Introduction

-Innate immunity is the first line of defense against infection or Natural inborn barrier against invading organisms

Characteristics:

•Present and act the same in all people against general antigens.
• It is monotonic; the same magnitude and speed of response each time
• Not specific, act against common microbial antigens
•Innate immune response is better than adaptive in recognizing self from non-self.
• set up at birth & heritable

1st line				2nd line			
Physical Factor	Biochemical Factors	Microbiological Barriers	Fever	Complement	Cells	Inflammation	Cytokines

1. Physical Factors

A. Skin: microbes sloughed off along with skin cells, Microbes must penetrate several layers
• Stratified and cornified epithelium provides a mechanical barrier
• Indigenous microbial flora competes with pathogens
• Acid pH inhibits growth of disease producing bacteria
• Bactericidal long chain fatty acids in sebaceous gland secretions
B. Mucous Membranes: produce mucus to trap microbes, Most lined with cilia

2. Biochemical Factors

A. Low pH in vaginal and urinary tracts, and stomach
B. Defensins: short antimicrobial peptides, insert into bacterial membranes and form pores
C. Lysozyme: degrades peptidoglycan
• Tears contain a high concentration of lysozyme (effective against gram positive microorganisms)
D. Interferon: are cytokines that trigger:
• macrophage activation
• production of substances to interfere with RNA viral reproduction

E. Antimicrobial Peptides/Defensins
• Originally isolated from frog skin based on their ability to kill bacteria
• Four hundred peptides described to date
• Defensins (four families in eukaryotes)
– a-defensins (neutrophils and intestinal Paneth cells)
– b-defensins (epithelial cells)
– Insect defensins
– Plant defensins
• Defensins appear to act by binding to outer membrane of bacteria, resulting in increased membrane permeability

• a+b Classified based on their secondary structural features.
• Cathelicidins (CATionic HELIcal bacteriCIDal proteIN) are α-helical peptides
• Human cathelicidin LL37 is highly expressed by PMNs and numerous mucosal and epithelial cell types.
• Defensins are β-strand peptides connected by disulfide bonds
• Most are short peptides (<100 amino acids) and carry a positive charge
• AKA – "cationic antimicrobial peptides"
• Interact with microbial cell membrane components to increase cellular permeability resulting in cell death. They also act to modulate the inflammatory response and wound repair.

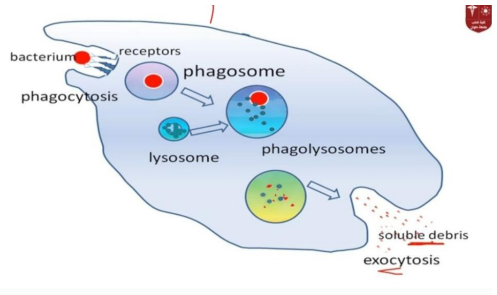
3. Microbiological Barriers
• Normal Flora: not part of immune system, but are part of first line of defense
• Protection they provide is considerable
– Competitive exclusion of invading microbes
– Produce compounds that are toxic to other bacteria
– Stimulates immune system, providing a moderate amount of "exercise" to system, thereby enhancing its function

4. Fever
• Results from
• release of pyrogens such as interleukin 1, interferons
toxins from infectious agents, drug reactions toxins, brain tumors
• Pyrogens
• released and circulate through the body
• target hypothalamus and cause release of prostaglandin E2
• raises temperature set point of hypothalamus
• Benefits of fever
• Inhibits reproduction of bacteria and viruses
• Promotes interferon activity
• Accelerates tissue repair
• Increases CAMs on endothelium of capillaries in lymph nodes
So,additional immune cells migrating out of blood
• Increases activity of adaptive immunity
• Recommended to leave a low fever untreated
• Risks of a high fever
•significant above 100 degrees F
• High fevers potentially dangerous above 1030in children
• Changes in metabolic pathways and denaturation of proteins
• Possible seizures, irreversible brain damage at greater than 1060, death above 1090

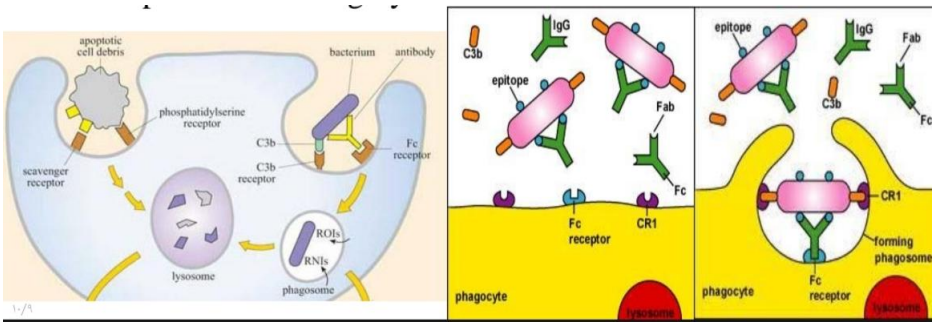
5. Innate Immune Cells
Phagocytic: neutrophils/macrophages/dendritic cells
Non-phagocytic: eosinophils/basophils/Natural killer

Phagocytosis is the capture and digestion of foreign particles

Steps of Phagocytosis
• Recognition
• Ingestion- pseudopods engulf microbe through endocytosis
• Vacuole Formation- vacuole contains microbe
• Digestion- vacuole merges with enzymes to destroy microbes
• Exocytosis- microbial debris is released



Opsonization is coating the microbe to make it obvious, molecules used for opsonization are:
1. Opsonization using IGG or IGM, which is classified into
a) Direct opsonization by IGG
b)Indirect opsonization by IGM + complement
2. Opsonization using C4b, C3b and C3bi complements
3. Opsonization using fibronectin and C-reactive proteins
4. Opsonization using cytokines
Note: 1&2 are the most important



Innate Immune Recognition
Innate immune cells recognize structures found only on microbes called PAMPs (pathogen associated molecular patterns) by pattern recognition receptors(PRRs).
- The PAMPs may be;
1. double stranded RNA in viruses
2. DNA in bacteria
3. Lipo-polysaccharides or endotoxins in G- bacteria

4. Teichoic acid in G+ bacteria
5. Mannose rich oligosaccharides

- The innate immune system also recognizes endogenous molecules that are produced by or released from damaged and dying cells. These substances are called damage-associated molecular patterns (DAMPs) 🫂

-We have 3 types of (PRRs):

• Extracellular & endosomal:

Toll like receptors (TLRs): receptors specific for ptn,CHO,lipids on the surface of microbes,present on the surface of immune cells and some recognise the genetic material so present in endosome

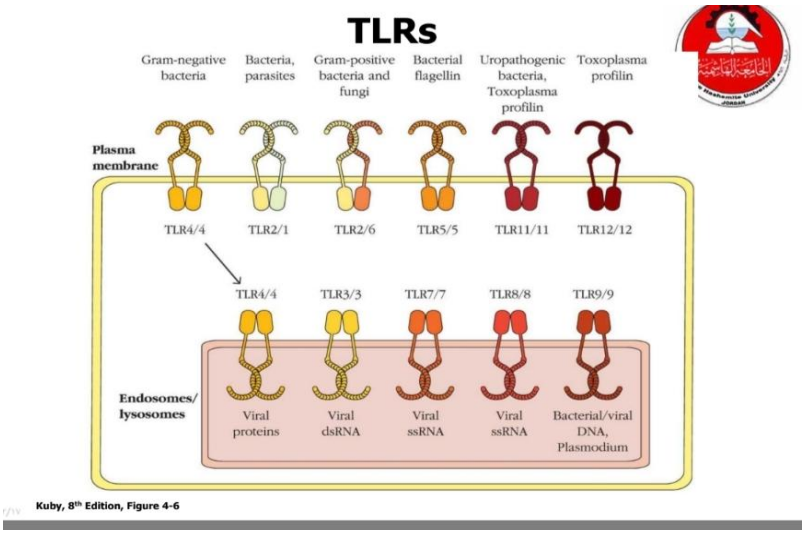
- Signals generated by TLRs activate transcription factors that stimulate expression of cytokines and other proteins involved in the inflammatory response and in the antimicrobial functions of activated phagocytes and other cells

mannose and scavenger receptors: bind to a range of ligands and enhance the

• Intracellular:

The NOD-like receptors (NLRs) are a large family of innate receptors that sense DAMPs and PAMPs in the cytosol of cells and initiate signaling events that promote inflammation or lead to programmed cell death.

• Secreted: some immune cells secrete these PRR : they are going to help the complement system in its activation process (ex. C-reactive protein, mannose binding lectin)



6. Cytokines

• Cytokines are a broad category of small proteins that are important in cell signaling,produced by a broad range of cells, including immune cells as well as endothelial cells, fibroblasts, and various stromal cell

• Cytokines act as
– Inflammatory mediators
– Communication between leukocytes and leukocytes and other cells

• 4 kinds:
– Chemokines: important in chemotaxis of immune cells
– Interferons: glycoproteins important in the control of viral infections; also help regulate cells involved in immune response
– Interleukins: important in innate immunity, inflammation, and adaptive immunity: The vast majority of these are produced by T-helper cells
– Tumor necrosis factors: help kill tumor cells, initiate programmed cell death (apoptosis)

Cytokine families
I. Hematopoietic (Interleukins) family
II. Interferon family
III. Tumor necrosis factor family
IV. Chemokine family

I, II, and III elicit physiological responses.
IV serves as a chemoattractant.y

Done by: Dr.mohammed farhoud

1-Some of the dust particles are not expelled by the sneeze and make their way further down the respiratory tract but not yet into the alveolar space. Here their elimination is the job of which of the following?
a. the released granular contents of your granulocytes.
b. the low pH of the environment.
c. the physical barrier produced by hairs.
d. phagocytosis by macrophages.
e. mucus combined with the movement of cilia of the lining cells.

2- A rare small dust particle reaches the alveolus (small terminal air sac where gas exchange occurs). At this anatomical site, you are protected by which of the following?
a. the released granular contents of your granulocytes.
b. the low pH of the environment.
c. the physical barrier produced by hairs.
d. phagocytosis by macrophages.
e. mucus combined with the movement of cilia of the lining cells

3- In order for a cell to ingest whole bacteria, the cell may employ which of the following?
a. pinocytosis.
b. antibodies and/or some complement components.
c. cytokines.
d. KIRs.

4-When an individual encounters Gram-negative bacteria (if the organisms survive the physical and chemical barriers), they may be recognized on first encounter by the innate immune system via which of the following?
a. antibodies.
b. coagulation cascade components.
c. Toll-like receptors (TLRs).
d. the membrane attack complex

Answers:e/d/b/c