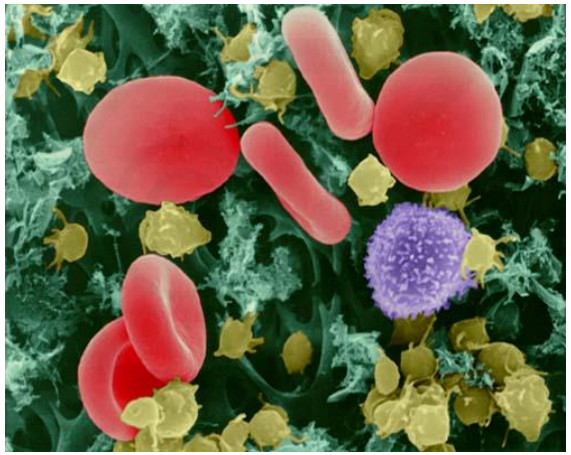
Medical bacteriology- Lecture 3

Host Immune Defenses against Bacterial Pathogens



Human blood contains most cellular and non cellular factors that participate in host immunity to bacterial pathogens

The Property of Host Defenses

- **The host and microbes are in a dynamic interaction. The outcome of such a relationship depends on the properties of the microbes and of the host;**

- 1- The virulence of the pathogen (invade, damage the host, resist the defenses of the host).
- 2- The degree of host resistance or susceptibility of the host (effectiveness of the host defense mechanisms)

- **Host Defenses**

A healthy human can defend itself against pathogens at different stages in the infectious disease process. The host defenses may be prevent entirely of infection. Or, if infection does occur, the defenses may stop the process before disease is apparent.

- **Typically the host defense mechanisms are divided into two groups:**
- **1. Innate Defenses**. Also known as ("natural" or "constitutive" resistance)

- **2. Adaptive Defenses**. Also known as (acquired or inducible immunity)

- **Adaptive Immunity is sometimes divided into two types**
- **1- Active immunity,** the host undergoes an immunological response and produces the cells and factors responsible for the immunity, i.e., the host produces its own antibodies and/or lymphocytes. Active immunity can persist a long time in the host.

- **2- Passive immunity** is acquisition by a host of immune factors which were produced in another animal, i.e., the host receives antibodies and/or immuno-reactive lymphocytes originally produced in another animal. Passive immunity is typically short-lived.

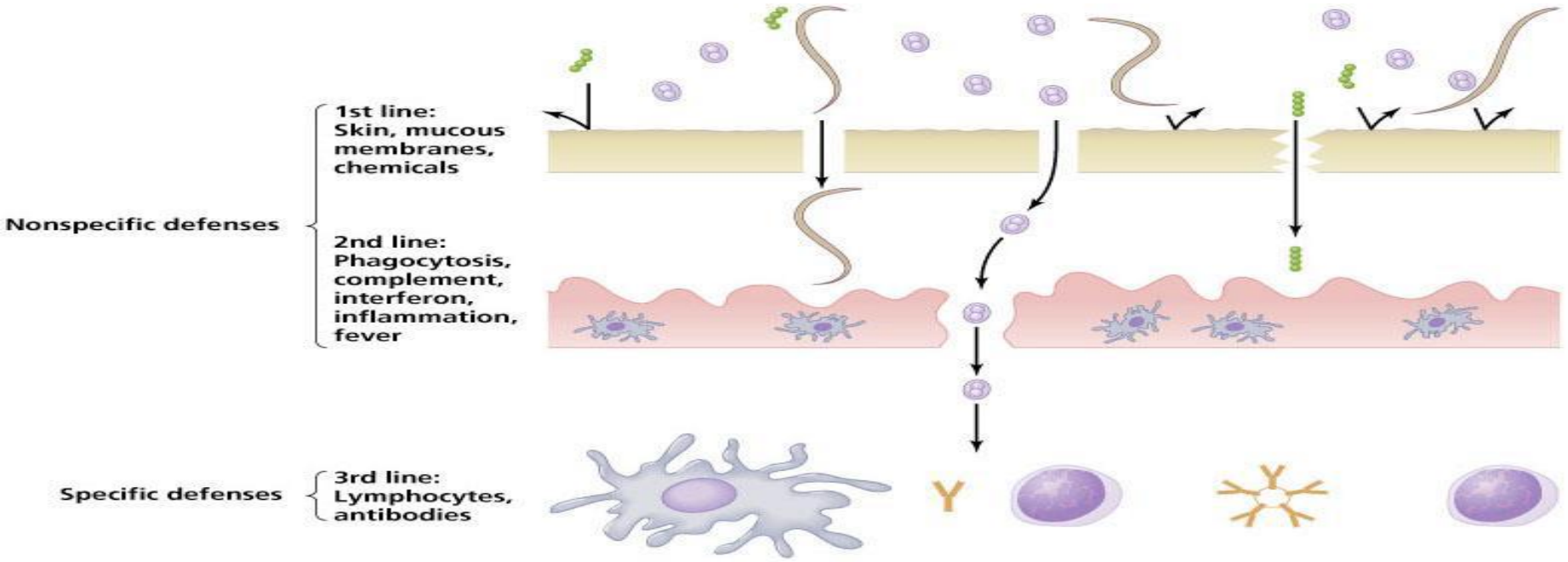
Innate defense Vs. Adaptive defense

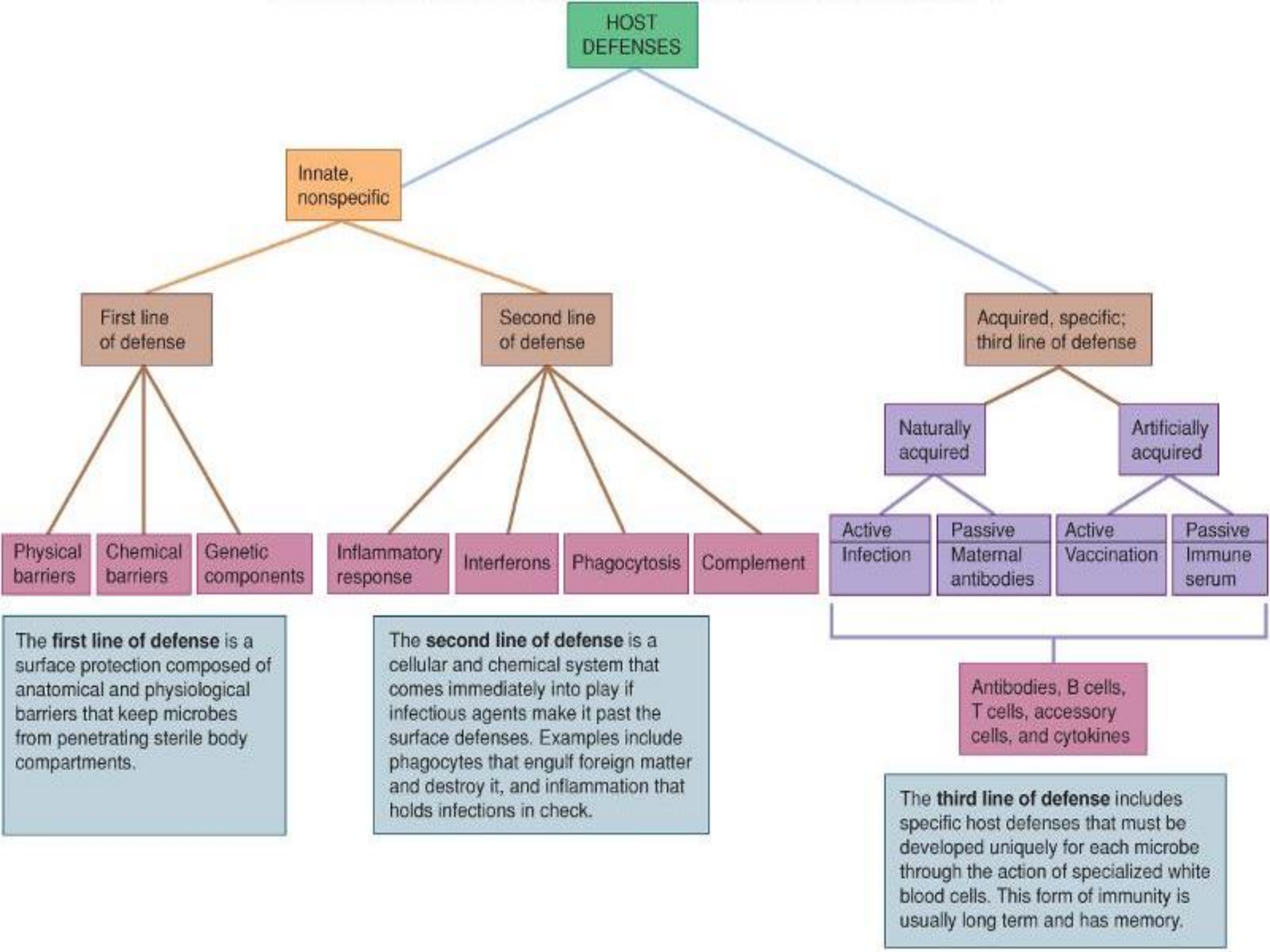
Innate defense	Adaptive defense
Common, inherent, natural to all healthy human. That meaning they are continually ready to respond and do not require a period of time for induction,	They are not immediately ready to come into play until after the host is exposed to the pathogen must be induced by host exposure to a pathogen (as during an infection).
Generally lacks specificity	Highly specific for a particular pathogen
Generally lacks memory	Possesses memory i.e. the onset of the response is fast successive exposures to the pathogen
First and second line of host defenses	Third line of host defense
Includes: anatomical and structural (physical) barrier - Inflammation - Complement- phagocytosis - the presence of normal flora	involve the immunological responses to a pathogen causing an infection. Antimicrobial chemicals, but no physical barriers
mast cells, monocytes/macrophages, natural killer (NK) cells, polymorphonuclear leukocytes (PMNL) , cells are primarily involved	Antigen-presenting cells, T lymphocytes and B lymphocytes are the major cellular components

Immunity

- **Innate immunity**
  - humoral: Complement system; Cytokines
  - cellular: Macrophages; Granulocytes; NK cells
- **Acquired immunity**
  - humoral: Antibodies
  - cellular: Lymphocytes; Dendritic Cells

Innate (Nonspecific) Immunity		Adaptive (Acquired) Immunity (Chapter 17)
First line of defense	**Second line of defense**	**Third line of defense**
• Intact skin • Mucous membranes and their secretions • Normal microbiota	• Natural killer cells and phagocytic white blood cells • Inflammation • Fever • Antimicrobial substances	• Specialized lymphocytes: T cells and B cells • Antibodies




HOST DEFENSES
Innate, nonspecific
Acquired, specific; third line of defense
First line of defense
Second line of defense
Naturally acquired
Artificially acquired
Physical barriers
Chemical barriers
Genetic components
Inflammatory response
Interferons
Phagocytosis
Complement
Active Infection
Passive Maternal antibodies
Active Vaccination
Passive Immune serum
The first line of defense is a surface protection composed of anatomical and physiological barriers that keep microbes from penetrating sterile body compartments.
The second line of defense is a cellular and chemical system that comes immediately into play if infectious agents make it past the surface defenses. Examples include phagocytes that engulf foreign matter and destroy it, and inflammation that holds infections in check.
Antibodies, B cells, T cells, accessory cells, and cytokines
The third line of defense includes specific host defenses that must be developed uniquely for each microbe through the action of specialized white blood cells. This form of immunity is usually long term and has memory.

Host Defense against Bacterial Infection

First Line of host defense

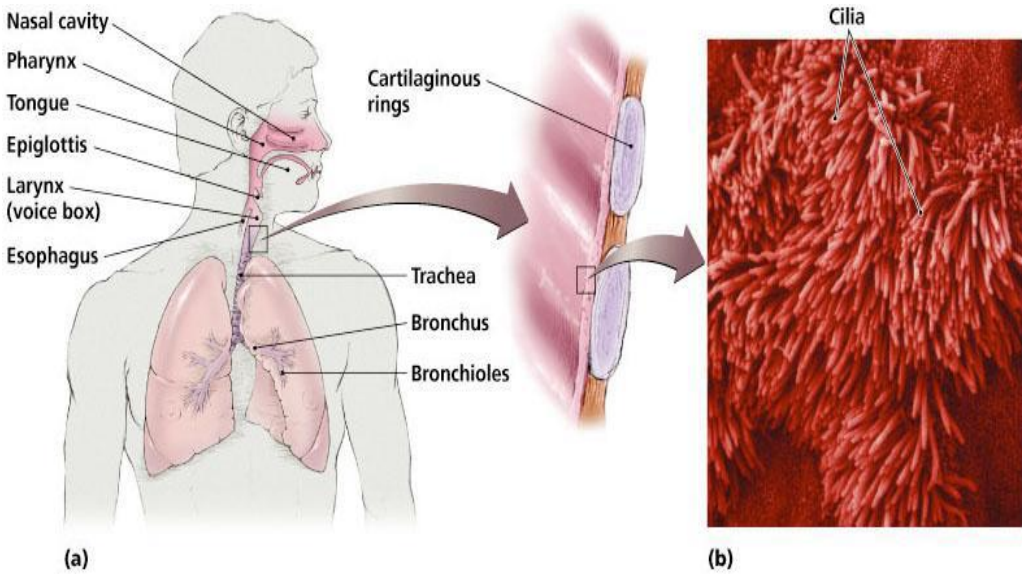
A- External Barriers:

- ### 1- Physical Barriers:

- **Skin:** The **intact surface-** rarely penetrated by bacteria. If the integrity of the epidermis is broken, invasive bacteria may enter. The **normal flora** of the skin, which metabolize substances secreted onto the skin, produce end products (e.g. fatty acids) that prevent the colonization of skin by pathogens. **Perspiration** contains **lysozyme** and other **antimicrobial substances**. **Salt-**inhibits growth of pathogen by drawing water from their cells, and Lysozyme-destroys cell wall of bacteria. **Lowers the pH** of the skin to a level inhibitory to many bacteria

- **Mucous membranes:** Line all body cavities open to the outside environment. Colonized with normal flora that restricted pathogens. The **normal flora** established on mucous membranes may antagonize pathogens. Mucus contains a number of types of anti-microbial compounds, including **lysozyme** and **secretory antibodies (IgA).**

- **Respiratory tract.** **hairs** of the nares (nasal membranes) entrap bacteria which are inhaled. Those which pass may stick to mucosal surfaces of trachea or be swept upward by the **ciliated epithelium** of the lower respiratory tract. **Coughing** and **sneezing** also eliminate bacteria. The lower respiratory tract (lung) is well protected by **mucus**, **lysozyme, secretory antibody,** and **phagocytosis.**



- **Mouth, stomach and intestinal tract.** Microorganisms entering by the oral route, more than any other, have to compete with the **normal flora** of the mouth and intestine. Most organisms that are swallowed are destroyed by **acid** and various secretions of the stomach. **Alkaline pH** of the lower intestine can prevent other organisms. The **action of the intestine** ultimately flushes out organisms which have not succeeded in colonization. **Bile salts** and **lysozyme** are present, which kill or inhibit many types of bacteria.

- **Urogenital Tract.** The **flushing mechanisms** and **acidity** of urine maintain the bladder and most of the urethra free of microbes. The vaginal epithelium of the female maintains a high population of *Lactobacillus acidophilus* whose acidic end products of metabolism **(lactic acid**) prevent colonization by most other types of microorganisms including potentially-pathogenic yeast (*Candida albicans*).

- **Eyes (Conjunctiva).** The conjunctiva of the eye is remarkably free of most microorganisms. **Blinking** mechanically removes microbes, the action of **tears** washes the surface of the eye, and the tears contain relatively large amounts of **lysozyme.**

- ## 2- Mechanical Barriers:
- ### Chemical Barriers:
- Many body organs secrete chemicals with antimicrobial properties
  (Stomach acid - Vaginal pH - Skin pH – Lysozyme- fatty acids-sweat)

- **Microbial flora:** The normal flora **antagonize** colonization of body surfaces by non indigenous bacteria. Normal microbiota help to protect the body by **competing** with potential pathogens. **Secrete antimicrobial substances** that limit pathogen growth. **Consumption of nutrients** makes them unavailable to pathogens. **Create an environment unfavorable** for pathogens by changing pH. **Helps stimulate the body defense**. Promote overall health by providing **vitamins** to host.

- **If these barriers are penetrated, the body contains cells that respond rapidly to the presence of the invader. These cells include macrophages and neutrophils that engulf foreign organisms and kill them. Bacterial invasion is also challenged by the activation of complement in blood and tissues and the inflammatory process which has the tendency to focus both the innate and adaptive immune defenses on the site of invasion.**

Host Defense Against Bacterial Infection

- **Second Line of host defense**
- **B- Internal barriers:**

- **Phagocytic cells:** Monocytes , Macrophages, Polymorphonuclear leukocytes (PMNs)
- **Lysozyme** (present in mucus and all body tissues and secretions).
- The internal tissues always contain **bactericidal substances**.
- **Iron Content.**
- **Chemotaxis (chemotactic factors such as: cytokines)**
- **Fever**
- **Complement system:** role in inflammation, phagocytosis and bacterial killing. Also play a role in adaptive immunity.

- **Third line of host defense**
- **Immunoglobulins (Antibodies):** IgM, IgA, IgG, IgE, IgD

- **Antigens:** chemical substances of high molecular weight, that stimulate the immune response. Bacteria are composed of various macromolecular components that are antigens in their host and bacterial antigens interact with the host immunological system in a variety of ways.

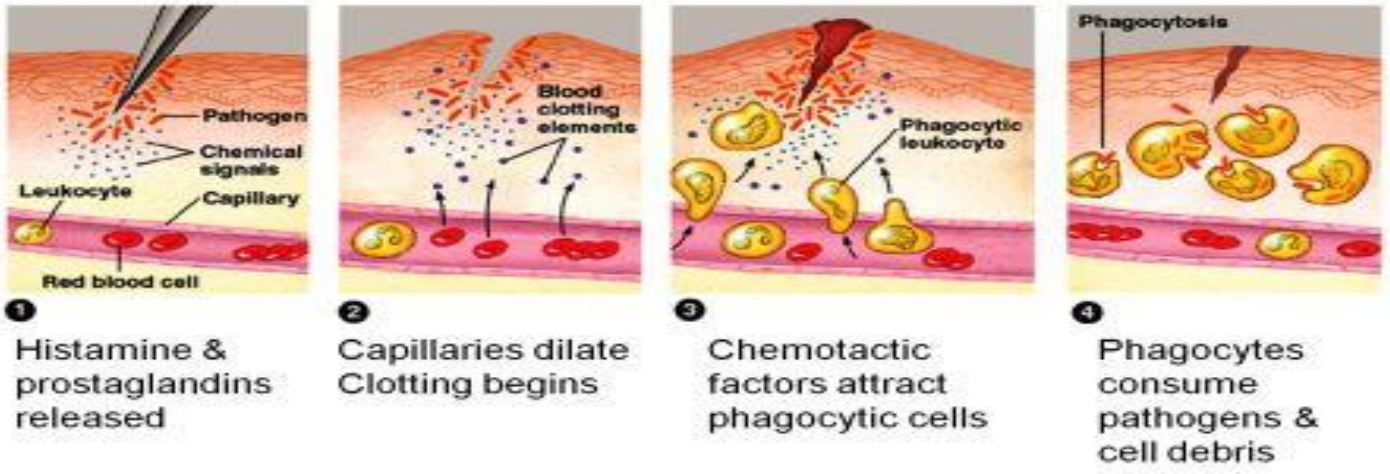
Inflammation (Non specific response)

The **inflammatory response** may be the most important for dealing bacterial infection.

Inflammation is necessary for all host defenses functions, because it focuses all circulating antimicrobial factors on the site of infection. (include phagocytes, lymphocytes, antibodies, complement and other antimicrobial components of plasma).

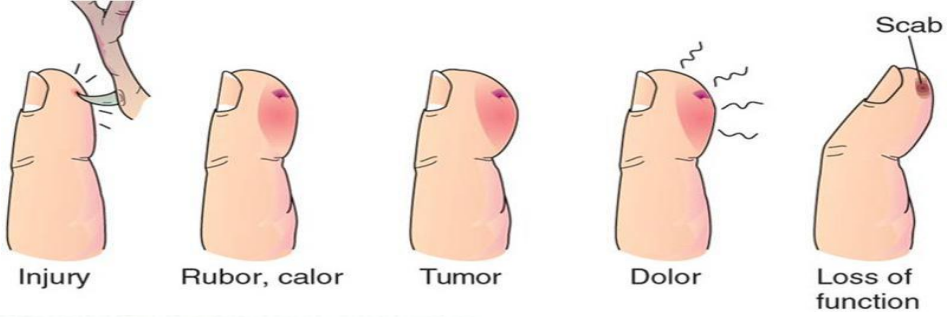
Inflammation is a tissue reaction to infection or injury, the **characteristic symptoms (**signs of inflammation) are **redness, swelling, heat** and **pain**. The redness is due to increased blood flow to the area of injury. The swelling is due to increased extravascular fluid and phagocytes to the damaged area. The heat is due to the increased blood flow and the action of pyrogens (fever-inducing agents). The pain is caused by local tissue destruction and irritation of sensory nerve receptors. If a whole organ or tissue is involved, **loss of function** may occur.

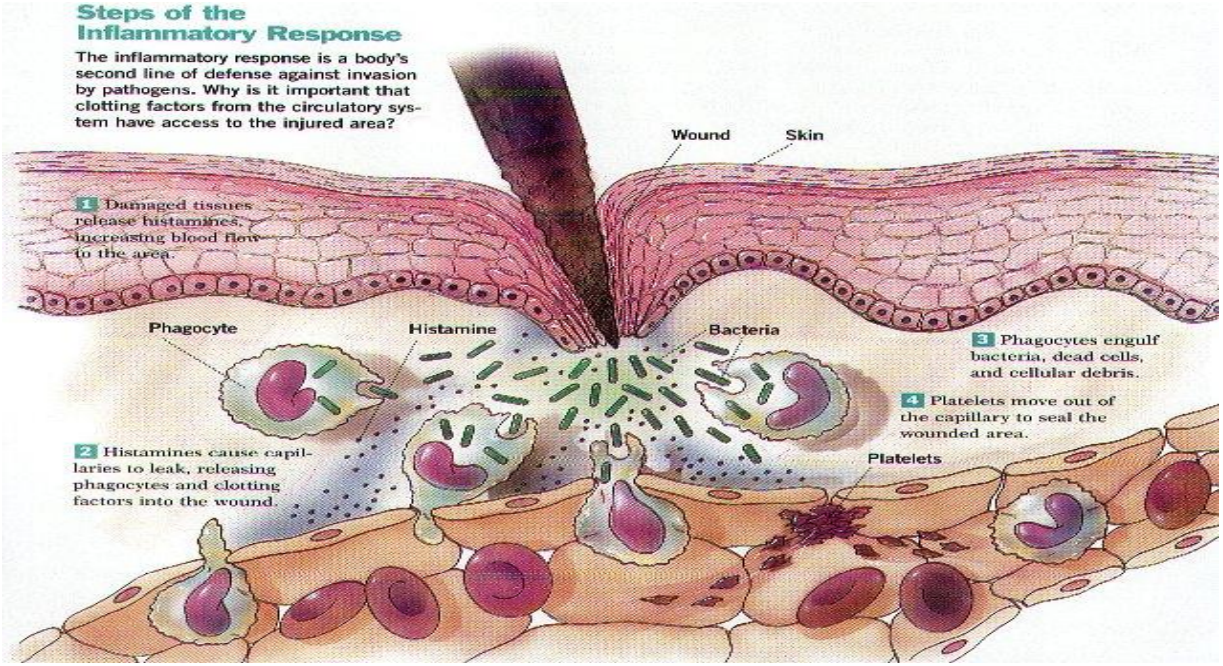
- Inflammation can be induced by certain **immunological reactions**, **tissue damage**, or the **entry of an injurious agent** (microbial or non microbial). Certain bacterial cells and/or their products (e.g. structural components or toxins) can induce an inflammatory response. Inflammation increases the blood supply and temperature in the inflamed tissues, which have maximal metabolic activity of the leukocytes, and lowers the pH slightly, which tends to inhibit the multiplication of many microorganisms.

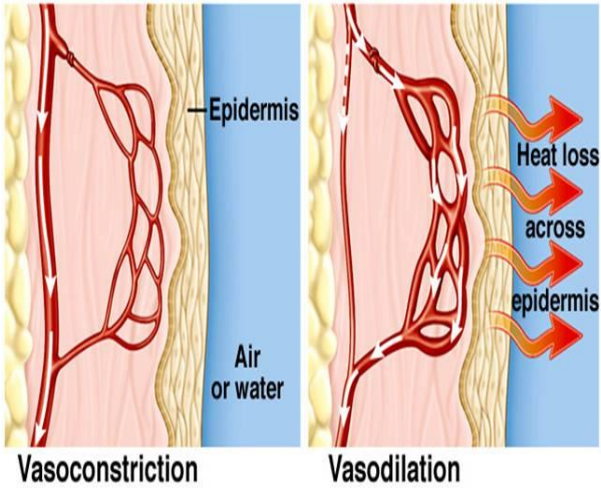


Signs of Inflammation

Inflammation is characterized by **4 signs: redness, heat, swelling & pain**







Inflammatory Response involves several steps:

1) Skin/cells are damaged.

2) Mast cells release **chemical messengers (**Histamine)-histamine causes blood vessels to expand. This causes redness & increased heat in the affected region. As a side effect, histamine causes itchiness. vessel walls more permeable or leaky

3) From the openings of blood vessels, phagocytes, Neutrophils & macrophages remove microbes or damaged tissue by phagocytosis (eating) and pus is formed. Also clotting factors, and platelets come out (healing). This causes swelling in the affected tissue.

Fever is triggered to kill pathogen.

animation

- Inflammatory Responces
- Inflammation
- Inflammation2

ANTIMICROBIAL SUBSTANCES OF HOST ORIGIN PRESENT IN BODY FLUIDS AND ORGANIZED TISSUES

Substance - Common Sources - Chemical Composition- Activity

*__Lysozyme -__ Serum, saliva, sweat, tears -Protein -Bacterial cell lysis

*__Complement__ - Serum – Protein -carbohydrate lipoprotein complex - Cell death or lysis of bacteria; participates in inflammation

*__Basic proteins & polypeptides__ (histones & other cationic proteins, tissue polypeptides) - Serum or organized tissues - Proteins or basic peptides- Disruption of bacterial plasma membrane

*__Lactoferrin & transferrin-__ Body secretions, serum, organized tissue spaces - Glycoprotein - Inhibit microbial growth by binding (withholding) iron

*__Peroxidase__ - Saliva, tissues, cells (neutrophils) - Protein - Act with peroxide to cause lethal oxidations of cells

*__Fibronectin__ - Serum & mucosal surfaces- Glycoprotein- Clearance of bacteria (opsonization)

*__Interleukins__ - Macrophages, lymphocytes - Protein - Cause fever; promote activation of immune system

Individual resistance

- **There are many reasons why some individuals may exhibit greater or lesser susceptibility to the same ineffective agent.**
- **Age.** development and status of the immunological system which varies with age- associated with changes in normal flora.
- **Sex.** presence and/or development of the sex organs- sex hormones.
- **Stress.** Stress is a complex of different factors that apparently has a real influence on health. shock, change in environment, climatic change, nervous or muscular fatigue, etc. are factors known to contribute to increases in susceptibility to infection. There are a number of relationships between stress-related hormones and the functioning of the immune defenses.
- **Diet, malnutrition.** Infections may be linked with vitamin and protein deficiencies, and this might explain partly why many infectious diseases are more prevalent and infant mortality rates are highest in parts of the world where malnourishment is a problem. Also, obese is more susceptible to infection. Diets high in sucrose predispose individuals to dental caries.
- **Intercurrent disease or trauma.** The normal defenses are impaired by organic diseases such as diabetes, AIDS, etc. Frequently, inflammatory or immune responses are delayed or suppressed. Colds or influenza may predispose an individual to pneumonia. Smoking tobacco predisposes to infections of the respiratory tract. Burned tissue is readily infected by *Pseudomonas aeruginosa.*
- **Therapy against other diseases.** Modern therapeutic procedures used in some diseases can render an individual more susceptible to infection. Under these conditions not only pathogens, but organisms of the normal flora and nonpathogens in the host's environment, may be able to initiate infection. Examples of therapeutic procedures that reduce the efficiency of the host's defenses are treatment with corticosteroids, cytotoxic drugs, antibiotics, or irradiation.

Review Questions

- Compare between Innate and adaptive immunity
- What do You Know about the External Barriers
- If the Pathogenic Bacteria Pass the External Barriers It Will be Faced by the
- Internal Barriers. Explain?
- Give Two Examples of The Phagocytic Cells
- What o you know about inflammation
- You studied the antimicrobial substances of host body fluids and tissues, explain them
- Why some individuals may exhibit resistant or susceptibility to the infections (only in points)