MUNI
PHARM

Immune Defence Mechanisms
Specific Defence
Inflammation

lecture from Physiology and Pathophysiology I

11. 10. 2022

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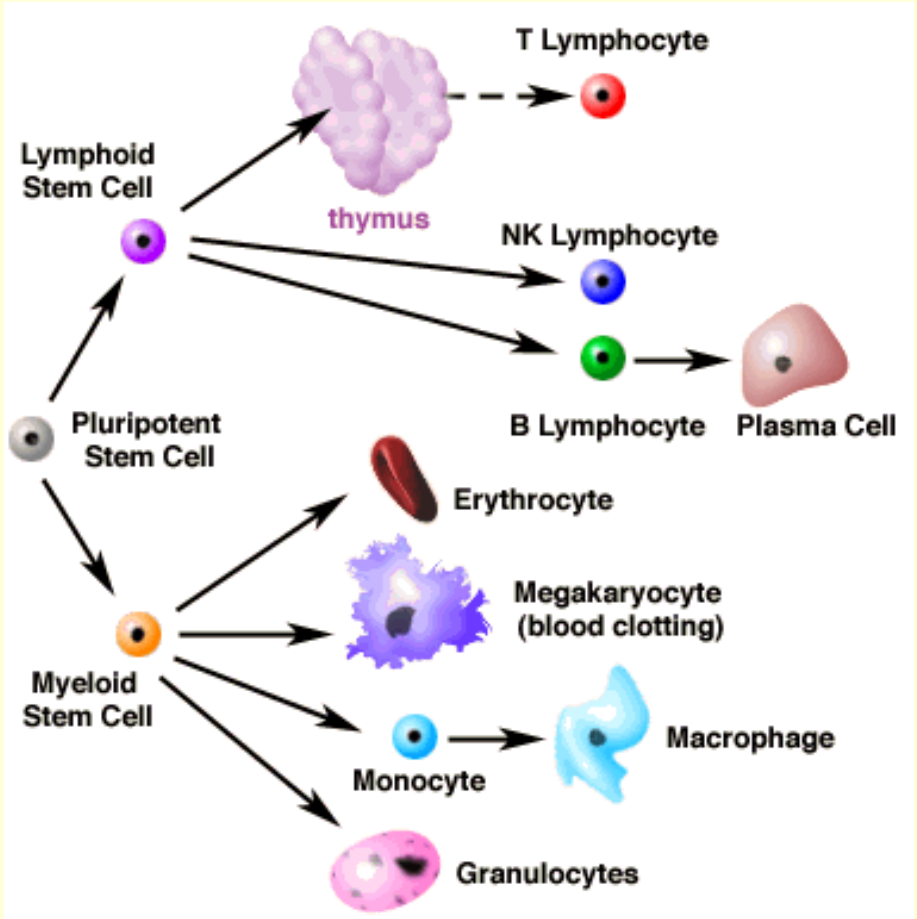
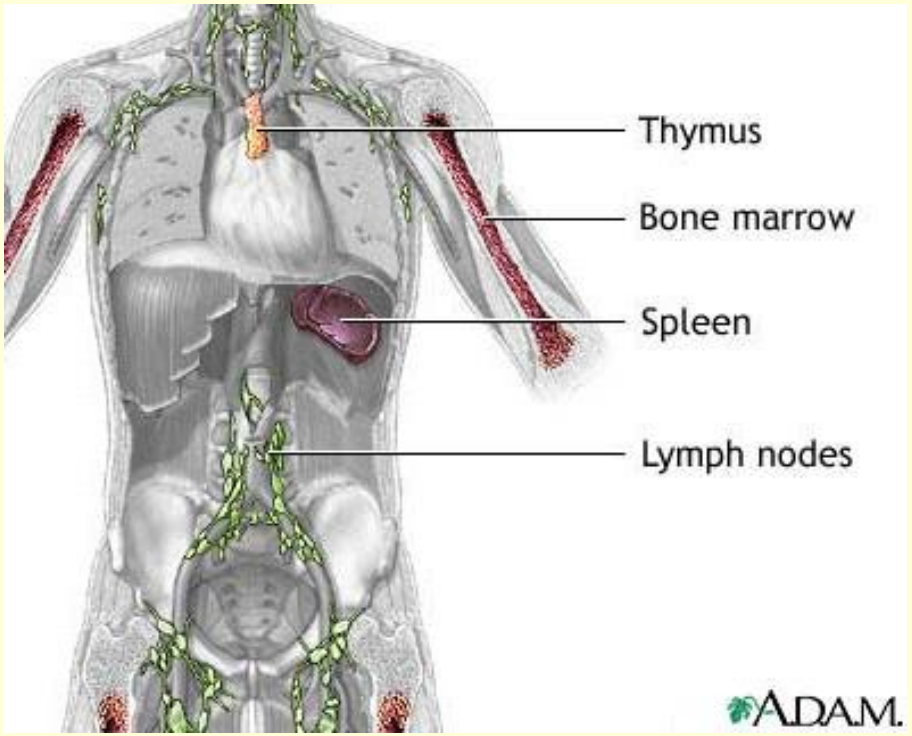
Immune System

- system of defence against pathogens (bacteria, viruses, fungi, parasites) and tumor cells





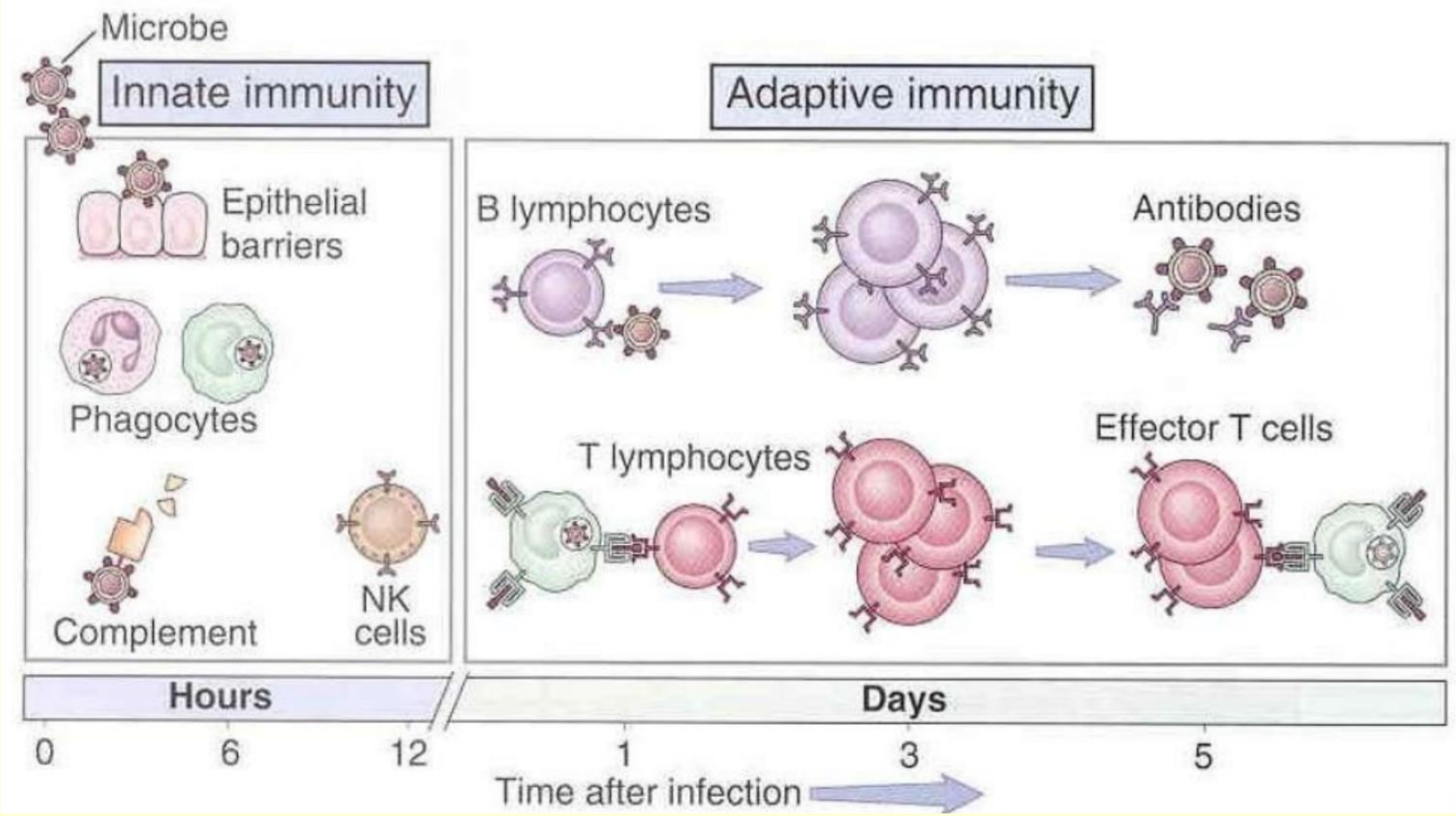
Nonspecific vs. Specific Defence

	Nonspecific/congenital	Specific/acquired
Cellular	polymorphonuclears monocytes–macrophages NK-cells	T-lymphocytes
Humoral	complement acute-phase proteins (CRP, ceruloplasmin...)	antibodies B-lymphocytes

Congenital vs. Acquired Immunity

Attribute	Congenital/Nonspecific Immunity	Acquired/Specific Immunity
Response time	Minutes/hours	Days
Specificity	Specific for molecules and molecular patterns associated with pathogens	Highly specific; discriminates even minor differences in molecular structure; details of microbial or nonmicrobial structure recognized with high specificity
Diversity	A limited number of germ line–encoded receptors	Highly diverse; a very large number of receptors arising from genetic recombination of receptor genes
Memory responses	None	Persistent memory, with faster response of greater magnitude on subsequent infection
Self/nonself discrimination	Perfect; no microbe-specific patterns in host	Very good; occasional failures of self/nonself discrimination result in autoimmune disease
Soluble components of blood or tissue fluids	Many antimicrobial peptides and proteins	Antibodies
Major cell types	Phagocytes (monocytes, macrophages, neutrophils), natural killer (NK) cells, dendritic cells	T cells, B cells, antigen-presenting cells

Congenital vs. Acquired Immunity



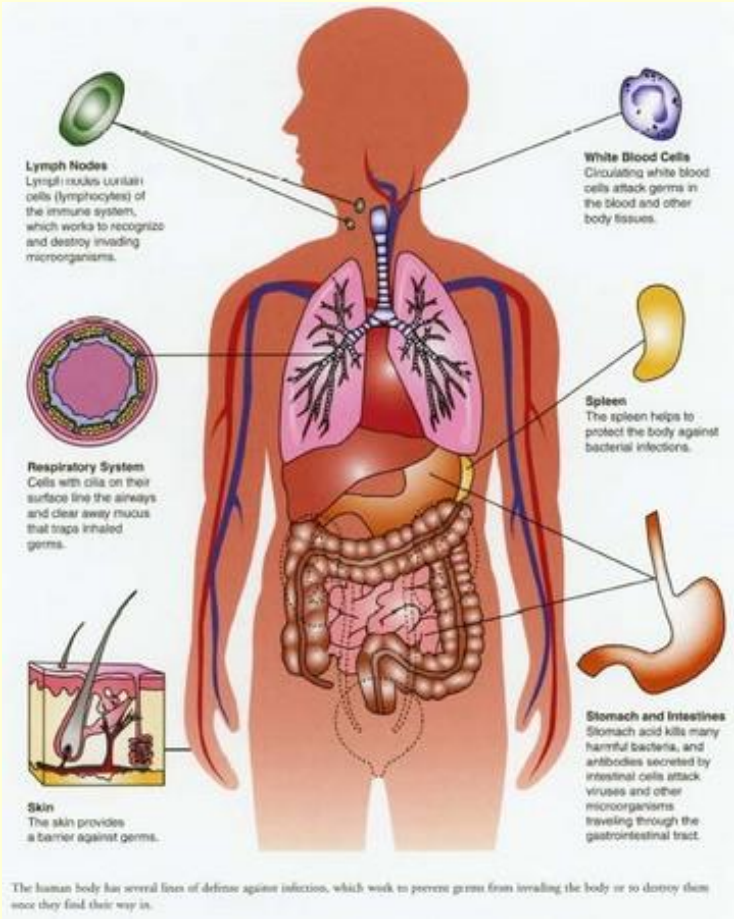
Surface Coverage
First Line of Defense

PHYSICAL FACTORS

- skin
- mucous membranes with lysozymes
- lacrimal apparatus
- salivary glands
- vaginal secretions
- flow of urine

CHEMICAL FACTORS

- sebum
- lysozyme
- gastric juice
- vaginal secretions
- urine



The human body has several lines of defense against infection, which work to prevent germs from invading the body or to destroy them once they find their way in.

Nonspecific Immune System
Second Line of Defense

- generalized responses to pathogen infection – do not target a specific cell type

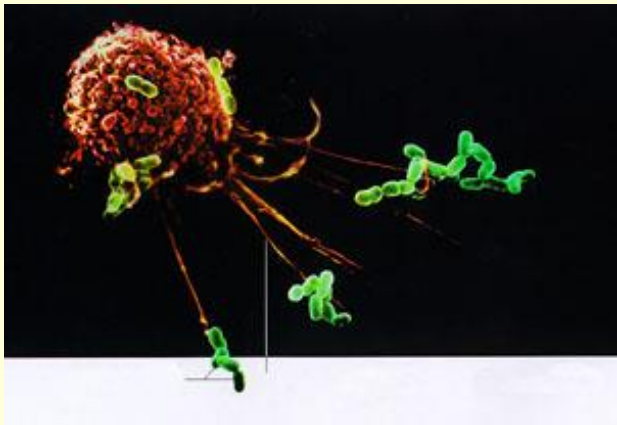
Phagocytes

- neutrophils
- eosinophils
- macrophages

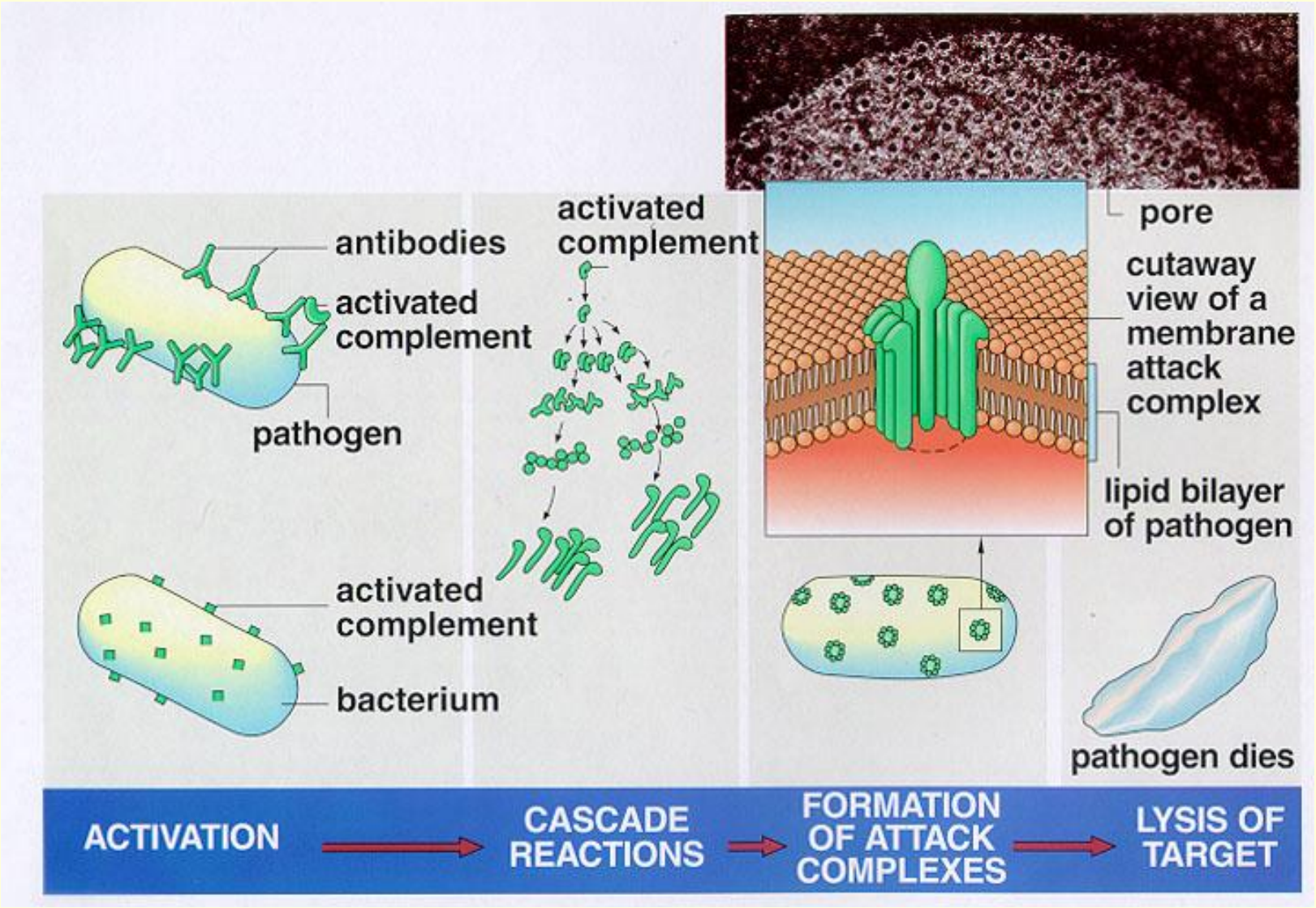
Non-phagocytic leucocytes

- basophils
- mast cells

Complement proteins



Complement


antibodies
activated complement
pathogen
activated complement
activated complement
bacterium
pore
cutaway view of a membrane attack complex
lipid bilayer of pathogen
pathogen dies
ACTIVATION
CASCADE REACTIONS
FORMATION OF ATTACK COMPLEXES
LYSIS OF TARGET

Specific Immune System
Third Line of Defense

HUMORAL (Ab-MEDIATED) IMMUNE SYSTEM

- antibodies
- B-cells (lymphocytes)

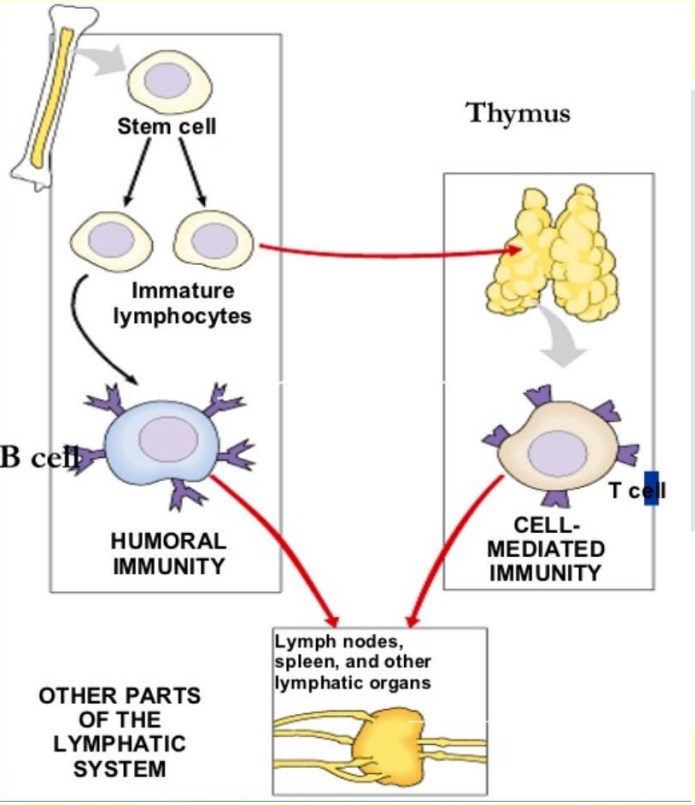
CELL-MEDIATED SYSTEM

- T-cells (lymphocytes)
- helper T lymphocytes (T_H)
  - produce and secrete chemicals that promote large numbers of effector and memory cells
- cytotoxic T lymphocytes (TC)
  - eliminate infected body cells and tumor cells

PHAGOCYTIC COMPONENTS

- macrophages, monocytes, neutrophils
- engulf foreign objects and inform T lymphocytes that a specific antigen is present

Lymphocytes

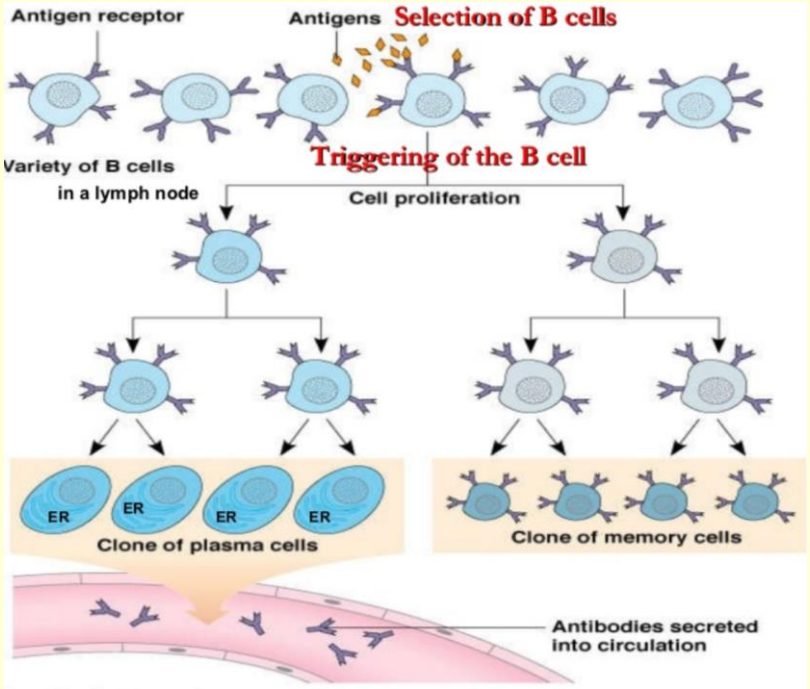


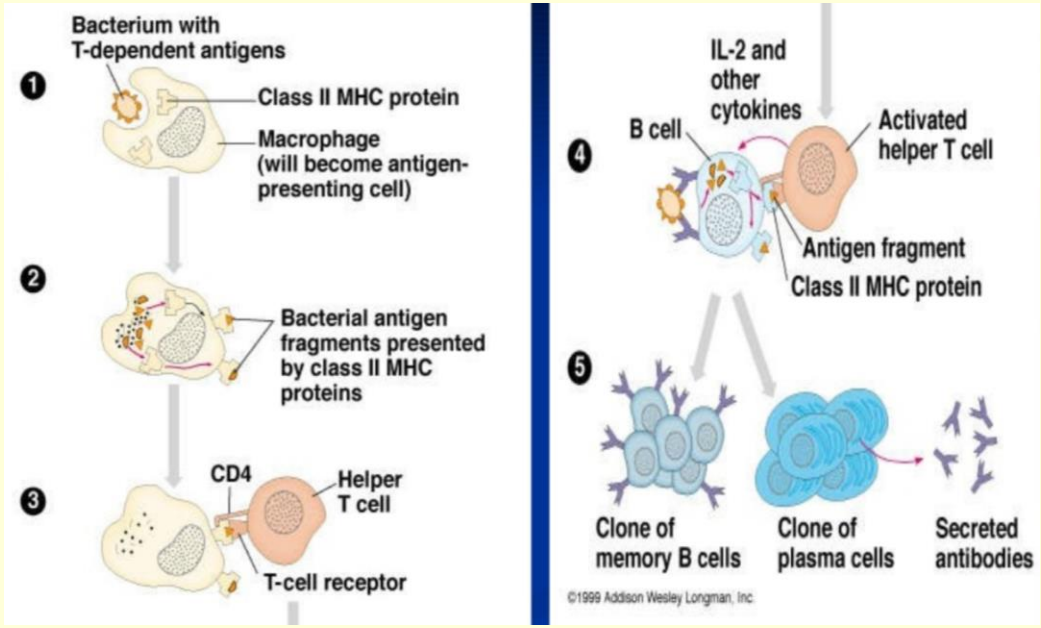
LYMPHOCYTES

B cells	Differentiate to form antibody-producing cells and memory cells
Plasma cells	Secrete antibodies
T cells	Kill virus-infected cells; regulate activities of other white blood cells
Natural killer cells	Attack and lyse virus-infected or cancerous body cells

Humoral (Antibody-Mediated) Immunity

- production of antibodies by B-cells
- B-cells migrate to the lymphoid organs (spleen, lymph nodes) after maturation

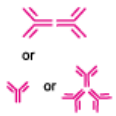




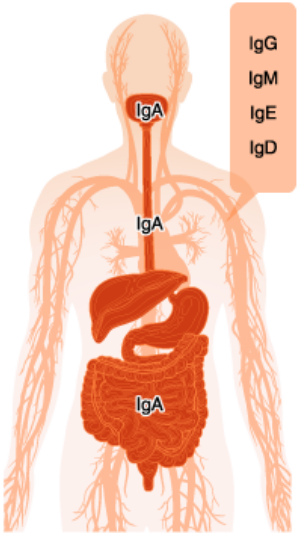
Antibodies

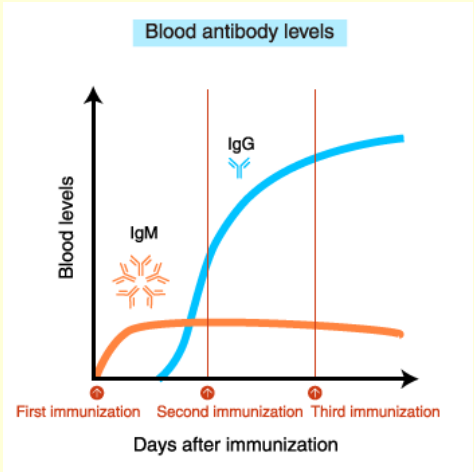
- synthesized by B-cells in soluble or cell-bound form
- each antibody recognizes one specific antigen
- **immunoglobulins** (5 classes) – glycoproteins
- **Ig G**
- **Ig M**
- **Ig A**
- **Ig D**
- **Ig E**

Types and characteristics of antibodies

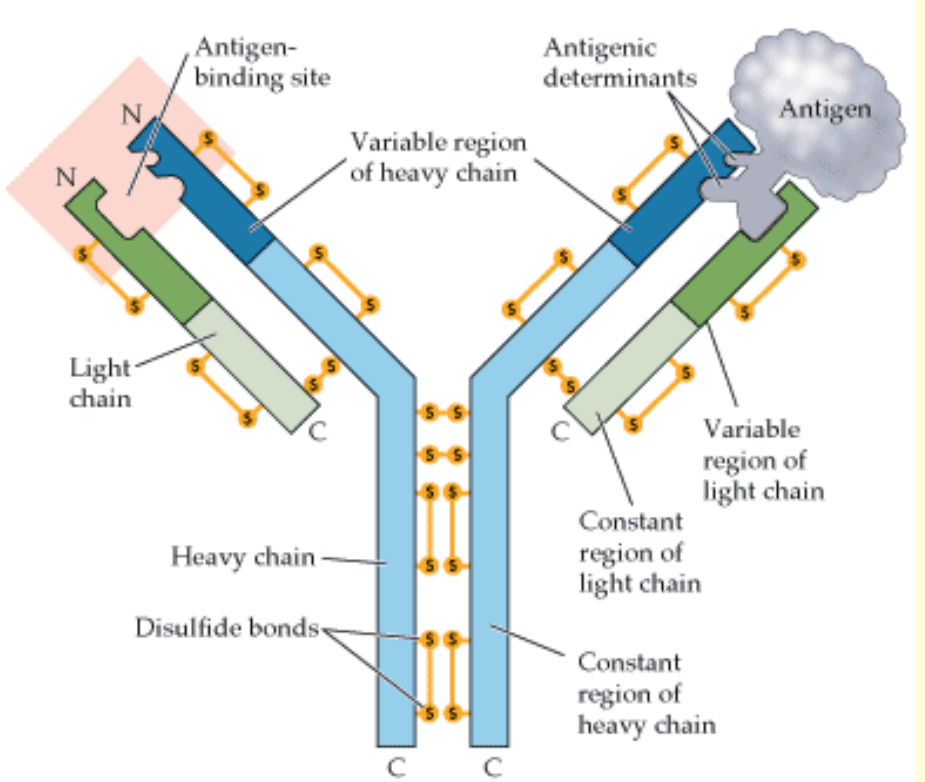
IgG		• Highest opsonization and neutralization activities. • Classified into four subclasses (IgG1, IgG2, IgG3, and IgG4).
IgM		• Produced first upon antigen invasion. Increases transiently.
IgA		• Expressed in mucosal tissues. Forms dimers after secretion.
IgD		• Unknown function.
IgE		• Involved in allergy.

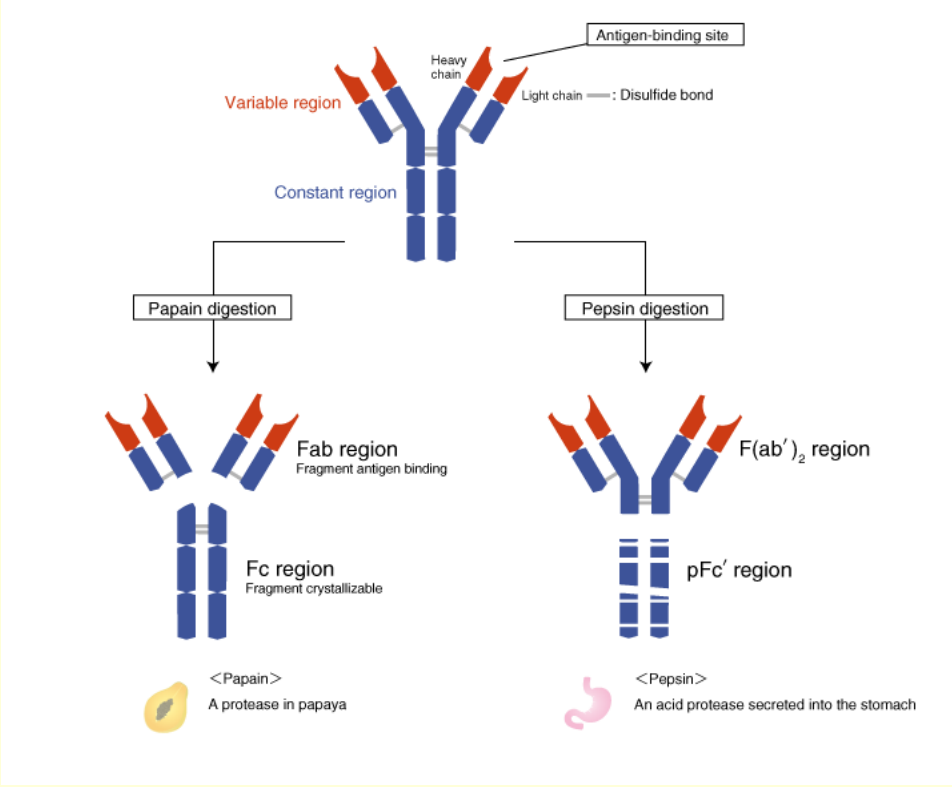
Distribution in the body



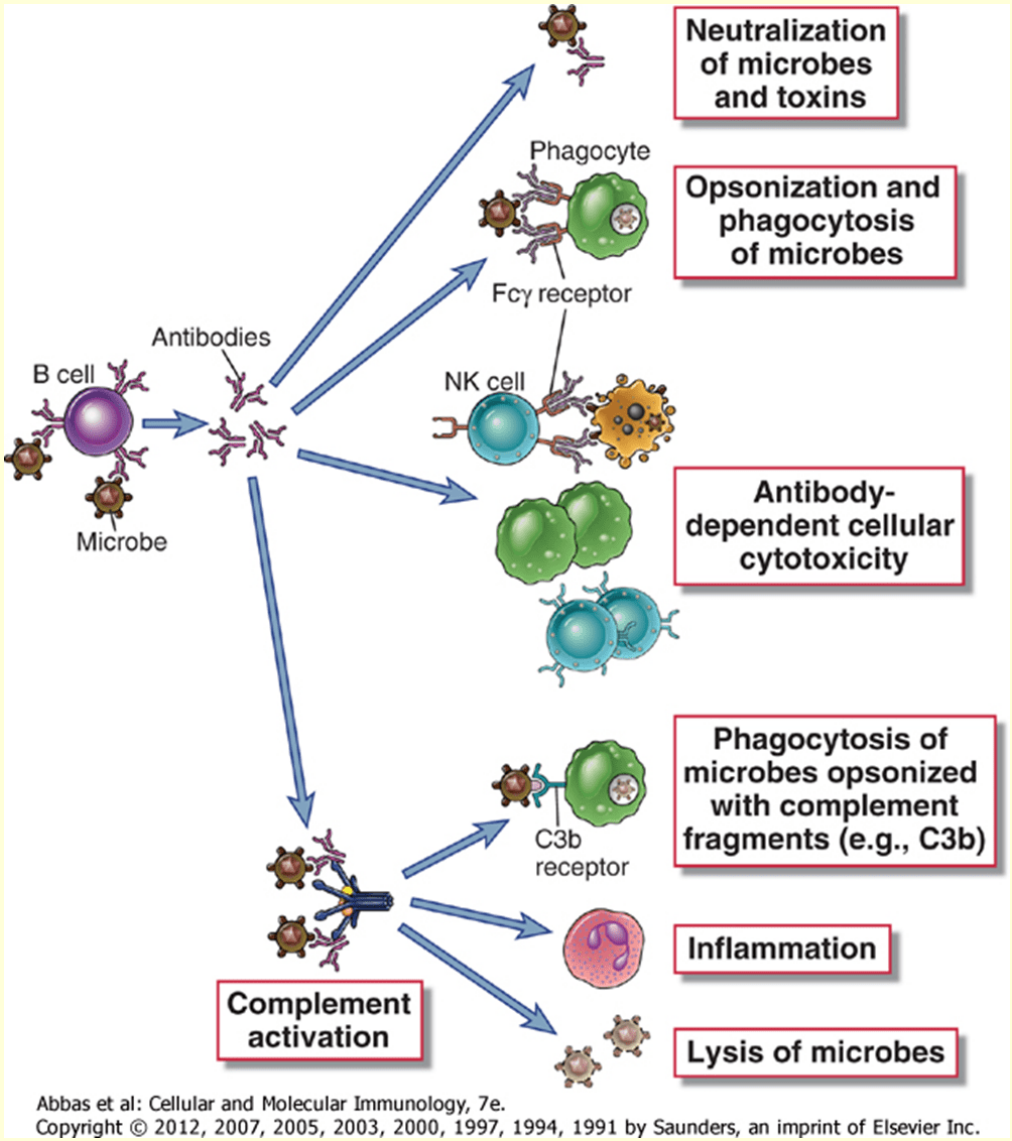


Antibodies Structure



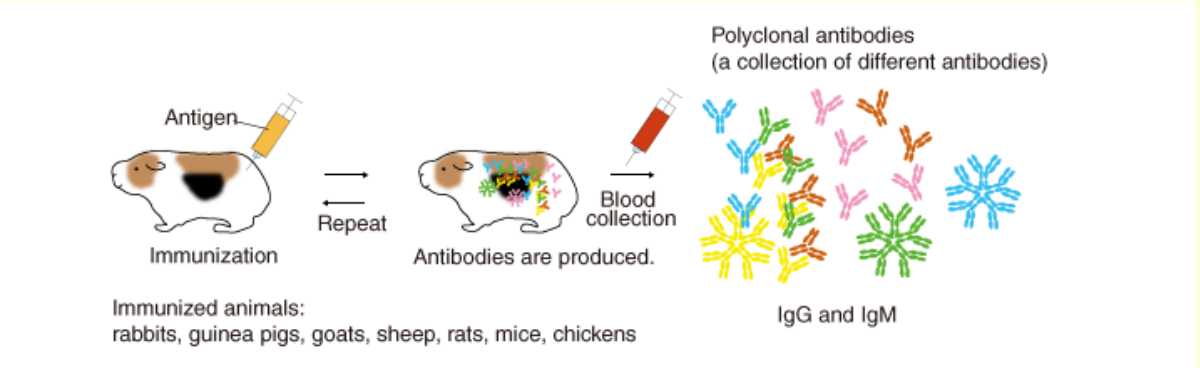


Antibodies Function

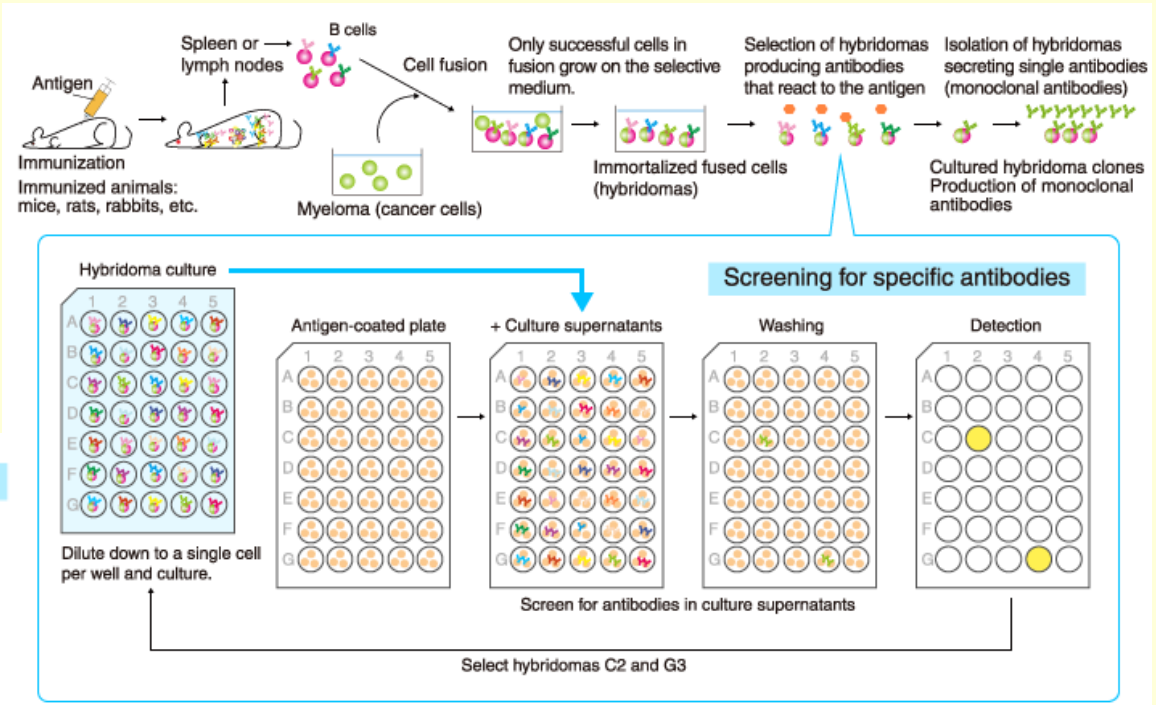


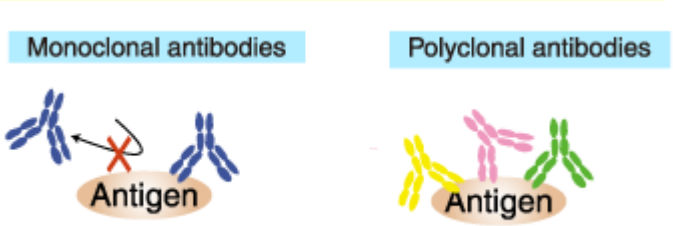
Antibodies Production

- **polyclonal**

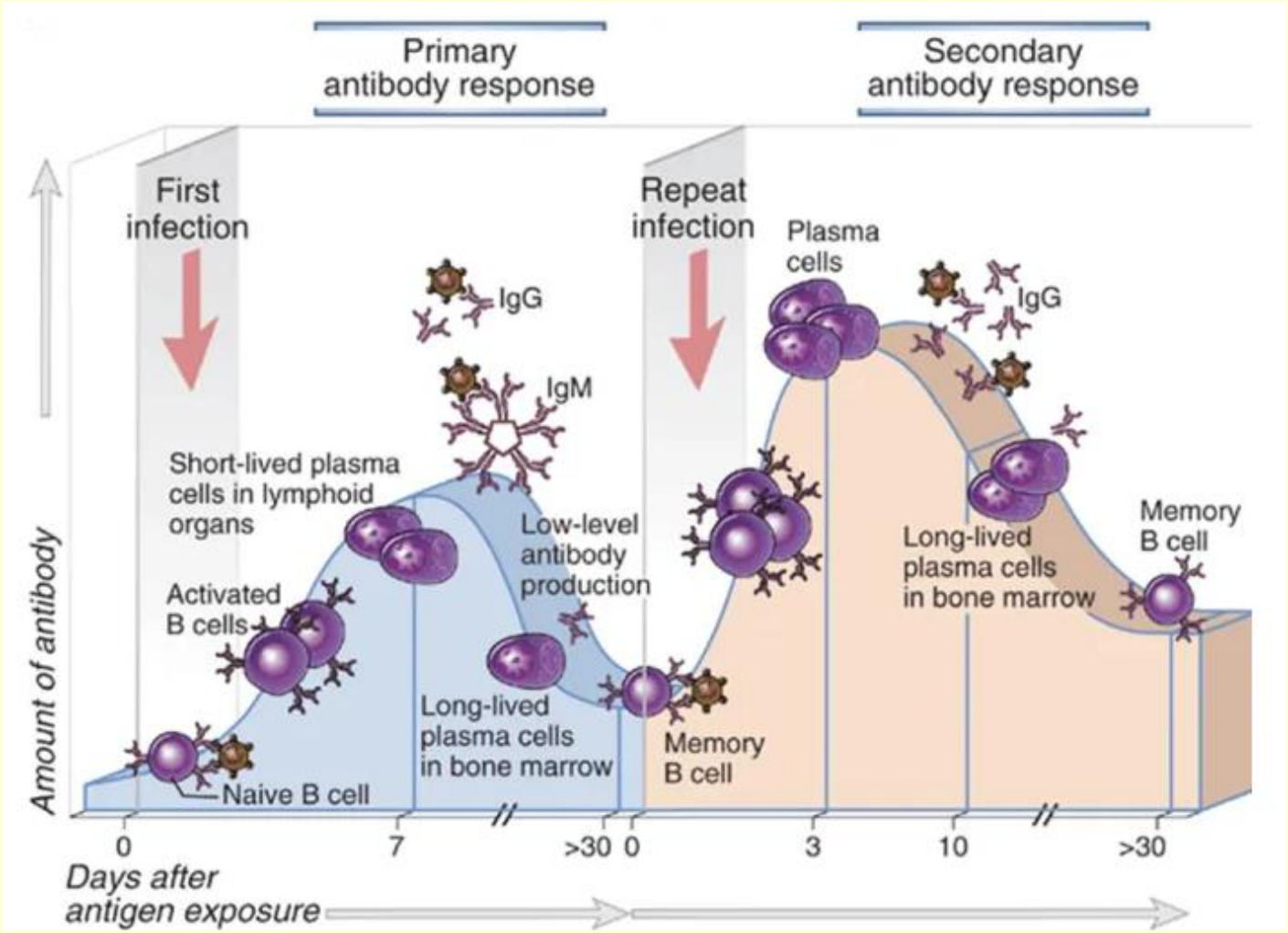


- **monoclonal**

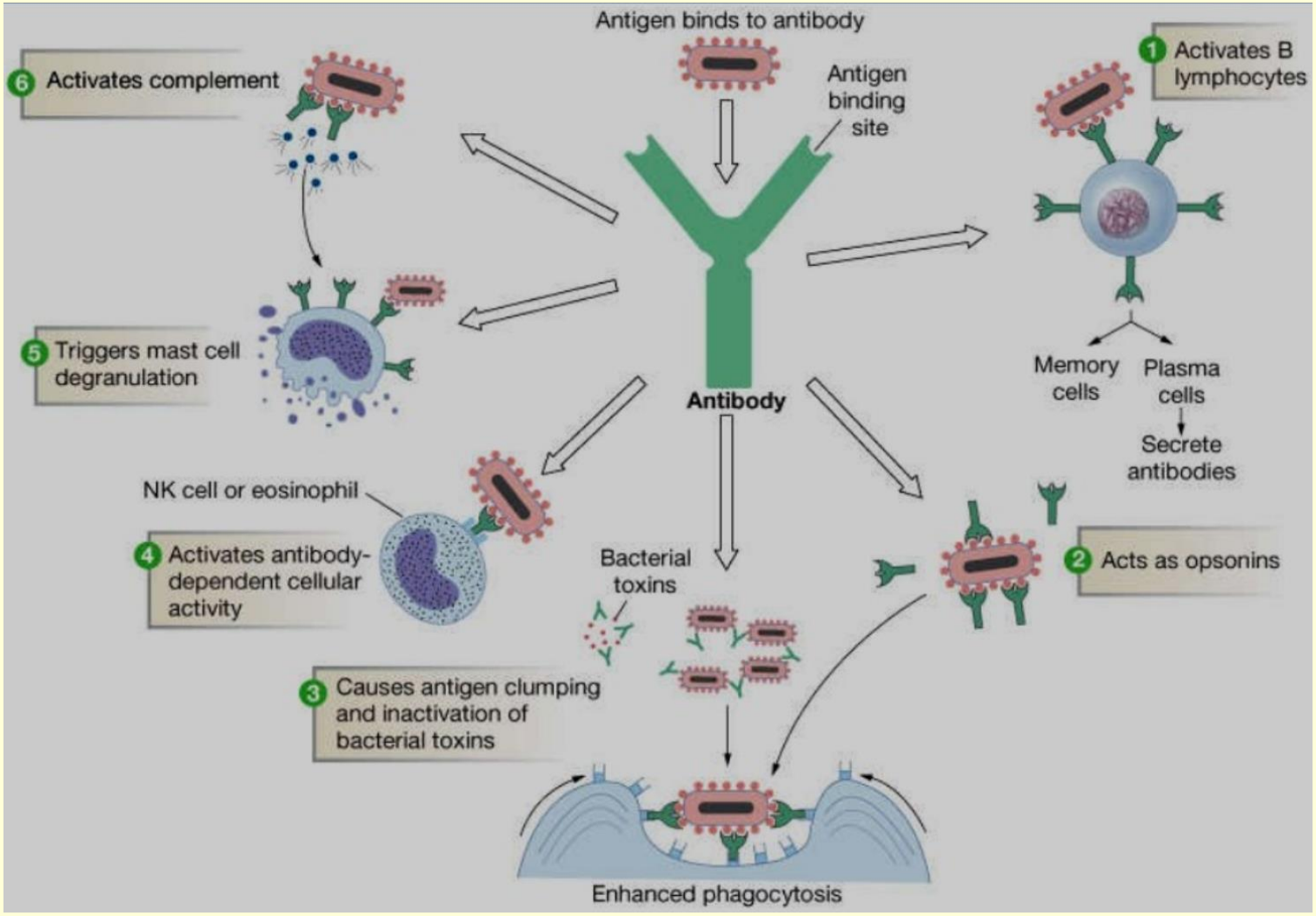




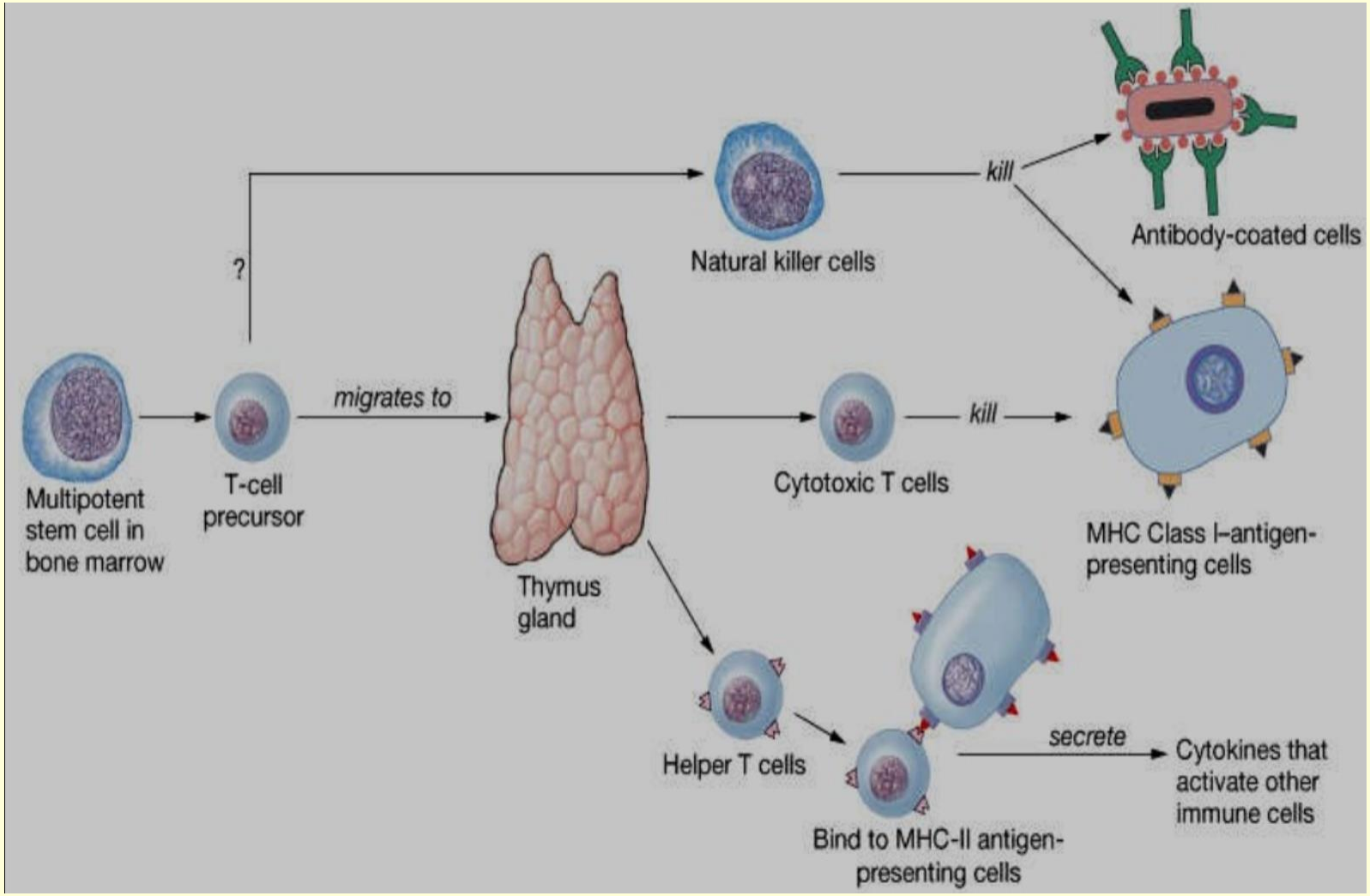
Primary and Secondary Antibody Response



Antigen-Antibody Response

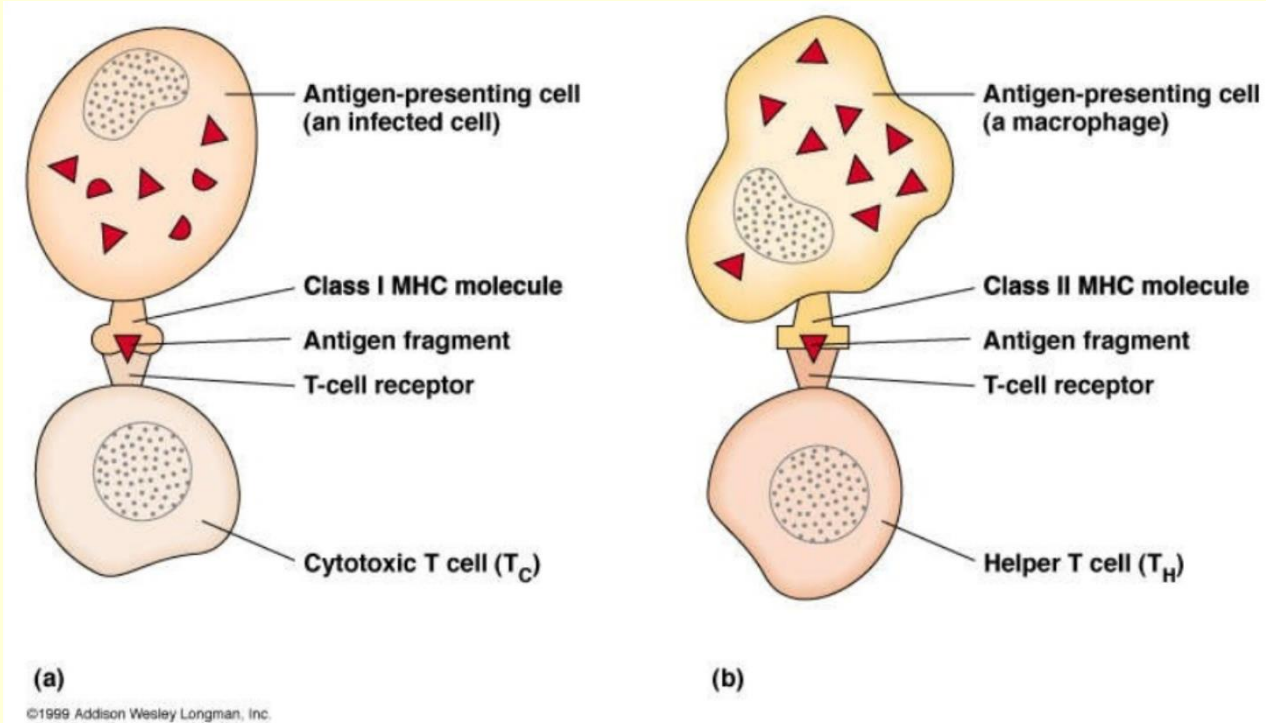


Cell-Mediated Immunity T-cells



Cell-Mediated Immunity T-cells

- T-cells recognize antigen associated with **MHC (major histocompatibility complex)** molecules in the cells
  - **MHC class I**
  - **MHC class II**

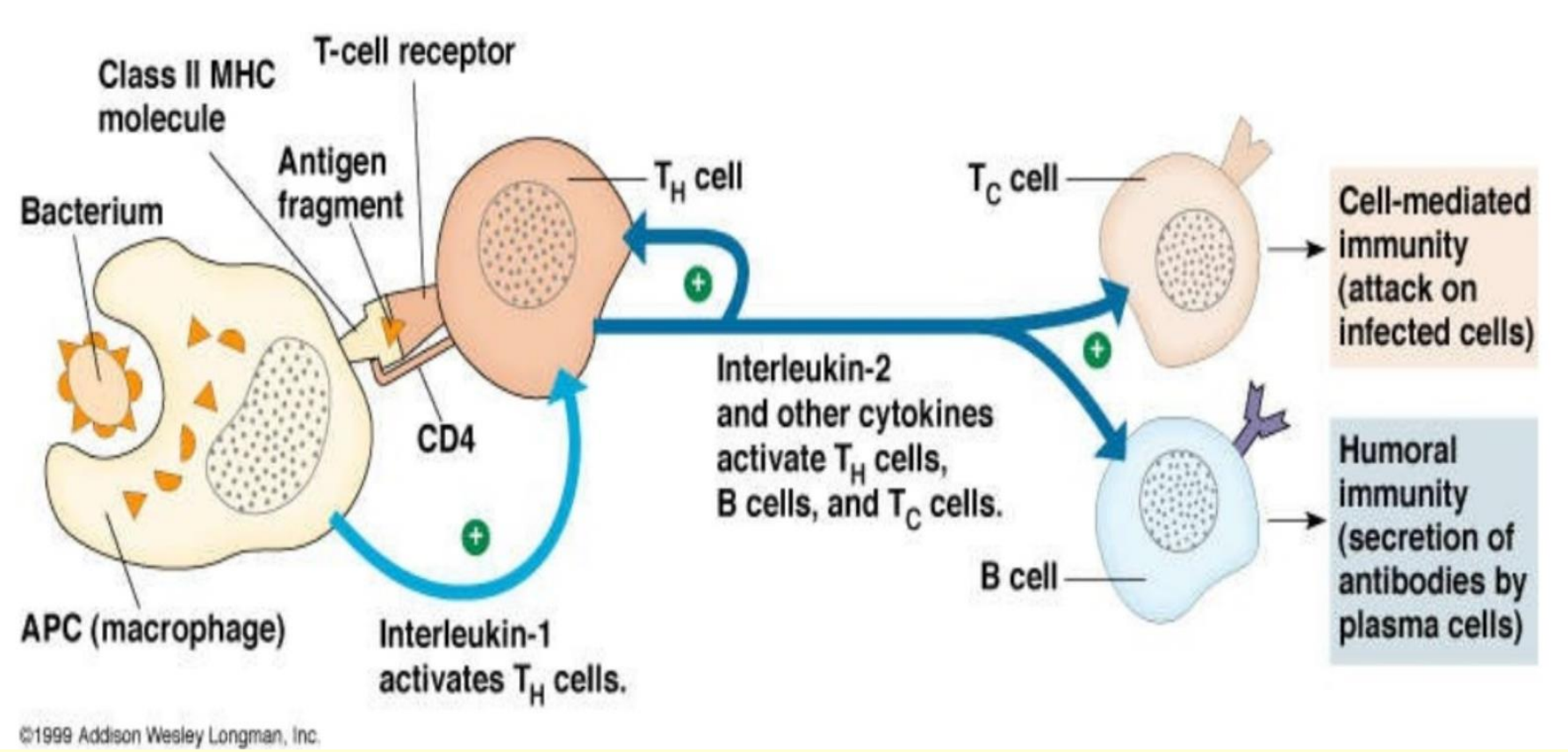


Cell-Mediated Immunity T-cells

T_H helper cells

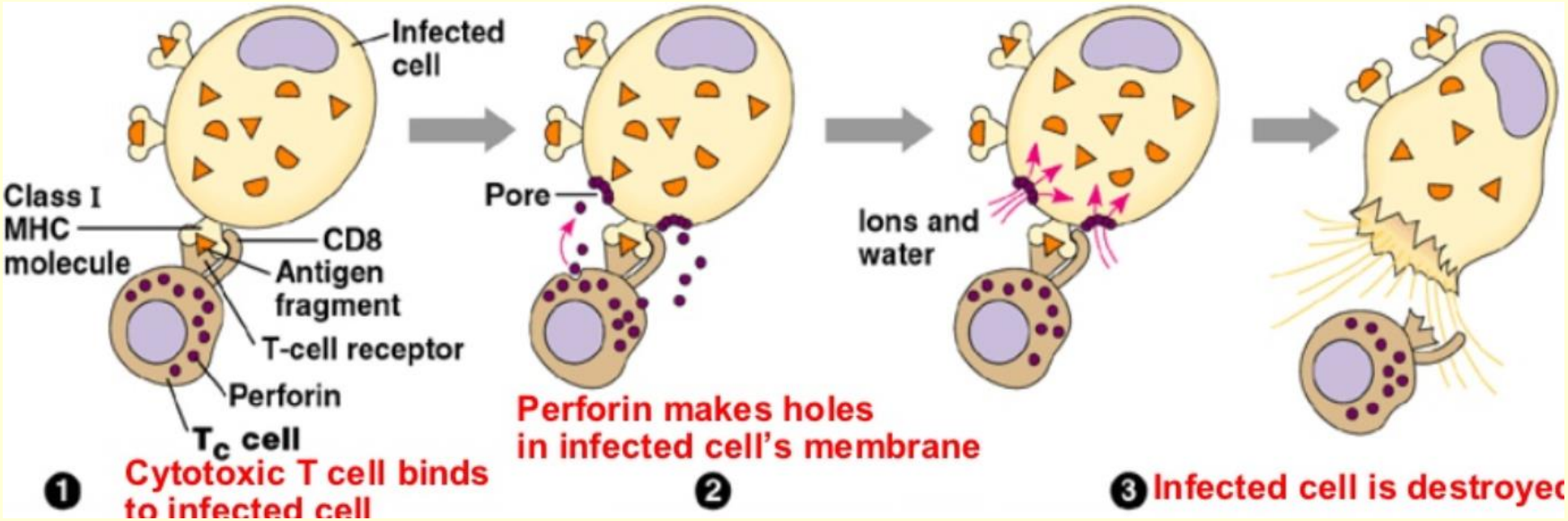
- T_H cells receptors recognize antigen on the surface of APC (macrophages)
- release of cytokines and activation of T_C and B-cells
- T_C cells directly attack and destroy infected cells ⟹ **CELL IMMUNE RESPONSE**
- B-cells (plasma cells) produce antibodies ⟹ **HUMORAL IMMUNE RESPONSE**

Helper T_H-cells



Cytotoxic T_C-cells

- recognize the antigens on the surface of the cells
- destroy infected cells (bacteria, viruses, fungi, parasites), tumour cells, transplanted tissue



Cytokines

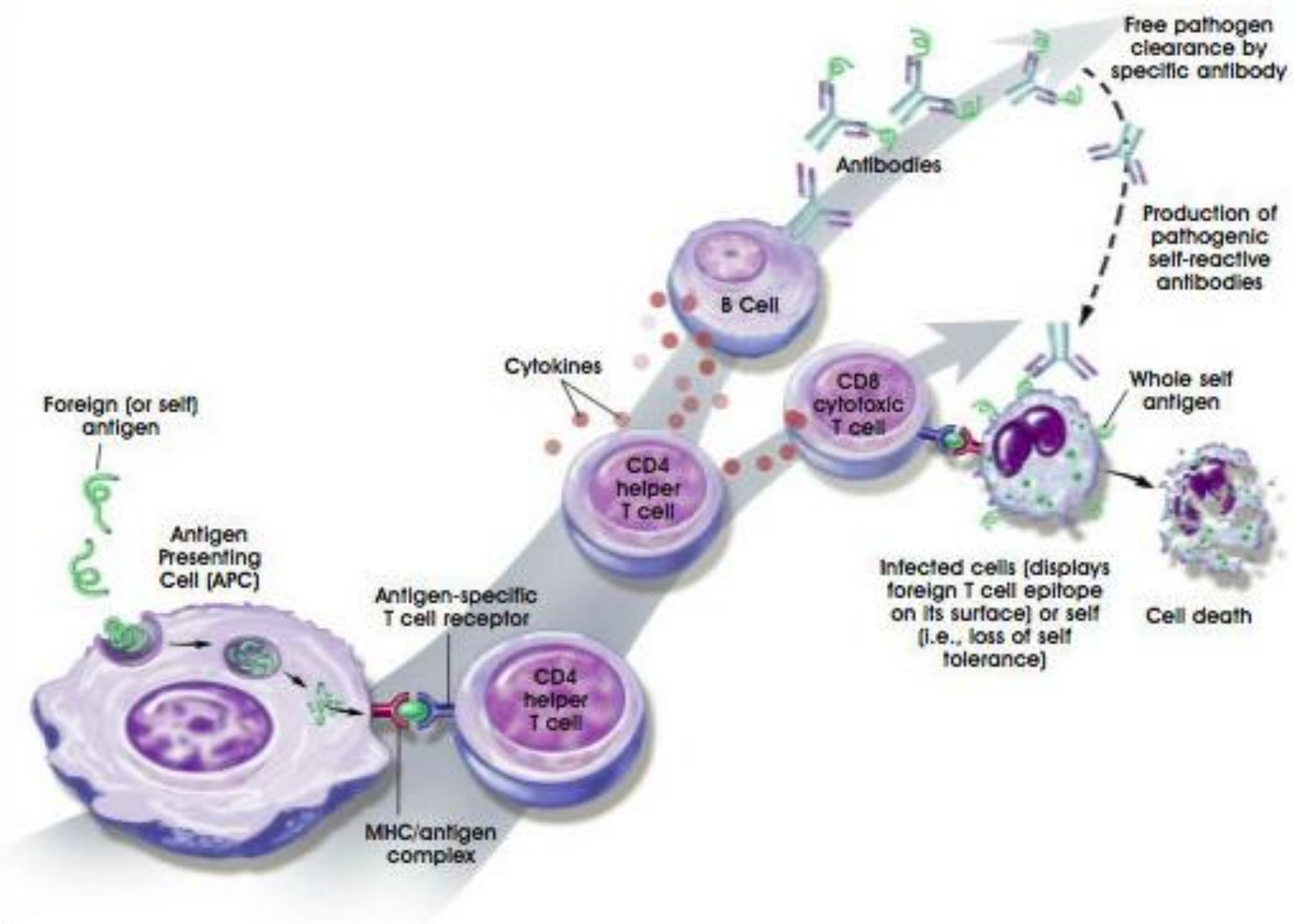
- small proteins involved in cell signaling
- amplify and regulate immune responses

- **interleukins** (IL-1, IL-2…)
- **TNF-α** (tumor necrosis factor alpha)
- **INF-γ** (interferon gama)
- **colony-stimulating factors** (G-CSF)

Complex Immune Reaction

- antigen ingested and presented by **antigen presenting cells (APC)**, like macrophages
- **helper T-cells** react with MHC-antigen complex
- **T-cell activation**, proliferation and cytokine production
- **cytokines** activate other cells (macrophages, NK cells, T_C cells)
- IL-2 stimulates **B-cells** to be developed to plasma cells with antibody production

Complex Immune Reaction



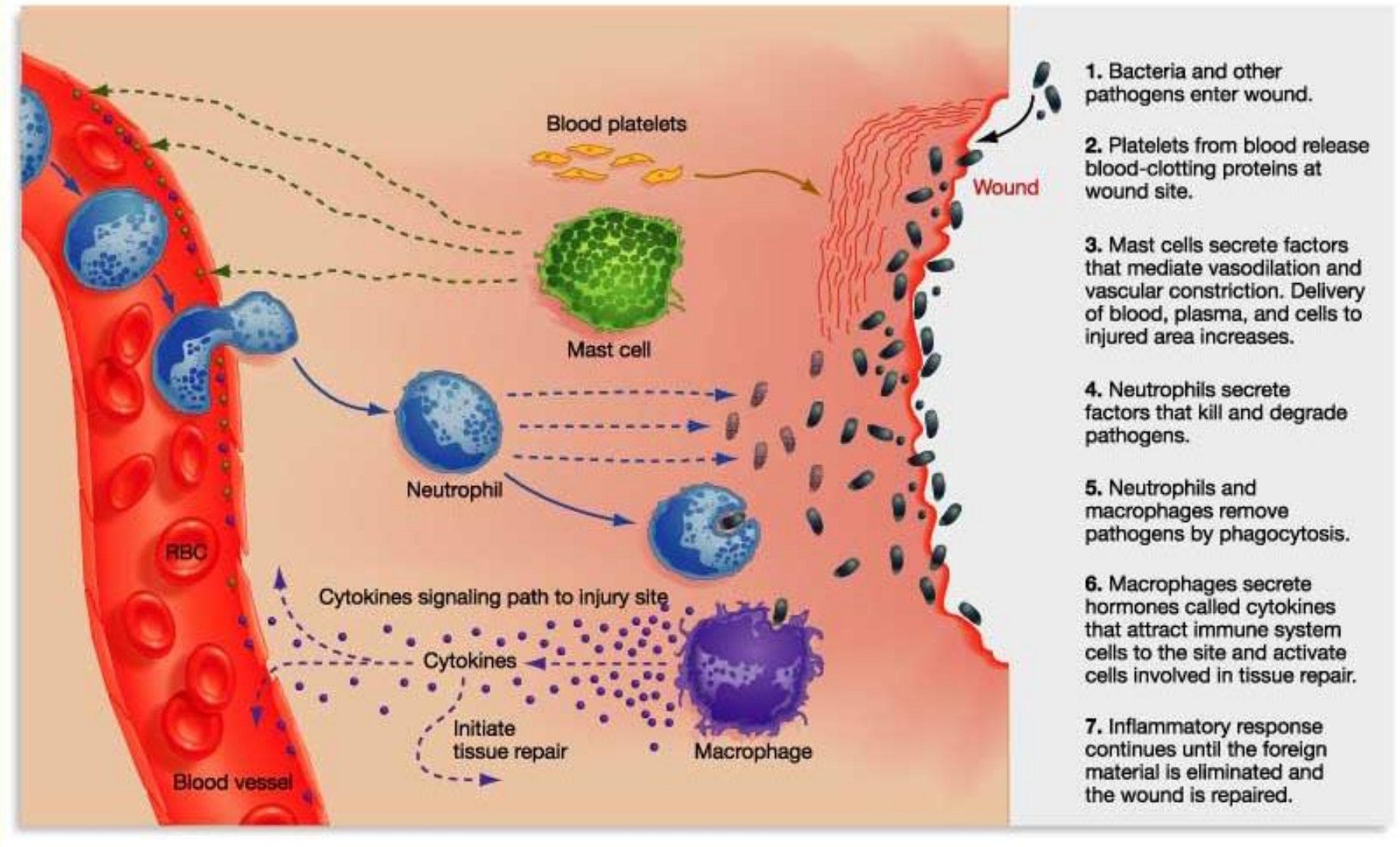
Inflammation

- defense reaction of the organism to injurious stimuli

MAIN AIMS

- to neutralize and destroy invading and harmful agents
- to limit the spread of harmful agents to other tissues
- to prepare any damaged tissue for repair

Inflammation



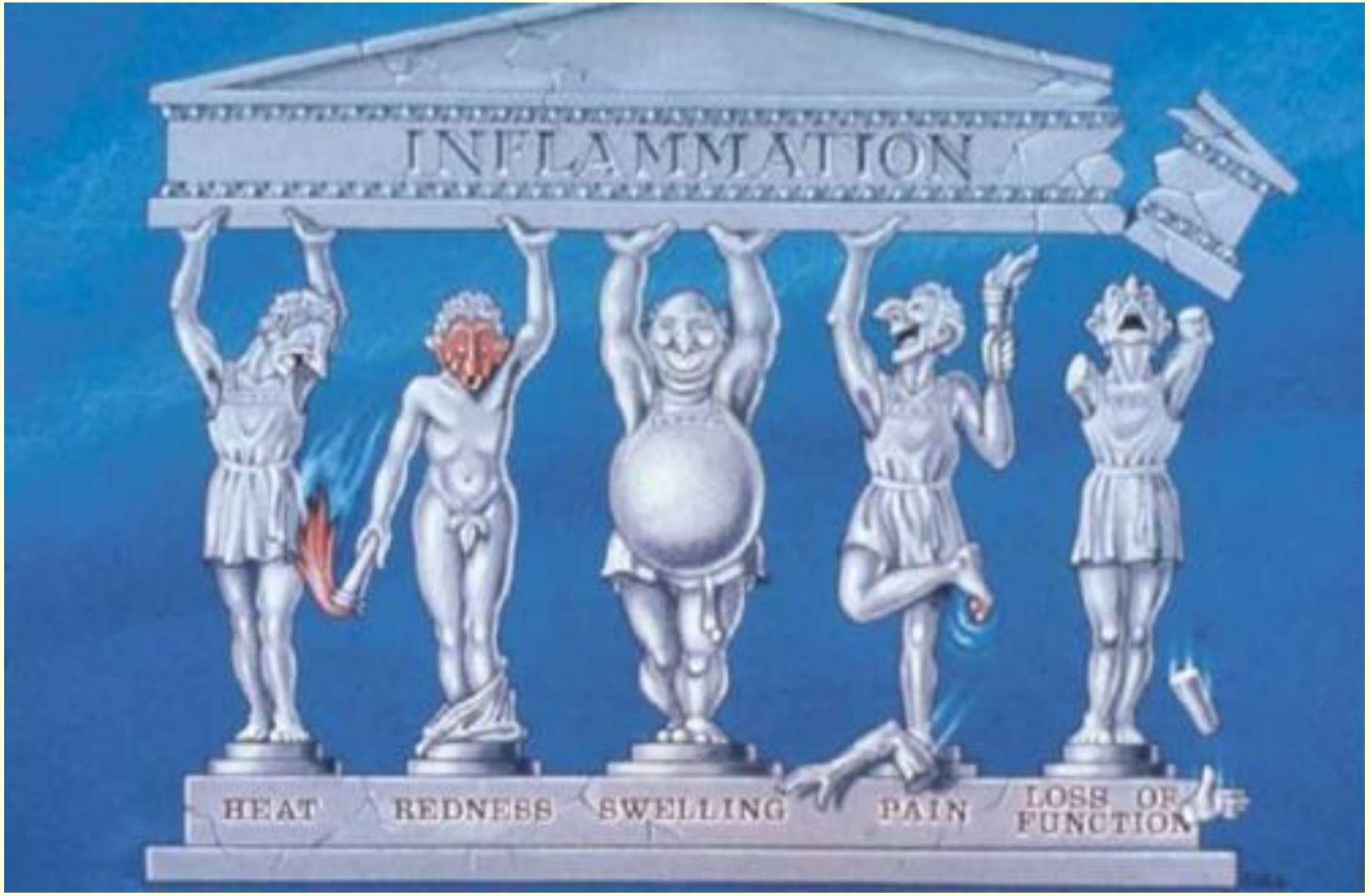
Local Signs of Inflammation

FIVE CARDINAL-LOCAL SIGNS OF INFLAMMATION:

1. RUBOR (REDNESS)
2. TUMOR (SWELLING)
3. CALOR (HEAT)
4. DOLOR (PAIN)
5. FUNCTIO LAESA (LOSS OF FUNCTION)

…. - ITIS

Inflammation



Inflammation

SYSTEMIC MANIFESTATION OF INFLAMMATION:

- fever
- Increased leukocyte counts (leukocytosis)
- lethargy
- muscle catabolism
- increased acute phase proteins (CRP C-reactive protein)
- increased erythrocyte sedimentation rate (ESR/FW)

Inflammation

INFLAMMATION AND INFECTION ARE COMMONLY CONFUSED BECAUSE THEY OFTEN COEXIST

INFECTION IS ALWAYS ACCOMPANIED BY INFLAMMATION;

HOWEVER,

NOT ALL INFLAMMATION INVOLVES AN INFECTIOUS AGENT

Inflammation

Causes of Inflammation

Biological
- bacteria, viruses, fungi, parasites

Physical
- UV, temperature, X-rays

Chemical
- strong acids and alkalies

Endogenous
- autoimmune diseases, disintegrating tumor cells

Surgery, trauma