Hematology

- Histology
- Biochemistry
- Pathology
- Pharmacology
- Physiology
- Microbiology

- Handout 3
- Slide
- Sheet

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- lecture number :
- Done BY :

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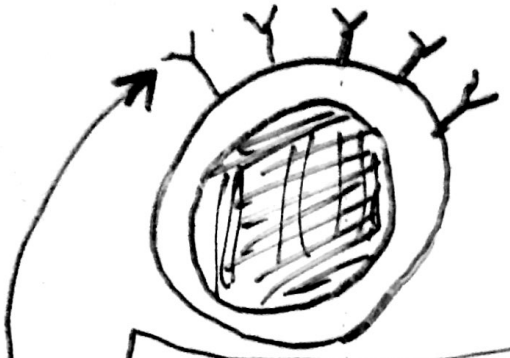
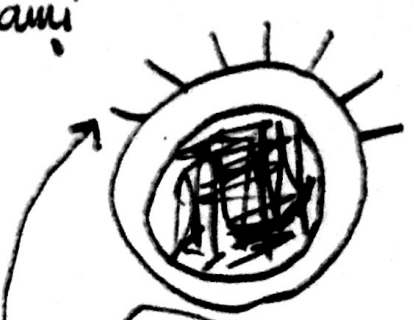
"Obeidat



B-lymphocyte

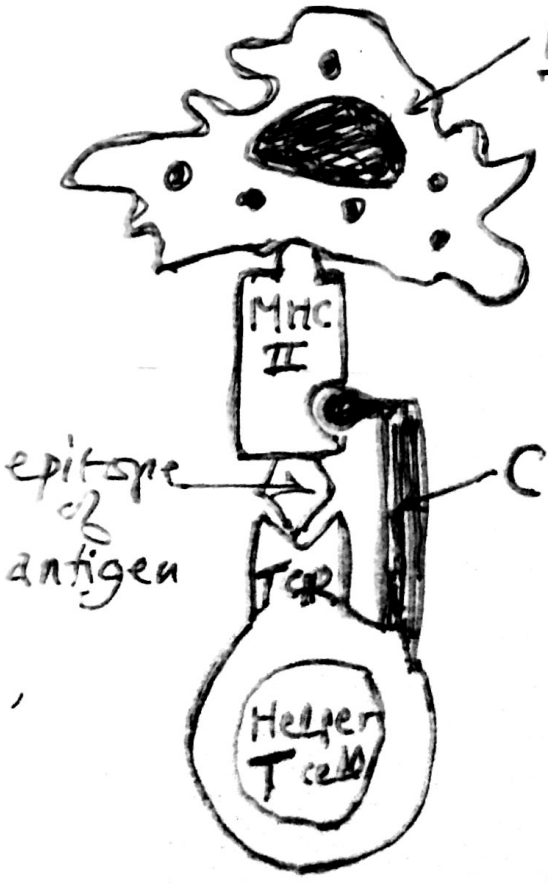
SIGs = surface immunoglobulins



T-lymphocyte

TCRs = T cell receptors

- differ in structure
- Both act as antigen Receptors
  - able to recognize & interact with specific antigen



APC (antigen presenting cell)

In addition to TCR molecules T cells express clusters of differentiation Proteins (CD molecules or CD markers)

↓

(The epitopes are short polypeptides that fit into a groove on the surface of MHC molecules)

↓

* T cells can recognize (bind) only peptide antigens associated with MHC molecules
* B cells ?? can recognize ..... Not associated with MHC

* Most T cells that display CD4 develop into helper T cell (TH) known as $CD4^+$ T cell
* T cells that display CD8 develop into cytotoxic T (TC) cells, also termed $CD8^+$ cells

↓

During development in the thymus

↓

{ developing T lymphocytes whose TCRs recognize self proteins or whose CD4 or CD8 molecules cannot recognize (bind) MHC I & MHC II } undergo apoptosis before they leave the cortex

↓

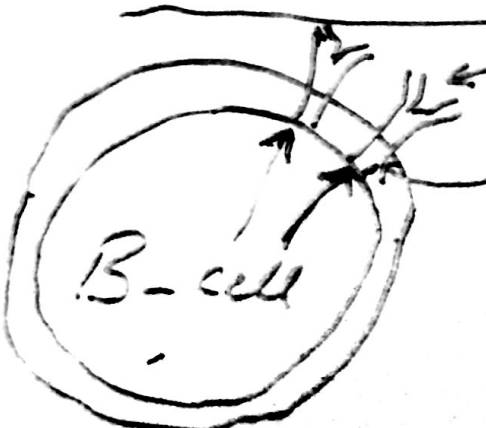
To function properly your T lymphocytes

① must be able to recognize your own MHC proteins
→ a process known as **Self Recognition**

② they must lack reactivity to peptide fragments from your own proteins
→ a process known as **self tolerance**

During development (the process of becoming immunocompetent) in the bone marrow

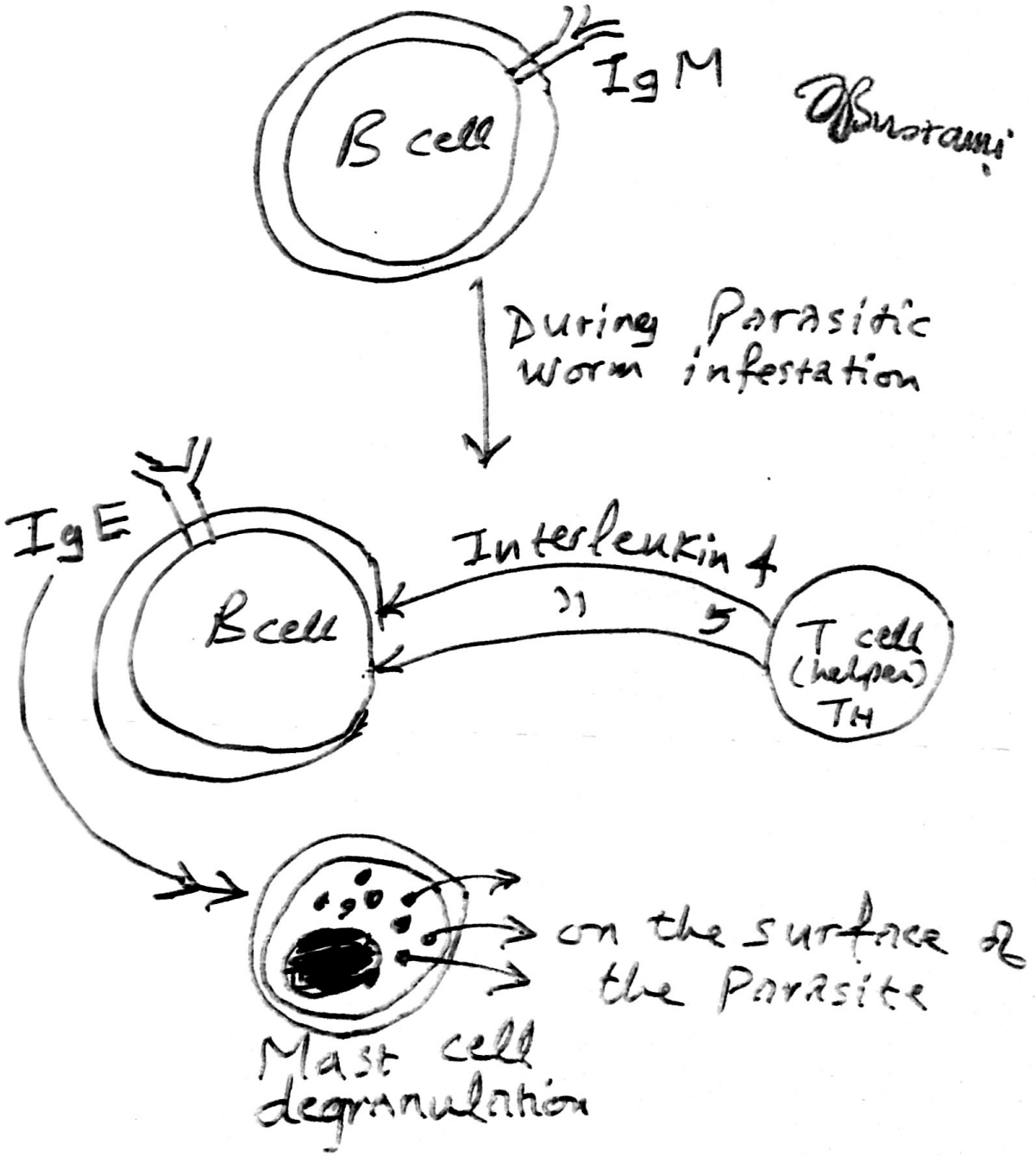
Each B cell produces 50.000 to 100.000 IgM and IgD immunoglobulins (SIGs) and INSERTS THESE IN ITS PLASMA MEMBRANE



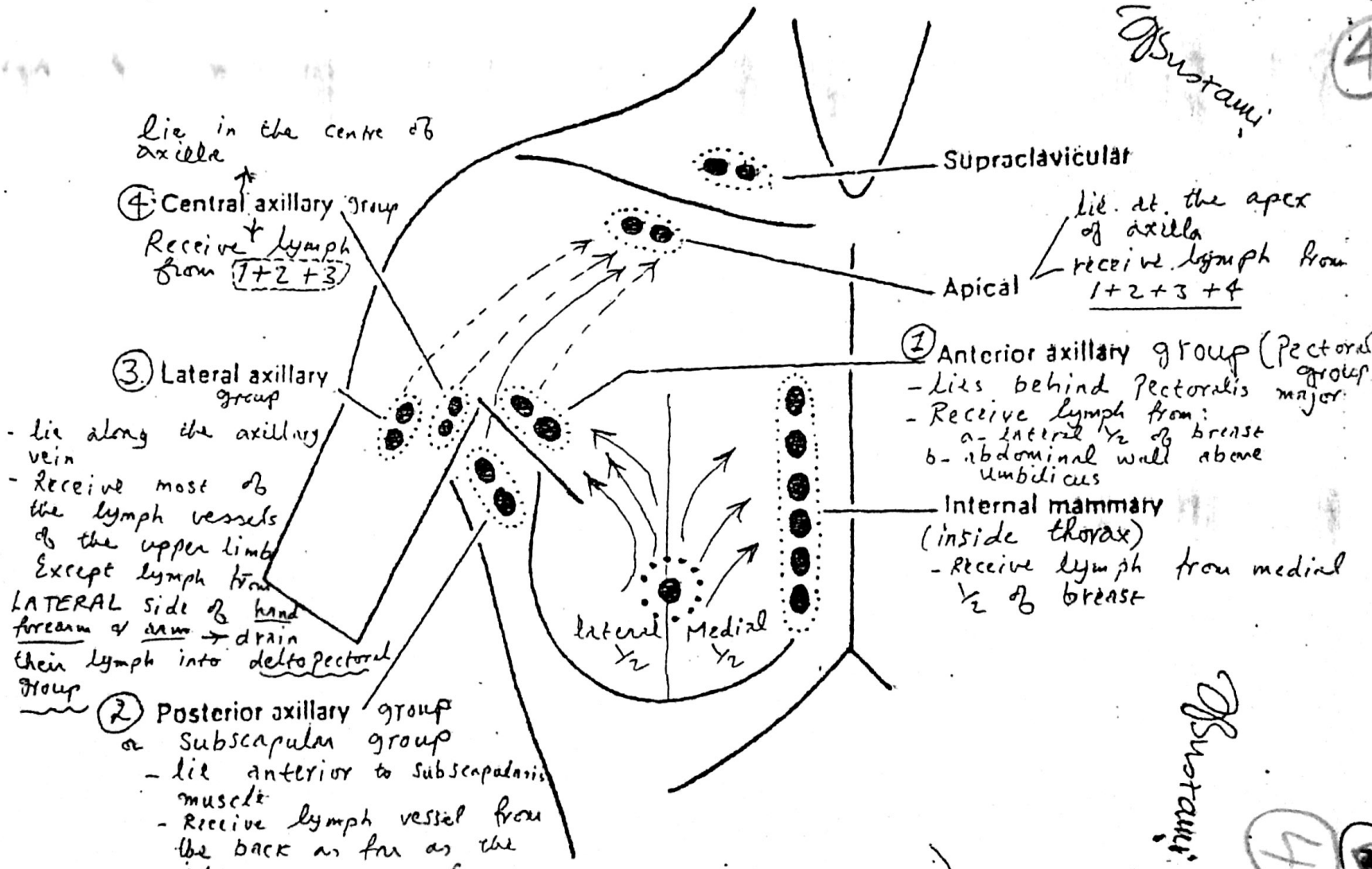
Class switching

once IgM is produced B cell can produce a different class of immunoglobulin

This ability is determined by a particular Cytokines present around the B cell & released by T-helper cells as a response to the Pathogen present



{Superficial lymphatics follow veins
deep " " " arteries}



lie in the centre of axilla

④ Central axillary group
Receive lymph from (1+2+3)

lie at the apex of axilla
receive lymph from 1+2+3+4

① Anterior axillary group (Pectoral group)
- lies behind Pectoralis major
- Receive lymph from:
  a- lateral ½ of breast
  b- abdominal wall above umbilicus

Internal mammary (inside thorax)
- Receive lymph from medial ½ of breast

③ Lateral axillary group
- lie along the axillary vein
- Receive most of the lymph vessels of the upper limb
Except lymph from LATERAL side of hand forearm & arm → drain their lymph into deltopectoral group

② Posterior axillary group
& Subscapular group
- lie anterior to subscapularis muscle
- Receive lymph vessel from the back as far as the iliac crest

Lymph nodes draining the breast

- The apical lymph nodes drain into the subclavian lymph trunk
- on the left this trunk drains into thoracic duct → venous circulation
- " " right " " " " Rt-lymph trunk → " "

SUPERFICIAL INGUINAL LYMPH NODES

The superficial inguinal lymph nodes are variable in their number and size. Their arrangement is 'T'-shaped, having a lower vertical group and an upper horizontal group. The upper nodes can be subdivided into the upper lateral and upper medial groups.

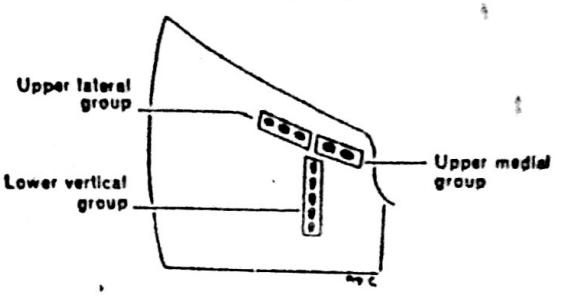


Fig. 5 Superficial inguinal lymph nodes.

1. The *lower vertical group* is placed along both sides of the upper part of great saphenous vein. It drains the skin and fasciae of the lower limb, except the buttock (to upper lateral group) and the short saphenous territory (to popliteal nodes).

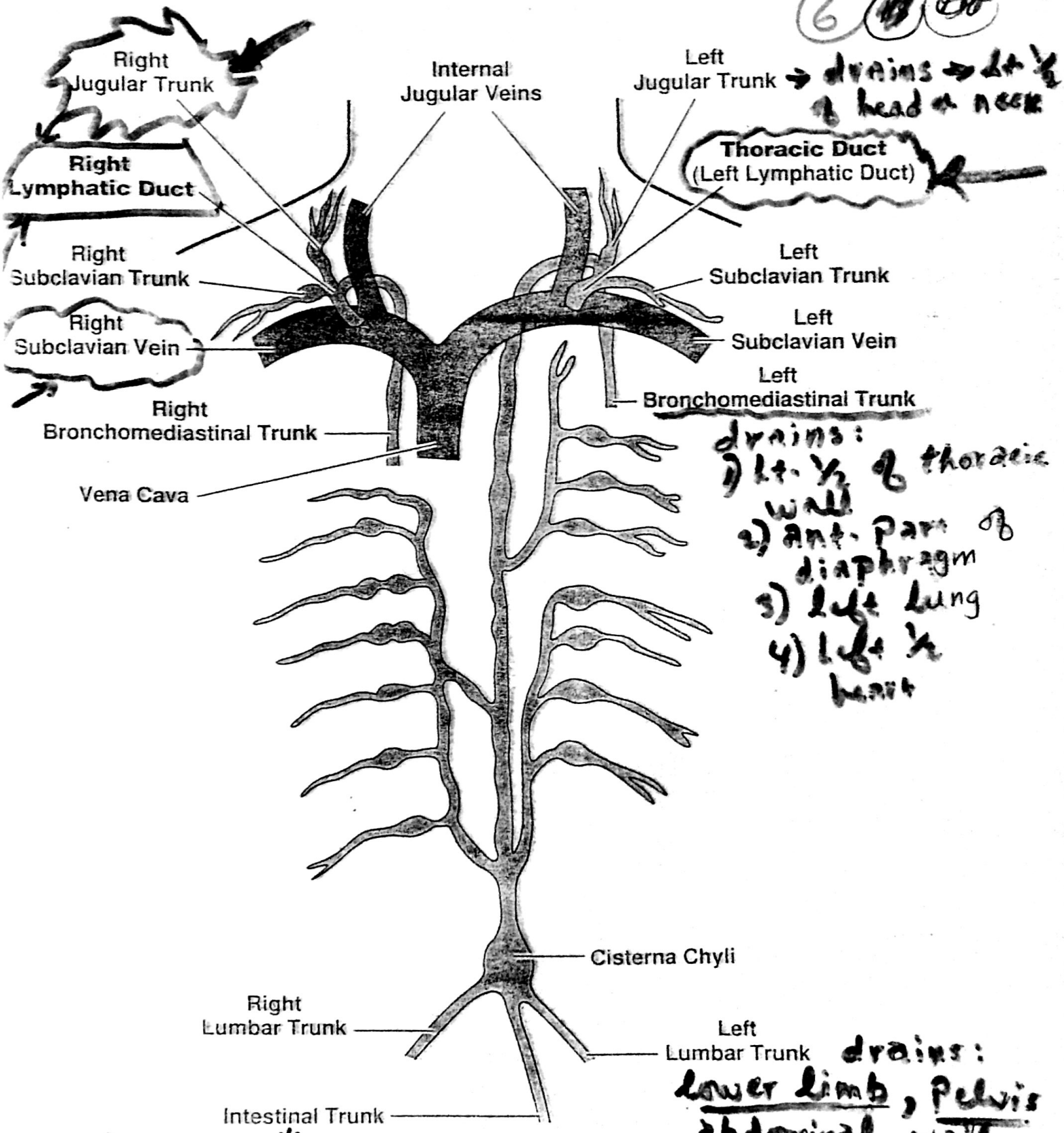
2. The *upper lateral group* is placed below the lateral part of inguinal ligament. It drains the buttock, flank and the back below the waist.

3. The *upper medial group* is placed below the medial end of the inguinal ligament; one or two nodes may lie above the inguinal ligament on the course of the superficial epigastric vessels. They drain anterior abdominal wall below the umbilicus, and the perineum.

* The *efferents* from all superficial nodes pierce the cribriform fascia, and terminate into the deep inguinal lymph nodes which lie along the upper part of the femoral vessels.

Painful enlargement of the superficial inguinal lymph nodes may therefore indicate a disease of the superficial parts of the lower limb including the buttock, infraumbilical part of anterior abdomial wall, perineum, external genitalia, anus, vagina and round ligament of uterus.

LYMPH TRUNKS AND LYMPHATIC DUCTS



drains → lt. ½ of head & neck

drains:
1) lt. ½ of thoracic wall
2) ant. part of diaphragm
3) left lung
4) left ½ heart

drains: lower limb, pelvis, abdominal wall

drains: stomach, intestines, pancreas, spleen & part of liver

Cell-Mediated immunity

Directly Kill specific ABNORMAL cells or FOREIGN cells

effective against

* Intracellular Pathogens: fungi, Protozoa, viruses inside body cells
* Cancer cells
* cells of tissue transplantation

Mechanism

Activation of Cytotoxic T cells

e.g virus

viruses attack body cells by injecting their nucleic acids into the cytoplasm → viral nucleic acids alter the DNA of the host cell causing it to produce viral proteins which are used to produce new viruses

SOME OF THE VIRAL PROTEINS ARE INSERTED IN THE PLASMA MEMBRANE OF THE HOST CELL COMPLEXED WITH MHC-I Proteins

→ since MHC-I proteins are present on all body cells this type of antigen-MHC-I complex can be formed by any virus-infected cell.

Tumour antigens → cancer cells result from genetic changes induced by viruses, chemicals or radiation
genetically altered cancer cells produce UNUSUAL PROTEINS NOT FOUND IN NORMAL BODY CELLS

SOME OF THESE CANCER-INDUCED PROTEINS CALLED TUMOR ANTIGENS ARE INSERTED IN THE PLASMA MEMBRANES OF TUMOR CELLS ASSOCIATED WITH MHC-I PROTEINS

* THE ANTIGEN-MHC-I complexes serve as BINDING SITES ~~for cytotoxic T~~ cells

Antigen Recognition

Refers to BINDING of an antigen to a T cell Receptor (TCR)

There are millions of different cytotoxic T cells
→ EACH WITH UNIQUE TCRs THAT CAN RECOGNIZE SPECIFIC ANTIGEN–MCH-I complexe

* When a resting (inactive) cytotoxic T cell encounters its antigen complexed with MHC-I Proteins on the surface of a virus-infected or Cancer cells it BINDS TO (Recognizes) the Complex

Activated cytotoxic T cells → Enlarge & divide forming a clone of cytotoxic T cells
→ At the same time memory cytotoxic T cells are produced

The activated cytotoxic T cells are carried by the BLOOD from the lymph nodes or spleen to all tissues of the Body → When they encounter cells that display their antigens complexed with MHC-I Proteins → they bind & RELEASE DAMAGING CYTOKINES

Attack by Cytotoxic T Cells

Cytotoxic T cells have three killing mechanisms :

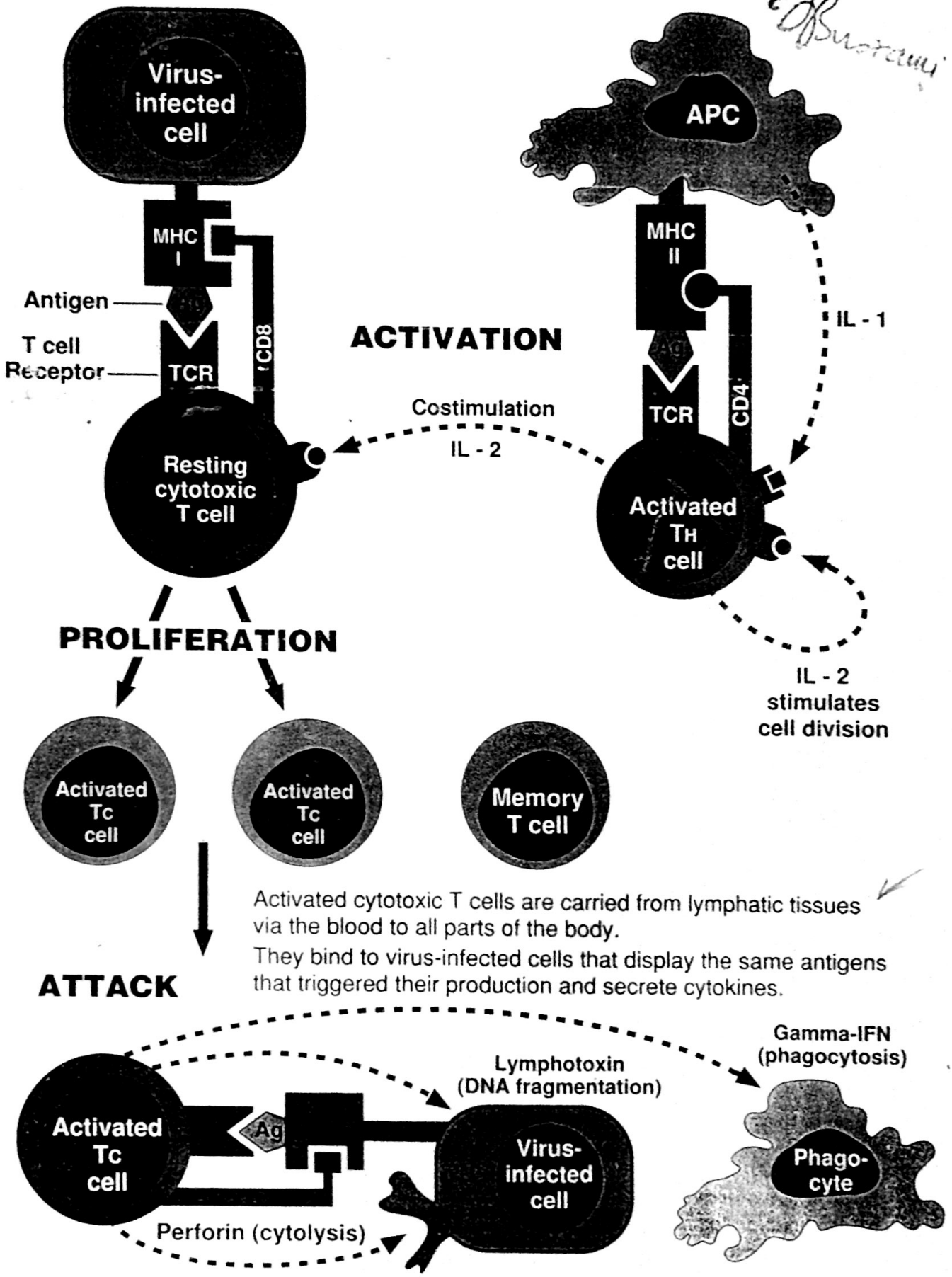
(1) Cytolysis (Lysis) A cytokine called *perforin* forms pores in the plasma membranes of target cells, causing them to burst and die.

(2) DNA Fragmentation A cytokine called *lymphotoxin* kills target cells by DNA fragmentation.

(3) Phagocytosis A cytokine called *gamma-interferon* enhances the phagocytic activity of macrophages, which ingest and kill the target cells.

Costimulation Macrophages phagocytize virus-infected cells and cancer cells. They process and insert fragments of the antigens into their plasma membranes associated with MHC II. The macrophages present these antigens to resting helper T cells located in lymphatic tissues. The helper T cells are costimulated by IL-1, which is secreted by the macrophages. The activated helper T cells proliferate and secrete a variety of cytokines, especially IL-2. The IL-2 acts as a costimulator for antigen-bound cytotoxic T cells. IL-2 also acts as an autocrine, increasing the proliferation of helper T cells (a positive feedback mechanism).

CELL-MEDIATED IMMUNITY



Activated cytotoxic T cells are carried from lymphatic tissues via the blood to all parts of the body.
They bind to virus-infected cells that display the same antigens that triggered their production and secrete cytokines.