BASIC Immunology
B (366)

FIRST LECTURE

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A Historical background of Immunology

Immunity *is* a resistance of a host to pathogens and their toxic effects . It is come from Latin term *immunis which* meaning free of burden or **exemption from civic duties and prosecution**

Immune system are the cells, tissues, and molecules that mediate resistance to infections

Immunology = is a science that study the structure and function of the immune system . Different sciences were derived from immunology like immunobiology , immunohistochemistry and serology and others .

Immune response = is a coordinated response against the foreign substances which introduced to an individual and mediated by the cells and molecules of the immune system

- ~ First attempts of immunity begin at 430 B.C during a Peloponnesian War, were the Thucydides in Athena describes plague – that the who had recovered from the disease could nurse the sick without getting the disease a second time

- 15th centurry: Chinese and Turks use dried crusts of smallpox as "vaccine"powder from crusts of smallpox pustules or vesicle fluid applied onto skin and the surface scratched or variolation. (Variolation is the process of taking fluid from pustules and scratching the fluid onto skin)

- Lady Montague in 1718: introduced variolation to Europe by having her children protected from smallpox by this process.

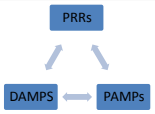
Types of immune response

- There are two types of immune response **innate immunity** and **adaptive immunity**.
- innate immunity means the immunity that preexists and functions independently of a microbial invader , also named native or natural consists of the defenses against infection that are ready for immediate action or rapid typically beginning within minutes when a host is attacked by a pathogen (viruses, bacteria, fungi, or parasites).

Edward Jenner (1749-1823):
Observed that milkmaids who had suffered from cowpox did not contract smallpox. Jenner protected a young boy from smallpox by deliberate immunization with cowpox and then challenging him with smallpox.

Louis Pasteur (1822 -1895) :
Studied attenuation of organisms and their subsequent use for vaccination eg. Chicken cholera and rabies. He called this attenuated strain a vaccine (from the Latin vacca, meaning "cow"), in honor of Jenner's work with cowpox inoculation.

- **10-During t**his response the pathogen can be recognized by cell surface or intracellular receptors called pattern recognition receptors (PRRs) that recognize
- pathogen associated molecular patterns (PAMPs) that is present in many microbes but not in human cells like beta –glucans of fungi , LPS and flagellin of bacteria and DS RNA of viruses.
- and damaged ,danger or dead associated molecular pattern (DAMPs) from aging damaged or dead cells.



11- Innate immunity does not recat against the host
12- The targets of the innate immunity are critical regarding the survival and infectivity of the microbes

- **1-** The innate immunity is considered a nonspecific response .
  2- first line of defense
- 3- relies on mechanisms that exist before infection
- **4-** Based on genetic make-up
- **5-** Relies on already formed components
- **6-** same molecules / cells respond to a range of pathogens
- **7-** Has no memory
- **8-** same response after repeated exposure
- **9- Does** not lead to clonal expansion or cell proliferation or differentiation
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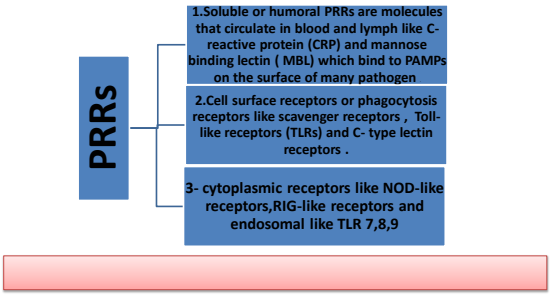
Factors affecting the innate immunity :
A host's innate immunity depends , in part , on some predisposing factors of disease resistance that are inherent in each host and in the host's environment .

1.Nutrition
Poor nutrition contributes to greater disease incidence. A diet containing the required amounts of proteins and vitamins is directly related to protection from microbial disease. Dietary proteins are used to make healthy tissues and serum proteins .Vitamins promote efficient metabolism and maintain integrity of skin and membrane surfaces .



3.Genetic factors
make certain races of people more susceptible or more resistant than other races to a particular infection . the likely basis for these susceptibility differences probably relates to differences in major histocompatibility complex (MHC) gene composition .

2.Species
- Resistance to infection varies with the species of animal or plant .
- and this may be explained by the basic physiological and anatomical characteristics of a species which can determined whether a microorganism can be pathogenic for that species .
- for example , because of the differences in normal body temperature , many diseases of mammals do not affect fish or reptiles .

Components of the innate immunity
Physical barrier

- The skin, the outermost physical barrier, consists of two distinct layers: **epidermis**, and **dermis**.
- The epidermis contains several tiers of tightly packed epithelial cells; its outer layer consists of mostly dead cells filled with a **waterproofing protein called keratin**.
- The dermis is composed of hair follicles, sebaceous glands, sweat glands which secret sebum(which contain fungistatic fatty acid) and lactic acid respectively, and scattered myeloid leukocytes such as dendritic cells, macrophages, and mast cells.

4.Age

Age of the host also plays a role in disease susceptibility, with the very young and the very old having the highest risk of infection .

- In a young child the immune system is less developed or experienced
- whereas in an elderly persons it is no longer as efficient .

5.Physical and emotional stresses

- Such as sleep deprivation ,fatigue, anxiety and depression – make a person more vulnerable to disease .
- In the stressed condition , there is enhanced production of adrenaline accompanied by altered levels of adrenal corticoid hormones ; this suppresses the function of many groups of defensive cells and depresses a wide range of defense mechanisms used by the body .

- **Mucus, the viscous fluid** secreted by specialized cells of the mucosal epithelial layers, entraps foreign microorganisms and acting as immunologic glue.
- In the lower respiratory tract, **cilia** ,the synchronous movement of cilia propels mucus-entrapped microorganisms from these tracts.

- In place of skin, the respiratory, gastrointestinal ,and urogenital tracts are lined by strong barrier layers of epithelial cells stitched together by tight junctions that prevent pathogens from squeezing between them to enter the body.

- **Coughing and sneezing** are the mechanical response that helps us get rid of excess mucus, with trapped microorganisms, that occurs in many respiratory infections.
- The flow of urine sweeps many bacteria from the urinary tract.
- Low ph of stomach also kill most pathogens

- A number of nonspecific physical and chemical defense mechanisms also contribute to preventing the entry of pathogens through the epithelia in these secretory tissues. For example, **the secretions of these tissues (mucus, urine, saliva, tears, and milk)** wash away potential invaders and also contain antibacterial and antiviral substances.
- The production of earwax (cerumen) protects the auditory canals from infectious disease .
- spermine and zinc in semen.

α- and β -defensins and cathelicidin.
Defensins and cathelicidin LL-37 (the only cathelicidin expressed in humans) are secreted constitutively by epithelial cells in many tissues, as well as stored in neutrophil granules where they contribute to killing phagocytosed microbes.

Surfactant protein SP-A and SP-D
bind differentially to sets of carbohydrate, lipid, and protein components of microbial surfaces and help to prevent infection by blocking and modifying surface components and promoting pathogen clearance.

Mannose-binding lectin (MBL),
A collectin with opsonizing activity, is found in the blood and respiratory fluids.

Chemical barriers
Lysozyme is an enzyme found in saliva, tears, and fluids of the respiratory tract that cleaves the peptidoglycan components of bacterial cell walls.

Lactoferrin and calprotectin
are two proteins that bind and sequester metal ions needed by bacteria and fungi, limiting their growth.

Psoriasin a small protein of the S-100 family(which also includes calprotectin) with potent antibacterial activity against *Escherichia coli*, an enteric (intestinal) bacterial species.

Complement components
A set of proteins which play different roles like opsonization

Type I Interferons (IFN-α,β)
Another major class of antimicrobial proteins the Type I interferons is generally recognize viral nucleic acids and other component

C-reactive protein (CRP)

- **A protein that** recognizes phosphorylcholine and carbohydrates on bacteria, fungi and parasites, and it is one of the acute phase proteins
- Researchers noted changes in the concentration of several serum proteins during the acute phase of the disease, the phase preceding recovery or death.
- The serum changes were collectively called the **acute phase response (APR)**, and the proteins whose concentrations rise during the acute phase are still called **acute phase response proteins (APR proteins)**.

- NK cells express a limited set of invariant, non-rearranging receptors that recognize infection, cancer, or damage that are expressed by other cells.
- NK cells respond immediately to appropriate stimuli, releasing from preformed secretory granules effector proteins that kill altered cells by inducing apoptosis.

2- Neutrophils

3- Monocytes and Macrophages

4- Dendritic cells

Cellular barrier

1-Natural Killer Cells

- A population of lymphocytes also recognizes components associated with pathogens, damage, or stress and generates rapid protective responses.
- **Natural killer (NK) cells** constitute a third branch of lymphoid cells, along with B and T lymphocytes of the adaptive immune system.

Biological barrier

- A totally different mechanism is that of microbial antagonism associated with the normal bacterial flora of the body (i.e. commensal bacteria).
- This suppresses the growth of many potentially pathogenic bacteria and fungi at superficial sites by competition for essential nutrients or by production of inhibitory substances.
- For example, invasion is limited by lactic acid produced by *Lactobacillus* sp. a commensal bacteria that metabolize glycogen secreted by the vaginal epithelium.
- Gut commensals may also produce colicins, a class of bactericidins that bind to the negatively charged surface of susceptible bacteria .
- When protective commensals are disturbed by antibiotics, susceptibility to opportunistic infections by *Candida* and *Clostridium difficile* is increased.