



**Disease of immune system**

**Lec. 1**

**Immunity**: refer to protection against infections.

**Immune system**: is the collection of cells and molecules that are responsible for defending us against the countless pathogenic microbes in our environment, **any deficiency in immune system** result in an increased susceptibility to infections, which can be life-threatening if the deficits are not corrected, **defense against microbes consist of two types of reactions**:

**1-Innate immunity (natural or native immunity)**: is mediated by cells and proteins that are always present and poised to fight against microbes and are called into action immediately in response to infection.

**The major components of innate immunity are:**

1. Epithelial barriers of skin, GIT, respiratory tract.
2. Phagocytic leukocytes (neutrophils & macrophages), and specialized cell type called the natural killer (NK) cell
3. Several circulating plasma proteins, the most important proteins of the complement system.

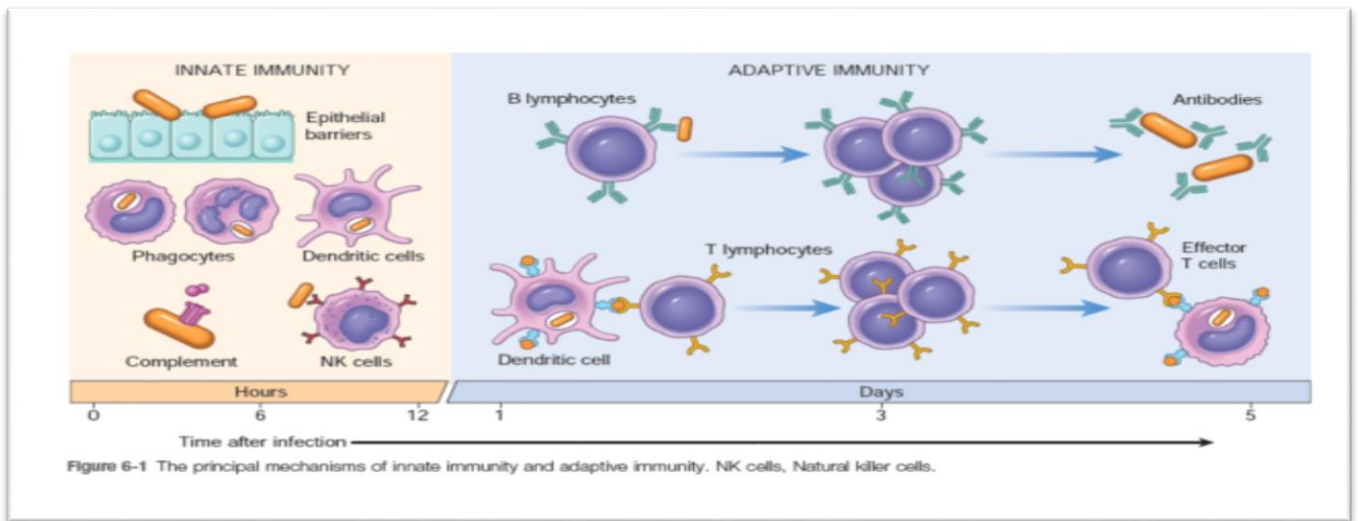
**2-Adaptive immunity (acquired)**: is normally silent and responds (or "adapts") to presence of infectious microbes by becoming active, expanding and more powerful to eliminate the microbes.

**There are two types of adaptive immunity:**

1. **Humeral immunity**: mediated by soluble antibody (Ab) produced by B-lymphocytes. Antibodies provide protection against extracellular microbes in blood, tissues & mucosal secretion.

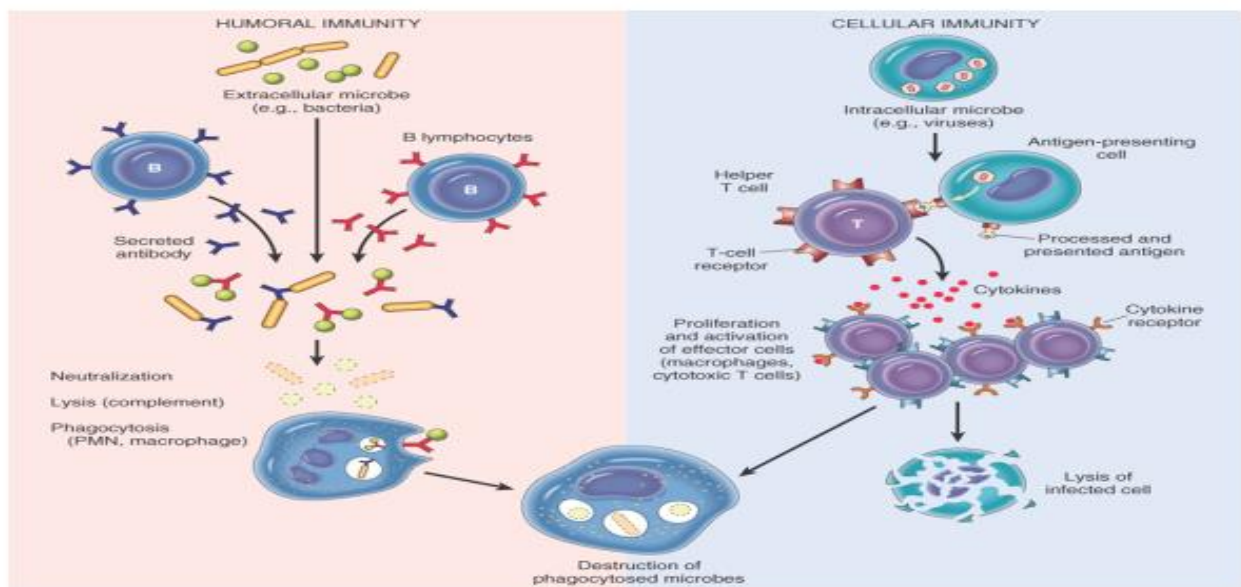
# Disease of immune system ..... Lecture 1

2. Cell- mediated (cellular) immunity mediated by T- lymphocytes, T- lymphocytes are important in defense against intracellular microbes



They work by either:

- 1-directly killing infected cells (accomplished by **cytotoxic T lymphocytes**)
- 2-or by activating phagocytes to kill ingested microbes, via the production of soluble protein mediators called **cytokines** (made by helper T cells)



## Cells of immune system

### 1-T-lymphocytes (thymus derived)

T (thymus-derived) lymphocytes: they are effectors cells in cellular immunity and there are 3 major population of T cells

1-Helper T lymphocytes (CD4+Tcells) stimulate B lymphocyte to make antibodies and activate other leukocytes e.g., phagocytes to destroy microbes.

2-Cytotoxic T lymphocytes (CTLs) (CD8+Tcells) kill infected cells

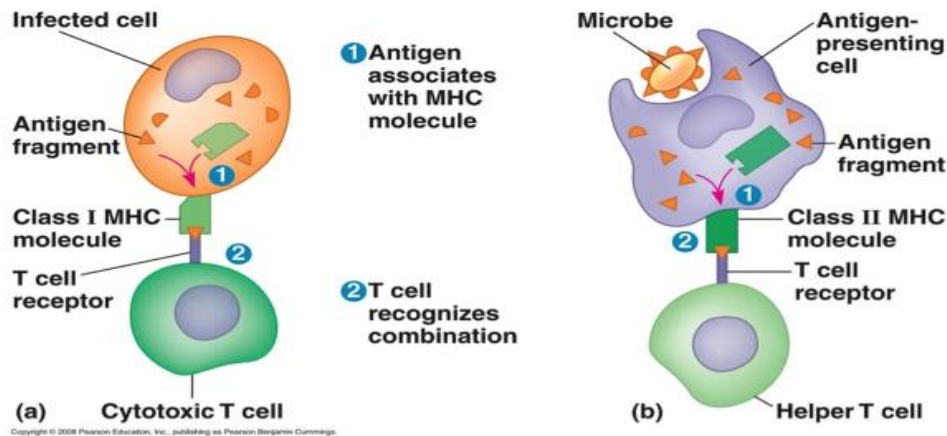
3-Regulatory T lymphocytes limit immune responses and prevent reactions against self-antigens.

They constitute 60-70% of lymphocytes in peripheral blood & the major lymphocytes population in splenic periarteriolar sheath & lymph node interfollicular zone.

T cells do not detect free or circulating antigens, the majority (>95%) of T-cells are recognizes only peptide fragments of protein antigens that are displayed on other cells bound to proteins of Major Histocompatibility Complex (MHC) (or in human called Human Leukocyte Antigen (HLA) complex (which known that the normal function of MHC molecules is to display peptides for recognition by T lymphocytes)

Each T cell recognizes specific cell-bound antigen by means of an antigen-specific TCR.

By limiting the specificity of T cells for peptides displayed by cell surface MHC molecules, called MHC restriction, the immune system ensures that T cells see only cell-associated antigens (e.g., those derived from microbes in cells or from proteins ingested by cells).



**MHC Molecules:** The MHC molecules are fundamental to T- cell recognition antigens, and variation in MHC molecules are associated with immunologic diseases , **the genes encoding MHC (in human called HLA) molecules are clustered on a small segment of chromosome 6**, on basis of their chemical structure, tissue distribution & function, MHC genes products fall in **two** major classes:

**1–Class I MHC:** are expressed on all nucleated cells and platelets, they are heterodimers consisting of a polymorphic  $\alpha$  chain, the  $\alpha$  chains are encoded by three genes, designated **HLA-A, HLA-B, and HLA-C**, that lie close to one another in the MHC locus. Class I–associated peptides are recognized by **CD8+ T lymphocytes**.

**2–Class II MHC:** are encoded in a region called HLA-D, which has three sub regions: **HLA-DP, HLA-DQ, and HLA-DR**, the class II–peptide complex is recognized by CD4+ Tcells, which function as helper cells, Class II MHC molecules are mainly expressed on cells that present ingested antigens and respond to T–cell help (macrophages, B lymphocytes, and dendritic cells).

The MHC locus also contains genes that encode some molecules which called (**Class III MHC molecules**) which include some complement components (**C2, C3**) and the cytokines **tumor necrosis factor (TNF)** and **lymphotoxin**, these molecules have no apparent role in the immune system.

**2-B- lymphocytes (Bone marrow derived):** are cells that produce antibodies & are the effector cells of humeral immunity, they constitute 10-20 % of peripheral lymphocytes, also present in bone marrow & in follicles of peripheral lymphoid tissue (lymph node, spleen, and tonsils), on antigenic stimulation B-cells differentiated to plasma cells which secrete immunoglobulin (Ig) that mediated the humoral immunity There are 5 types of Ig (IgG, IgM, IgA, IgE & IgD).

### 3-Antigen presenting cell (APC)there two types:

**1-Dendritic cells:** cells with dendritic morphology, occur as two functionally distinct types:

**A-Interdigitating D.C:** they are located in lymphoid tissue, they are non-phagocytic that express high level of class II MHC & T cell co stimulatory molecules to capture & express antigens to T cells.

**B-Follicular D.C:** located in the germinal centers of lymphoid follicles and bear receptors for Fc portion of IgG & complement proteins, these cells display the antigens to activate B- lymphocytes.

**2- Macrophages:** ingest microbes and other particulate antigens and display peptides for recognition by T lymphocytes, these T cells in turn activate the macrophages to kill the microbes, the central reaction of cell-mediated immunity.

**4-Natural killer (NK) cells:** Are lymphocytes that arise from the common lymphoid progenitor that gives rise to T and B lymphocytes. It kills the cells that are infected by some microbes, or are damaged beyond repair.

NK cells express inhibitory receptors that recognize self MHC molecules that are normally expressed on healthy cells, and are thus prevented from killing normal cells.