Lecture 7
14 Aug 2023

Neutrophils

- 60% of WBCs
- 'Patrol tissues' as they squeeze out of the capillaries.
- Large numbers are released during infections
- Short lived – die after digesting bacteria
- Dead neutrophils make up a large proportion of pus.
- Primary granules: Azurophilic granules; young neutrophils contains:cationic proteins, lysozyme, defensins, elastase and **myeloperoxidase**
- Secondary granules: Specific for mature neutrophils
  contains: lysozyme, NADPH oxidase components, **lactoferrin and B12-binding protein**

Macrophages

- Larger than neutrophils.
- Found in the organs, not the blood.
- Made in bone marrow as monocytes, called macrophages once they reach organs.
- Long lived
- Initiate immune responses as they display antigens from the pathogens to the lymphocytes.

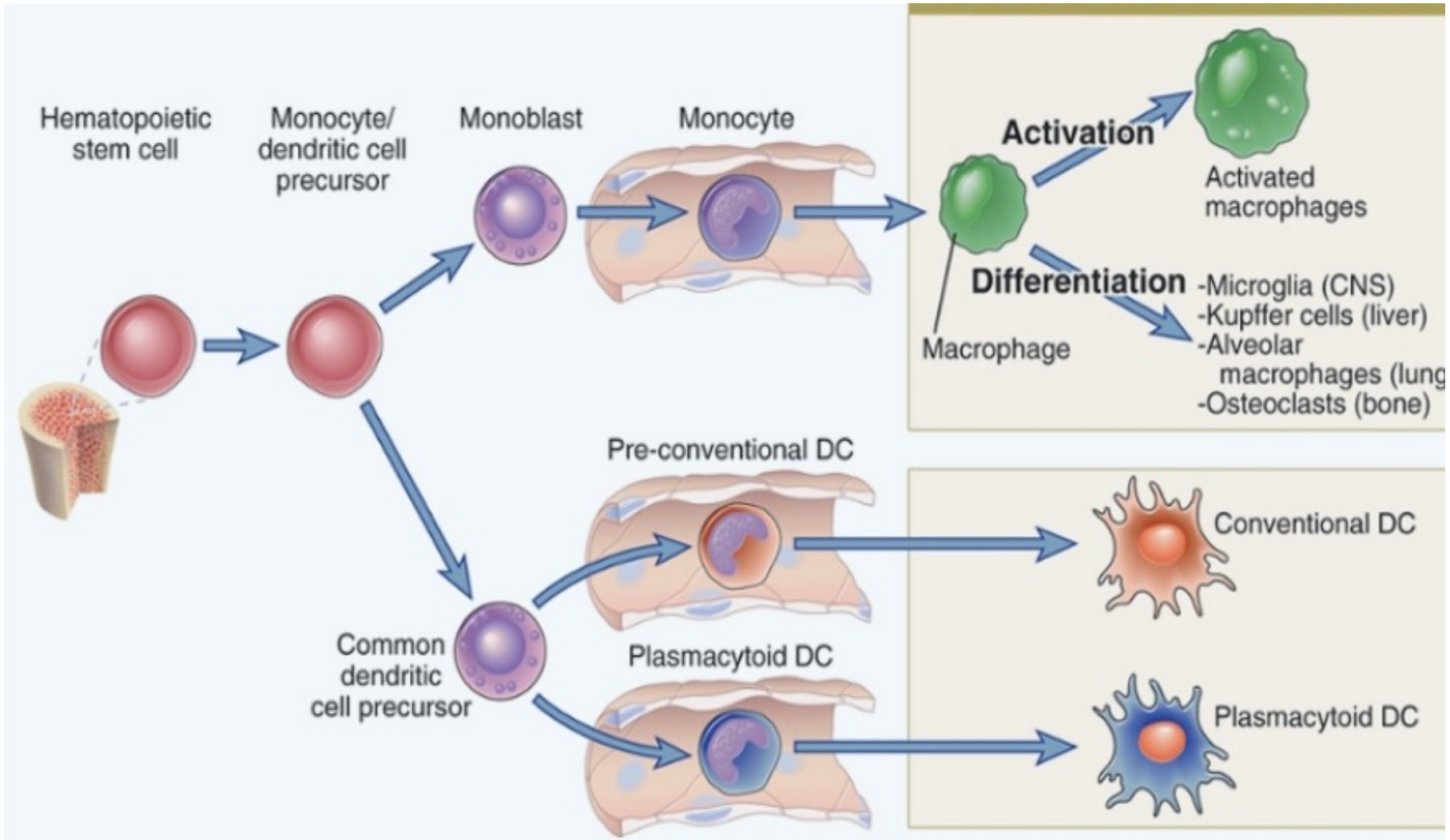
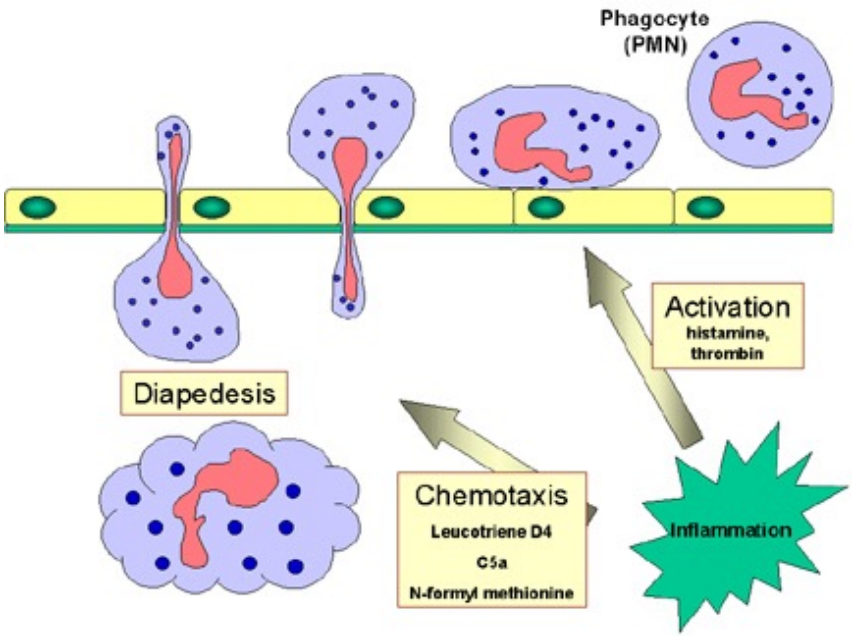


Figure 2–2 **Maturation of mononuclear phagocytes and dendritic cells.** Both dendritic cells and…

Macrophages…

Phagocyte response to infection



- The SOS signals
  - N-formyl methionine-containing peptides
  - Clotting system peptides
  - Complement products
  - Cytokines released by tissue macrophages
- Phagocyte response
  - Vascular adherence
  - Diapedesis
  - Chemotaxis
  - Activation
  - Phagocytosis and killing

Phagocytosis and Killing of Microbes

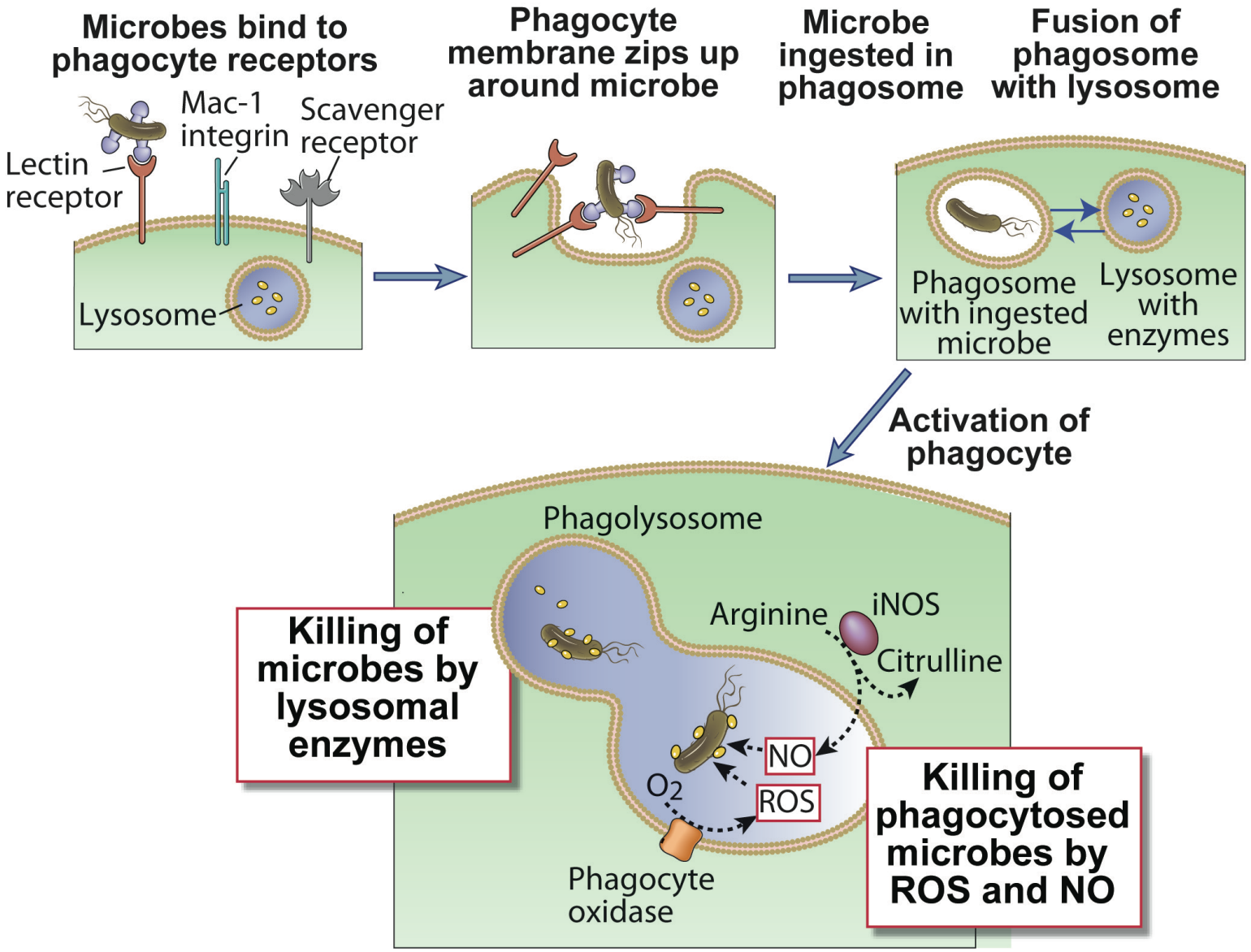
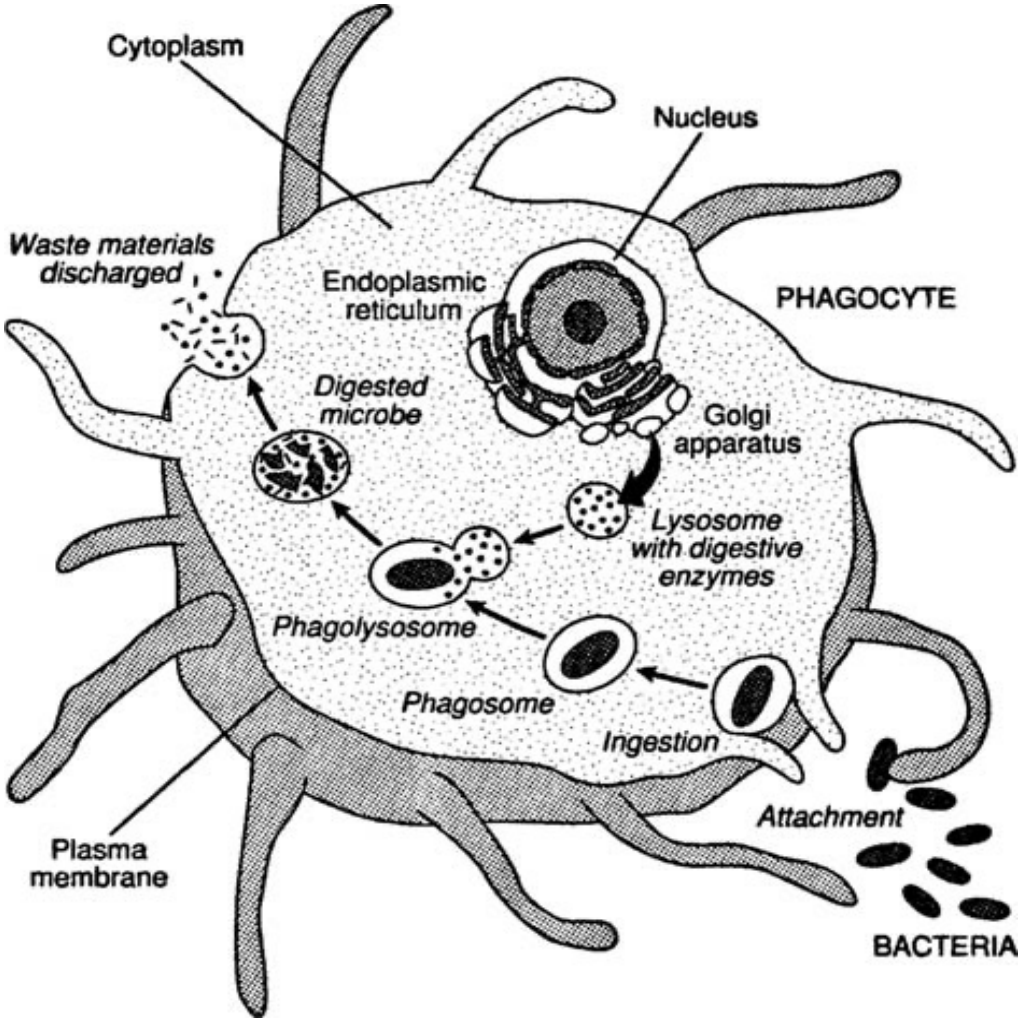


Fig. 4-12

How phagocytes act?

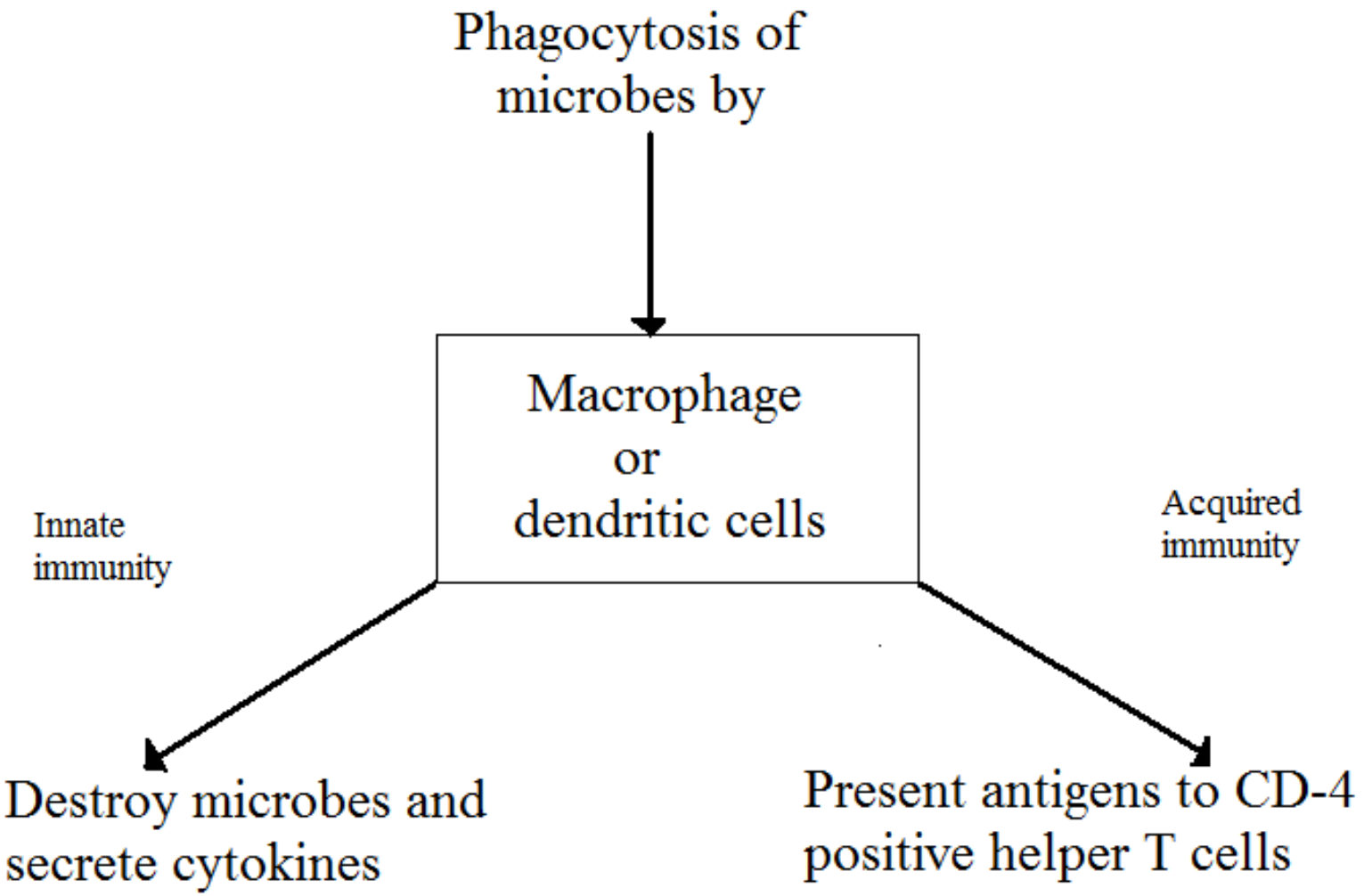
- Phagocytic cells reach the site of inflammation
- Attracted by chemo tactic substances
- Ingest particle material



Cells of the immune system: APC

- Cells that link the innate and adaptive arms
  - Antigen presenting cells (APCs)
    - Heterogenous population with role in innate immunity and activation of Th cells
    - Rich in MHC* class II molecules
  - Examples
    - Dendritic cells
    - Macrophages
    - B cells
    - Others (Mast cells)

*MHC: major histocompatibility complex



Macrophages and other antigen presenting cells such as dendritic cells, participate in both the innate arm and acquired arm of the immune system. They are in effect a bridge between the two arms. As part of the innate arm they ingest and kill various microbes. They also present antigens to helper T cells which is the essential first step in the activation of the acquired arm.

Effector Functions of Macrophages

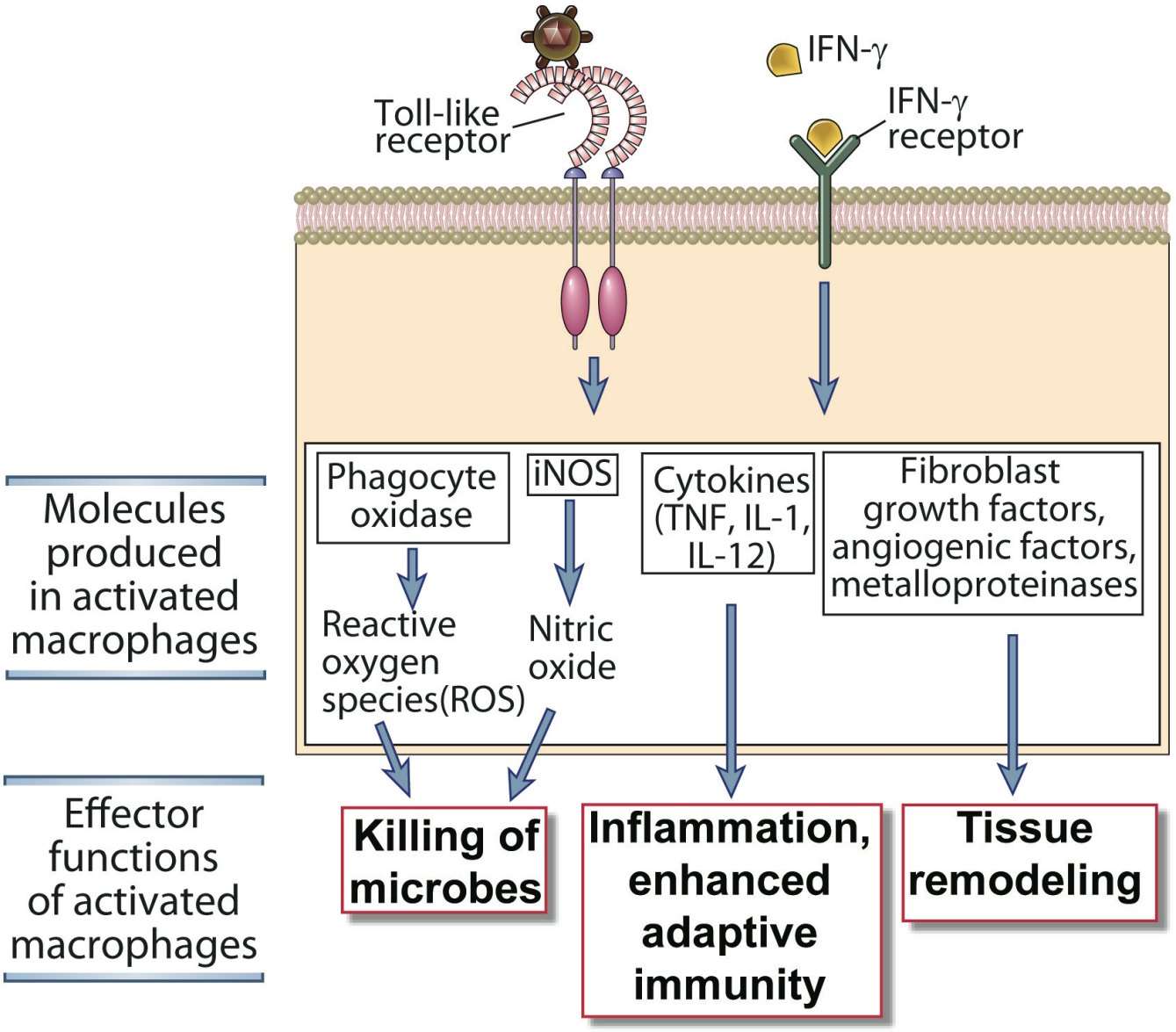
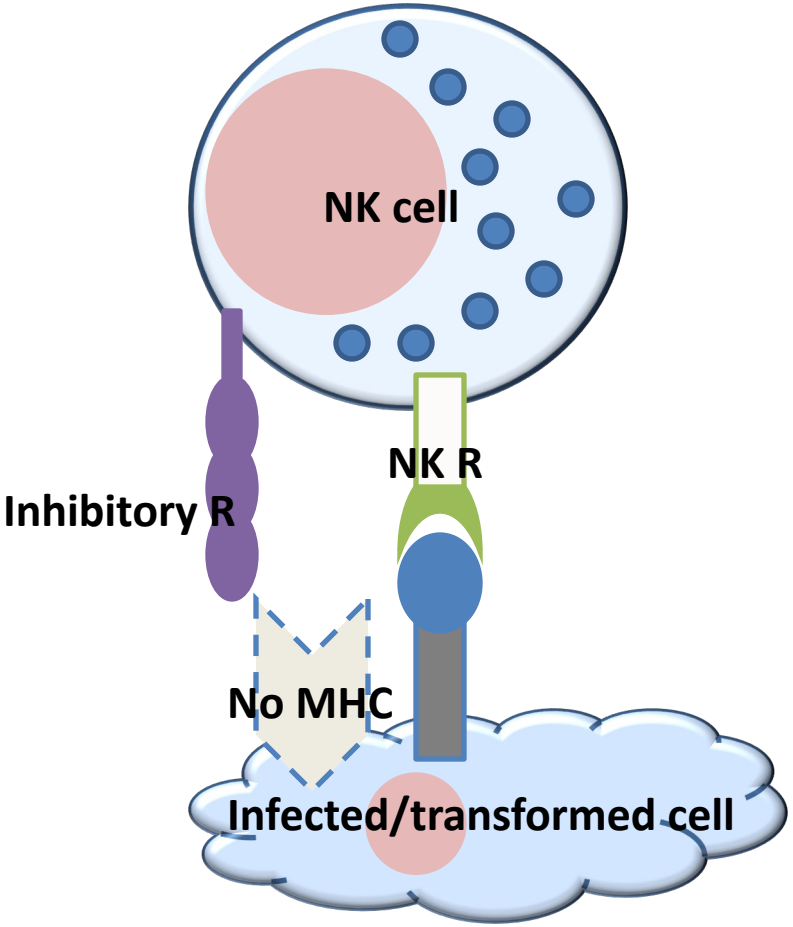


Fig. 4-13

NK cell: Innate response to virus infection and altered self



- Infected or altered self (transformed) cell downregulates MHC*
- NK does not receive inhibitory signal
- Signals kill infected cell

*MHC: major histocompatibility complex

Lecture 8
16 Aug 2023

Role of NK cells

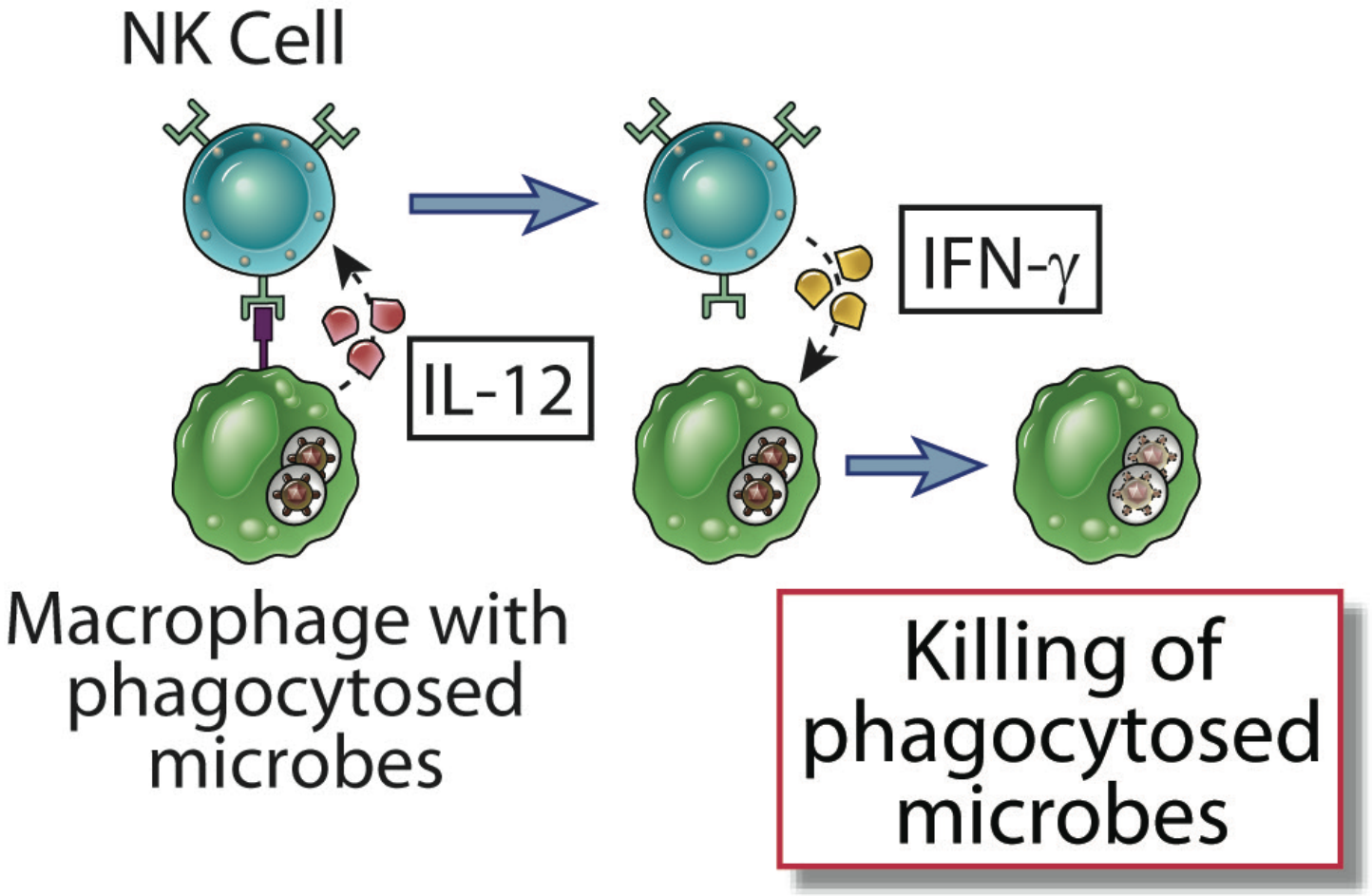
- **NK cells**

are a type of cytotoxic lymphocyte that constitute a major component of the innate immune system.

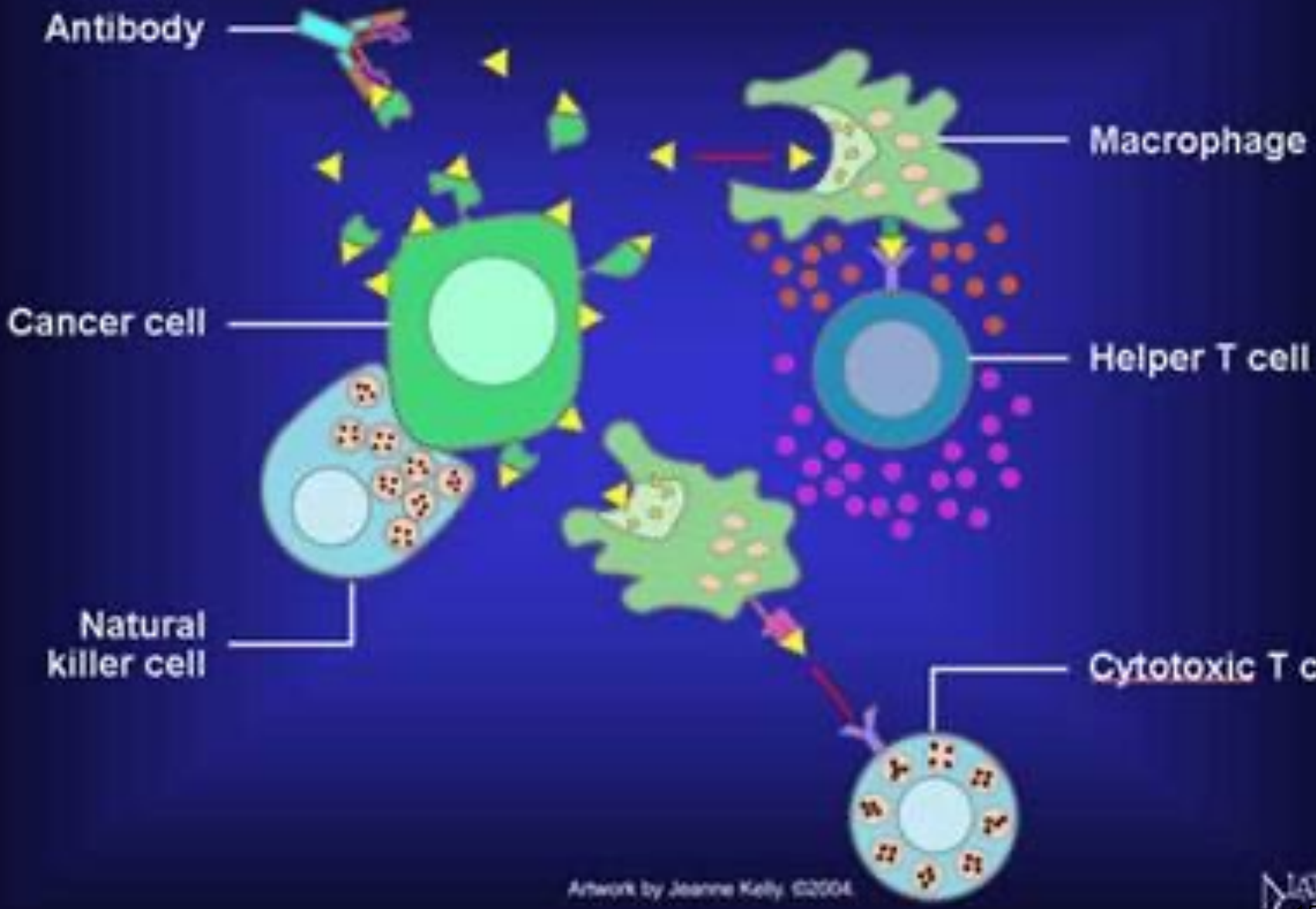
- plays a major role in the rejection of tumours and cells infected by viruses.

- The cells kill by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the target cell to die by apoptosis

NK Cells Activate Macrophages



Immunity and Cancer

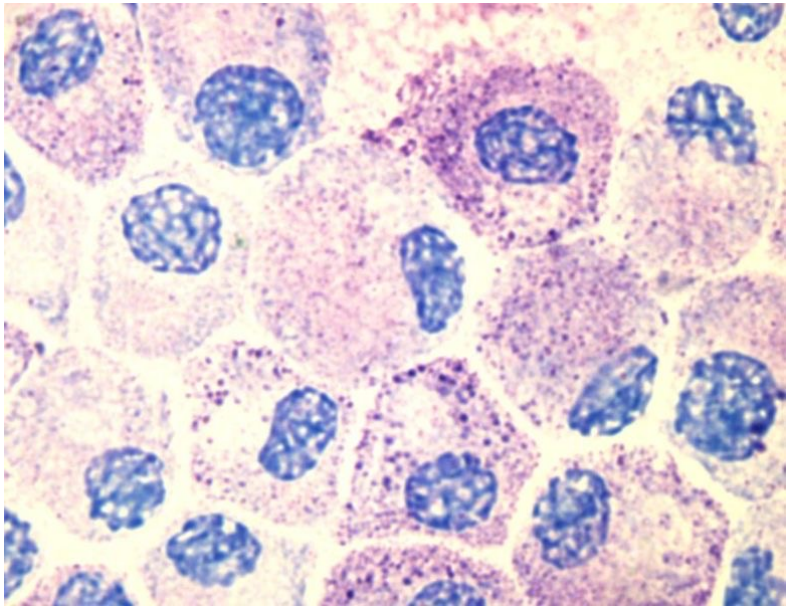


Eosinophils

Source: Bristol Biomedical Image Archive, used with permission

- Characteristic bi-lobed nucleus
- Cytoplasmic granules, stain with acidic dyes (eosin)
  - Major basic protein (MBP)
  - Potent toxin for helminths
- Kill parasitic worms

Mast cells



- Characteristic cytoplasmic granules
- Responsible for burst release of preformed cytokines, chemokines, histamine
- Role in immunity against parasites

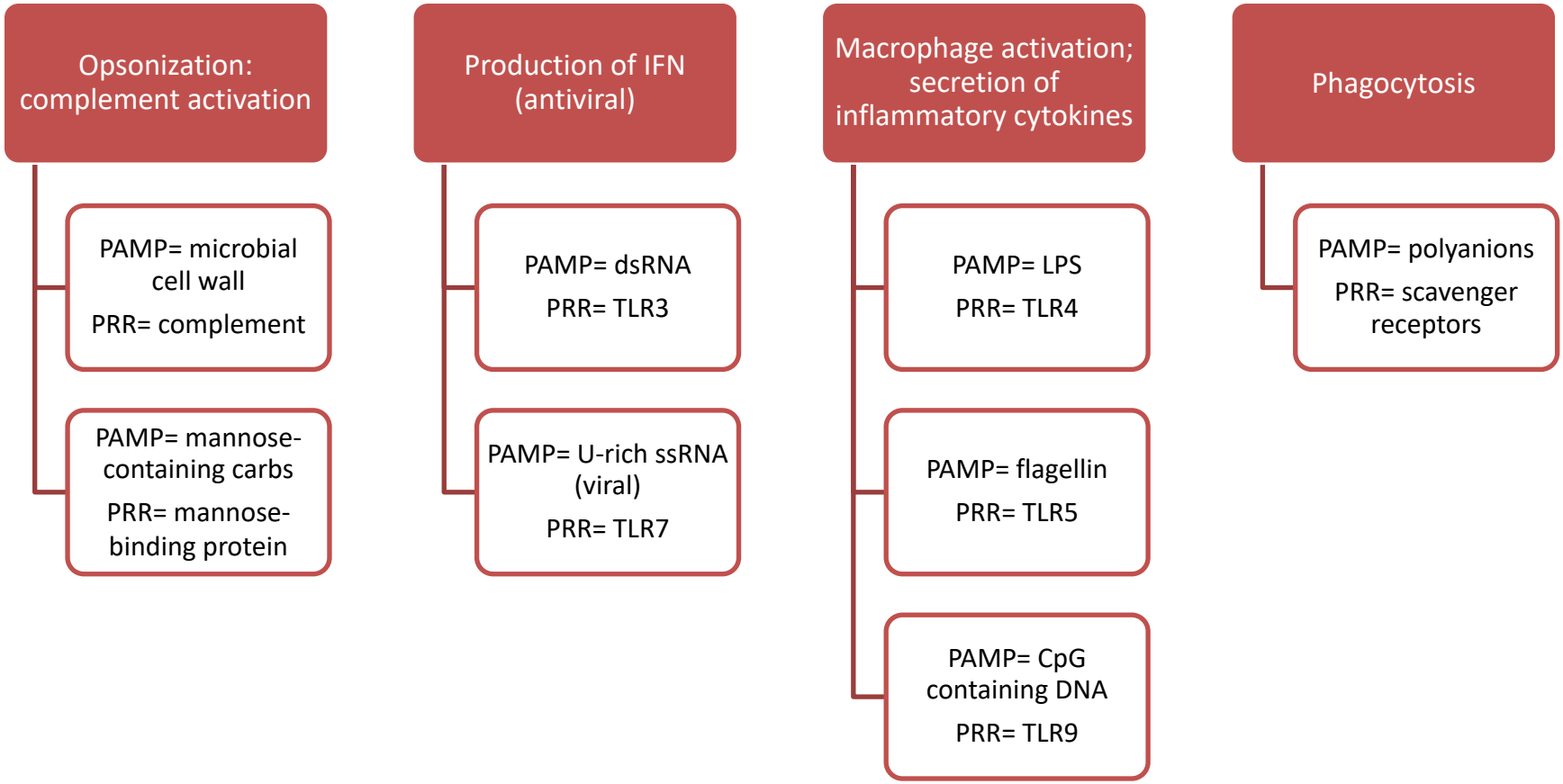
Determinants recognized by the innate immune response

- PAMPs- pathogen associated molecular patterns
- PRRs- pattern recognition receptors

Pathogen-associated molecular patterns (PAMPs)

- Non-specific (not antigen specific) receptor recognition
- Part of innate antimicrobial defense
- Toll-like receptors on macrophages bind pathogen and cause activation

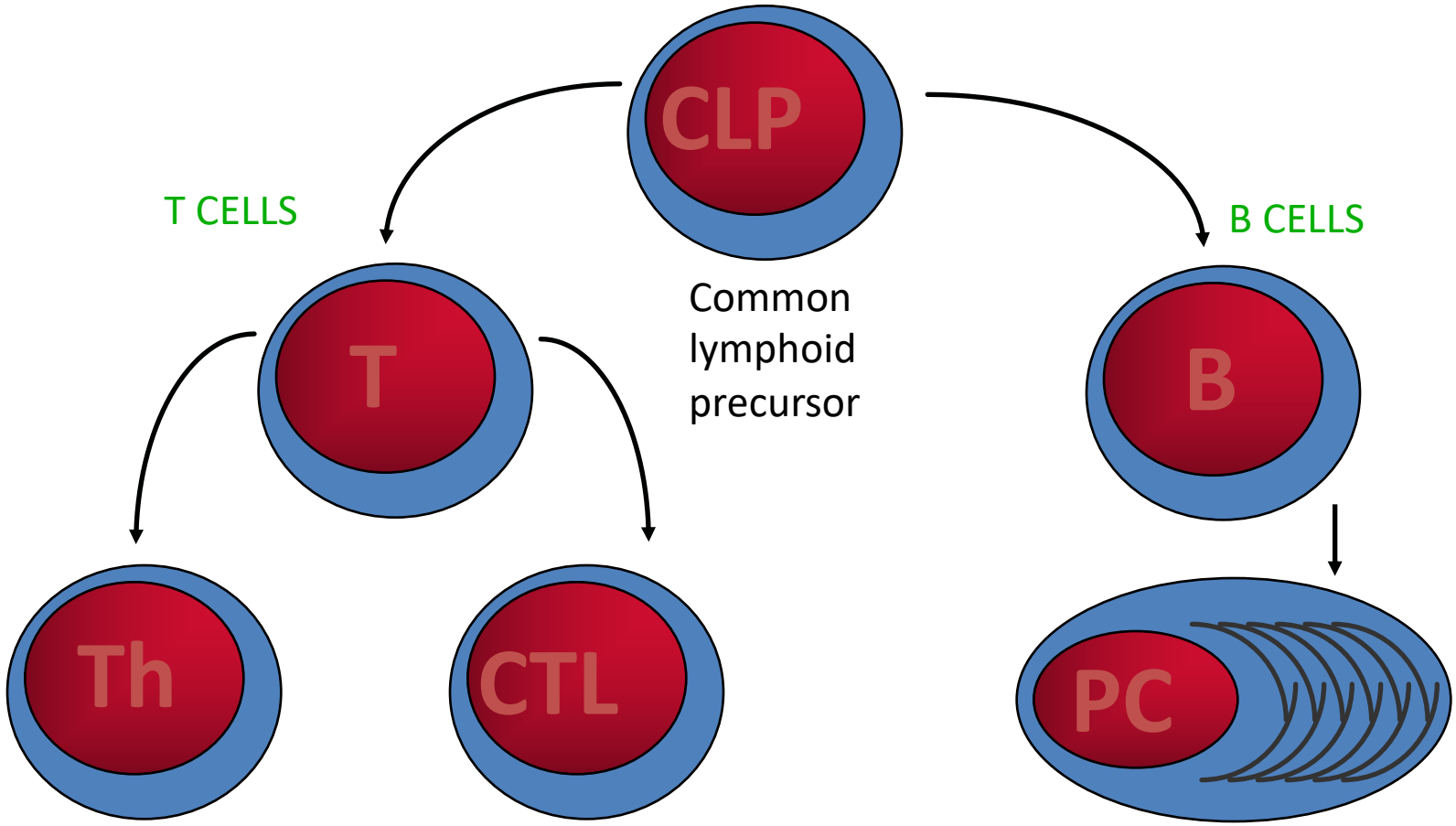
Determinants recognized by the innate immune system



Cells of the immune system: adaptive

- Lymphocytes
  - B cells
    - Plasma cells (Ab producing)
  - T cells
    - Cytotoxic (CTL)
    - Helper (Th)
      - Th1
      - Th2
      - Th17
      - T-reg

Lymphocyte subsets



Lecture 9
17 Aug 2023

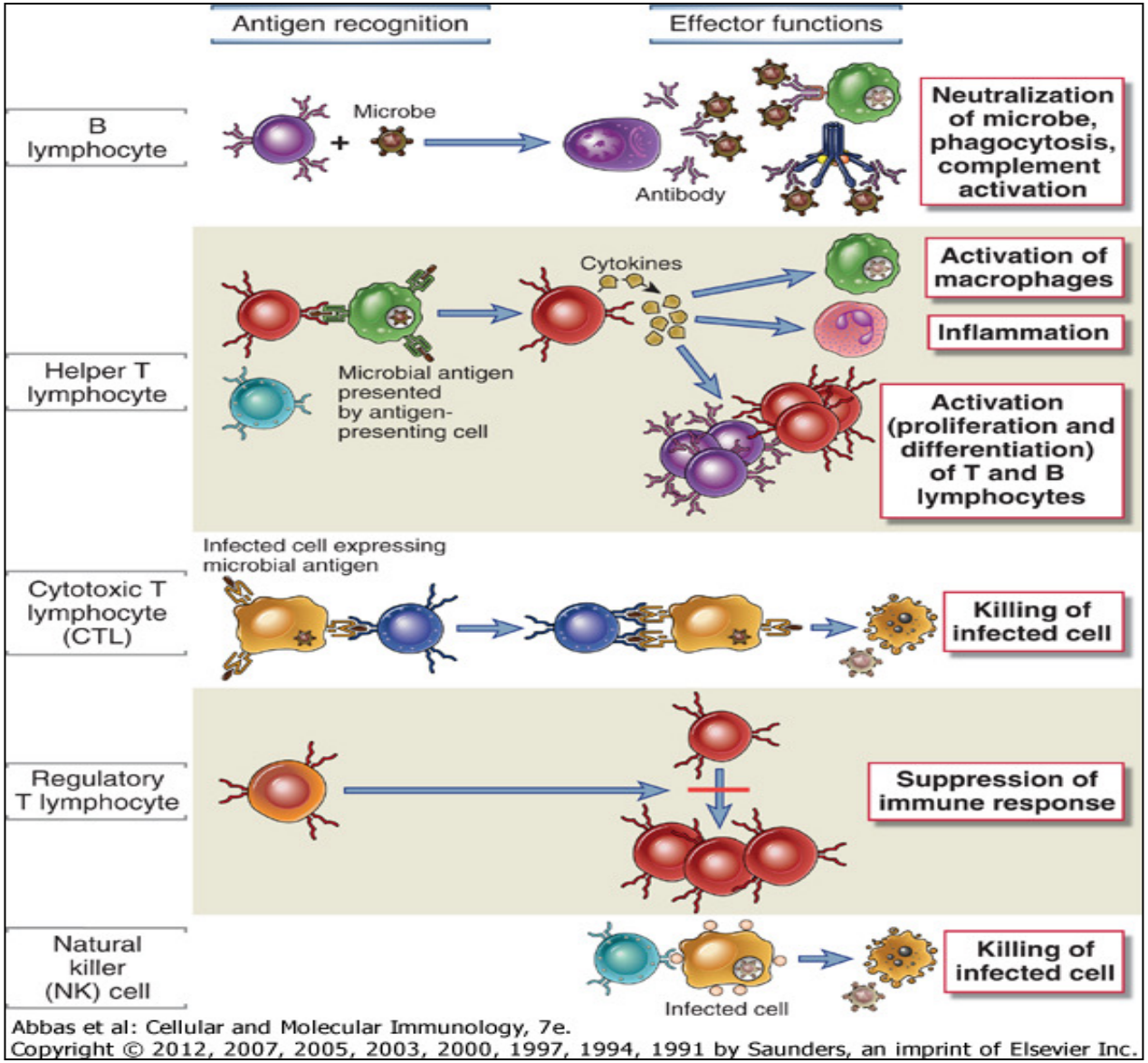
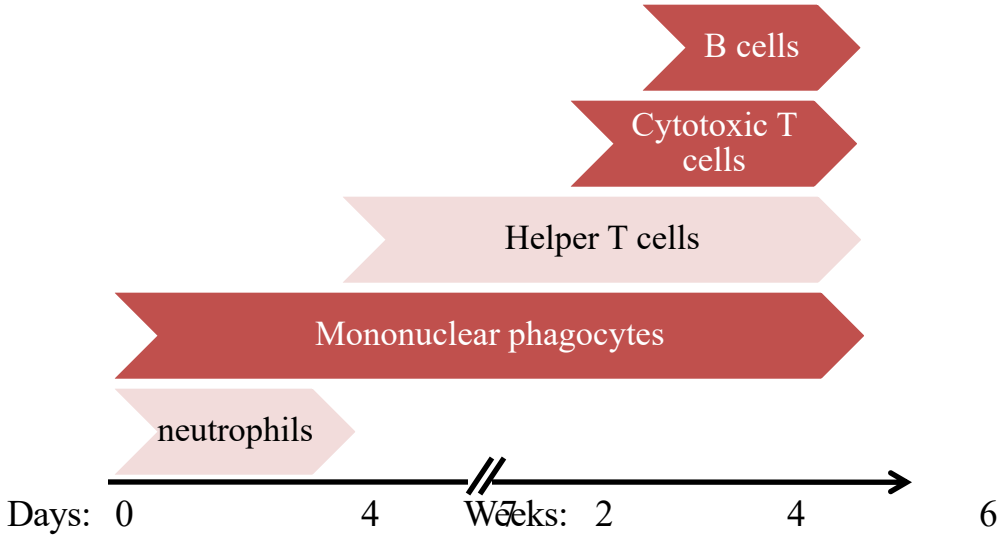


Figure 1-5 Classes of lymphocytes. B lymphocytes recognize soluble antigens and develop into antibody-secreting cells. Helper T lymphocytes recognize antigens on the surfaces of antigen-presenting cells and secrete cytokines, which stimulate different mechanisms of immunity and inflammation. Cytotoxic T lymphocytes recognize antigens on infected cells and kill these cells. Regulatory T cells suppress and prevent immune response (e.g., to self antigens). NK cells use receptors with more limited diversity than T or B cell antigen receptors to recognize and kill their targets, such as infected cells.

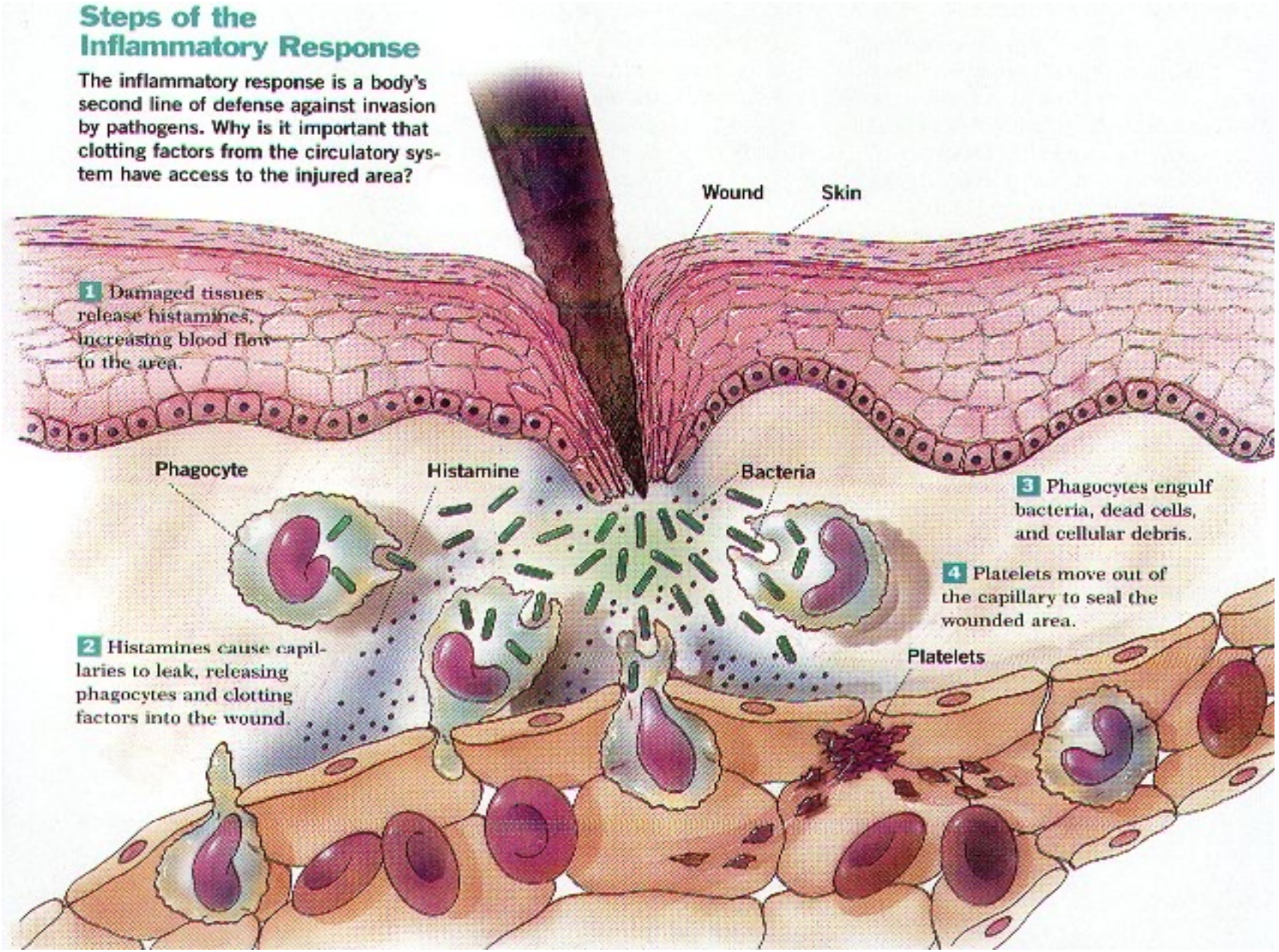
Immune response to damage

- Dependent on what, where and how bad
- Phased response with critical timing
  - Requires chemokine signalling, receptor binding, etc



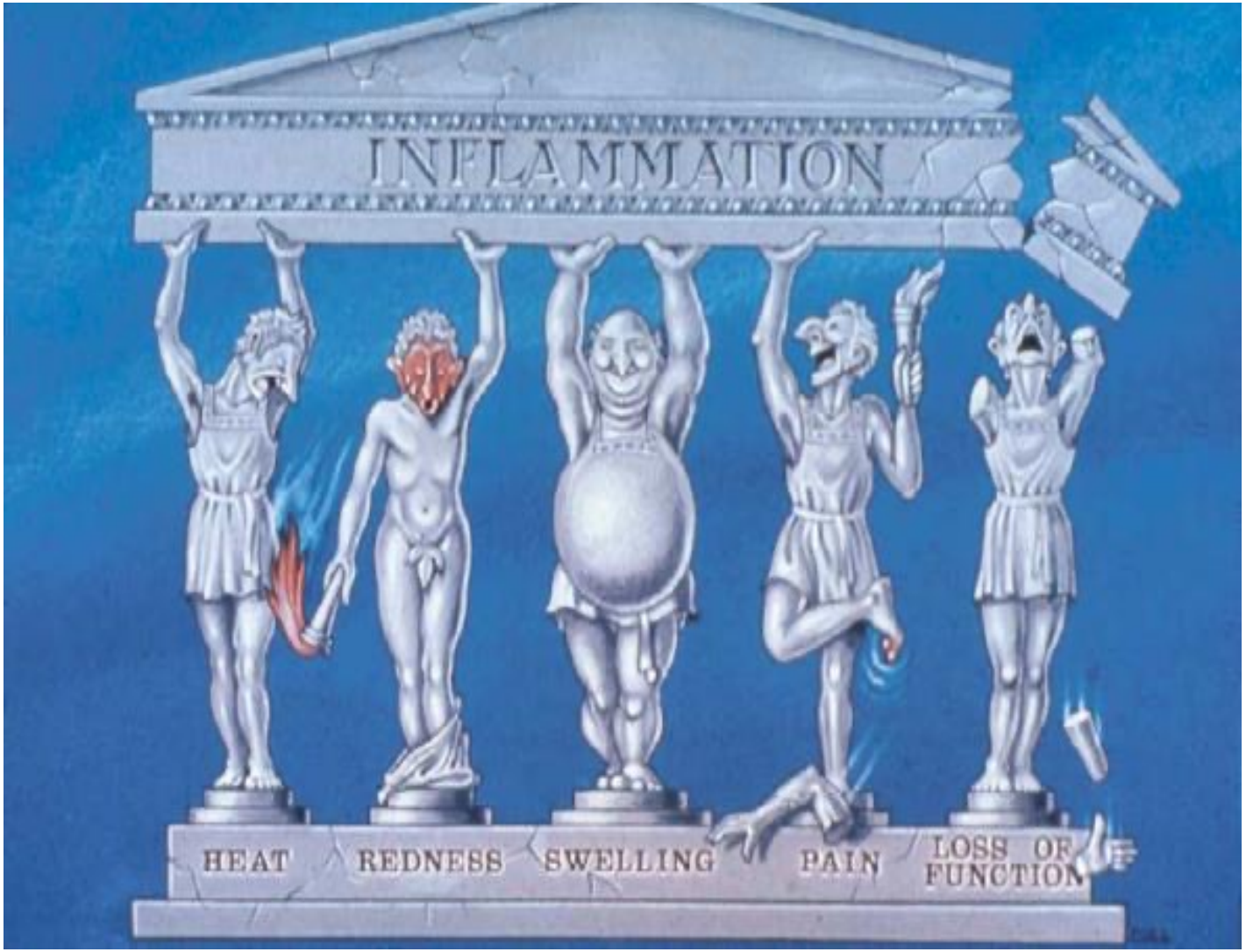
Role of inflammation

- Inflammation is signaled by mast cells, which release histamine.
- Histamine causes fluids to collect around an injury to dilute toxins. This causes swelling.
- The temperature of the tissues may rise, which can kill temperature-sensitive microbes.


Steps of the Inflammatory Response
The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?
Wound
Skin
1 Damaged tissues release histamines, increasing blood flow to the area.
Phagocyte
Histamine
Bacteria
3 Phagocytes engulf bacteria, dead cells, and cellular debris.
4 Platelets move out of the capillary to seal the wounded area.
2 Histamines cause capillaries to leak, releasing phagocytes and clotting factors into the wound.
Platelets

Inflammation…

- Tissue Injury
- Irritation
- Arterioles constrict initially and then dilate
- Slow the blood flow and results in margination of leucocytes
- Escape into tissues by diapedesis and accumulate in large numbers


INFLAMMATION
HEAT
REDNESS
SWELLING
PAIN
LOSS OF FUNCTION