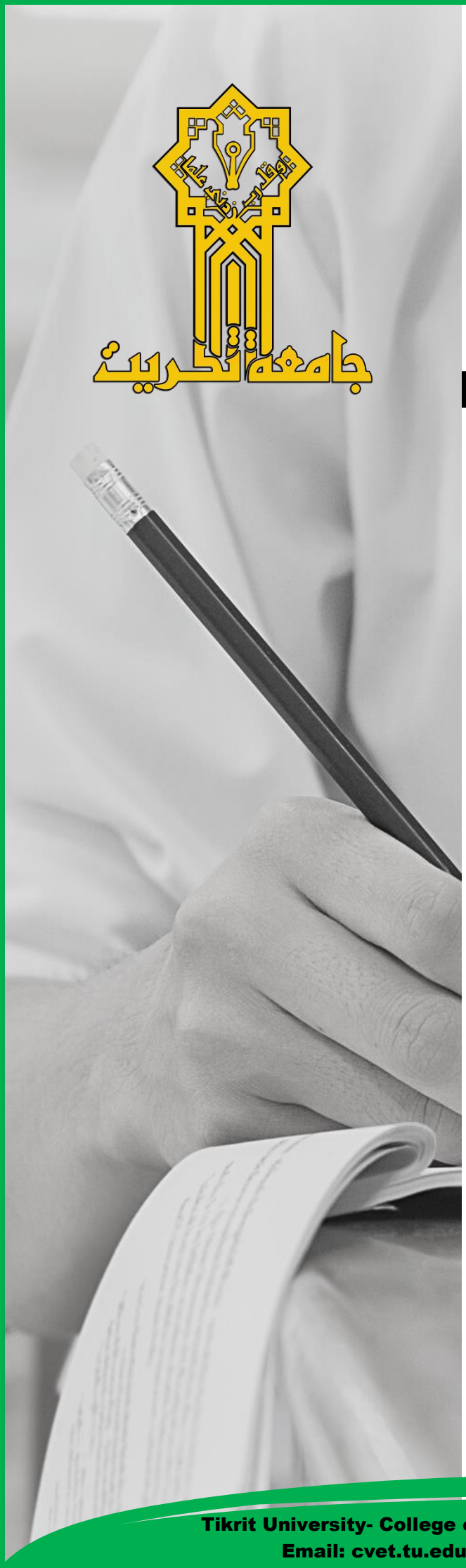

Tikrit University
College of Veterinary Medicine

Lect. 6-Immunology

Subject name: Innate Immunity Part 2
Subject year:2024-2023

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Lecturers link

Types of Immunity

There are two major types of immunity

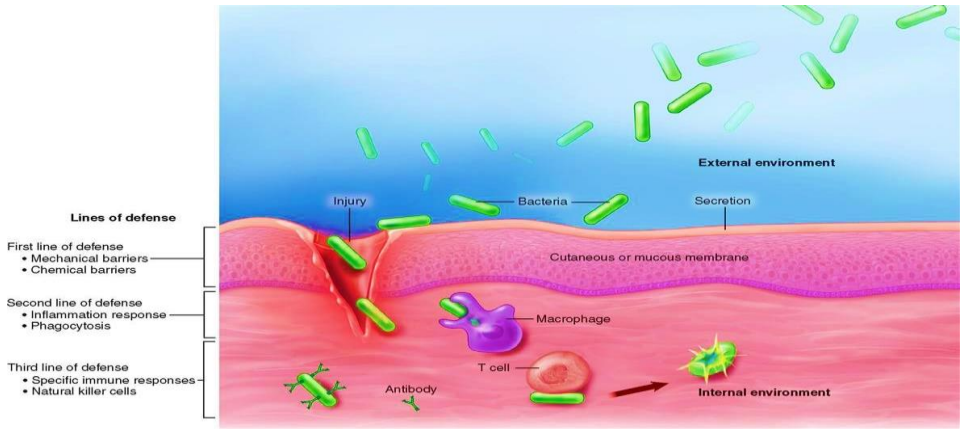
1. **Innate or natural or nonspecific immunity. Innate immunity is inherited by the organism from the parents and protects it from birth through life**
2. **Acquired or adaptive: The immunity that an individual acquires after the birth is called acquired or adaptive or specific immunity. It is specific and mediated by antibodies or lymphocytes or both which make the antigen harmless**

Innate immunity

Because all multicellular organisms are subject to microbial attack, innate immunity has evolved in animals and plants, in vertebrates, and in invertebrates Innate immune mechanisms have evolved in different ways and at different times in response to different threats.

Innate immunity (also called nonspecific or natural immunity) refers to ability of the body resistant, and is genetically transmitted from one generation to the next.

- **This immunity offers resistance to any microorganism or foreign material**
- **Innate immunity lacks immunological memory.**
- **The resistances can be at individual level or racial level or species levelIt is based on age, sex, nutritional level, lifestyle, and hormones.**



The principal components of innate immunity are:

- Physical and chemical barriers - e.g., skin, epithelial cells, tears etc.
- Cellular Barriers - Phagocytic cells (neutrophils, macrophages)and NK (natural killer) cells, phagocytosis.
- Plasma Protein Mediators:: Acute-Phase Proteins, Complement
- and Cytokines
- Genetic Factors
- Inflammation process
- Temperature-dependent innate defense.

A. Physical and chemical barriers :

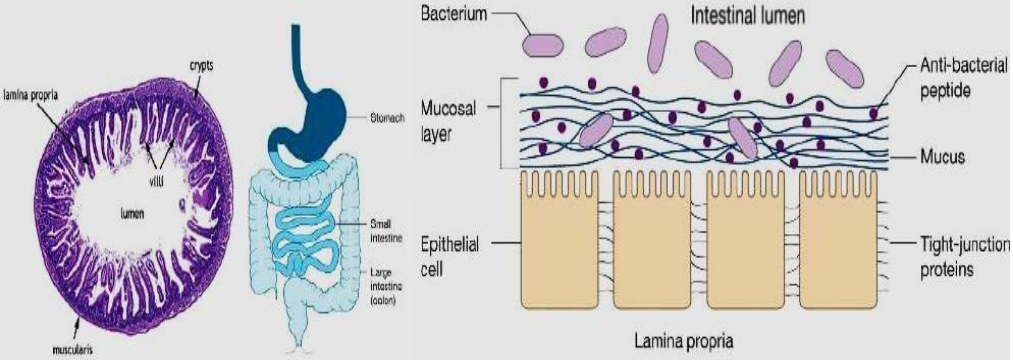
Physical and chemical barriers of the body are processes that occur in response to pathogens in order to remove them from the system and vary depending on the location and situation.

1) These barriers prevent the attachment and penetration of infectious pathogens to the host body these are; Intact skin, mucus, whipping of cilia, coughing and sneezing, flushing actions, urine, saliva, tears, vomiting, and diarrhea.

- The skin is the physical barrier of body. Its acts as a major barrier to various invading microorganisms: Breaks in the skin results from scratches ,wound or abrasions.These breaks are the routes of infection . The skin may also be penetrated by biting insects: mosquitoes, mits, ticks, fleas and sandflies.
- Acid of the stomach kills most ingested microorganisms.
- Bile salts not allow growth of microorganisms.
- Cerumen (ear wax) traps dust particles ,kills bacteria and repels insects.
- **Lysozyme** is present in tissue fluids and in almost all secretions except in cerebrospinal fluid ,sweat and urine. Lysozyme attacks Bactria and dissolves their cell walls.
- Nasal Hair they filter out microbes from urethra.
- Urine washes microbes out of body.
- Sebum: It forms a protective acid film over the skin surface that inhibits growth of many microbes.
- Tears wash all the pathogens and they have high salts concentration which cannot allow pathogens and have lysozyme that digests or kills the pathogens.

2) Gastro-intestinal tract:

The gastro-intestinal tract contains residential bacteria paly an important role in the control of potential pathogens The gastric pH may be sufficiently low to have an antimicrobial effect. In addition to antimicrobial peptides, lysozyme is synthesized in the gastric mucosa and in macrophages within the intestinal mucosa.



3) Respiratory tract:

A blanket of mucus gel produced by goblet cells lines the upper respiratory tract. **The mucus contains soluble host defense molecules such as lysozyme, lactoferrin, surfactant proteins,**

and cationic peptides such as the defensins and cathelicidins. Most microorganisms that enter the mucus layer are likely to be killed rapidly.

4) Urogenital tract

The flow of the urine and low pH provides the lumen of urogenital tract sufficient protection.The anaerobic degraded of glycogen upon the epithelial surface of genital organs **by lactobacilli result in produce lactic acid which act as a deterrent of pathogenic infection**

5) Mammary glands

Milk contains bacterial inhibitors called **lactenin** . The lactenin include complement , lysozymes ,and iron –binding protein called lactoferrin and lactoperoxidase enzyme.

B. Cellular Barriers: Circulating Phagocytes and Natural killer (NK) cells:

- Neutrophils and macrophages (monocytes in blood) identify, ingest and destroy the microbes by **phagocytosis**
- Neutrophil are recruited at the site of infection within a few hours of infection otherwise they undergo programmed cell death and usually phagocytosed by resident macrophages in the liver and spleen.
- Macrophages play important role in both innate and adaptive immunity.
- Natural killer (NK) cells kill viruses, intracellular bacteria, and NK cells produced IFN-γ to help the macrophages in phagocytosis.

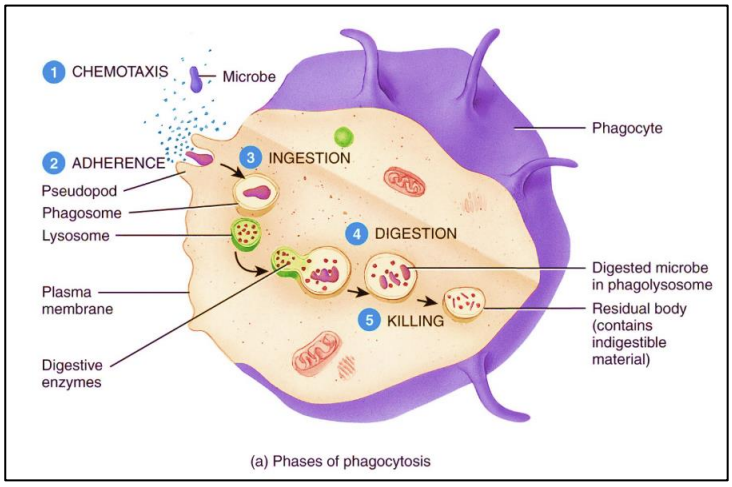
Phagocytosis of microbes Élie Metchnikoff (1845–1916) made his original observations in the 1880s while studying invertebrate marine organisms. He found special cells attacking small thorns placed into starfish larvae. Based on these findings, he later moved into immunology and championed the concept of cellular immunity. For his contributions he was awarded the Nobel Prize in 1908 . He shared the prize with Paul Ehrlich, a supporter of humoral immunity. Together they provided the bases for modern immunology

1. **Phagocytosis is a cellular process for ingesting and eliminating particles larger than 0.5 µm in diameter, including microorganisms, foreign substances, and apoptotic cells**. Phagocytosis: Greek (phage-engulf/eat; cyte –cell).
2. Phagocytosis is found in many types of cells and **it is essential not only for microbial elimination, but also for tissue homeostasis**. Professional phagocytes accomplish phagocytosis with high efficiency including : **macrophages, neutrophils, monocytes, dendritic cells, and osteoclasts** These cells are in charge of **eliminating microorganisms and of presenting them to cells of the adaptive immune system**
3. The process of phagocytosis involves several phases:
   a. **Detection of the particle to be ingested** : **Chemotaxis**
      phagocytes are attracted by and move toward a variety of substances generated in the immune response; this process is called chemotaxis.
   b. **Activation of the internalization process:**
      Phagocytes must recognize a large number of different particles that could potentially be ingested by variety of discrete receptors on the plasma membrane

of phagocytes. They can be divided into(a)nonopsonic: some receptors that directly bind PAMPs(pathogen-associated molecular patterns) and seem to be phagocytic receptors include Dectin-1, mannose receptors, CD14, and scavenger receptor A (SR-A) and (b)opsonic receptors : Opsonins include antibodies, complement, fibronectin, mannose-binding lectin, and milk fat globulin (lactadherin) The best characterized and maybe most important opsonic phagocytic receptors are the Fc receptors (FcR) and the complement receptors (CR).

c. **Formation of a specialized vacuole called phagosome.**

d. **Maturation of the phagosome to transform it into a phagolysosome to digest the foreign particles :** The phagosomes vesicles contain the ingested foreign particles and /or break away from the plasma membrane and toward the endocytic pathway. Then the **phagosome** moves toward the interior of cell and fuse with lysosome to form **phagolysosome**



(a) Phases of phagocytosis

The stages in the process of phagocytosis

e. **Destruction of ingested microbes:Ingested particles are destroyed by the different mechanisms:**

- **Oxygen dependent pathway:** By release of reactive oxygen intermediates (ROIs), called as respiratory burst. By release of reactive nitrogen intermediates e.g. nitric oxide.\
- Oxygen independent pathway: By lysosomal enzymes or other hydrolytic enzymes, defensins and other cationic proteins.

C. Plasma Protein Mediators:

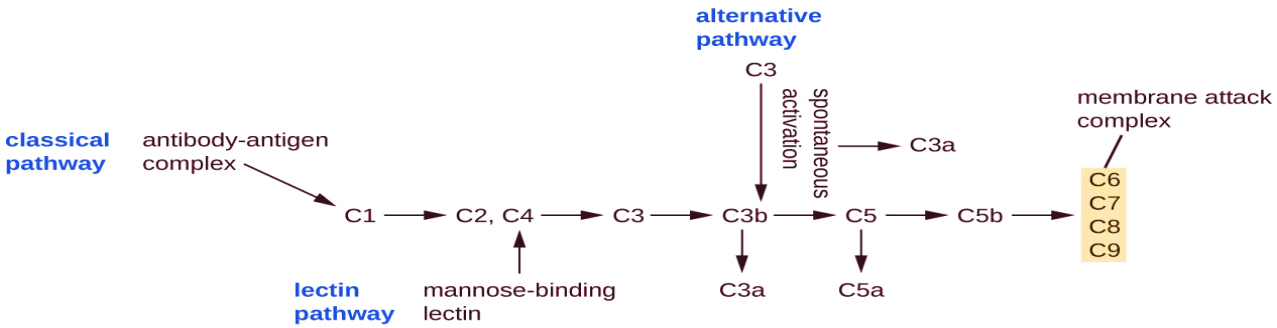
Many nonspecific innate immune factors are found in plasma, the fluid portion of blood. Plasma contains electrolytes, sugars, lipids, and proteins, each of which helps to maintain homeostasis, clotting factors and proteins such as acute-phase proteins, complement proteins, and cytokines, involve in nonspecific innate immune response

1) Acute-Phase Proteins

The acute-phase proteins are another class of antimicrobial mediators. Acute phase proteins (APP) are a class of proteins whose plasma concentration some are increased and called . Positive APP with inflammatory response and the Negative APP are those which shows a decrease in serum concentration with increase in inflammation. Examples of acute-phase proteins include C-reactive protein, serum amyloid A, ferritin, transferrin, fibrinogen, and mannose-binding lectin. Each of these proteins has a different chemical structure and inhibits or destroys microbes in some way.

2) Complement

Complement is a group of more 30 proteins, many of which are enzyme precursors and are produced by the liver They are found circulating in the blood plasma and within tissues throughout the body.



complement activation pathways

3) Cytokines

Cytokines are soluble proteins that act as communication signals between cells. In a nonspecific innate immune response, various cytokines may be released to stimulate production of chemical mediators or other cell functions, such as cell proliferation, cell differentiation, inhibition of cell division, apoptosis, and chemotaxis. Kinds of cytokines include interleukins produced by leucocytes, tumor necrosis factor and interferons (IFNs).Interferons are a soluble proteins that

protects against viral infection of cells .They interfere with the replication of the virus that has entered.

D. Natural immunity is due to genetic factors including ;

1) **Species immunity**:

Species (species resistance) is that in which a disease affecting one species dose not affect the other species . For example , humans do not affect by cattle plague ,chicken cholera , hog cholera ,infectious horse anemia, while animals are not affected by many human diseases such as enteric fever ,scarlet fever , syphilis ,gonorrhea, measles.

2) **Racial Immunity :**

Racial immunity (racial resistance) is that in which various races (breeds) show marked differences in their resistance to certain infectious diseases. A well known example is that Brahman cattle are resistance to tick fever compare to other breeds of cattle.

3) Individual immunity :

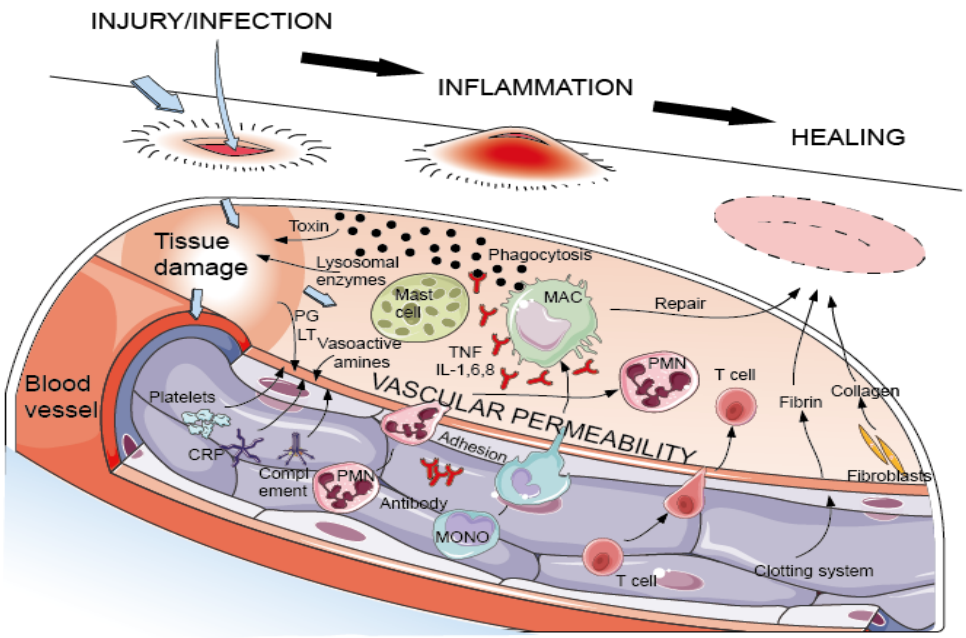
Having the same racial background and opportunity for exposure, some individuals of race experience fewer or less sever infections than other individuals of the same race.

E. Inflammation

Inflammation: a localized physical condition in which part of the body becomes reddened, swollen, hot, and often painful, especially as a reaction to injury or infection Inflammation is a defensive response of the body to tissue damage.

The conditions that may produce inflammation are pathogens, scrapping off, chemical irritations, distortion or disturbances of cells and extreme temperatures.

Inflammation is an attempt to dispose of microbes, toxins, or foreign material at the site of tissue repair. Thus, it helps restore tissue homeostasis.



Inflammation response

F. Temperature-dependent innate defense.

1. Temperature is important in determining the innate immunity. It is non specific defence mechanisms in which body temperature is raised when the body is infected.
2. The generation of fever involves the following steps :(1) Exogenous pyrogens initiate fever for example, by Endotoxin of Gram-negative bacteria, with their pyrogenic component lipopolysaccharide
3. Exogenous pyrogen enhance host cells (primarily macrophages) to produce and release endogenous pyrogens such as interleukin-1. which are transmitted to the hypothalamic thermoregulatory center of the brain increase the body temperature which is called Fever.
4. At high temperature, the pathogens are destroyed
5. The higher temperature inactivate some enzyme and toxins produced by microbes
6. Increase in temperature can higher the level of immune response increasing the rate of chemical reactions
7. Mild fever strengthens the defense mechanism by activating the phagocytes and by inhibiting the growth of microbes.
8. Fever makes the person, feel ill and forces him to take rest
9. Fever also stimulates the production of interferons which are antiviral