Lecture 1 - Introduction to Immunology: Innate Immunity & Cell Types.

Suggested reading: Chapter 1 & 2

Learning objectives:

- Definition of: pathogen, antigen, immunogen, tolerance.
- Compare and contrast innate and acquired immune system
- Describe and differentiate between physical/physiological/cellular barriers
- Cell lineage of: B, T, NK, neutrophil, basophil, eosinophil, mast cell, monocyte, macrophage, dendritic cell.
- Pathogen destruction by intracellular process.

Some Definitions

Pathogen: bacteria, virus, fungi (yeast), parasite. ; cancer
→ cause harm to organism

Antigen: "thing" recognized by immune system.

Immunogen: Antigen that promotes an initial immune response

Tolerance: hapten: small organic (not immunogens, but can be antigens)
hapten + protein = immunogen.
- lack of immune response, self tolerance important.
fails = auto immune disease

Functions of the immune system:

Protect body against harmful (pathogens)

What are some consequences of dysfunction of the immune system?
- auto immune disease, immunodeficiency, allergy

Branches of the Immune System:

Innate ⟶ ⟵ Acquired (Ab, T-cells)

Immune response:

Recognition ✓ ✓

Response ⤳ common mechanisms

→ Killing

2. Properties of the Branches of the Immune System:

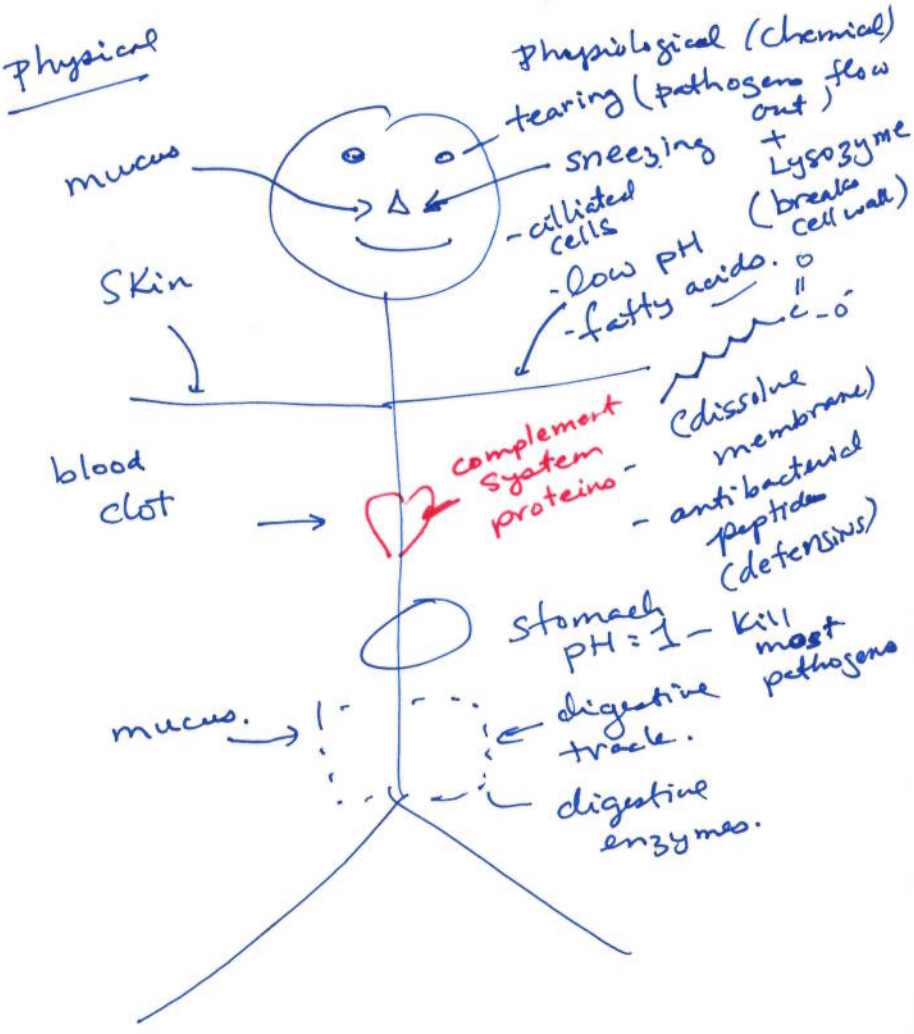
Innate	Acquired
present all the time	Induced.
fast. (sec)	Slow < primary response (1) 7-14d; Secondary response (2) 4d
No memory	memory → memory cells B Mem T Mem
low specificity - N-formyl peptide. (bacteria)	high specificity - one Ab recognizes one antigen.
Not adaptable	high adaptable → increase in binding affinity of Ab to antigen

Innate Immune System:

Barriers to Infection

i) **Physical/anatomic** barriers
- Skin: effective if intact
- Mucus traps pathogens. Respiratory, gastrointestinal, and genitourinary tracts: mucosal cell layer continuous with skin.
- Blood clotting - post injury

ii) **Physiological/chemical defenses** -present in body cavities and fluids.

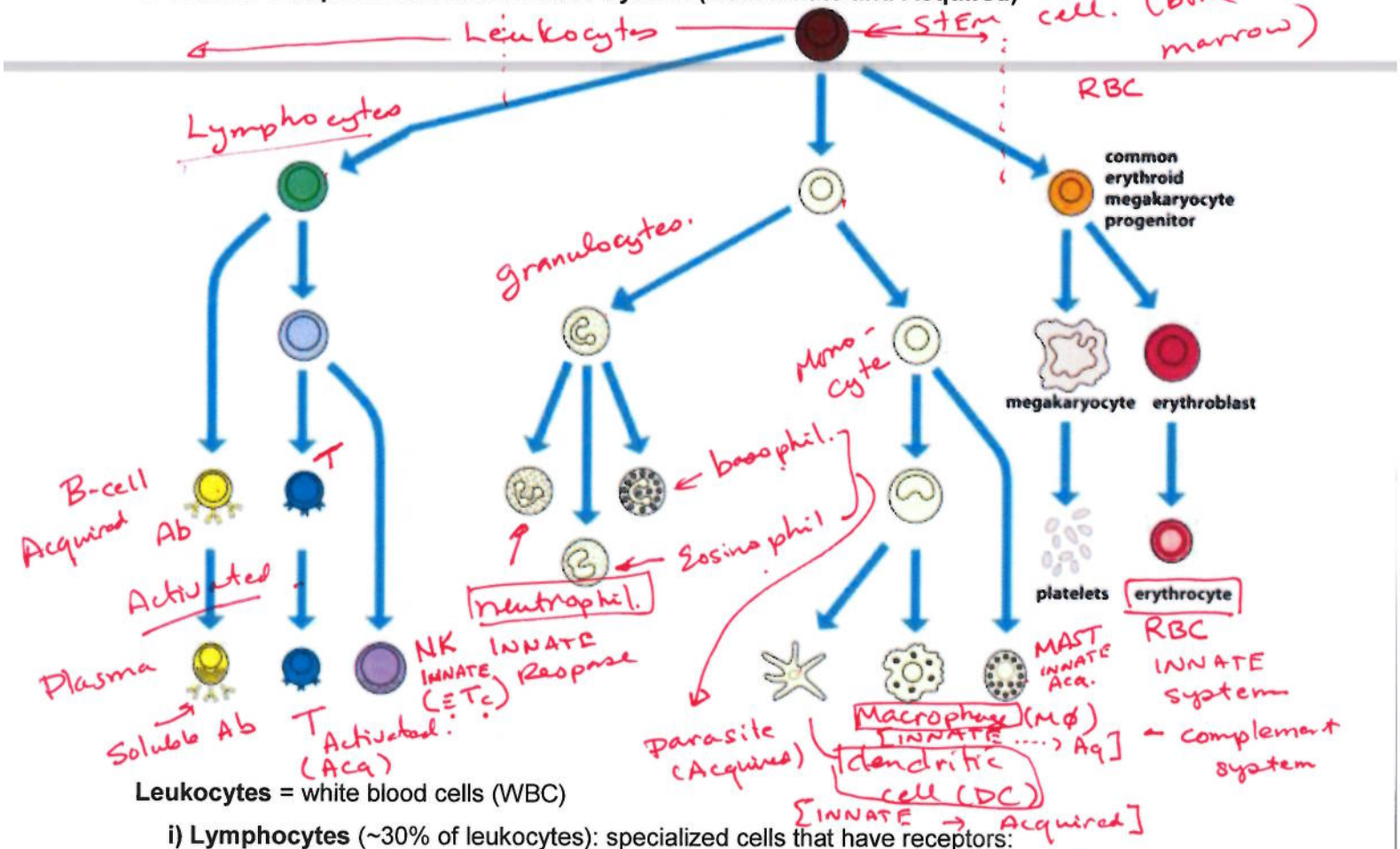


- Skin: low pH (sweat), fatty acids, hydrolytic enzymes (lysozyme),anti-microbial cationic peptides (defensins).
- Mechanisms such as tearing, coughing, sneezing, vomiting
- Respiratory, gastrointestinal, and genitourinary tracts: acidic secretions, degradative enzymes, Removal of mucus via ciliated cells.
- Circulation: soluble proteins such as the complement system, cytokines, acute phase proteins.

iii) **Cellular barriers** (Killing of pathogens & infected cells)

- Granulocytes (Mast cells)
- Phagocytes (neutrophil, macrophages)
- NK cells
- Native microbial biofilms (commensal bacteria)

3. Cellular Components of the Immune System (Both Innate and Acquired)



Leukocytes = white blood cells (WBC)

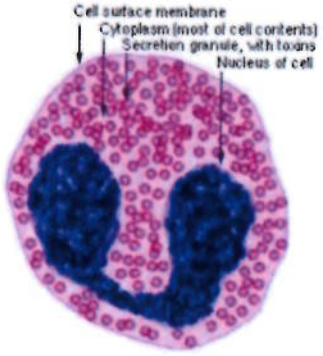
i) Lymphocytes (~30% of leukocytes): specialized cells that have receptors:

B lymphocytes (B cells):
T lymphocytes (T cells):
Natural Killer (NK) cells:

T_H (helper) → Activate B cells
→ Activate T_C cells

T_C Activated $\xrightarrow{T_H}$ T_{CTL} cytotoxic T lymphocyte. Kill virally infected cells, cancer

ii) Granulocytes, sometimes called polymorphonuclear leukocytes (PMN; ~64% of leukocytes): have a multi-lobed nucleus and intracellular granules, which contain degradative enzymes and vasoactive proteins.



Neutrophils (~60% of leukocytes): found in circulation, short-lived (7 hr. half-life), recruited to site of injury within 30-60 minutes. Released from bone marrow.

Eosinophils (~3% of leukocytes): found in circulation.

Basophils (~1% of leukocytes): found in circulation.

iii) **Monocytes** (~6% of WBC): found in blood, recruited to site of injury within 4-6 hrs, Monocytes develop into the following three cell types:
Macrophages: found in tissues near blood vessels. Tissue specific forms, e.g. Kupffer cells in the liver, microglial cells in the central nervous system
Dendritic cells are found primarily in the skin, intense communication with acquired system.
Mast cells involved in inflammatory response, allergic response

4. Killing of Pathogens (Neutrophils, Macrophages, Dendritic Cells)

i) pathogen internalized by:

- phagocytosis
- receptor mediated endocytosis (enhanced by **opsonization:** innate (C3b is the opsonin) & acquired (IgG is the opsonin)

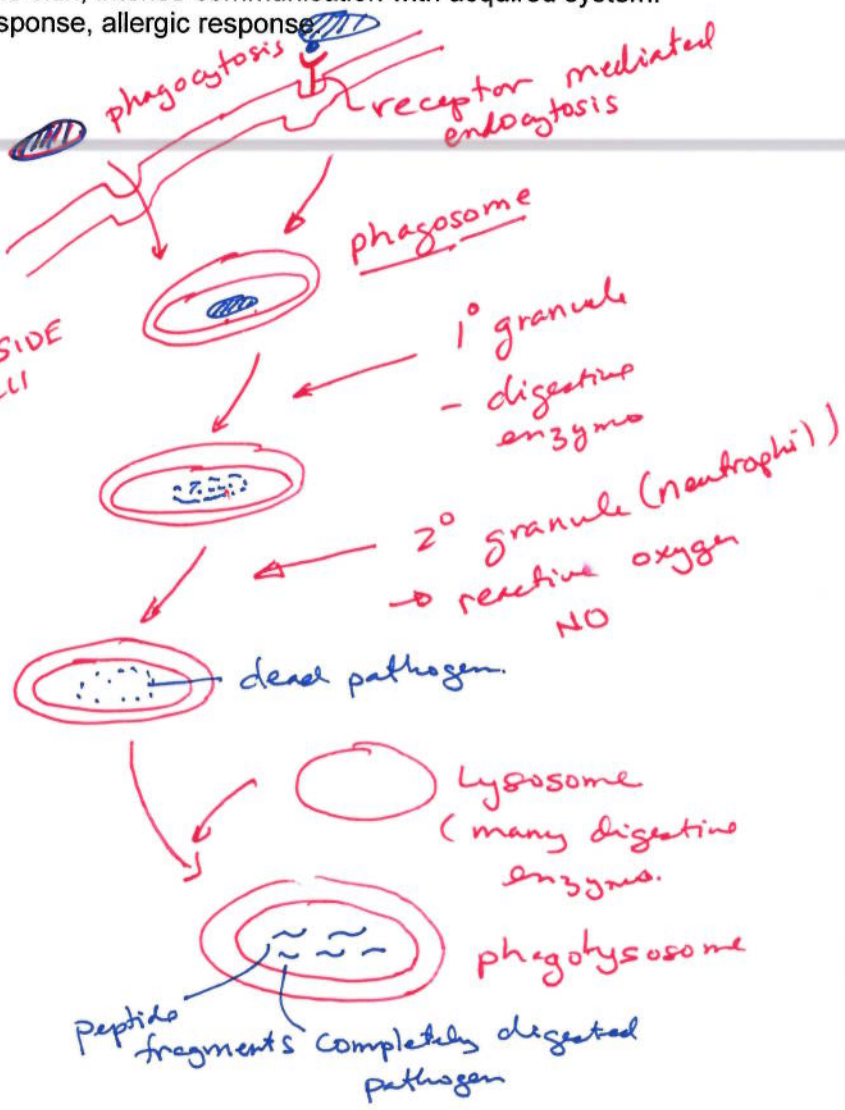
ii) Phagosome fuses with:

- primary granuales (lysozyme, α-defensins)
- secondary granuales (lactoferrin, oxidases=cytochrome b_{558})

$NADPH + O_2 \longrightarrow NADP^+ + O_2^-$

iii) Respiratory burst (largely neutrophils) generates

- Superoxide, hydrogen peroxide, NO
- Increase in pH, which activates enzymes from primary granuales



v) phagosome fuses with lysosome, making phagolysosome - acidic environment activates proteases that complete degradation.

5. Compare and Contrast: Neutrophils, macrophages, and dendritic cells:

	Neutrophil (INNATE)	Macrophage	Dendritic Cell
Killing ability	+++	++	+
Location initial	blood	tissue	tissue
post-response	infected tissue.	infected tissue.	Lymph node
Communication between Innate & Acquired	0	+	+++