a disease but it may be a part of the normal flora. Not contain virulence factor.
- **Infection:** The colonization and / or invasion and multiplication of pathogen in the host with or without manifestation of disease. Infectious disease are complex and involve a series of shifting interactions between host and pathogen.
- For the pathogen; the interactions depends on the ability to **evade or overcome host defenses**
- **increase insufficient numbers**
- **transmit to new host**
- For the host, the interactions depends on: **the host having useful functioning defenses.**
- **the host s susceptibility to infection**

# Basic terms describing aspects of pathogenesis

- **Virulence:** a measure of pathogenicity, ( the degree of disease)
- 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 microorganisms required to cause lethality ( death) in 50% of the tested animal.
- **Determinants of Virulence**
- Pathogenic bacteria are able to produce disease because they possess certain **structural** or **biochemical** or **genetic** traits ( Virulence factors) that render them pathogenic or **virulent**.
- The sum of the characteristics that allow a given bacterium to produce disease are the pathogen's **determinants of virulence**.
- 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*, which have hardly any invasive characteristics, 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 more complete range of diseases that affect different tissues in their host.

# (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 and the conjunctiva.
- **2. Colonization** Establishment of the pathogen at the appropriate portal of entry (staying in)
  - The first stage of bacterial infection
  - 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**.
    - **The receptors** are usually specific carbohydrate or peptide residues on the eukaryotic cell surface.
    - **The bacterial ligand**, called also an **adhesion**, is typically 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
  - After establishment at a primary site of infection, they grow in the host and spread
  - Infection can spread through tissues or via the lymphatic system to bloodstream.
  - Bloodstream infection (bacteremia) can be transient or persistent.
  - Bacteremia allows bacteria to spread widely in the body and permits them to reach tissues suitable for their
  - multiplication

## Terms used to describe Adherence factors in Host Bacteria interaction

<b>Adhesion- Ligand</b>	A surface macromolecule structure that binds a bacterium to a specific surface receptors
<b>Receptor</b>	A complementary macromolecular binding site on a ( eukaryotic) surface that binds specific adhesions or ligand
<b>Lectin</b>	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
<b>Capsule</b>	A detectable layer of polysaccharide (rarely polypeptide) on the surface of a bacterial cell which may mediate specific or nonspecific attachment.
<b>Lipopolysaccharide (LPS)</b>	A distinct cell wall component of the outer membrane of Gram-negative bacteria- mediate specific adherence
<b>Teichoic acids &amp; lipoteichoic acids (LTA)</b>	Cell wall components of Gram- positive bacteria that may involved in nonspecific or specific adherence



# Specific Adherence of Bacteria to Cell and Tissue Surfaces

- **1- Tissue tropism:** bacteria are known to have a preference for certain tissues over others, 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- Species specificity:** certain pathogenic infect only certain species of animals, e.g. *Niesseria gonorrhoeae* infections are limited to humans; *Strep. pyogenes* infections occur only in humans.
- **3- Genetic specificity within a species:** certain strains are genetically immune to a pathogen, e.g. certain pigs are not susceptible to *E . coli* (K – 88) infections.

- **3. Invasion**

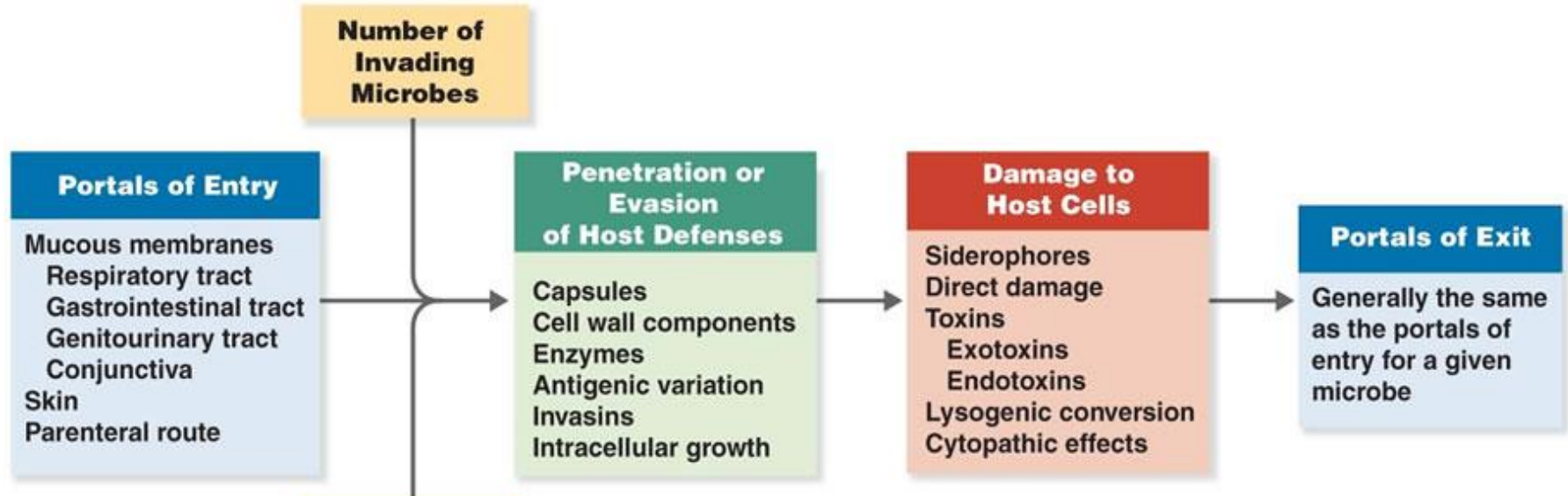
- The Invasion of a host by a pathogen may be aided by the production of bacterial extracellular substances which act against the host by breaking down primary or secondary defenses of the body. Most invasions are proteins (enzymes) that act locally to damage host cells and/or have the immediate effect of facilitating the growth and spread of the pathogen.
- The extracellular proteins produced by bacteria which promote their invasion are not clearly distinguished from some extracellular protein toxins ("exotoxins") which also damage the host.
- Exotoxin typically are more specific and more potent in their activity than invasions . Some classic exotoxins (e.g . Diphtheria toxin, anthrax toxin) may play some role in colonization or invasion in the early stages of an infection, and some invasions (e. . Staphylococcal leukocidin) have a relatively specific effect.

- **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*).

- **5. Transmission**                      Be transmissible

# Mechanism of Microbial Pathogenic



## Key Concept

Several factors are required for a microbe to cause disease. After entering the host, most pathogens adhere to host tissue, penetrate or evade host defenses, and damage host tissues. Pathogens usually leave the body via specific portals of exit, which are generally the same sites where they entered initially.

# 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** (Streptolysin); 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** a 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 Question

- 1- What do you know about: Tissue tropism with examples?
- 2- Definitions: Invasiveness, Toxigenesis, virulence, virulence factors, colonization, spreading factors, pathogens, pathogenicity, opportunistic pathogens, LD50, Infection
- 3- Compare between ligand and receptor- lipopolysaccharide and Teichoic acid ?
- 4- You studied different types of spreading factors, what they are?
- 5- Compare between the three bacterial host relationships with examples?
- 6- One of the most common opportunistic pathogens of humans, what is it?
- 7- Pathogens must be able to accomplish the steps requirements for infection, what is it ( in points) explain only first and second steps?
- 8- 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. Explain with examples?
- 9- How can you differ between pathogenic bacteria and non pathogenic bacteria?
- 10- Give three example of the normal flora which may be a true pathogen?