Immunology

Lec.1

Introduction to immunology & the immune system:

Immunology: is the science which studies immunity. It is a relative new branch of medical sciences. Many of the observations in immunology were made by microbiologists at the beginning of the last century through the researches for protection against infectious diseases.

The Latin term "immunis", meaning "exempt", is the source of the English word immunity, meaning the state of protection against foreign organisms or substances.

Components of immunity:

The immune system is designated to produce a coordinated response to the introduction of foreign substances into the body. It is divided into TWO complementary arms:

1- non-specific component → Innate immunity
2- specific component → Adaptive immunity

Innate (natural, native) immunity:

Non-specific host defenses that exist to a particular pathogen. This type of immunity present since birth (pre-exist) & it is the main, first line of defense against microbial invaders.
It's characteristics are that:
1- It's preexist, it present for life.
2- It has no specificity (it can't discriminate between different types of foreign substances).
3- It has no memory (it can't remember any previous exposure).
4- It is non-adaptive or acquired.

Innate immunity comprises three types of defensive barriers:
1- Mechanical barriers
2- Humoral (chemical) barriers
3- Cellular barriers

1-Mechanical barriers: these barriers inhibit the attachment & penetration of infectious agents, they include the following:

A/ Intact skin & mucous membrane: these are the first line of defense against infection. The keratinized outer layer of dead cells, the successive layers of epidermis, & the contiguous mucosal epithelium are impenetrable to microbe.

B/ Mucous: it coats the epithelial cells of mucosa. Bacteria & other particles are trapped in viscous mucous & are removed by other mechanisms:
I- beating of cilia of epithelial cells in respiratory tract removes contaminating microbes that become trapped in mucous.
II- coughing & sneezing enhance dislodge & help to expel mucous blanket.
C/ Shedding of cells that carry microbes provide a mechanical cleansing action.

D/ Flushing action of saliva, tears, urine, & other body fluids assist in washing microbes from the body.

E/ Vomiting, peristalsis, diarrhea... etc. also eliminate pathogenic organisms.
However, some invaders may pass the mechanical barriers, so they will face the *Humoral barriers*.

2- *Humoral barriers*: are numerous substances found in body secretions & provide a natural defenses against microorganisms (m.o) that invade the body. They include:

1- **Tears** → contain lysozymes which lyses bacteria by destroying the peptidoglycan layer of bacterial cell wall.

2- **Fatty acids of skin** → inhibit growth of m.o. by denaturizing the protein of cell membrane.
(Sebaceous glands of skin secrete sebum which is an oily secretion consist of lactic acids & fatty acids & it maintains the pH of skin between 3-5).

3- **Saliva** → contains enzymes that cause damage to the microbial cell wall & membrane & cause leakage of cytoplasm.
Also it contains complement components & antibodies that help in the opsonization & lyses of m.o.

4- **Gastric acid** → acidity of stomach can kill most ingested m.o. It causes denaturation of cell wall protein.

5- **Bile acids** → interfere with vital function of cell membrane.
6- Trypsin $\rightarrow$ Hydrolyze protein of cell membrane & cell wall.

7- spermin $\rightarrow$ it is a pH-dependent poly amine found in sperms & seminal fluid. It inhibits growth of gram - positive bacteria.

8- Lactoferrin & Transferrin $\rightarrow$ these are iron binding proteins, they sequester iron required for bacterial growth as an essential metabolite.

* Other humoral factors are:

- **Complement components**: complements are a series of about 20 serum proteins which are functionally inactive, but once activated, they play a major role in HDM (host defense mechanism) & inflammatory processes.
  
  Complement is a lytic system, non-specific in its mode of killing & causing lyses of the invaders.

- **Interferons (IFNs)**: these proteins are not antiviral by themselves but induce an antiviral state in other cells following viral infection.
  
  INFs combine with specific receptors on cytoplasmic membrane & activate cellular genes to produce an anti-viral proteins that interfere with translation of viral m-RNA.

  They are of 3 types:

  IFN-α ◊ secreted by macrophages & other leukocytes.

  IFN-β ◊ secreted by fibroblasts.

  IFN-γ ◊ secreted by T-lymphocytes.

* If the m.o. manages to pass the second barrier, it will be faced by another barriers which are the **cellular barriers**.
3- Cellular barriers:

- Cells of phagocytosis:

**Phagocytosis** is the process by which particulate substances such as bacteria are ingested by a cell & destroyed.

a. **Neutrophils (polymorph nuclear leukocytes- PMNs):**
   These are granulocytes that circulate in blood & migrate quickly in response to local invasion by m.o.

b. **Monocytes:**
   Also circulate in blood but in much lower number than neutrophils. They migrate to tissues, where they differentiate into macrophages, which reside in all body tissues.

   e.g. - **kupffer cells** are macrophages in liver
   - **histiocytes** are macrophages in connective tissue
   - **splenocytes** in spleen

- Other types of cells:

  **Natural killer cells (NK):** these are **cytotoxic granular lymphocytes** that play an important role in innate host defenses. They are specialized in killing virus-infected cells & mutated (precancerous) cells by secreting cytotoxins (perforins & granzymes).

**Physiological factors contribute to innate immunity:**

1- The inflammatory process
   As a result of inflammation, body fluids & phagocytic cells are brought into the site of injury.

2- Body temperature
   Some organisms do not infect human because they grow poorly at 37°C

3- Hormonal balance
4- Age
People who are very young < 3 yrs old
Very old >75 yrs old
are more susceptible to infection because their immune response is suboptimal.
If the invader manages to pass natural HDM, it will face another limb of defense mechanism which is the specific immunity.

**Adaptive immunity:**
Adaptive (acquired, specific) immunity, is capable of recognizing & selectively eliminating foreign microorganisms & molecules. These host defenses are mediated by **TWO** interrelated & interdependent mechanisms:

1- **Humoral immunity** primarily involves bone marrow-derived B-lymphocytes or B-cells. Interaction of B-cells with antigen results in proliferation & differentiation into antibody secreting plasma cells.

2- **Cell-mediated (cellular) immunity** primarily involves thymus-derived T-lymphocytes or T-cells.

**Characteristics of adaptive (acquired) immunity:**
1- The ability to distinguish self from foreignness (self/non-self recognition).
2- It has specificity:
Cells of the immune system react only with matching (homologous) immunogens.
3- Immunologic memory:
The immune system remember homologous immunogens & respond rapidly to them on subsequent exposure.
4- Diversity:
The human immune system is capable of producing a vast number of different antibody molecules, each with its own specificities.

Specific immunity may be acquired by natural or artificial processes:

1-Naturally acquired:
   a- placental transfer of antibody (passive)
   b- Recovery from disease (active)

2-Artificially acquired:
   a- administration of antitoxin (passive)
   b- Vaccination (active)

Antigens & Immunogens:
Antigens are molecules that react with antibodies, whereas immunogens are molecules that induce an immune response. Immunogens have the capacity to stimulate the immune system to produce an immune elements & react specifically to it.

Criteria of immunogenicity:

1- Foreignness: it must be recognized as foreign.

2- Molecular weight: The size of a molecule is important in determining its ability to induce an immune response. Usually the larger the molecule, the better the immunogen, because it provides the opportunity for more chemical complexity. Proteins are the most potent immunogens due to its high molecular weight.
   In general, mol.wt. > 100000 dalton ---- potent immunogen
   mol.wt. < 10000 dalton ---- weak immunogen
3- Chemical structural complexity:
It enables the formation of numerous different structures, called **Epitopes**, that are the units to which antibodies are directed.
Proteins are the most potent immunogens because they are built from 20 amino acids and more, and thus can include many distinct epitopes, while most polysaccharides are weak immunogens because they are constructed of only a few monosaccharaides & hence they do not possess sufficient chemical diversity for full immunogenicity

4- Dose & route of antigen administration
Generally, minimal doses and excessive large doses of antigen impair the immune response.
- The subcutaneous or intramuscular routes of antigen injection are best for inducing an antibody response, while I.V. route minimize the immune response.

5- Genetic constituents of the host

6- Antigenic determinants (Epitopes)
Immunogens & antigens possess unique cluster of chemical grouping that serve as the B-cell &T-cell stimulating sites in the molecule. These sites are called epitopes.

**Epitope** is that portion of an antigen with which antibodies & T-cell receptors react.

- **Structure of epitopes:**
  - Size: they consist of 4-5 amino acids of a protein or an equal-size area of polysaccharide.
  - Conformation: epitopes could be linear or conformational (folded)
  - Site: topographic or internal
• **Function:**
Epitopes determine the specificity of the antigen molecule. Antigens that share one or more identical or similar epitopes are cross-reactive antigens.

![Epitopes Diagram](image)

**Adjuvants:** These are chemical substances that enhance the immune response to an immunogen. They act non-specifically by stimulating the immunoreactive cells or by releasing immunogen slowly. **Ex.** Some human vaccines contain adjuvants such as aluminum hydroxide or lipid.

**Hapten:**
A small organic molecules that are non-antigenic & non-immunogenic. Chemical coupling of a hapten to large protein (existing Ag), called **carrier**, yield an immunogenic hapten-carrier conjugate. Hapten can add a new epitope (i.e. a new specificity) when combined to an existing Ag.