Immunology of T and B cells
Cells of Immune System

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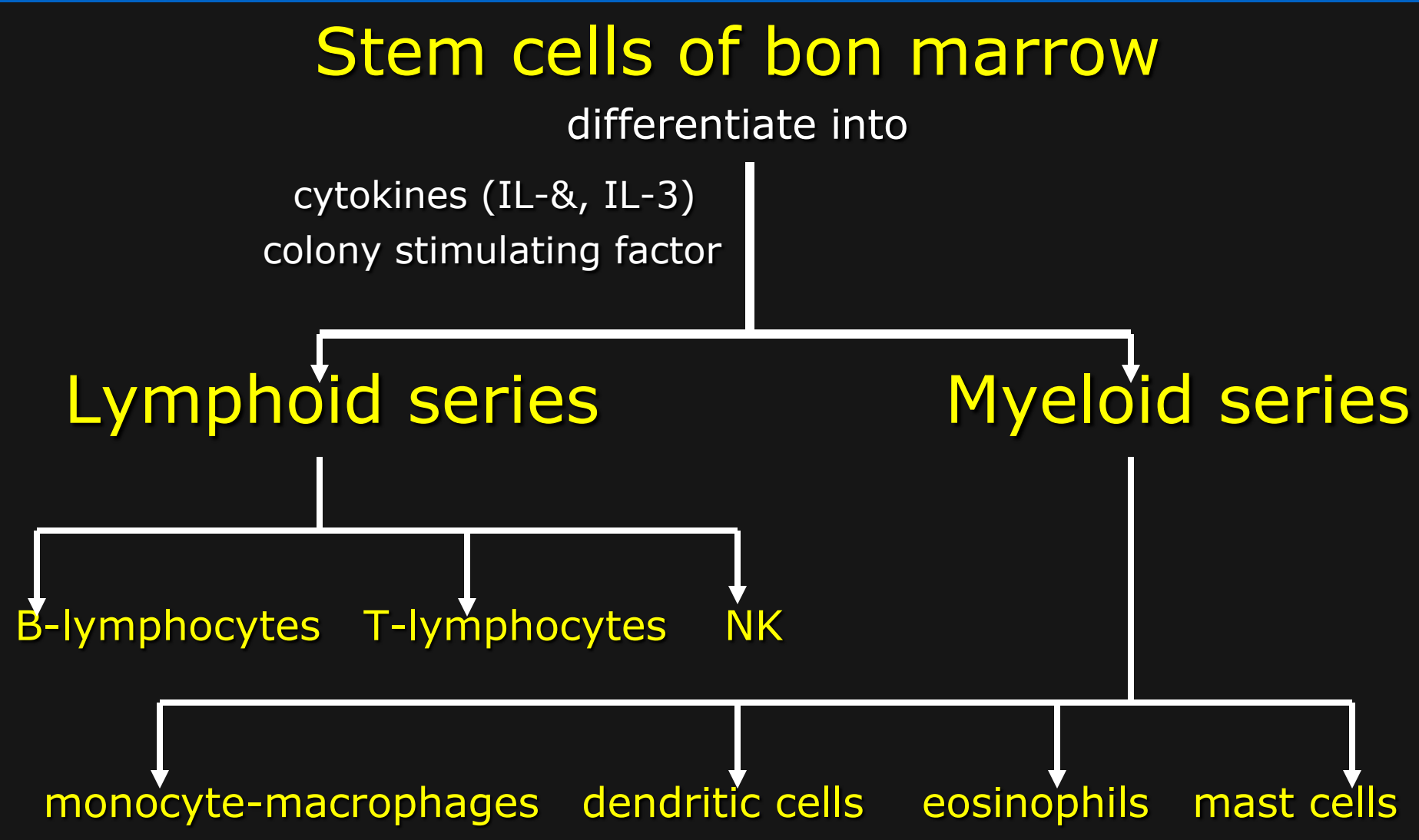


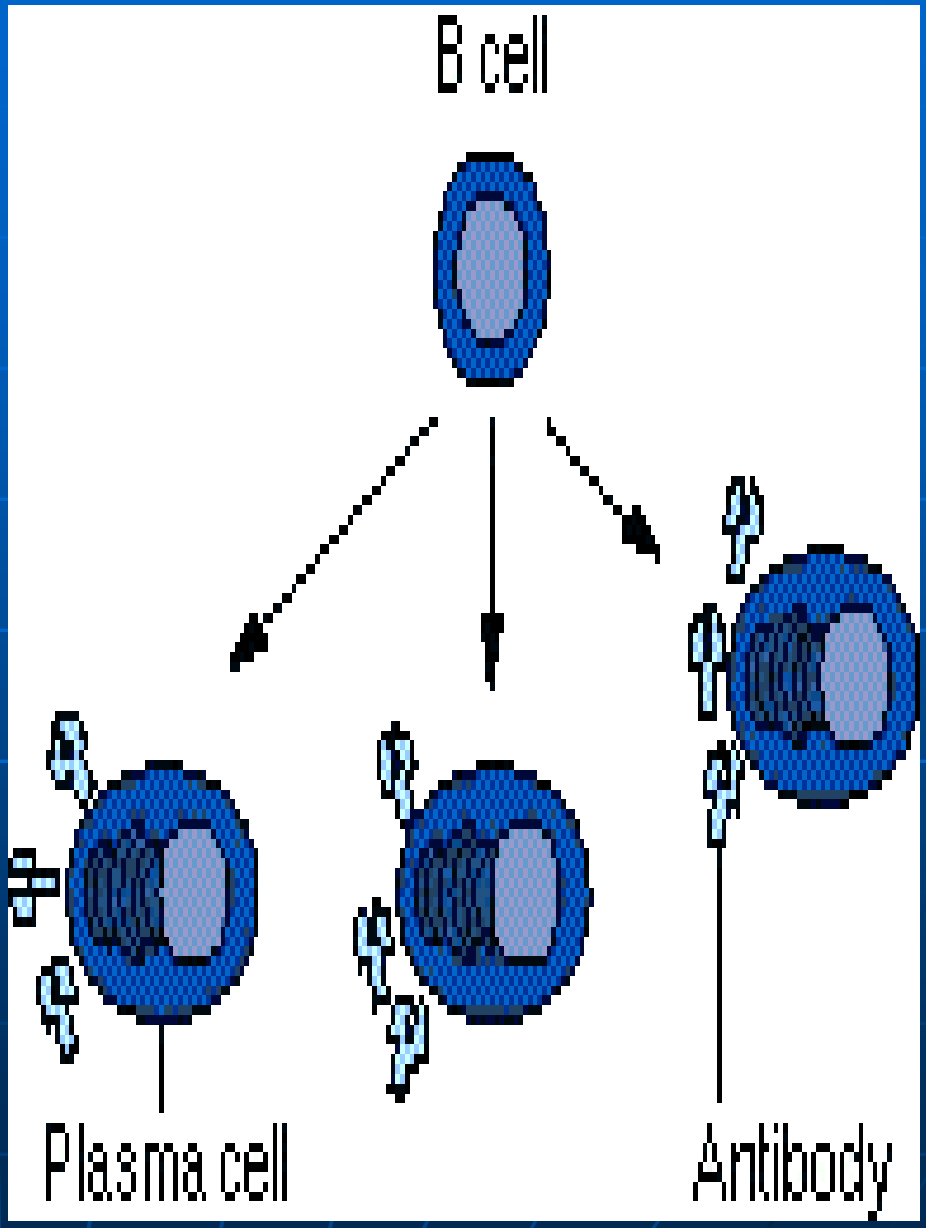
The Life Of The B Cell

- B lymphocytes are formed within the bone marrow and undergo their development there
- In Birds Bursa of Fabricious is the origin of B cells

They have the following functions:

- To interact with antigenic epitopes, using their immunoglobulin receptors
- To subsequently develop into plasma cells, secreting large amounts of specific antibody, or
- To circulate as memory cells
- To present antigenic peptides to T cells, consequent upon interiorization and processing of the original antigen

* B cells become plasma cells, which produce antibodies when a foreign antigen triggers the immune response



B-lymphocytes

in bon marrow

* The lymphoid stem cells differentiate into B cells

* B-cells precursors mature, differentiate into immunocomptent B-cells with a single antigen specificity

* Immature B-cells that express high affinity receptors for self antigens, die or fail to mature

  i.e negative selection or clonal deletion

* This process induces central self tolerance and reduces autoimmune diseases

B-lymphocytes

* Immature B cells express IgM receptors on the surface

* Mature B cells express IgM, IgD molecules on surfaces

* IgM and IgD molecules serve as receptors for antigens

* Memory B-cells express IgG or IgA or IgE on the surface

* B-cells bear receptors for Fc portion of IgG and a receptor for C3 component of the complement

* They express an array of molecules on their surfaces tha are important in B-cells interactions with other cells such as MHC II, B7 and CD4.

Mechanism of Humoral immunity

* Antibodies induce resistance through:

1) Antitoxin neutralize bacterial toxins (diphtheria, tetanus)

Antitoxin are developed actively as a result of:

a- Previous infection

b- Artificial immunization

c- Transferred passively as antiserum

* Neutralization of toxin with antitoxin prevents a combination with tissue cells

Mechanism of Humoral immunity

2) Antibodies attach to the surface of bacteria and

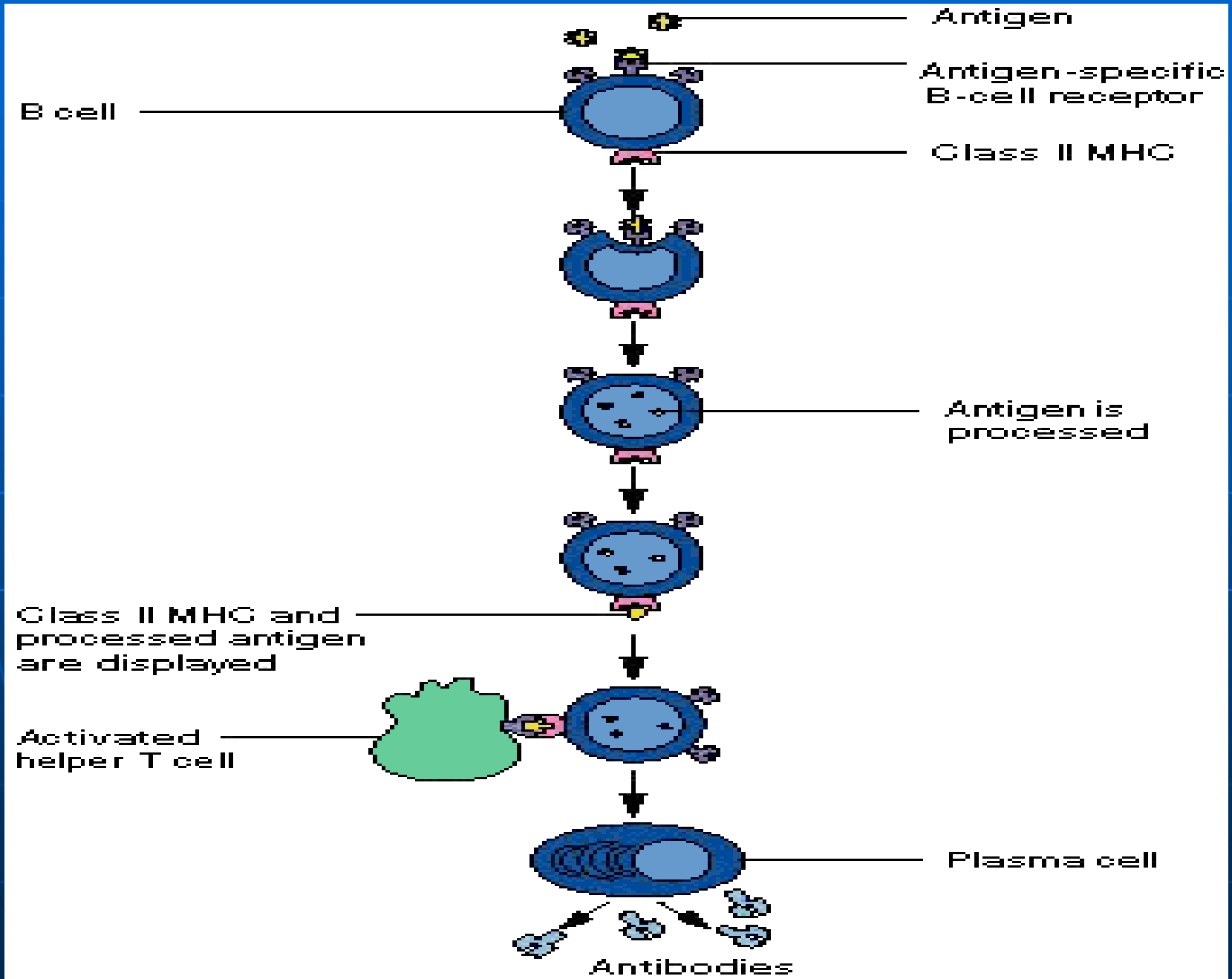
a- act as opsonins and enhance phagocytosis.

b- prevent the adherence of microorganisms to their target cells, e.g. IgA in the gut

c- Activate the complement and lead to bacterial lysis

d- Clump bacteria (agglutination) leading to phagocytosis

Activation of B cells to make antibody



T-Lymphocytes

T-lymphocytes migrate from bon marrow to enter thymus

1) In the outer cortex of thymus:

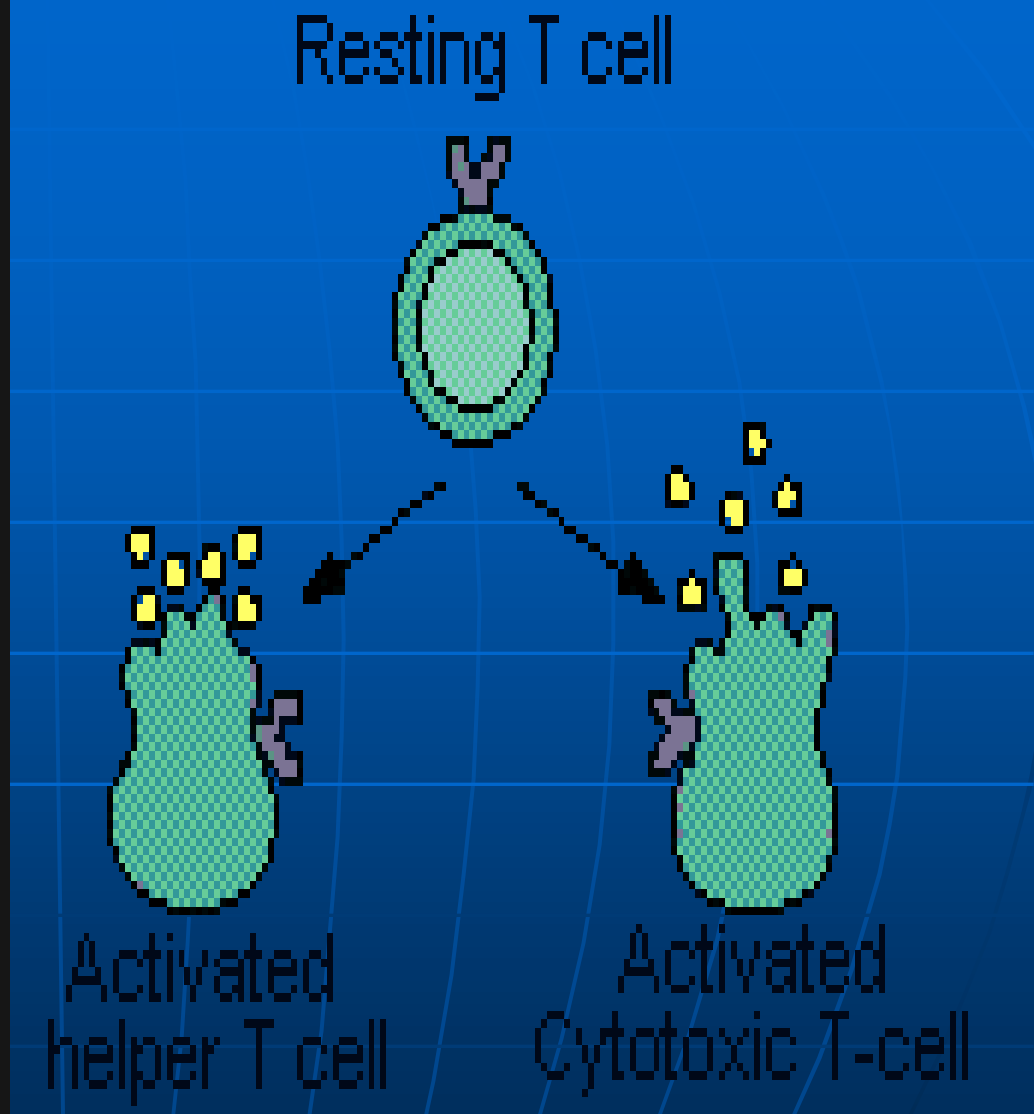
- T-lymphocytes acquire specific receptors (TCRs)

- This receptor commit lymphocyte to a single antigen specificity

- Responding by proliferation and production of a clone of cells (clonal selection)

- They differentiate to express CD3, both CD4 and

* T lymphocytes become CD4+ (helper T cells)
or
* CD8+ cells (which in turn can become killer T cells) also called cytotoxic T cells



T-Lymphocytes

2) In the medulla of thymus:

- TCRs recognize MHC molecules, loaded with normal self-peptides (p-MHC)

- TCRs capable of binding with low affinity to p-MHC will receive positive selection signals to divide and establish clones

- TCRs that bind too strongly to p-MHC undergo (negative selection)

- This selection process will eliminate the potentially most harmful self reactive T-cells (central self tolerance)

T-Lymphocytes

3)Immature T-cells express both CD4 and CD8.

As they mature

* T-cell with TCRs that have affinity to bind to MHC class II will become helper T-cells with CD4 molecule only

* T-cell with TCRs that have affinity to bind with MHC class I will become cytotoxic T-cells with CD8 molecule only

T-Lymphocytes

4) Mature positively selected T-cells are MHC restricted

* CD4 T-cells are MHC II restricted and only recognize specific foreign peptide only when they are presented in association with specific MHC II molecules

* CD8 T-cells are MHC I restricted and recognize specific foreign peptides only when they are presented in association with specific MHC I molecules

T-cell surface markers

These are molecules that by witch we can identify T-cells and divide them to subsets

They are required to for interactions between T-cells and APC and for antigen recognition

These are TCRs, CD3, CD4, CD8, CD2, CD28,and CD40 on activated T-cells

T-cell subpopulation

1) CD4 T helper lymphocytes (TH)

- TH lymphocytes recognize antigen on the surface of APC in association with class II MHC molecules

- They are activated and secrete several cytokines

- There are two main subsets of TH cells (THI and TH2)

- The two subsets are differentiated on basis of the cytokine they produce

1) CD4 T helper lymphocytes Subsets

Th1 produce mainly :

- Cytokines of CMI and inflammation

  e.g. IFN-γ, TNF- β, IL-3 and IL-2

TH2 produce mainly:

- Cytokines that stimulate B-cells
- Suppressor cytokines

  e.g. Il-4, IL-5, IL-6 and IL-10

2) CD8 Cytotoxic T-lymphocytes (CTLs)

* They constitute 35% of peripheral T-cells

* CTLs recognize antigen on surface of target cells (infected APC or other infected nucleotide cell) in association with MHC-I

* They are activated and kill the virus infected cell or tumor cell

Professional APCs

Dendritic cells, macrophages, and B-lymphocytes

Dendritic cells:

- They are the most efficient APCs
- They are the main inducers of primary immune response
- Presenting antigen to and activating native T-cells in the recognition phase
- They express class I and class II MHC molecules
- Dendritic cells are primarily located under skin and mucosa of most organs
- They capture foreign antigens and transport them to local lymph nods
- They present antigen to native helper T-cells

Macrophages

* Derived from myeloid stem cells in bon marrow

* They exist as free cells in blood e.g. monocytes and fixed cells in tissues e.g. Kupffer cells of liver

* They are important link between innate and acquired immune responses

* They are activated and attracted to the site of foreign material by action of different cytokines
  e.g. IFN-γ , C5a

Functions of Macrophages

1) Phagocytosis

2) Opsonization

3) APCs: they ingest foreign material, process it, and fragments of antigen are presented on its surface (in association with MHC molecules) for interaction with T-cells

4) Macrophages may kill antibody coated infected cells or tumor cells through release of lytic enzymes

5) They produce IL-1, IL-6, IL-12, IL-15, TNF-alpha

6) They secret prostaglandins and synthesize complement components

Natural killer (NK) Cells

* Large granular lymphocytes which lack most surface markers of B and T-cells

* They comprise 5-10% of the peripheral lymphocytes

* They function mainly in innate immunity

* They have spontaneous non-specific cytotoxic activity on virus infected cells, tumor cells and graft cells

* They are not MHC restricted and MHC I inhibits their killing functions

* The mechanism of NK mediated cytolysis is as that of CTLs

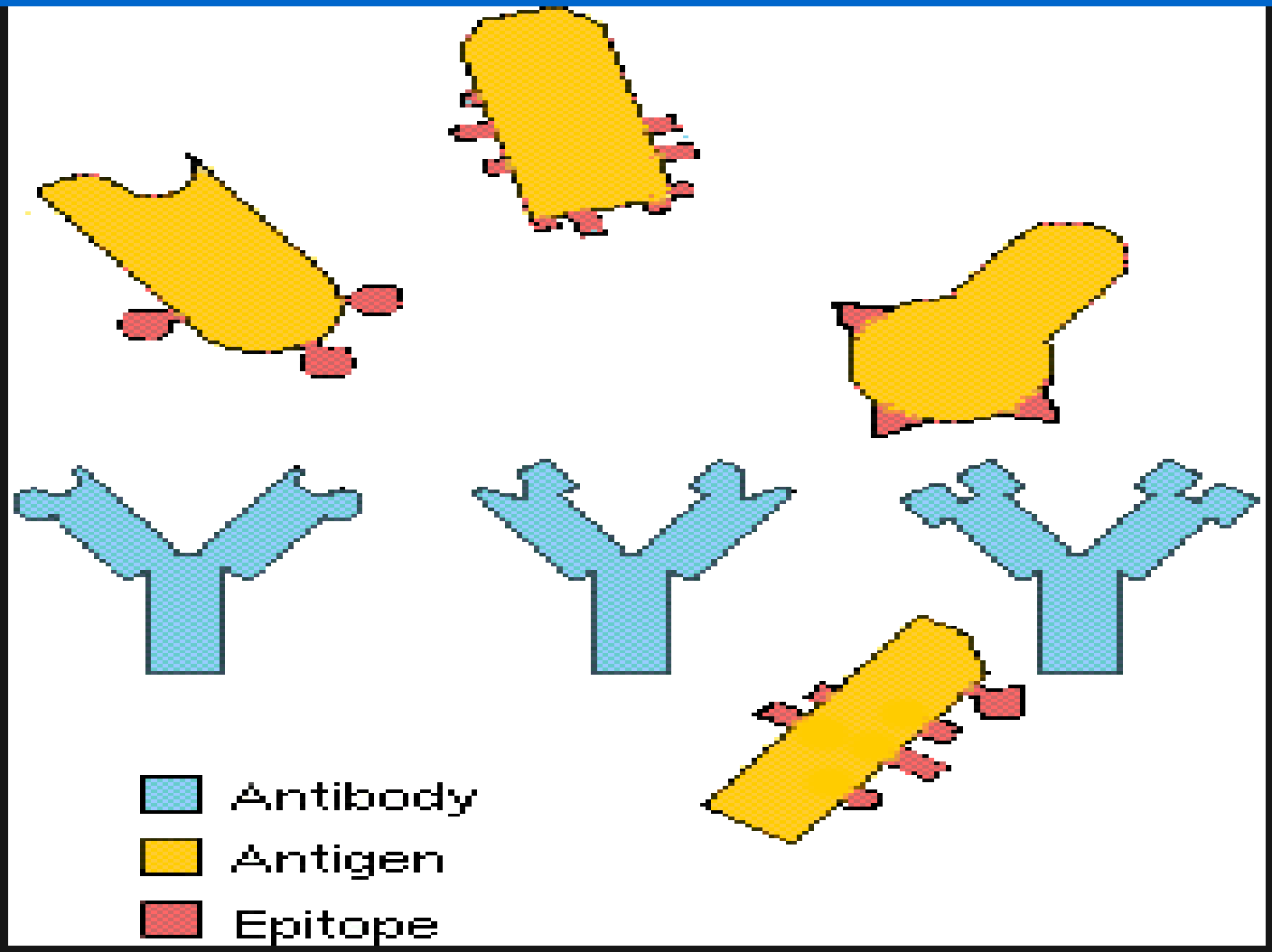
NK cells differ from CTLs in

1)They are non-specific

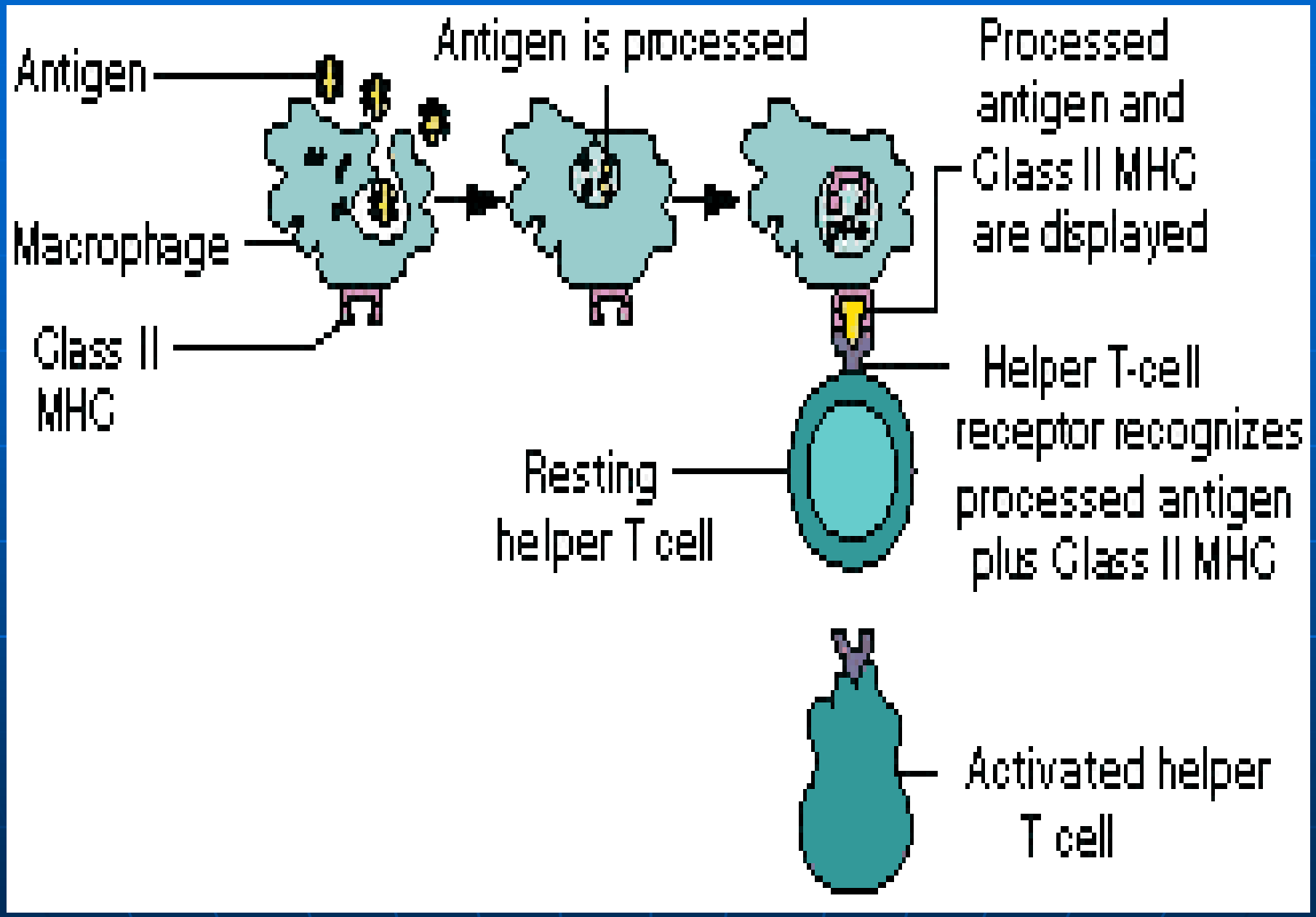
2)They act spontaneously without prior recognition or activation

3)They do not require antigen presentation by MHC

4)They destroy cells coated with antibodies,
a mechanism called antibody dependent cellular cytotoxicity (ADDCC)

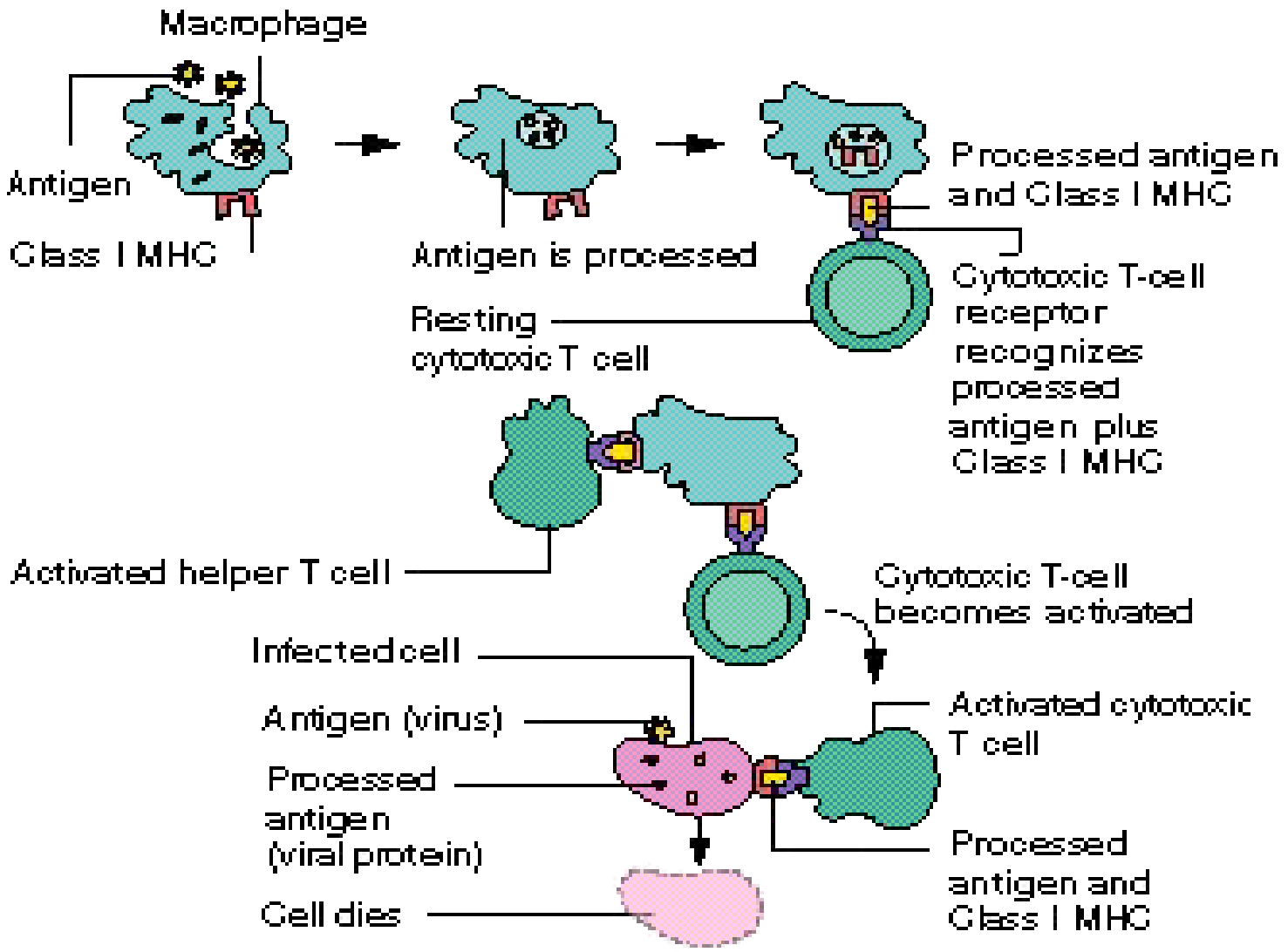


Antibodies produced by B-cells of the immune system recognize foreign antigens and mark them for destruction



Activation of helper T cells

Activation of cytotoxic T cells



Primary And Secondary Response

- Primary Response:
- Slow in Onset
- Low in Magnitude
- Short Lived
- IgM

- Secondary Response:
- Rapid in Onset
- High in Magnitude
- Long Lived
- IgG (Or IgA, or IgE