White blood cells

(leukocytes)

Medical physiology

ILOs

- Enumerate different types of WBCs and normal count
- Demonstrate functions of each type.
- Recognize the different lymphatic organs
- Explain the functions of lymphatic system.

Leukocytes

white blood cells ~ WBC

agranular

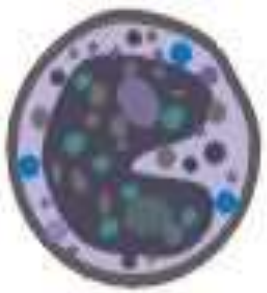
lymphocytes
20 - 25 %

T-cell, B-cell, NK Cell

monocytes
3 - 8%

granular

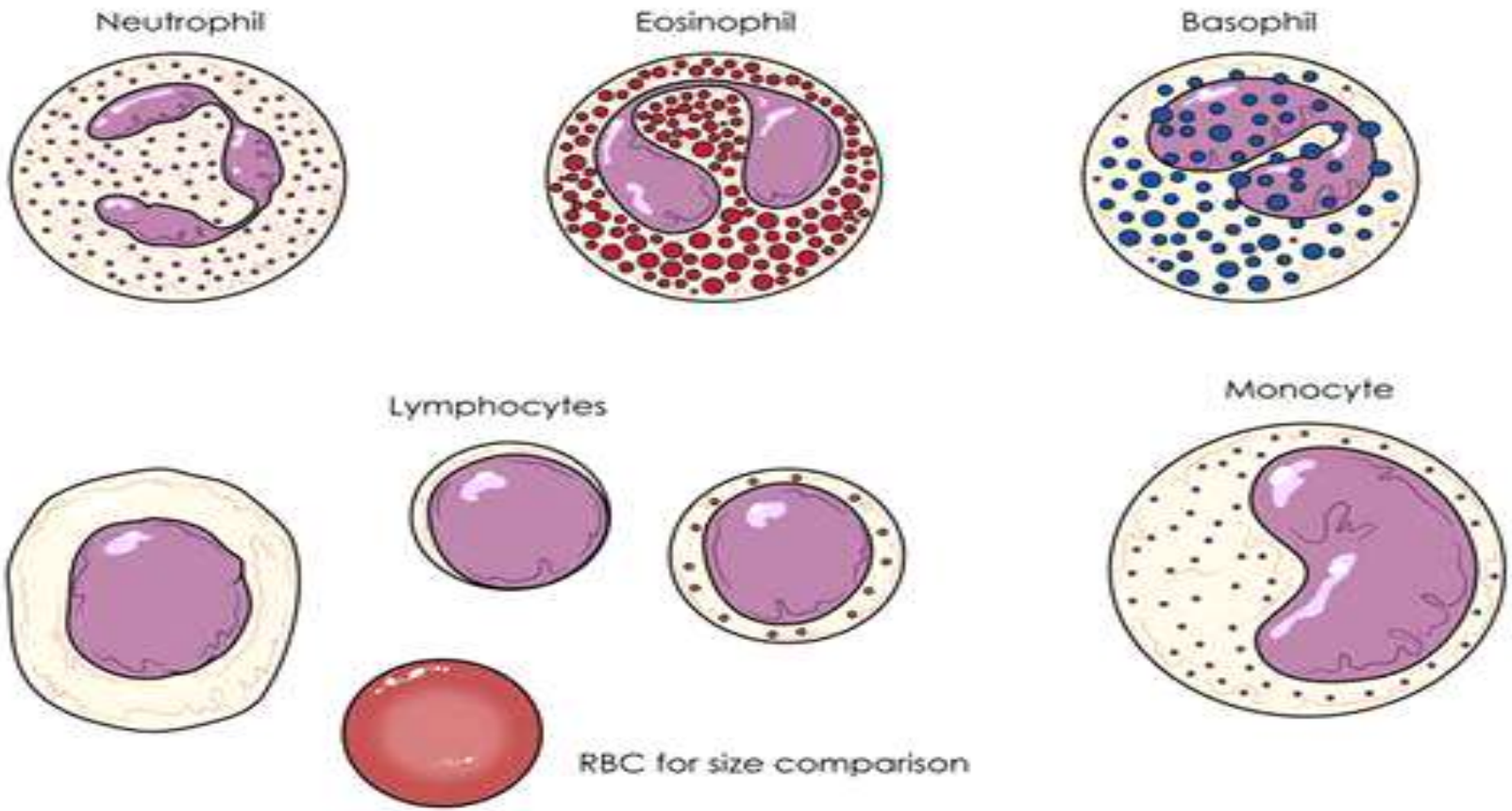
basophils
.5 - 1%



neutrophils
60 - 70%

eosinophils
2 - 4%

WBCs


Neutrophil
Eosinophil
Basophil
Lymphocytes
Monocyte
RBC for size comparison

White blood cells (leukocytes)

White blood cells (WBCs) are the mobile units of the body defensive system

They work in two different ways to prevent diseases:

1) Phagocytosis

2) Formation of antibodies & sensitized lymphocytes.

Site of formation:

In bone marrow: granulocytes, monocytes & few lymphocytes.

In lymphoid tissue: lymphocytes & plasma cells.

Count: 4000 – 11000/mm^3.

- **Leukocytosis:**

Increase WBCs to 20.000 as in acute inflammation e.g. tonsillitis.

- **Leucopenia:**

Decrease WBCs as in exposure to irradiation & drugs.

Leukemia:

Malignant disease of Bone marrow→increase number of WBCs

Types of WBCs

Granulocytes: They have granules in their cytoplasm, include:

Neutrophils: 50-70 % of WBCs

Eosinophils: 1-4 %

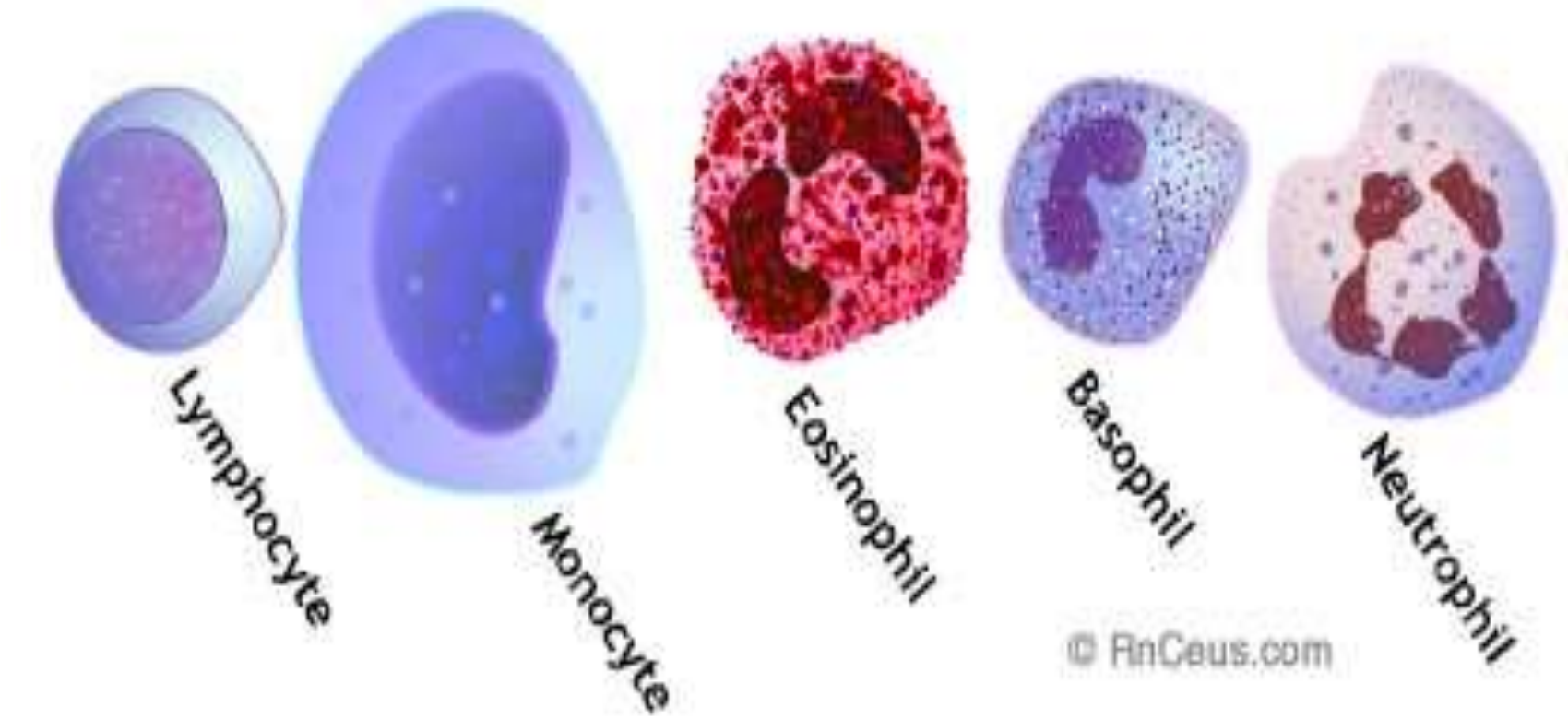
Basophils: 0.4 %

Agranulocytes: They have no granules in their cytoplasm, include:

Lymphocytes: 20 – 40%

Monocytes: 2-8 %

Types of leukocytes



Function of leukocytes:

(1) Eosinophils:

- Attack parasites, that are to large to be engulfed by phagocytosis
- They produce leukotriene in allergic diseases.
- They are involved in mucosal immunity e.g. GIT, respiratory system, lower urinary tract.
- Eosinophils, produce profibrinolysin as they migrate into blood clots
- They are weak phagocytes & they show chemotaxis.

(2) Basophils:

- Contain histamine, heparin & leukotriene.
- Responsible for immediate type of hypersensitivity reactions (allergy).
- Mast cells are similar to basophils but found in tissues as epithelial surfaces & in areas rich in connective tissue.

(3) Neutrophils (mature cells)

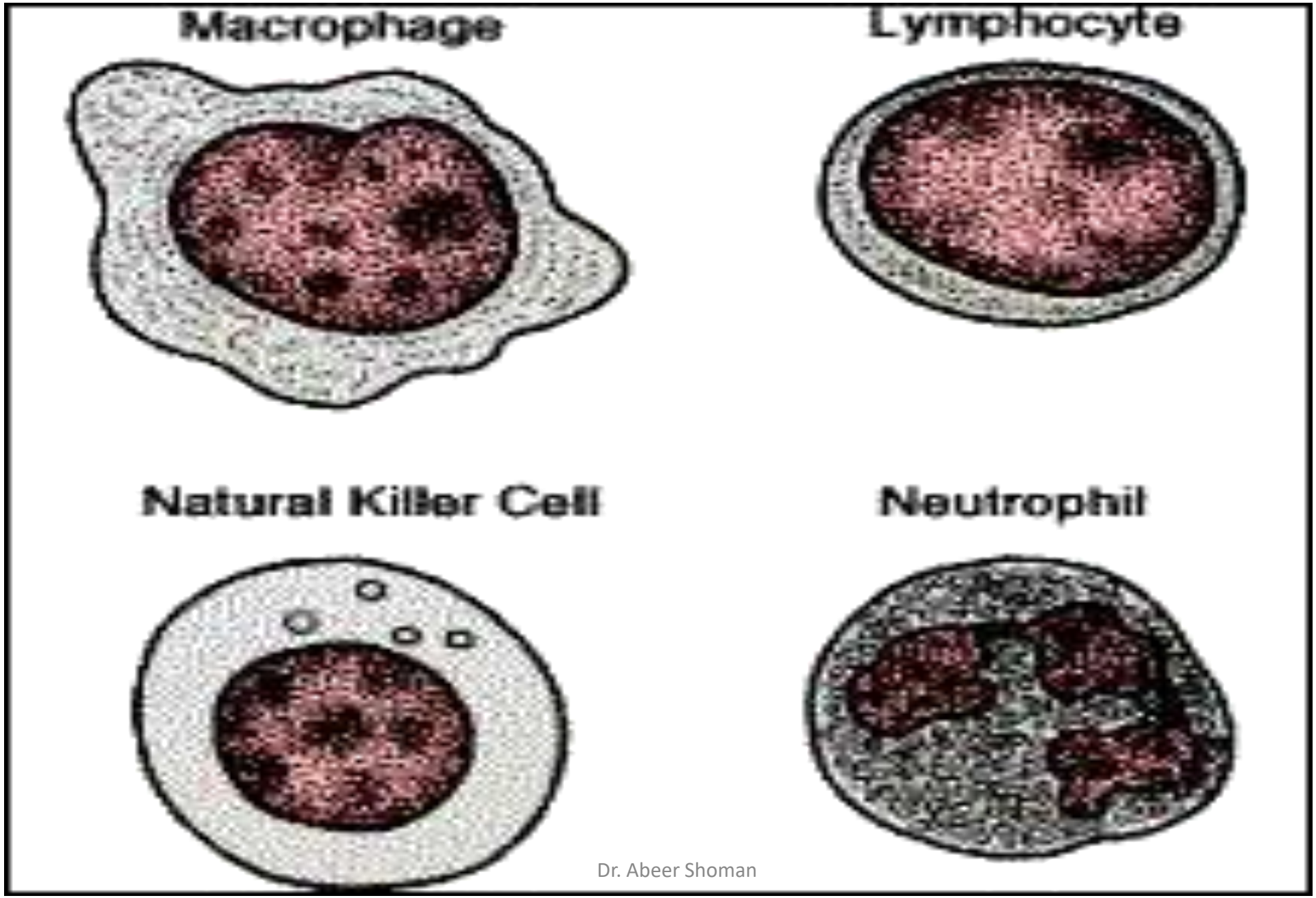
- Half-life is 6 hours.
- They ingest & kill bacteria.

4-Lymphocytes:

- They are formed in lymph nodes, thymus & spleen.
- They enter blood stream via lymphatics.
- Their life span: few days to several months.
- They are the key cells of immunity.

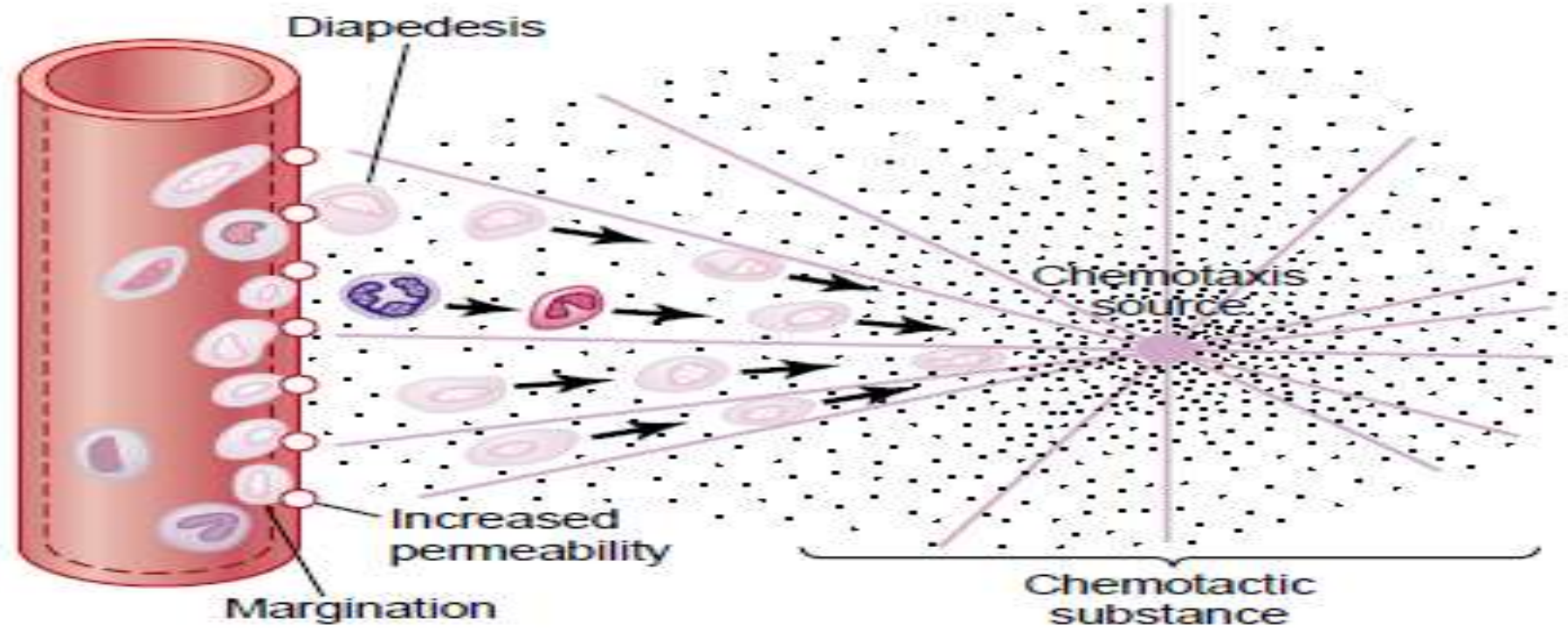
5-Monocytes: …..immature cells

- Little defense mechanism.
- Have amoeboid movement & pass to area of inflammation after neutrophils.
- Circulate for 72 hours & then enter the tissues.
- In the tissues, they become macrophages which have high defense mechanism e.g. Kupffer cells of liver, osteoclast in bone.


Macrophage
Lymphocyte
Natural Killer Cell
Neutrophil

The inflammatory response:

- is response of living tissue to injury like infection, trauma & chemicals.
- It is characterized by local vasodilatation causing redness & increase vascular permeability (edema).
- The cells involved are **neutrophils & monocytes**.



Movement of neutrophils by *diapedesis* through capillary pores

Steps of inflamatory response

1-Margination: WBCs stick to the inflamed capillary wall.

2-Diapedesis: WBCs squeeze themselves through capillary pores.

3-Amoeboid movement: through tissue to reach bacteria.

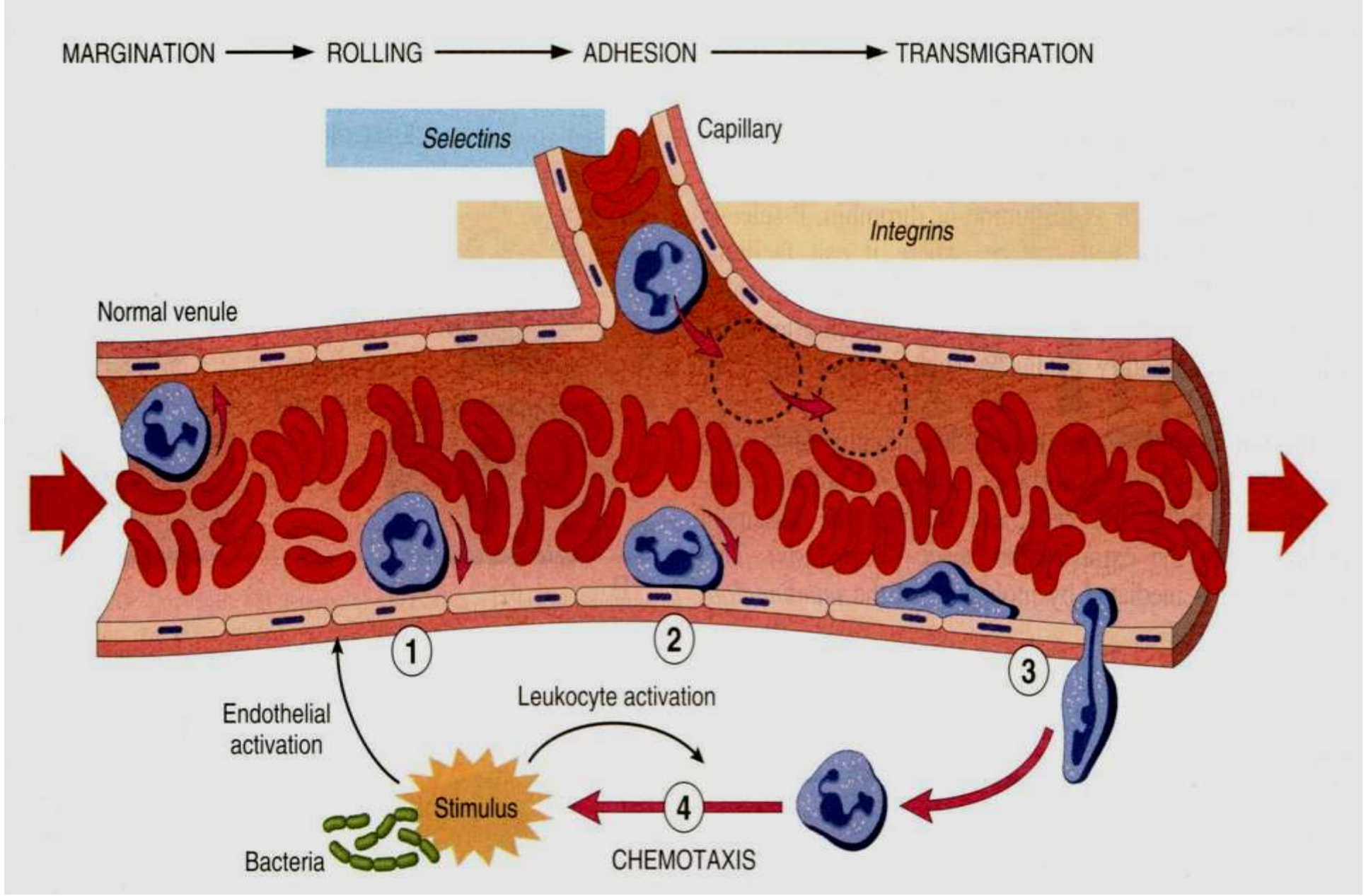
4-Chemotaxis: Positive: attraction of cells towards bacterial toxins & site of inflammation by chemotactic agents e.g. Complement & leukotriene

Negative: repulsion of cells away from bacteria.

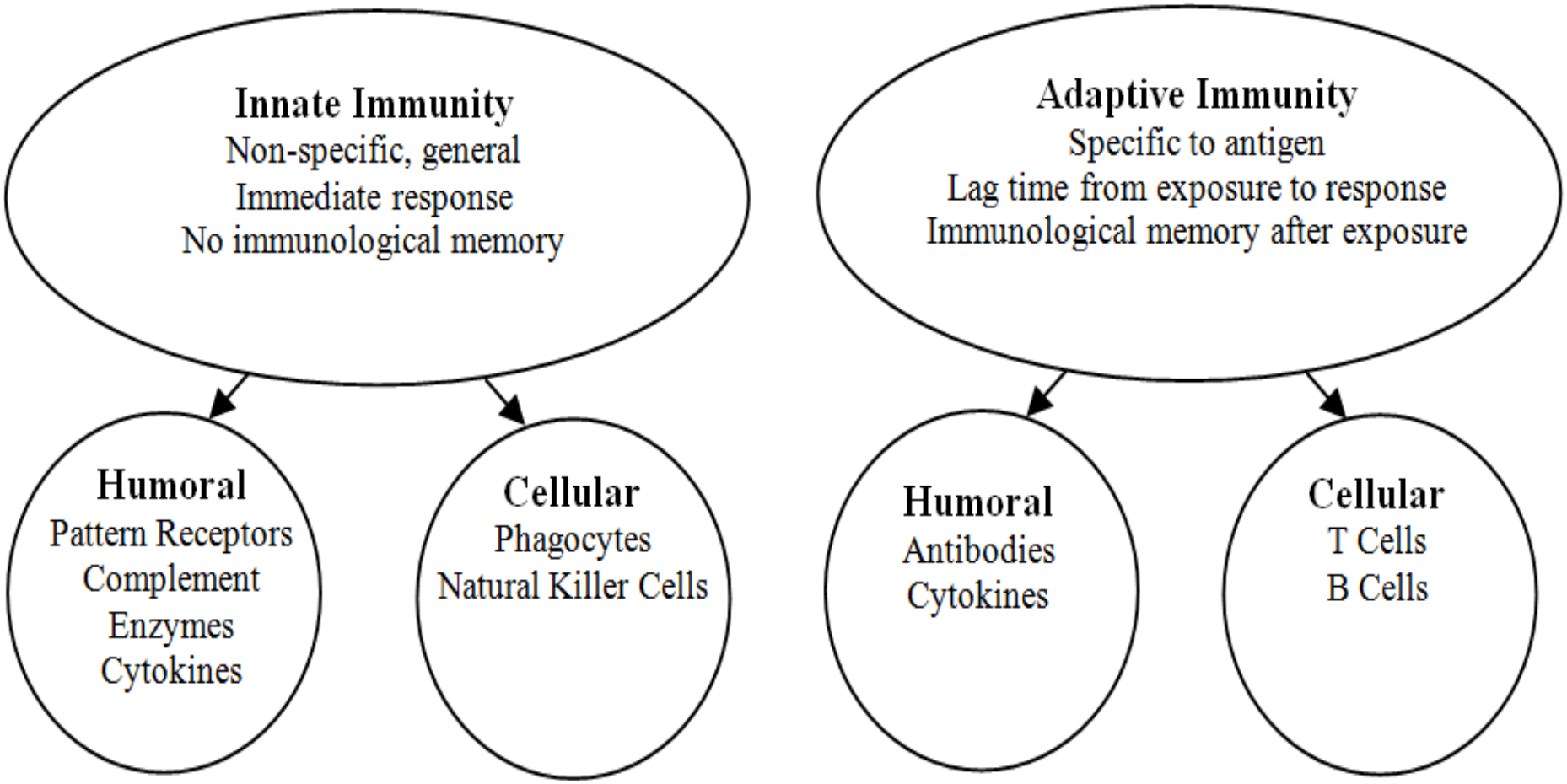
5-Opsonization: preparation of bacteria to be tasty to phagocytes.

- Opsonins are immunoglobulin G (IgG) & complement proteins.
- Opsonins coat bacteria then bind to receptors on phagocyte cell membrane and then engulfed by Phagocytosis.

6-A **phagocytic vacuole** is then formed with which lysosomes & release enzymes to kill bacteria.


MARGINATION
ROLLING
ADHESION
TRANSMIGRATION
Selectins
Capillary
Integrins
Normal venule
1
2
3
4
Endothelial activation
Leukocyte activation
Stimulus
Bacteria
CHEMOTAXIS

Immunity


Innate Immunity
Non-specific, general
Immediate response
No immunological memory
Humoral
Pattern Receptors
Complement
Enzymes
Cytokines
Cellular
Phagocytes
Natural Killer Cells
Adaptive Immunity
Specific to antigen
Lag time from exposure to response
Immunological memory after exposure
Humoral
Antibodies
Cytokines
Cellular
T Cells
B Cells

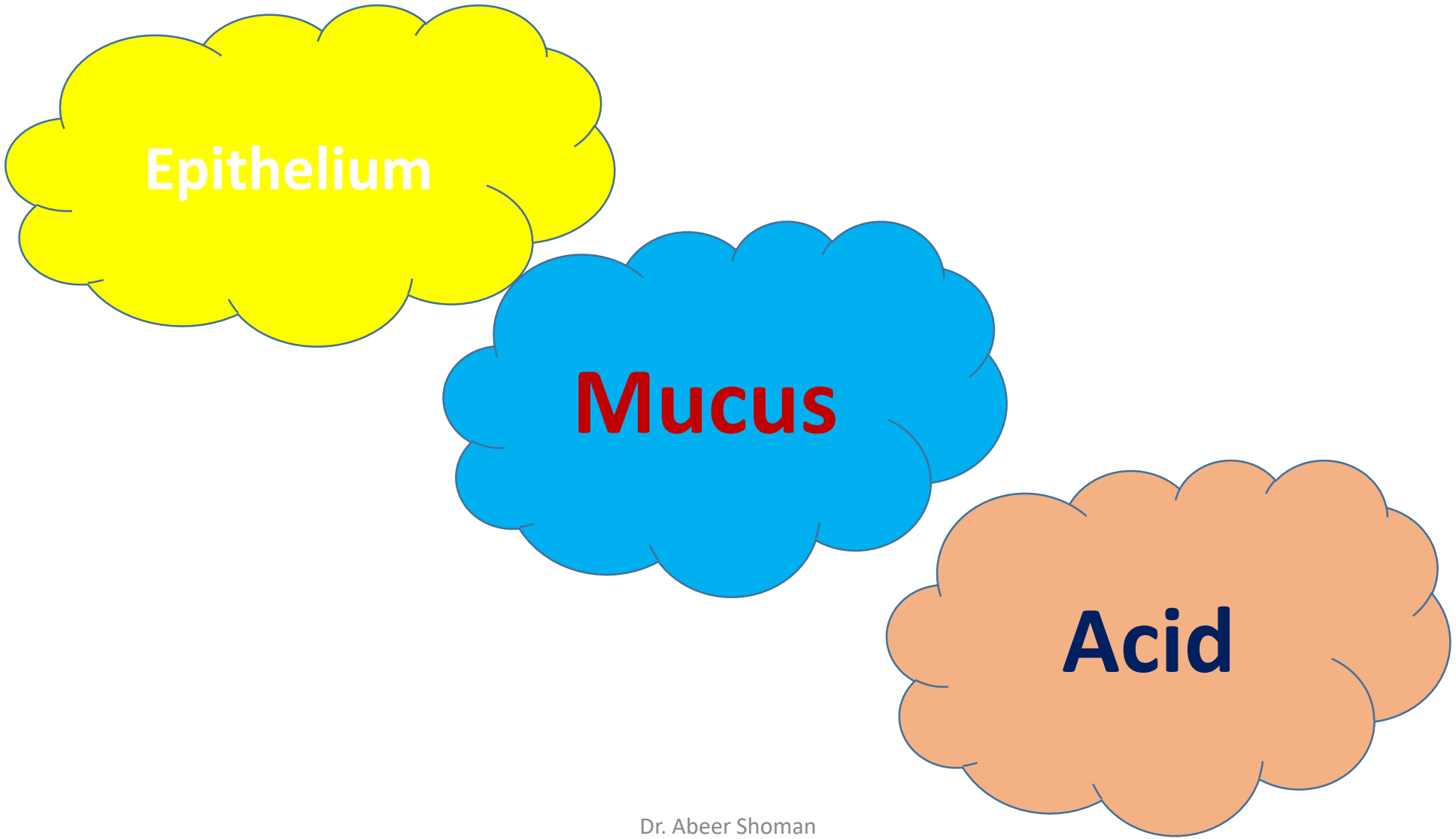
A] Nonspecific (innate) immunity

- **1- Mechanical & chemical barriers**.

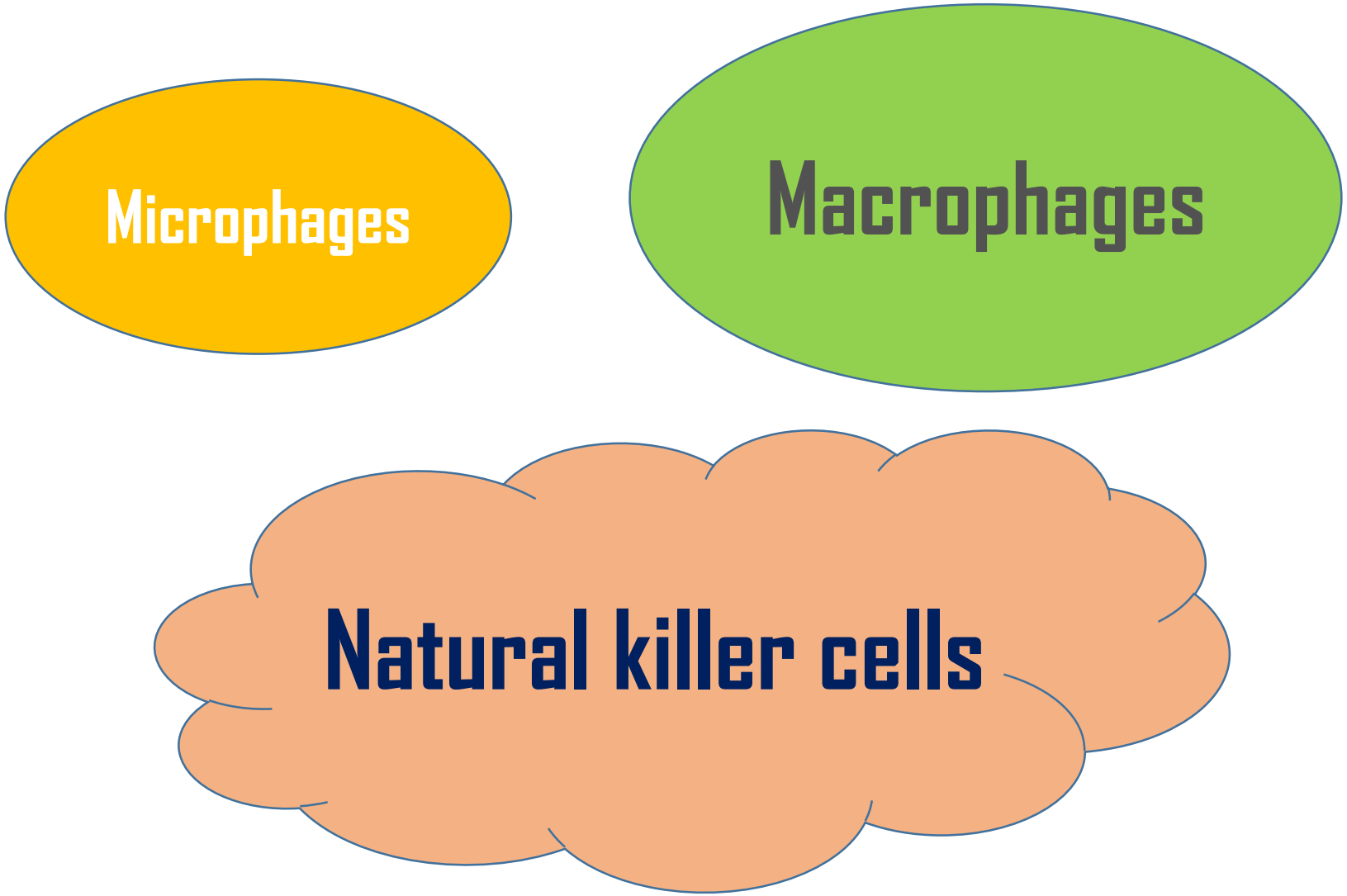
- 2- **Non specific cellular mechanism**

- **3- Nonspecific humoral mechanism**

1- Mechanical & Chemical barriers



2- Non specific cellular immunity



3- Nonspecific humoral mechanism

1) Lysozymes
2) Interferon's (IFN)
3) Properdin system
4) Acute phase proteins
5) Complement system

Nonspecific humoral mechanism:

A-Lysozymes: mucopolysaccharide that dissolve bacteria.

B- Interferon's (IFN): proteins released from virus infected cells

-They are α , β & Υ IFN

1- Alpha: - antiviral & increase activity of NK cells
- Used in treatment of cancer

2- Beta: antiviral

3- Gama: increase the activity of macrophages

C- Properdin system: A complex system of proteins that can activate complement

D- Acute phase proteins: formed in liver during acute inflammation & tissue destruction. They are anti-inflammatory proteins e.g. C-reactive proteins.

E- Complement system:

-A system of 11 plasma protein enzymes (C1→C9) & C9 is 3 subunits.

-They mediate humoral & cellular immunity.

2]Specific (Aquired)immunity

- It is the ability of immune system to respond to foreign molecules called antigens.
- **Antigen:** is a substance which stimulates immune response and reacts specifically with antibodies.

Ag. is Foreign, Usually protein, Large M.W. > 10.000.

Has a determinant group

- **Classification of specific immunity:**

1-Cell mediated immunity

2-Humoral immunity

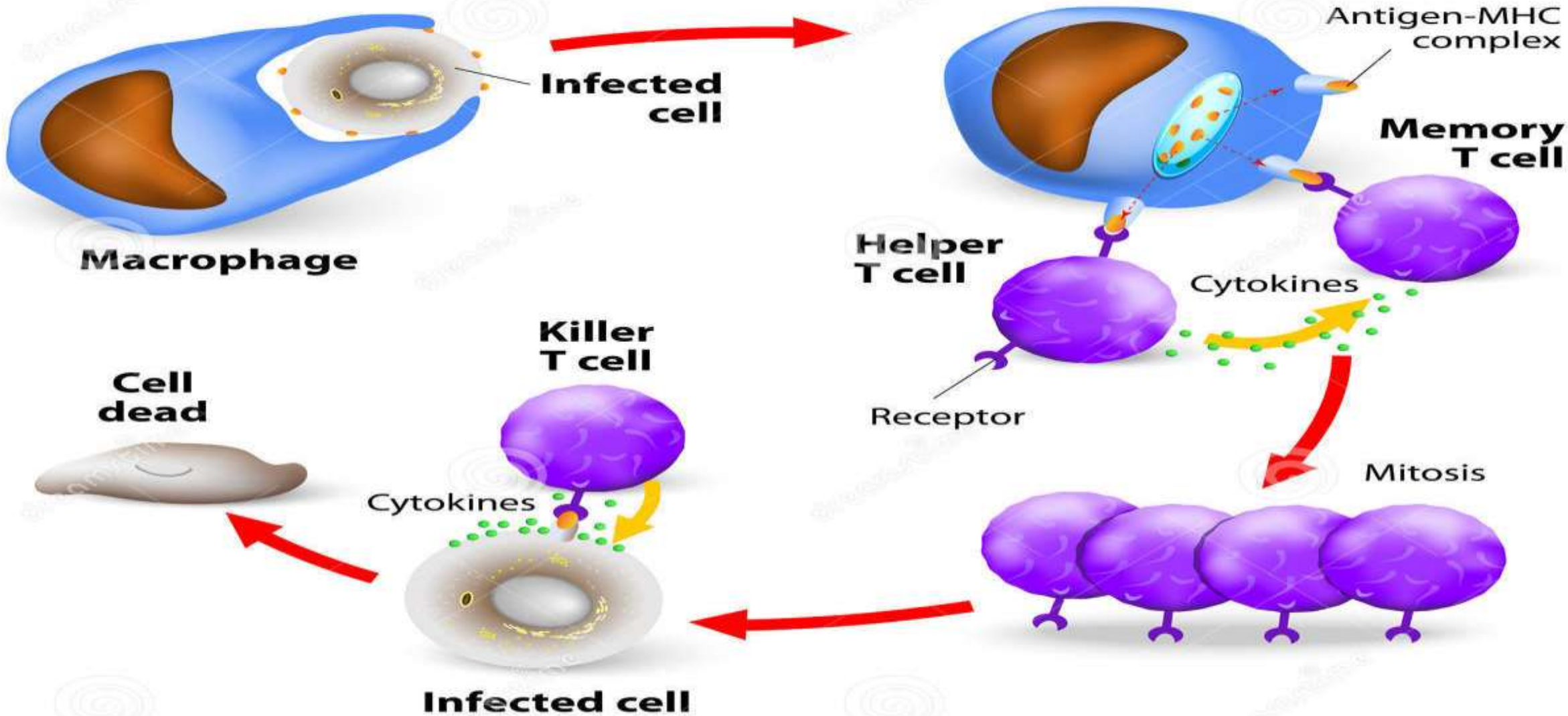
Cell mediated immunity

1] Helper T-lymphocytes
(Th)-CD4

2] Cytotoxic T-lymphocytes
(TC)-CD8

3] Suppressor T–lymphocytes (Ts)-
CD8

CELL-MEDIATED IMMUNE RESPONSE



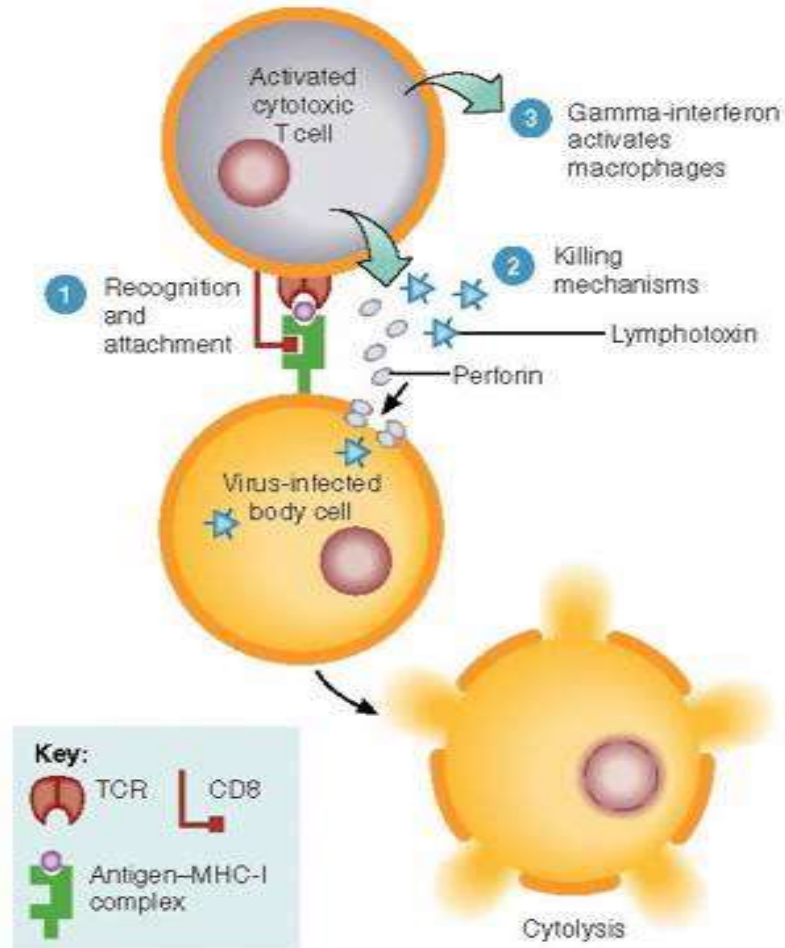
I. Cell Mediated Immunity

Elimination of invaders by Cytotoxic T cells

1) **Cytotoxic T cells** migrate to site of invasion
2) Bind to target cells bearing MHC I-antigen complex
3) Destroy infected cells by secreting two substances:

Perforin: Perforates the target cell membrane

Granzyme: Enters via pores, degrades and activates apoptosis



Humoral immunity

1- Plasma cells

2-Memory B cells

- **1ry immune response**
- **2ry immune response**

Antibodies

Types, Functions

Humoral Immune response

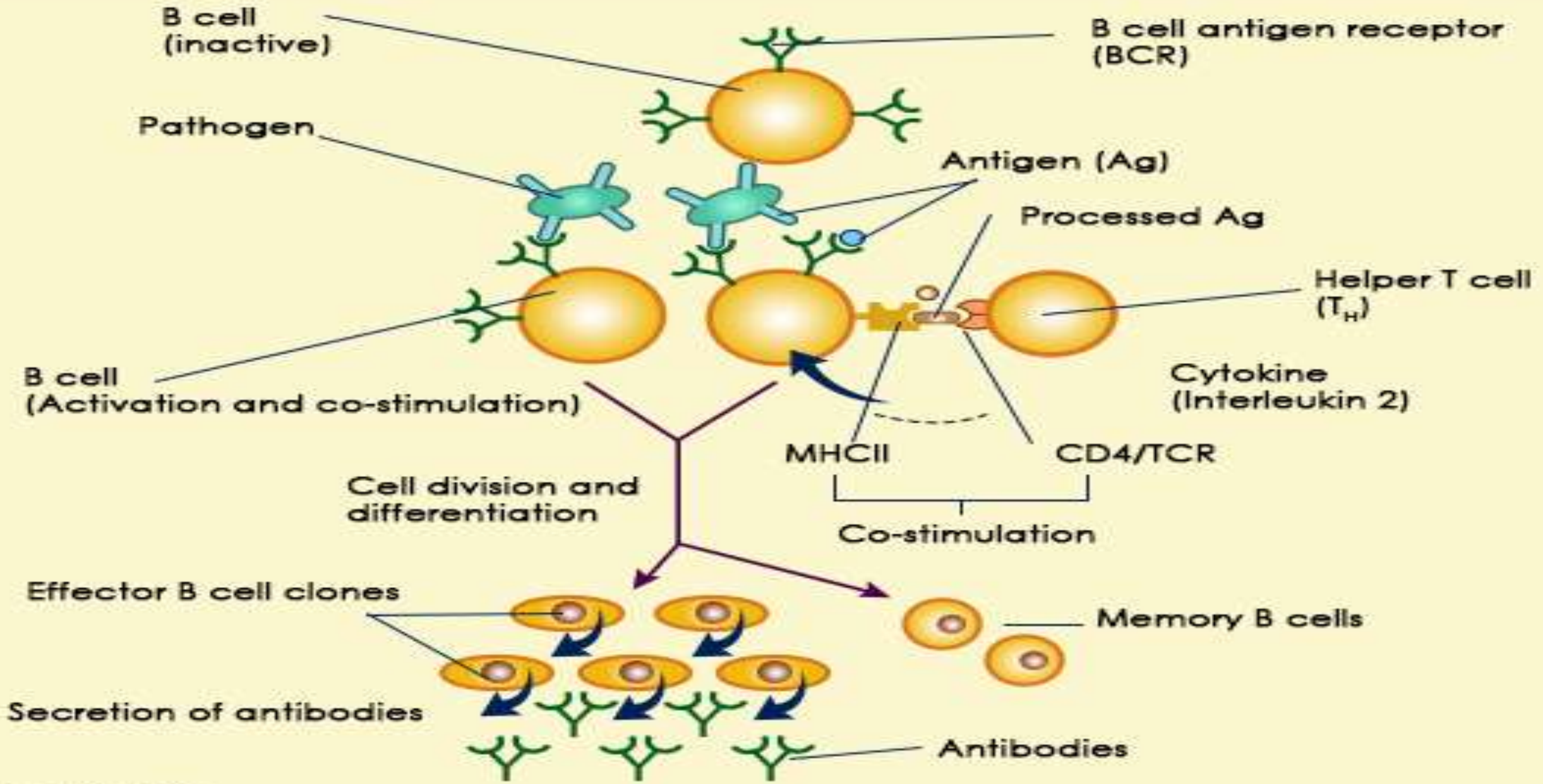
1-B lymphocytes recognize Ag via antibodies on their surface.

2-B lymphocytes differentiate into:

- **Plasma cells** have well developed granular ER which forms large quantities of antibodies (immunoglobulins).
- **Memory B cells** : on second exposure to the same antigen produce secondary response ⟶ more rapid and more potent response than primary response. .
- Memory cells persist in the body for months or years.

NB: T helper cells (Th2) are needed for full activation of B-lymphocytes through productions of IL-4,5 & 6

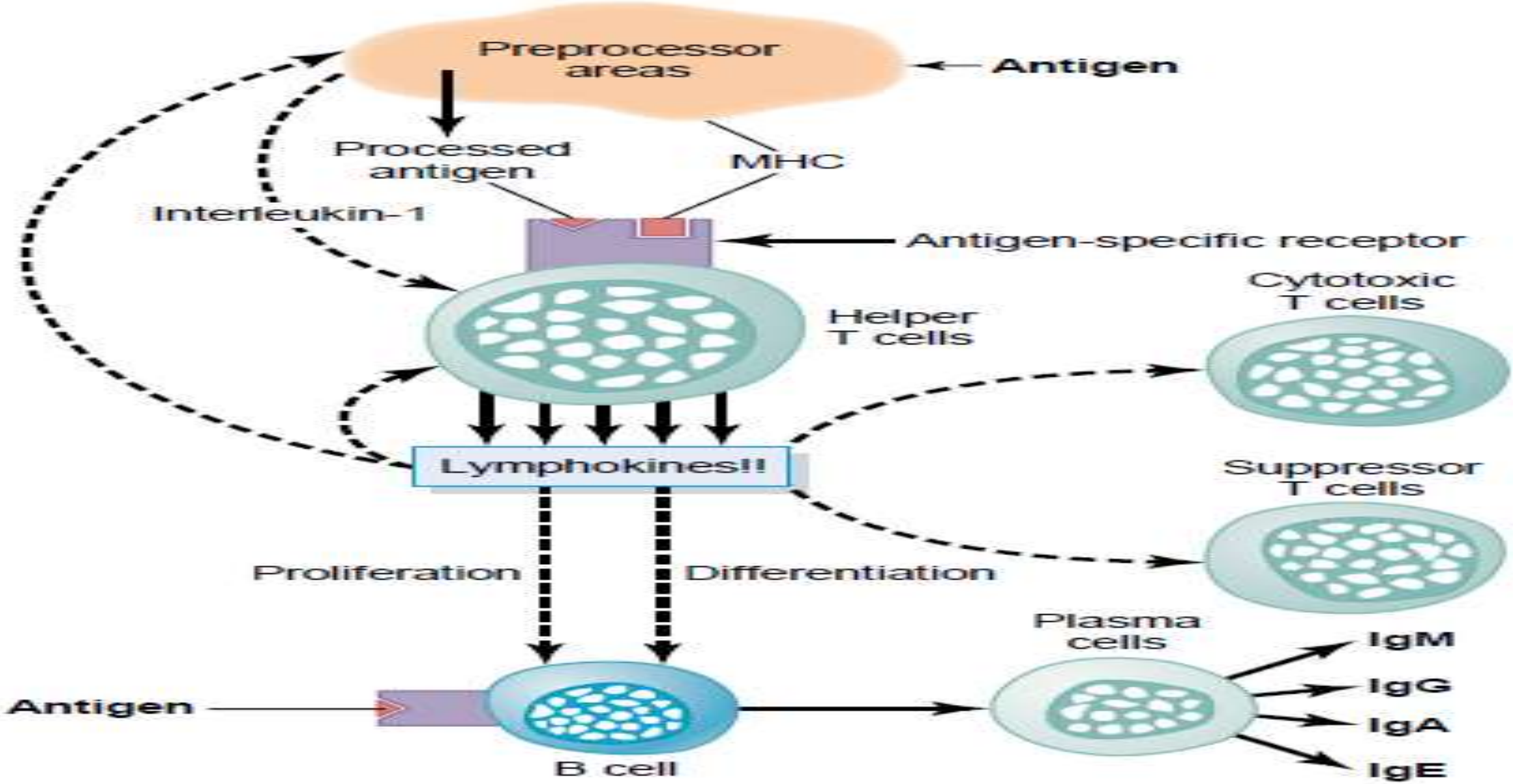
HUMORAL IMMUNITY



Primary & Secondary antibody response:

- **Primary response**: Following an initial exposure to foreign antigen, antibodies start to appear in the plasma after 8 days incubation period, reach a high level in few weeks then decline rapidly. Antibodies formed are IgM.

- **Secondary response**: On exposure to the same antigen, the concentration of the antibody produced is much higher than the first exposure. Antibodies formed are IgG



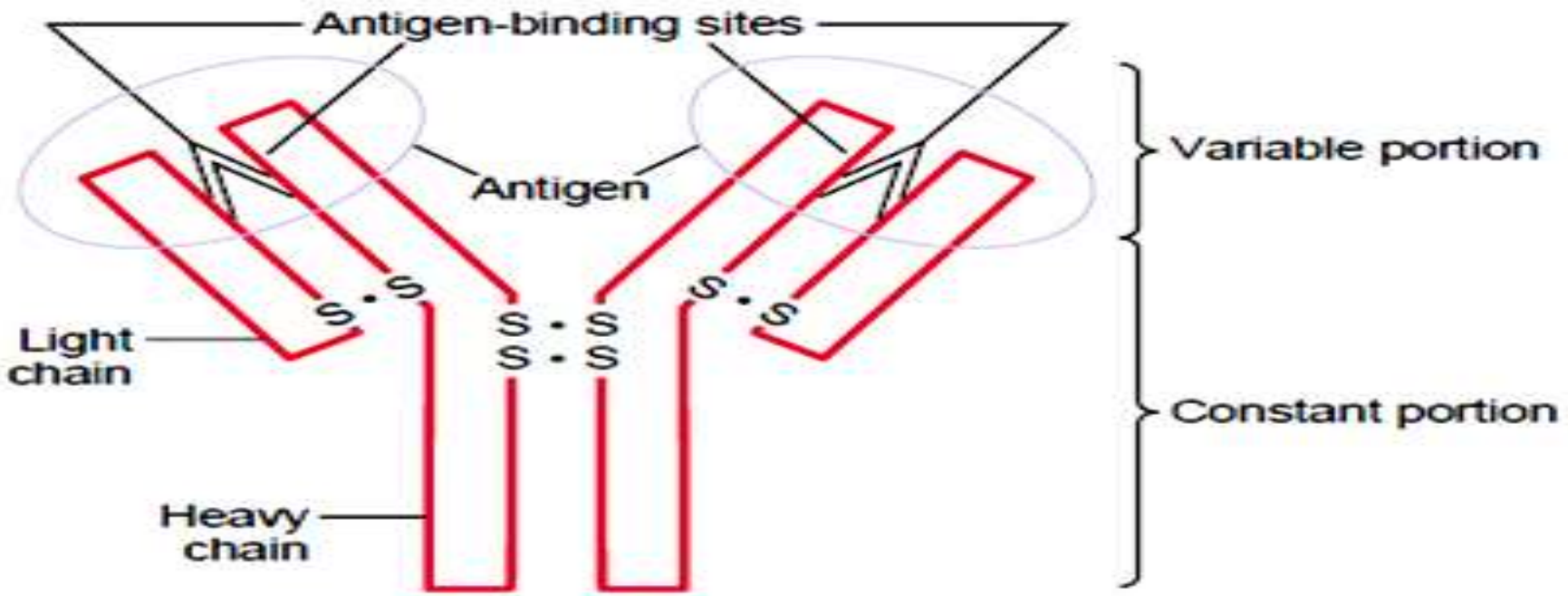
Regulation of the immune system, emphasizing a pivotal role of the *helper T cells*. MHC, major histocompatibility complex.

Antibodies

-Antibodies are gamma globulins called immunoglobulins (IGs).

-They have MW between 90.000 &150.000 .

Types of antibodies: Immunoglobulins (IG) M A G E D



Structure of the typical IgG antibody, showing it to be composed of two heavy polypeptide chains and two light polypeptide chains. The antigen binds at two different sites on the variable portions of the chains.

	IgG	IgM
Structure	Monomer: 2 sites for antigen binding	Pentamer: 10 sites for antigen binding
M.W	Lowest molecular weight	Highest molecular weight
Functions	1) Passive immunity 2) Rh antibody are IgG, so can cross the placenta 3) Complement activation 4) Responsible for secondary response 5) Act as Opsonins activating phagocytosis, Produces major antiviral, antibacterial activity	1) Active immunity 2) ABO antibody are IgM, so not cross the placenta 3) Complement activation 4) Responsible for primary response

IgA (Secretory immunoglobulins):

- Monomer, dimer or trimmer.
- Found in body secretions (mucous, saliva, tears, milk & colostrum).
- It protects against superficial infection e.g. eye , nasopharynx and also in urinary tract.
- It is first line at mucosal level against viral infection.

IgD:

- It is responsible for antigen recognition by B cells.
- It is present as an antigen receptor in B- lymphocytes.

IgE:

- It binds to specific receptors on basophils & mast cells.
- If reacts with antigen, it leads to release of histamine, heparin & leukotriens.
- It plays a role in allergic condition & parasitic infestation.

Functions of antibodies:

Antibodies bind antigens & cause their destruction by:

- Agglutination of the antigen.
- Neutralization of the toxic site of the antigen.
- Opsonization
- Activation of Natural killer (NK) cells.
- Activation of the complement system by the classic pathway

-The structure of the antibody is complementary to its antigen (Key & its lock)

-The interaction may be one or more of the above mentioned effects.

Disturbance of immunity

➢ Acquired immune deficiency Syndrome (AIDS)

HIV virus → - Decrease T helper

- Decrease T cytotoxic
- Decrease B cells
- There is loss of immune function.

➢ Autoimmune disease:

- Normally immune system distinguishes between self & non self-cells.
- Sometimes, antibodies are formed against self-constituents e.g. insulin dependent diabetes in which antibodies is formed against Pancreas B cells.

Thank You