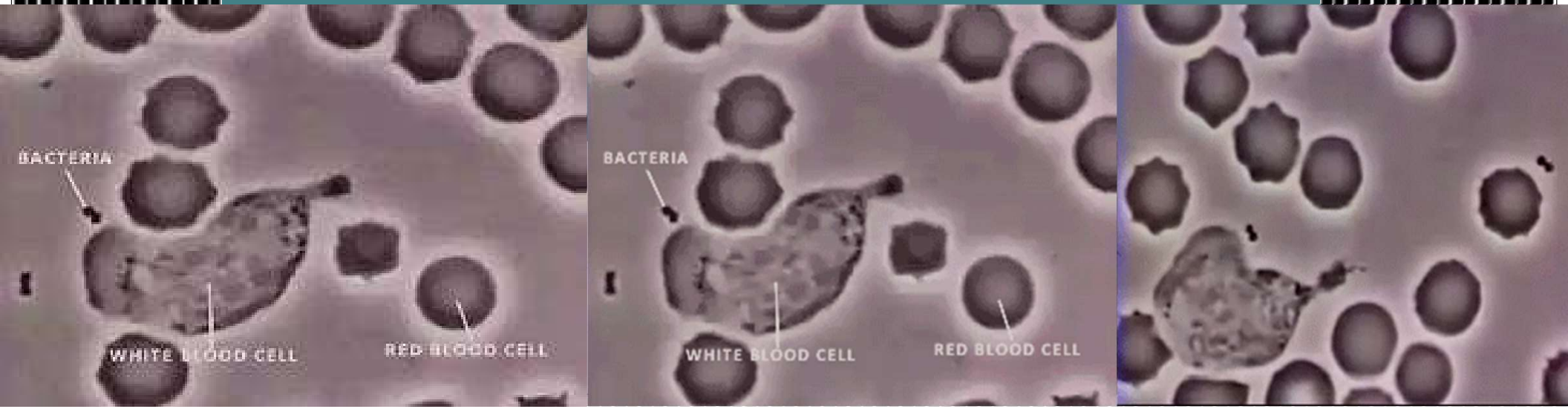
Immunology or licensed to kill
Lecture 2025

D.HAMMOUDI.MD



Generality

ANTIGEN:

A molecule **recognized by the immune system** (specifically by **B-cell receptors, T-cell receptors, or antibodies**).
•Can be a **protein, polysaccharide, lipid, or nucleic acid**.(**CAN BE ANYTHING, MOSTLY PROTEIN, CARDIOLIPID [ONLY LIPID]**
•**Not all antigens elicit an immune response** on their own. **"Antigen = Recognized"** (but not necessarily responded to).

Examples:
•**Blood group antigens (A, B)** — recognized by antibodies.
•**Bacterial surface proteins** — e.g., flagellin.
•**Viral capsid proteins** — e.g., hepatitis B surface antigen (HBsAg).
•**Allergens** — e.g., pollen proteins.

- **Antigen(ic) specificity**
  - **is the ability of the host cells to recognize an antigen specifically as a unique molecular entity and distinguish it from another with exquisite precision**

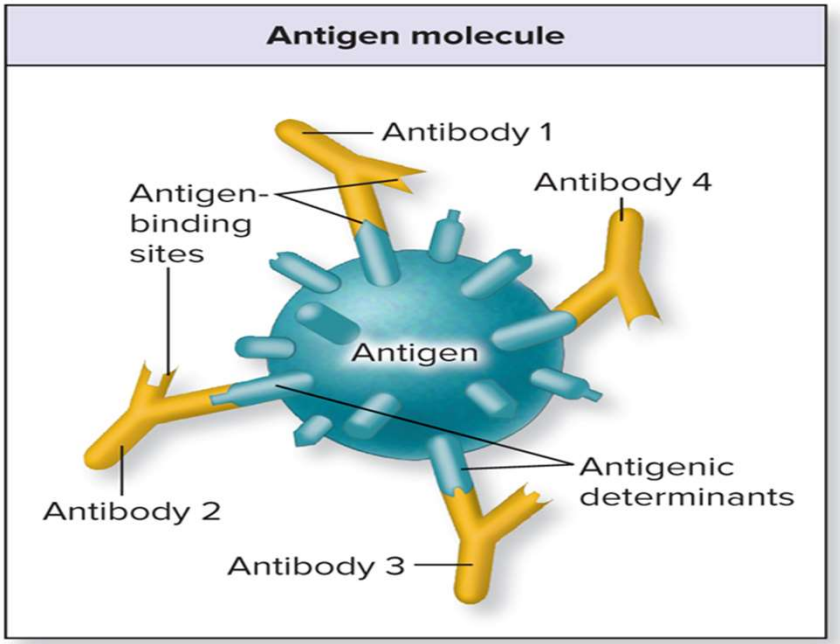
Antigenicity

- is the **ability to combine specifically with the final products of the immune response (i.e. secreted antibodies and/or surface receptors on T-cells).**
- **Although all molecules that have the property of immunogenicity also have the property of antigenicity, the reverse is not true**

- **Antigenic determinant**
  - **Also known as *epitope***
  - **Specific site on antigen recognized by immune system**
  - **and bound by an antibody, B cell receptor (BCR), or T cell receptor (TCR).**
  - Each has a different shape
  - Pathogenic organisms can have multiple determinants

Scenario	Connection to Antigenic Determinants
Vaccines	Designed to present key **epitopes** to generate protective antibodies
Monoclonal antibodies	Target specific **epitopes** (e.g., rituximab targets CD20 epitope on B cells)
Autoimmunity	Immune system mistakenly targets **self-epitopes**
Escape mutants	Viruses mutate epitopes to **evade recognition** (e.g., HIV, Influenza drift)

"**Epitope = Exact Point**" the immune system recognizes.



A vaccine induces antibodies that recognize a specific 8–amino acid region on a viral capsid protein. What term best describes this region?

A. Immunogen
B. Hapten
C. Antigenic determinant
D. MHC molecule
E. Antibody idiotype

✅ **Correct Answer: C. Antigenic determinant**
🧠 Because it's the **specific part of the antigen** that the immune system targets.

Generality

- IMMUNOGEN • **LARGE ENOUGH TO HAVE AN IMMUNE REACTION**

A substance that is **capable of provoking an immune response**.

•Triggers **both innate and adaptive immunity**.

•Usually a **large, complex, foreign protein**.

•Must be **processed and presented by APCs** for T cell activation.

All immunogens are antigens because they are recognized by the immune system.

"Immunogen = Initiates immunity."

Examples:

•**Tetanus toxoid** — used in vaccines, stimulates adaptive immunity.
•**Viral spike proteins (e.g., SARS-CoV-2 spike)** — targeted by mRNA vaccines.
•**Bacterial exotoxins** — like diphtheria toxin.
•**Whole pathogens** (attenuated/killed) — polio vaccine.

- **Immunogenicity**
  - **is the ability to induce a humoral and/or cell-mediated immune response**

Generality

- HAPTEN **TOO SMALL FOR A IMMUNE REACTION**

"Hapten = Half-antigen" — needs a partner (carrier protein) to spark a response.

A **small molecule** that **cannot elicit an immune response** **on its own** but becomes immunogenic **when attached to a larger carrier protein**.

•Alone → **not immunogenic**.

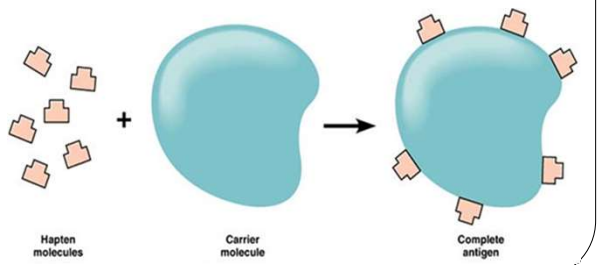
•Hapten + carrier protein → becomes an **immunogen**.

•Important in **drug allergies** (e.g., penicillin binds to proteins and forms hapten-carrier complexes that trigger hypersensitivity).

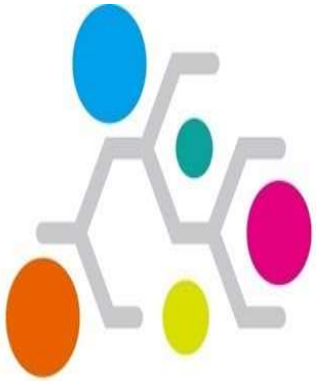
- Some haptens can induce autoimmune disease. Ex: **hydralazine**, a blood pressure-lowering drug that occasionally can produce **drug-induced lupus erythematosus** in certain individuals.
- This also appears to be the mechanism by which the anaesthetic gas halothane can cause a life-threatening hepatitis, as well as the mechanism by which penicillin-class drugs cause autoimmune hemolytic anemia.

Examples:

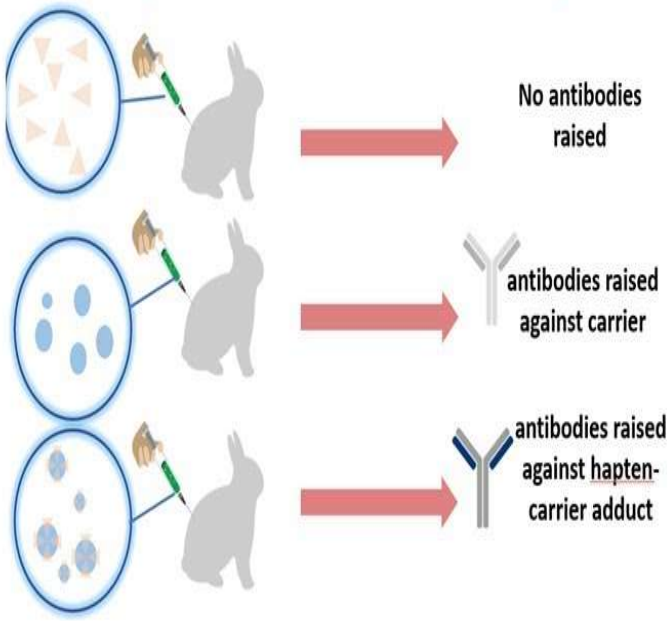
1. **Penicillin**: Binds to host proteins → becomes immunogenic → triggers **drug allergy**.
2. **Nickel (Ni^{2+})**: Causes **contact dermatitis** when bound to skin proteins.
3. **Urushiol** (poison ivy): Binds skin proteins → triggers T-cell response.
4. **Dinitrophenol (DNP)**: Classic experimental hapten in immunology research.

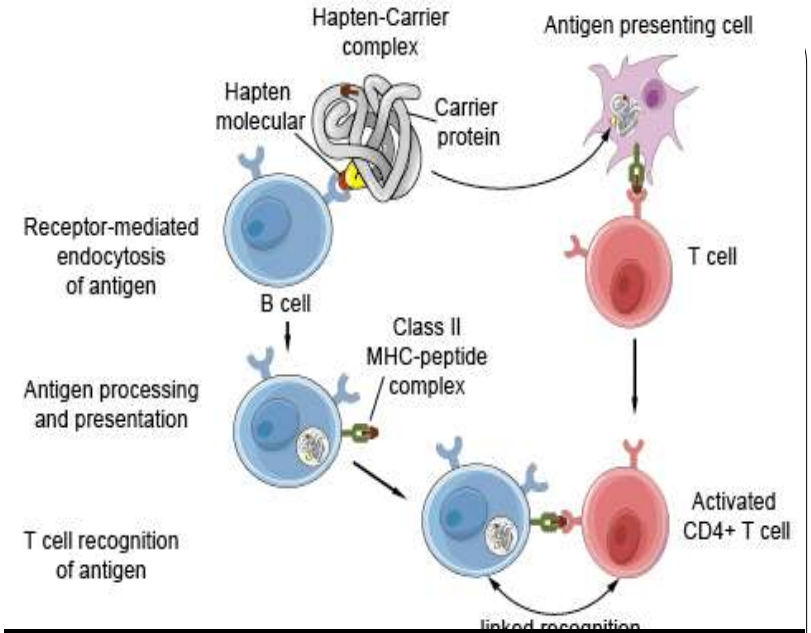


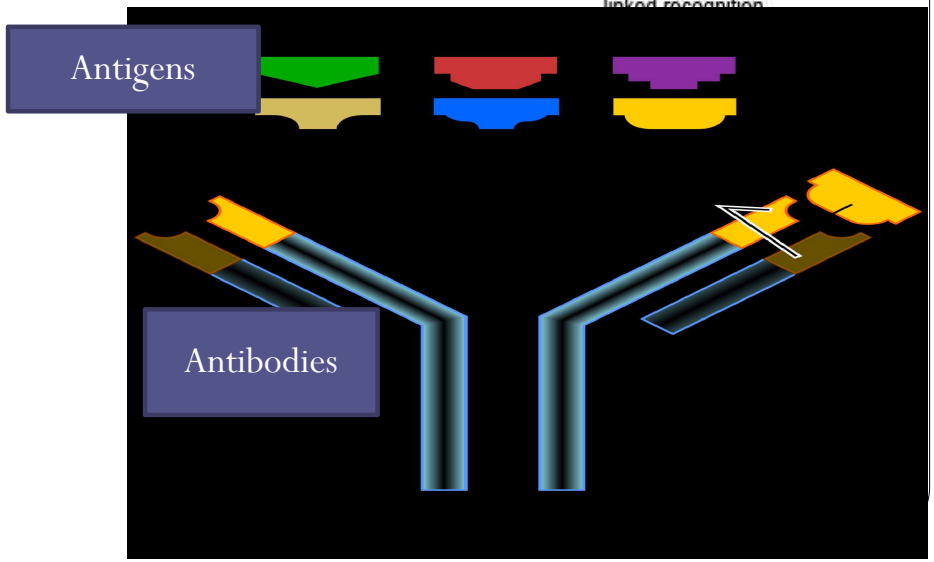
Hapten



Haptens are minute molecules that elicit an immune response only when attached to a large carrier







Property	Antigen	Immunogen	Hapten
Recognized by immune system?	✅ Yes	✅ Yes	✅ (when bound to carrier)
Triggers immune response?	❌ Not always	✅ Yes	❌ Not by itself
Requires carrier?	❌ No	❌ No	✅ Yes
Example	Bacterial LPS	Viral protein	Penicillin

- **Vaccines** use immunogens, not just antigens.
- **Hapten-carrier model** helps explain **Type I and Type IV hypersensitivity**.
- **Contact dermatitis**, **drug-induced hemolysis**, and **autoimmune hemolytic anemia** can involve **hapten formation**.

Concept	Real-world Example	Association
Antigen	ABO blood group antigens	**Hemolytic transfusion reaction**
Immunogen	Tetanus toxoid vaccine	**Vaccine-induced active immunity**
Hapten	Penicillin binds RBCs → immune attack	**Drug-induced hemolytic anemia** (Type II hypersensitivity)

ANTIGEN VERSUS IMMUNOGEN

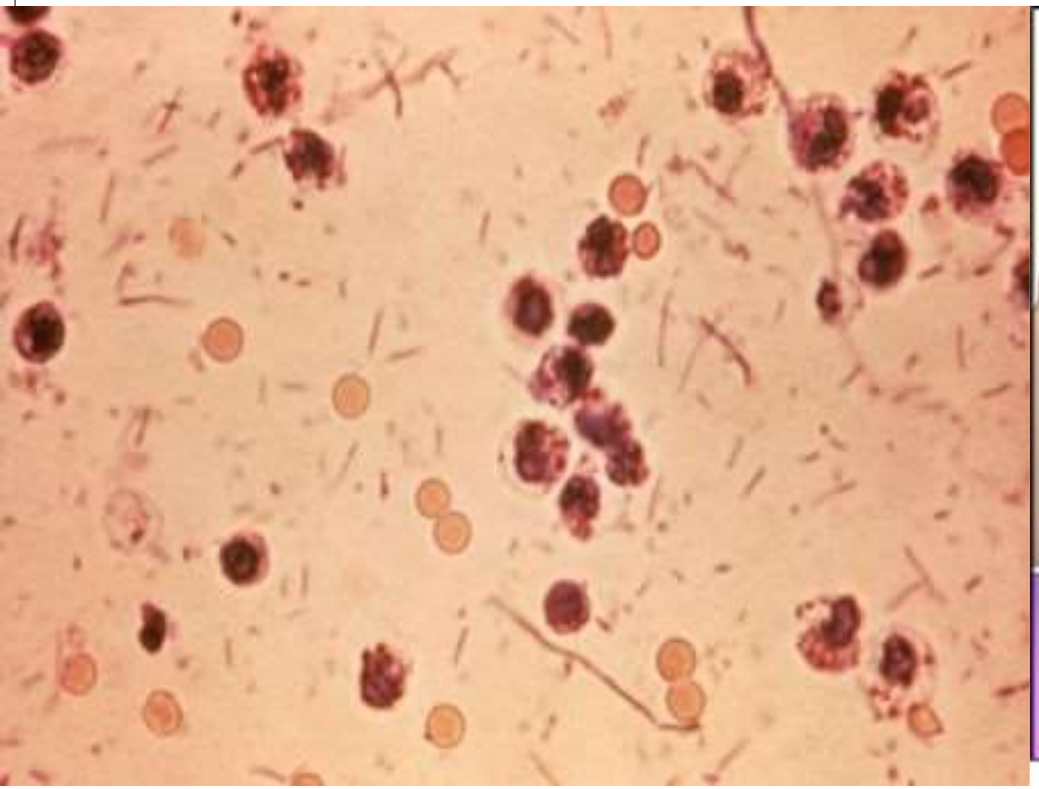
ANTIGEN	IMMUNOGEN
A substance specifically bind to antibodies or a cell surface receptors of B cells and T cells	An antigen capable of inducing an immune response
Can be either immunogenic or non-immunogenic	Immunogenic
Not all are immunogens	All are antigens
Can be either proteins, polysaccharides, lipids or nucleic acids	Normally proteins and large polysaccharides
Haptens are low-molecular-weight molecules, which bind to antibodies	Haptens become immunogenic when binding to larger carrier molecules

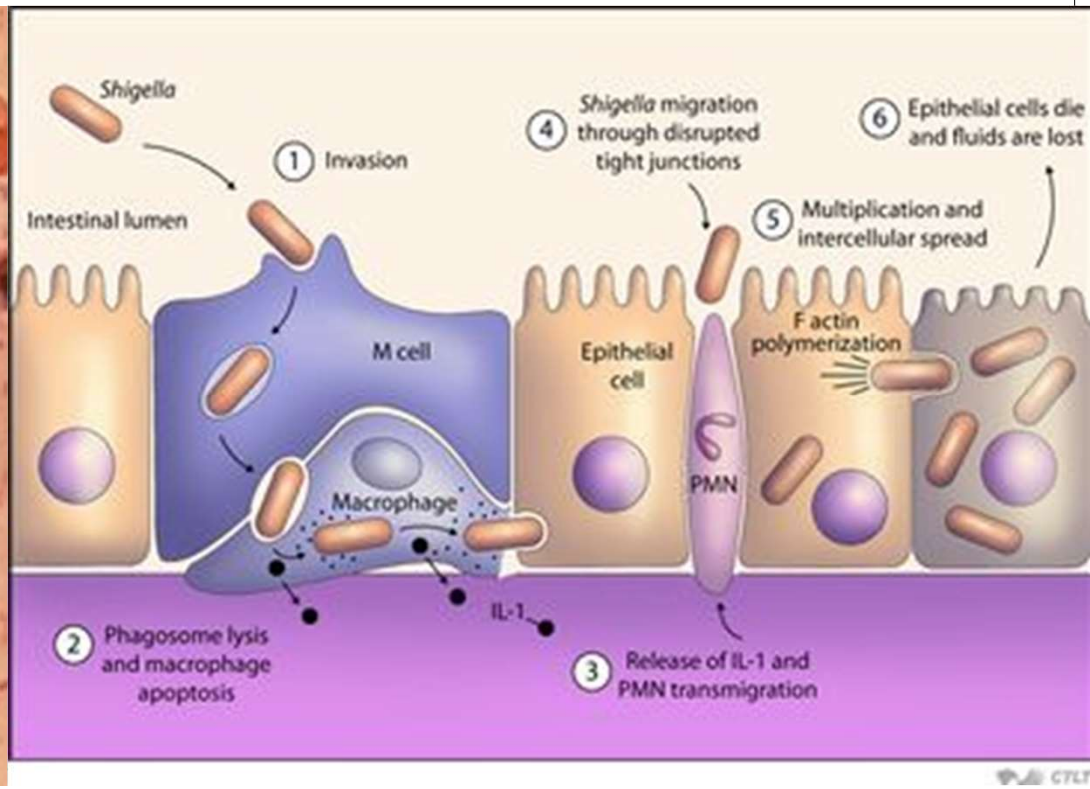
THE MOST IMMUNOGENIC BACTERIA

=

SHIGELLA

[ONLY 8 TO 10 OF THEM WILL GET YOU SICK.





Immunogen vs Antigen

- immunogen induces immune response
- antigen reacts with products of the immune response
- immunogenicity
  - nature of the immunogen
  - ability of immune system to react
  - possible to manipulate

Feature	Antigen	Immunogen
📌 **Definition**	Any substance that is **recognized** by the immune system (BCR/TCR/antibodies).	A substance that is **both recognized AND elicits an immune response**.
🔍 **Immune recognition**	✅ Yes	✅ Yes
💥 **Immune response**	❌ Not necessarily	✅ Always
🧬 **Includes**	All immunogens + non-immunogenic substances (like haptens)	Only substances that can **trigger an immune response**
⚠️ **USMLE Tip**	An antigen may **bind**, but not always **activate**	Immunogens **bind AND activate**

All immunogens are antigens, but not all antigens are immunogens."
Think:
Antigen = A for Aware (immune system sees it)
Immunogen = I for Immune reaction (actually triggers a response)

epitope (antigenic determinant)

- **recognized by antibody**
- **recognized by T-cell receptor**

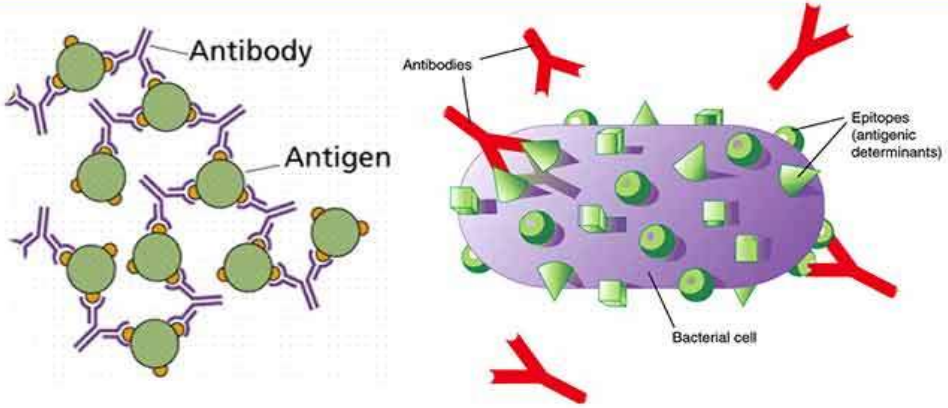
A 30-year-old man develops a rash after receiving penicillin. The drug binds to host proteins and is recognized by the immune system. What is the best classification of penicillin in this context?

A. Immunogen
B. Antigen
C. Epitope
D. MHC molecule
E. Cytokine

✅ **Answer: B. Antigen**

🧠 Penicillin acts as a **hapten** — not immunogenic alone, but becomes an **antigen** when bound to a protein.

Differences Between Antigen and Antibody



"Antigen = ANTIbody GENerator"

•It **generates** a response that leads to antibody production.

"Antibody = Anti-BODYguard"

•Acts as a **defender** that neutralizes invaders (antigens).

Feature	Antigen	Antibody
Definition	A molecule that is **recognized by** the immune system (B cells, T cells, antibodies)	A **protein** produced by **B cells (plasma cells)** in response to an antigen
Function	**Triggers** an immune response (can be self or foreign)	**Neutralizes, marks, or eliminates** antigens
Structure	Can be any substance: proteins, polysaccharides, lipids	Y-shaped glycoprotein (immunoglobulin: IgG, IgA, etc.)
Origin	Comes from pathogens, toxins, allergens, or even self-tissue	Made by **activated B lymphocytes (plasma cells)**
Recognition	Has **epitopes** that are recognized by antibodies or T/B cell receptors	Has **paratopes** that bind specifically to epitopes
Reusability	May appear multiple times (e.g., virus spike protein)	Produced in response to **each unique epitope**

Condition	Antigen Role	Antibody Role
Hepatitis B	HBsAg (surface antigen) → diagnostic marker	Anti-HBs → protective immunity
Systemic Lupus (SLE)	Nuclear antigens = triggers	Anti-dsDNA = diagnostic
Rh incompatibility	Fetal Rh^+ RBC = antigen to mom	Maternal anti-Rh antibodies can destroy fetal RBCs

A patient receives a vaccine containing viral protein. Several weeks later, their serum contains high levels of specific IgG molecules. Which of the following best describes the relationship between the protein and the IgG?

A. The IgG is an antigen and the protein is an antibody
B. The IgG is an antibody and the protein is an antigen
C. Both are antigens
D. Both are antibodies
E. The protein is a cytokine

✅ **Correct Answer: B**

🧠 The viral protein is the **antigen** that stimulated the immune system to produce **IgG antibodies**.

Cytokines

Cytokines: small proteins that regulate immune activity

- Produced by cells of both innate and adaptive immune system
- Chemical messengers released from one cell that bind to receptors of target cells
  - Can act on cell that released it (autocrine); on local cells (paracrine); or on distant cells after circulating through blood (endocrine)
  - Have short half-life
- **Effects**
  - Signaling cells (including non-immune cells, e.g., neurons)
  - Controlling development and behavior of immune cells
  - Regulating inflammatory response
  - Destroying cells

- **Cytokines are essential for coordinating the immune response and maintaining homeostasis.**
- They act through specific receptors on target cells, triggering various intracellular signaling pathways that lead to changes in gene expression and cellular function.

- **Their balanced production and regulation are critical for effective immune responses and for preventing excessive inflammation or immune-mediated damage.**

Cytokines

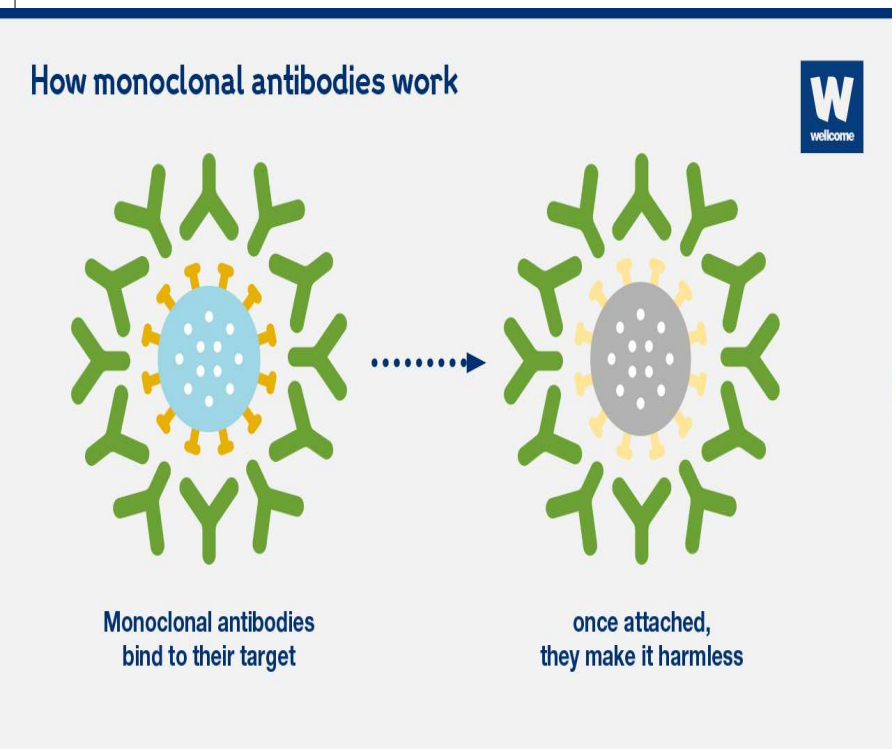
- **Cytokine** characteristics
  - Small soluble proteins
  - Produced by cells of both innate and adaptive immune system
  - Released from one cell and bind specific receptor of target cell
    - action similar to that of a hormone
    - can act on cell that released it (autocrine)
    - can act on local cells (paracrine)
    - can circulate in the blood to act systemically (endocrine)
  - Have short half-life
- Cytokine functions
  - Regulate and facilitate immune system activity
  - Means of communication between cells
  - Control behavior of effector cells of immunity
  - Regulate inflammatory response
  - Serve as weapons to destroy cells
  - Influence non-immune cells, e.g., nervous system
- Cytokine categories
  - Interleukin (IL)
    - e.g., IL-2
  - Tumor necrosis factor (TNF)
    - e.g., TNF-α
  - Colony-stimulating factor (CSF)
    - e.g., granulocyte CSF
  - Interferon (IFN)
    - e.g., INF-α

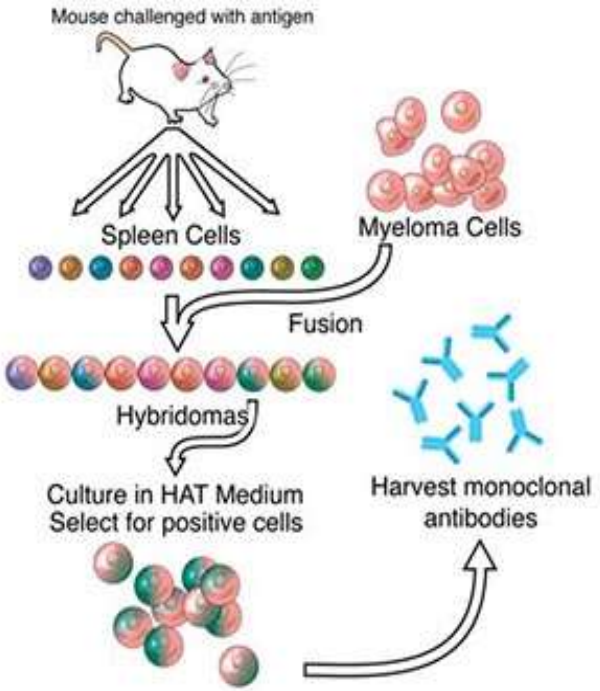
Cytokine	Primary Functions
Interleukin-1 (IL-1)	Promotes inflammation, induces fever, stimulates production of acute-phase proteins.
Interleukin-2 (IL-2)	Stimulates growth and differentiation of T cells, enhances NK cell activity.
Interleukin-4 (IL-4)	Promotes differentiation of naive T cells to Th2 cells, stimulates B cell proliferation and antibody production.
Interleukin-6 (IL-6)	Promotes inflammation, induces fever, stimulates production of acute-phase proteins, supports B cell growth and differentiation.
Interleukin-10 (IL-10)	Anti-inflammatory cytokine, inhibits cytokine production by macrophages and dendritic cells, promotes B cell survival.
Interleukin-12 (IL-12)	Enhances NK cell activity, promotes differentiation of naive T cells to Th1 cells.
Interleukin-17 (IL-17)	Promotes inflammation, stimulates production of pro-inflammatory cytokines and chemokines.
Interleukin-23 (IL-23)	Supports maintenance and proliferation of Th17 cells, promotes inflammation.
Interferon-alpha (IFN-α)	Antiviral effects, enhances MHC class I expression, activates NK cells.
Interferon-beta (IFN-β)	Antiviral effects, enhances MHC class I expression, modulates immune response.
Interferon-gamma (IFN-γ)	Activates macrophages, enhances antigen presentation, promotes Th1 cell differentiation.
Tumor Necrosis Factor-alpha (TNF-α)	Promotes inflammation, induces fever, mediates septic shock, stimulates acute-phase protein production.

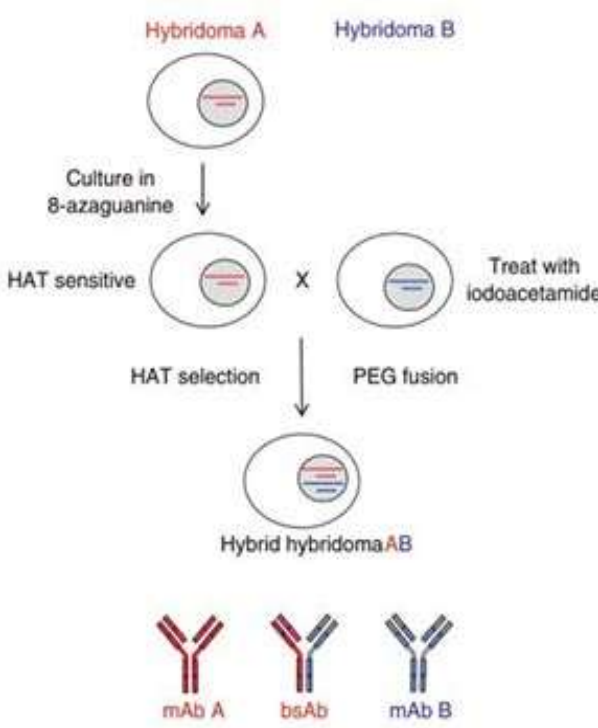
Chemokine (e.g., IL-8/CXCL8)	Attracts neutrophils to sites of infection and inflammation, promotes angiogenesis.
Transforming Growth Factor-beta (TGF-β)	Anti-inflammatory cytokine, promotes tissue regeneration and repair, inhibits T cell proliferation and differentiation.
Macrophage Colony-Stimulating Factor (M-CSF)	Promotes differentiation of hematopoietic stem cells into macrophages.
Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)	Stimulates production and differentiation of granulocytes and macrophages from hematopoietic progenitor cells.

Hybridomas

hybrid cells produced by the fusion of an antibody-producing lymphocyte with a tumor cell and used to culture continuously a specific monoclonal antibody.

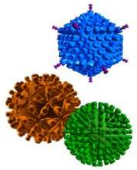


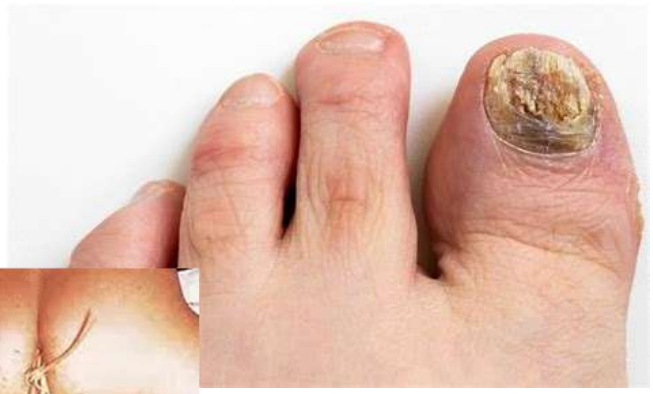


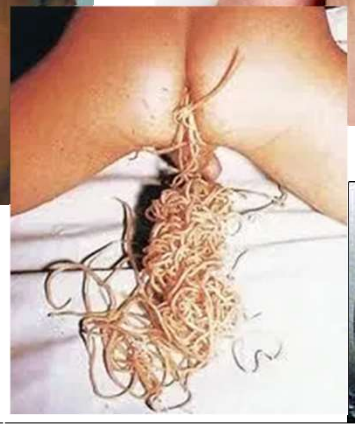


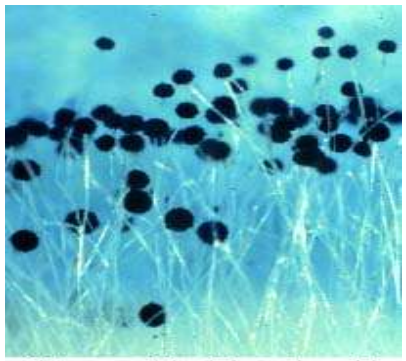
The Invaders . . .

- **Bacteria**
- **Viruses**
- **parasites : protista, & worms**
- **fungi**
- **Prion**









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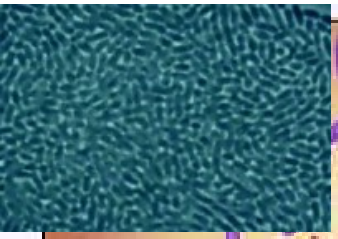
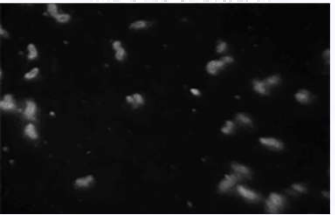
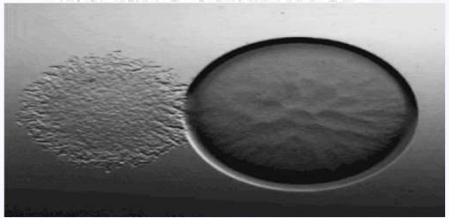


a Bacteria invade.



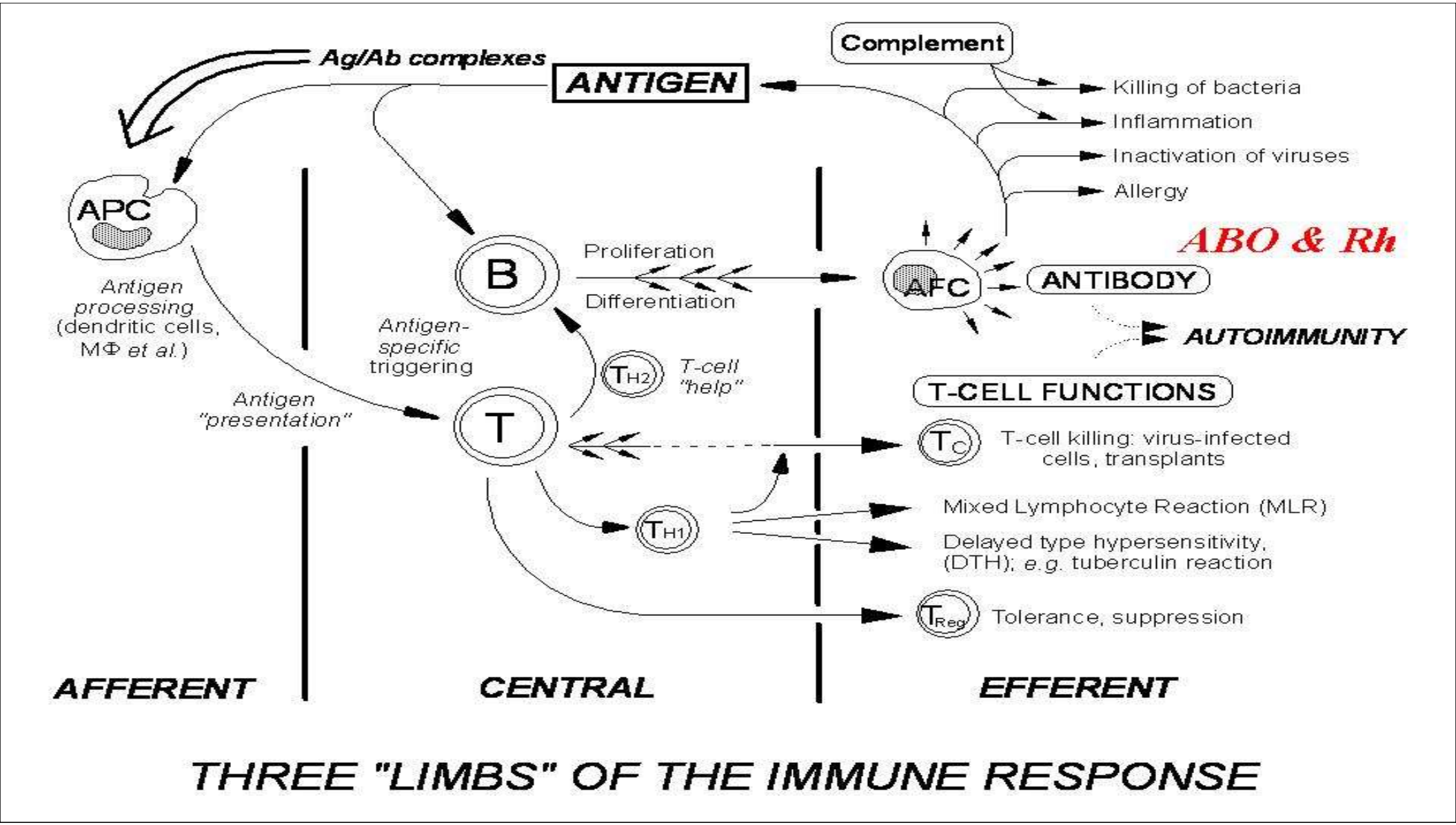
b Substances accumulate.



c The substances make plasma and proteins escape.

d Plasma proteins attack bacteria, phagocytes, or repair damage.

e Phagocytes engulf bacteria.



THREE "LIMBS" OF THE IMMUNE RESPONSE

CELLS OF THE IMMUNITY

Immune Cells and Their Locations (review white cells blood)

Leukocytes (white blood cells)

- Formed in red bone marrow
- Include:
  - Granulocytes: neutrophils, eosinophils, basophils
  - Monocytes
    - Become macrophages when they leave blood and enter tissues
  - Lymphocytes
    - B-lymphocytes, T-lymphocytes, NK (natural killer) cells

Immune Cells and Their Locations

Structures that house immune system cells

Most leukocytes are in body tissues (instead of blood)

Secondary lymphatic structures

- T- and B-lymphocytes,
- macrophages,
- dendritic cells,
- NK
- **cells housed in**
  - lymph nodes,
  - spleen,
  - tonsils,
  - MALT,
  - lymphatic nodules)

Select organs house macrophages

May be permanent residents of the organ, or migrating macrophages

Some permanent ones named for location (e.g., alveolar macrophages

Immune Cells and Their Locations 3

Structures that house immune system cells (*continued*)

Epithelial layers of skin and mucosal membranes house dendritic cells

- These dendritic cells are usually derived from monocytes
- Engulf pathogens and migrate into lymph

Connective tissue houses mast cells

- Mast cells typically in close proximity to small blood vessels
- Abundant in dermis and mucosa of respiratory, GI, and urogenital tracts
- Also found in connective tissue of organs (e.g., endomysium of muscle)

Internal Defenses: Cells and Chemicals

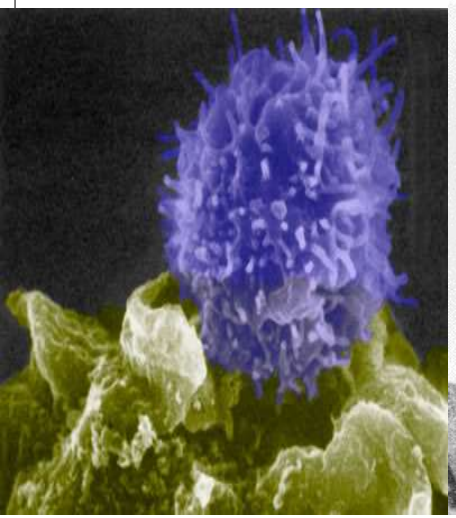
- **The body uses nonspecific cellular and chemical devices to protect itself**
  - **Phagocytes and natural killer (NK) cells**
  - **Antimicrobial proteins in blood and tissue fluid**
  - **Inflammatory response enlists macrophages, mast cells, WBCs, and chemicals**
- **Harmful substances are identified by surface carbohydrates unique to infectious organisms**

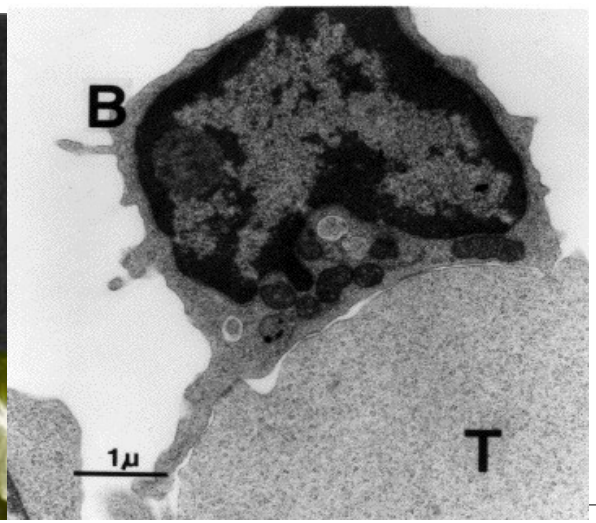
Inflammatory Chemicals

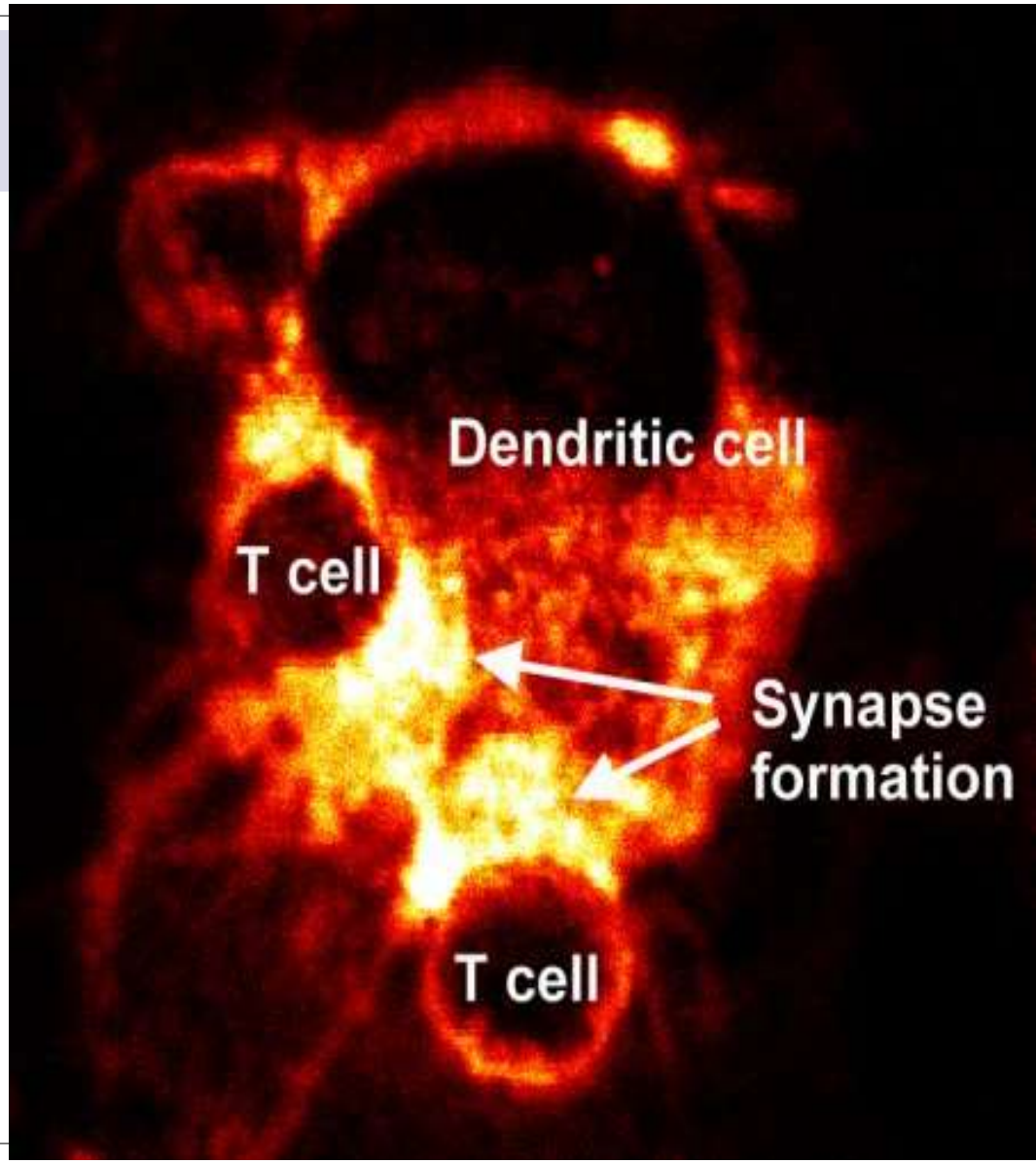
CHEMICAL	SOURCE	PHYSIOLOGICAL EFFECTS
Histamine	Granules of basophils and mast cells; released in response to mechanical injury, presence of certain microorganisms, and chemicals released by neutrophils	Promotes vasodilation of local arterioles; increases permeability of local capillaries, promoting exudate formation
Kinins (bradykinin and others)	A plasma protein, kininogen, is cleaved by the enzyme kallikrein found in plasma, urine, saliva, and in lysosomes of neutrophils and other types of cells; cleavage releases active kinin peptides	Same as for histamine; also induce chemotaxis of leukocytes and prompt neutrophils to release lysosomal enzymes, thereby enhancing generation of more kinins; induce pain
Prostaglandins	Fatty acid molecules produced from arachidonic acid—found in all cell membranes; generated by enzymes of neutrophils, basophils, mast cells, and others	Sensitize blood vessels to effects of other inflammatory mediators; one of the intermediate steps of prostaglandin generation produces free radicals, which themselves can cause inflammation; induce pain
Platelet-derived growth factor (PDGF)	Secreted by platelets and endothelial cells	Stimulates fibroblast activity and repair of damaged tissues
Complement	See Table 21.2 (p. 796)	
Cytokines	See Table 21.4 (pp. 817–818)	

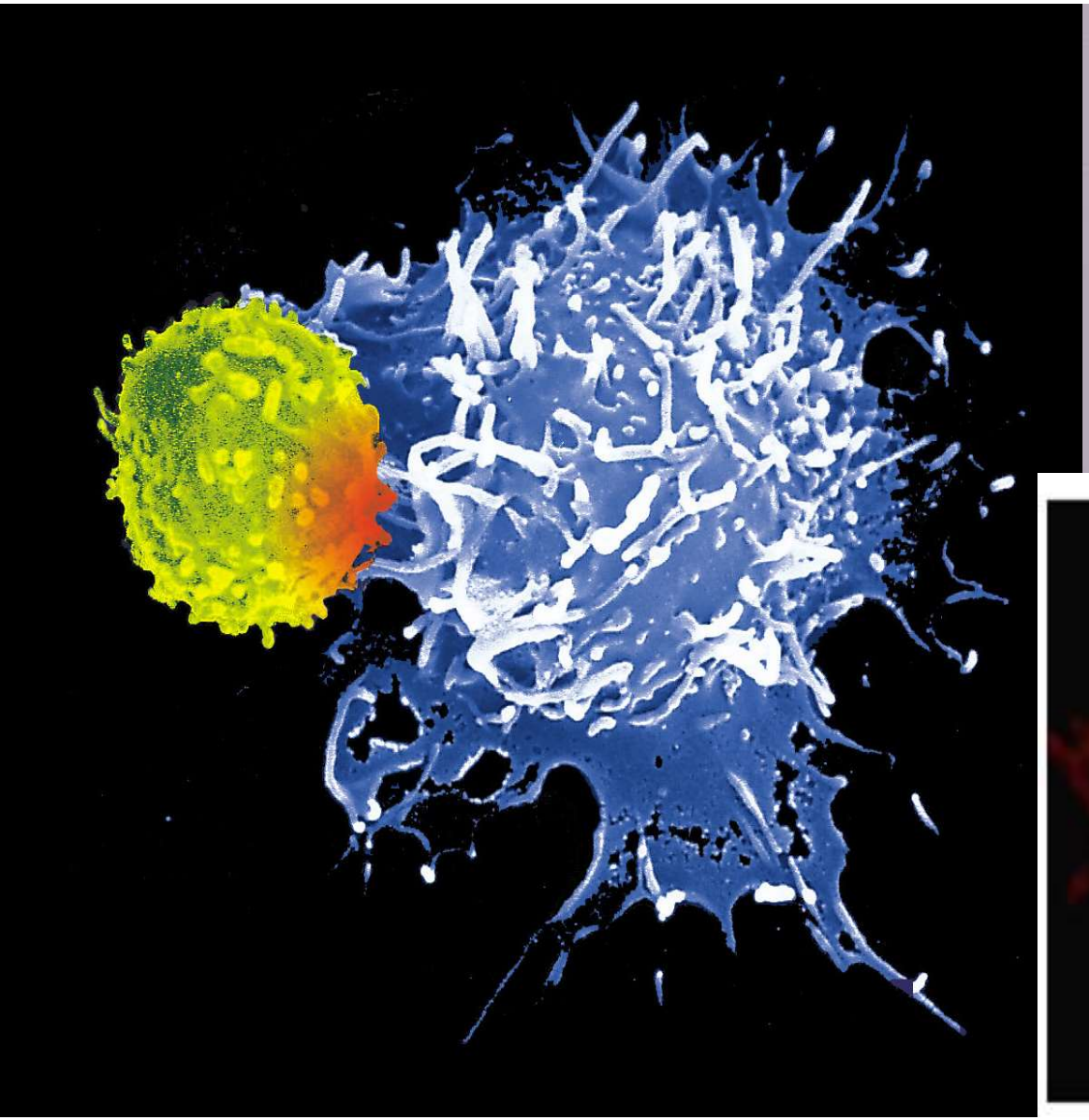
Immunological Synapse

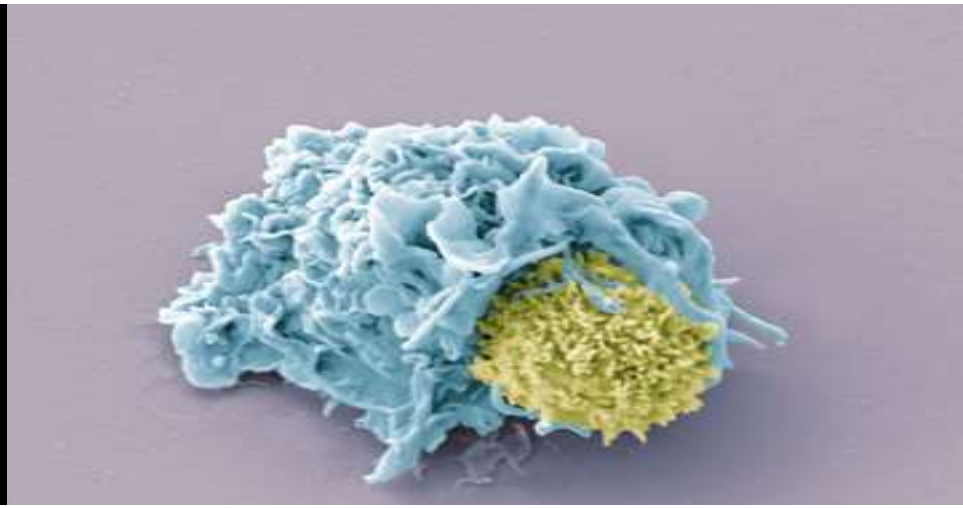
Is the interface between an antigen-presenting cell and a lymphocyte

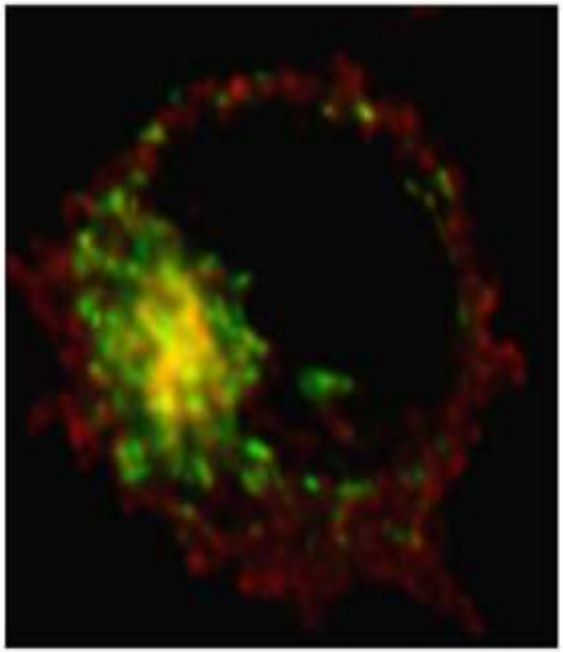




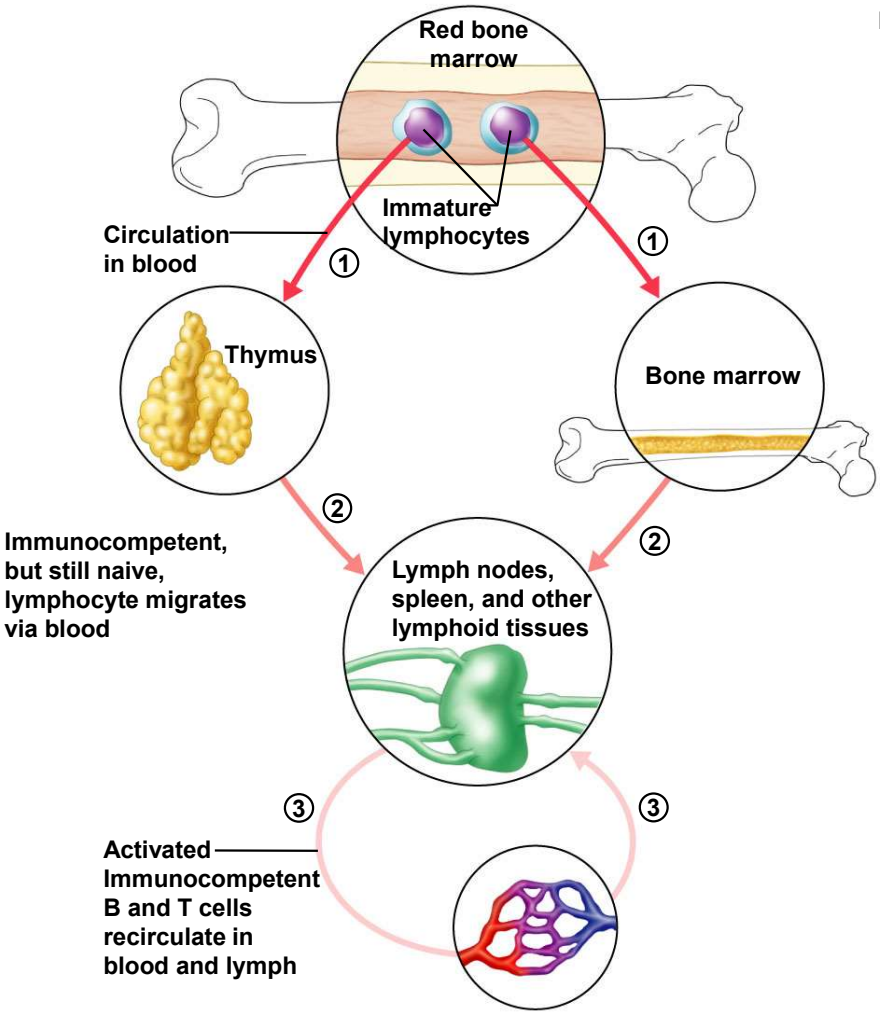








HIV-1-infected T cell displaying Lck (red) retained in recycling endosomes (marked by the transferrin receptor, green). Yellow color indicates the co-localization of both proteins



Key:
- = Site of lymphocyte origin
- = Site of development of immunocompetence as B or T cells; primary lymphoid organs
- = Site of antigen challenge, activation, and final diff erentiation of B and T cells

① Lymphocytes destined to become T cells migrate to the thymus and develop immunocompetence there. B cells develop immunocompetence in red bone marrow.

② After leaving the thymus or bone marrow as naïve immunocompetent cells, lymphocytes "seed" the lymph nodes, spleen, and other lymphoid tissues where the antigen challenge occurs.

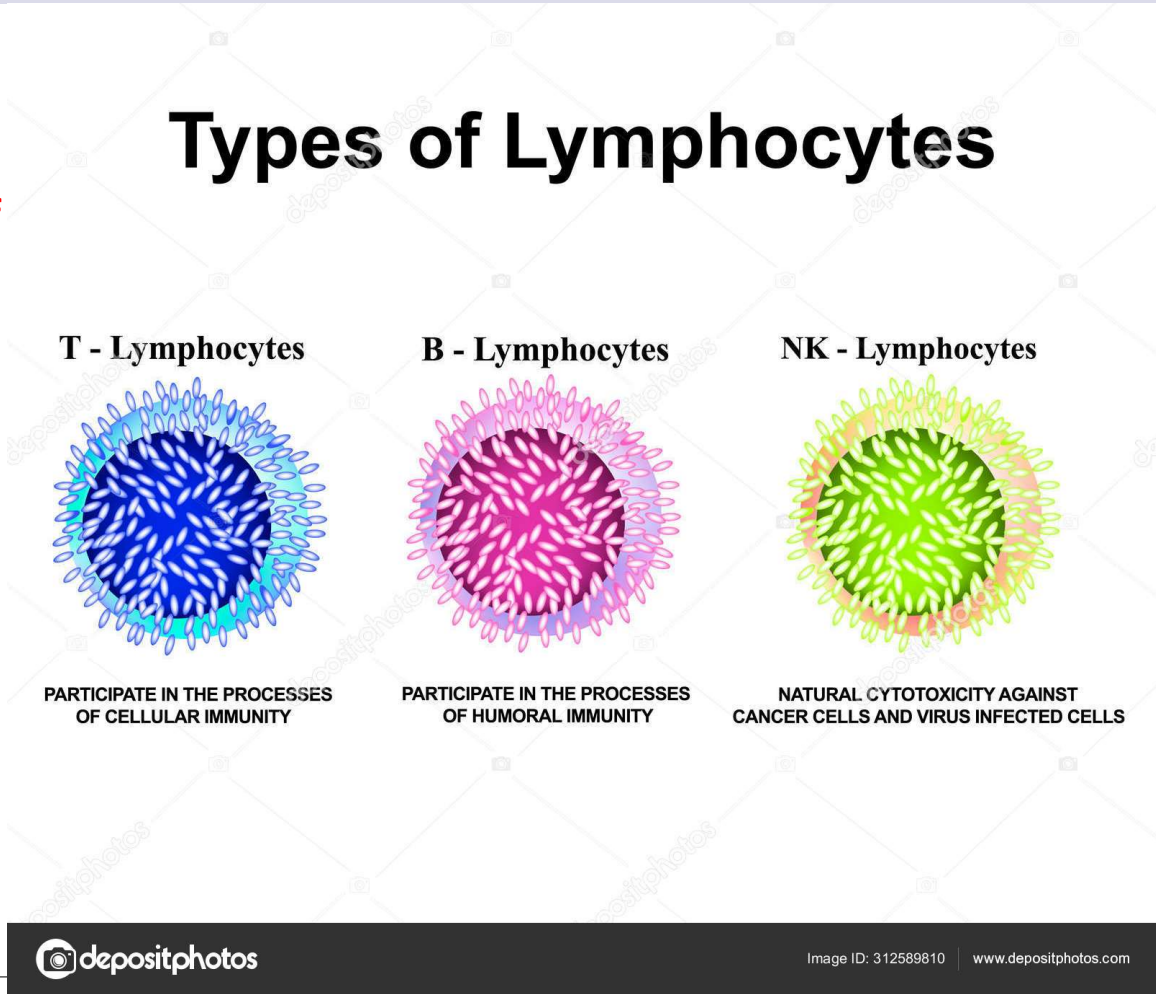
③ Antigen-activated immunocompetent lymphocytes circulate continuously in the bloodstream and lymph and throughout the lymphoid organs of the body.

Figure 21.8

Cells of the Adaptive Immune System

- Two types of lymphocytes
  - **B lymphocytes – oversee humoral immunity**
  - **T lymphocytes – non-antibody-producing cells that constitute the cell-mediated arm of immunity**
- Antigen-presenting cells (APCs):
  - **Do not respond to specific antigens**
  - **Play essential auxiliary roles in immunity**

- **Immature lymphocytes released from bone marrow are essentially identical**
- **Whether a lymphocyte matures into a B cell or a T cell depends on where in the body it becomes immunocompetent**
  - **B cells mature in the bone marrow**
  - **T cells mature in the thymus**



T - Lymphocytes

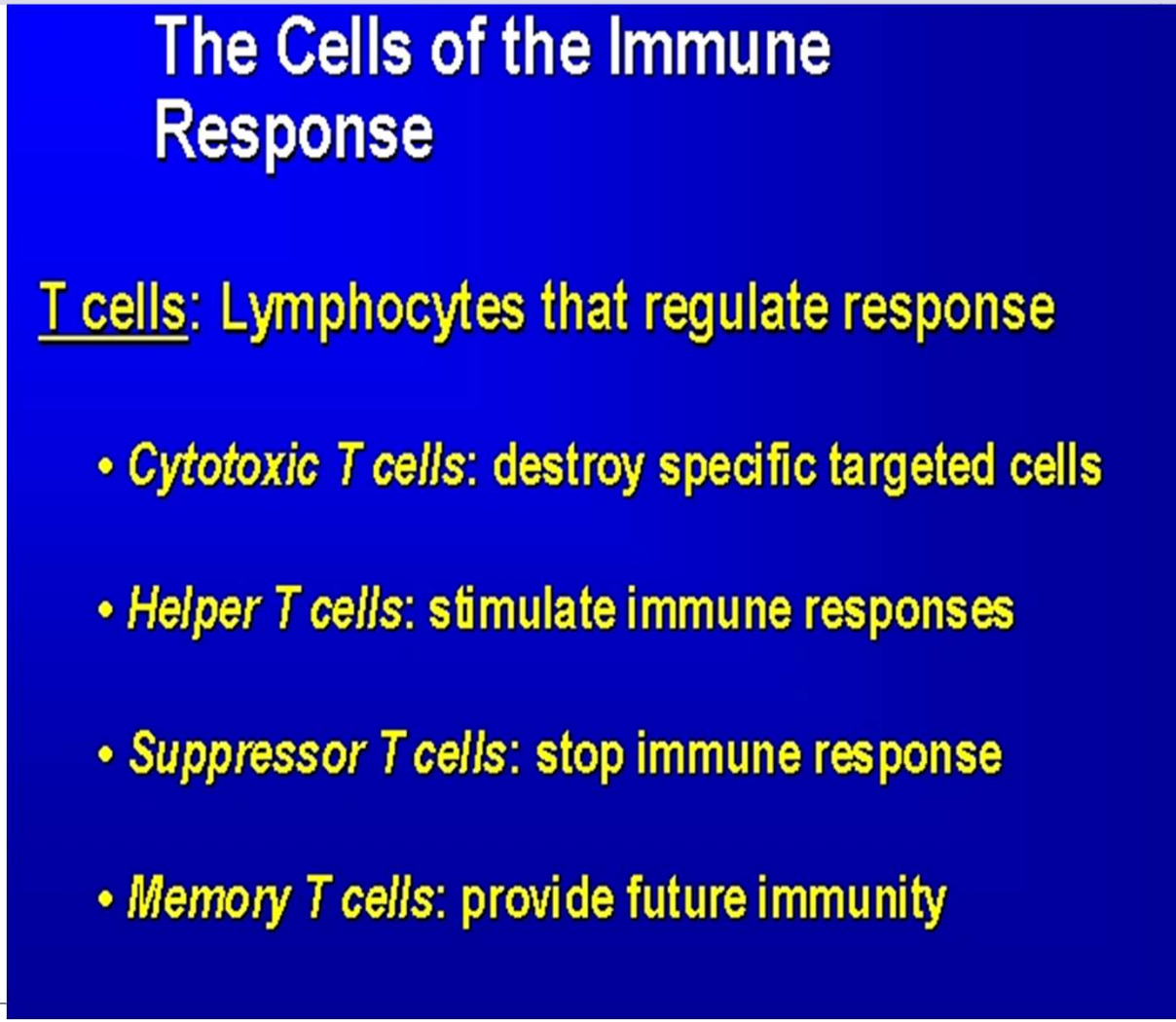
Subtype	Surface Marker	Function
Helper T (Th)	CD4+	Secrete cytokines; activate B cells, macrophages
Cytotoxic T (Tc)	CD8+	Kill virus-infected, tumor, or graft cells
Regulatory T (Treg)	CD4+, CD25+, FOXP3+	Suppress immune response, maintain tolerance

Antigen Recognition:

•Recognize **processed antigens** presented by **MHC molecules**:

- CD4+ → MHC class II
- CD8+ → MHC class I

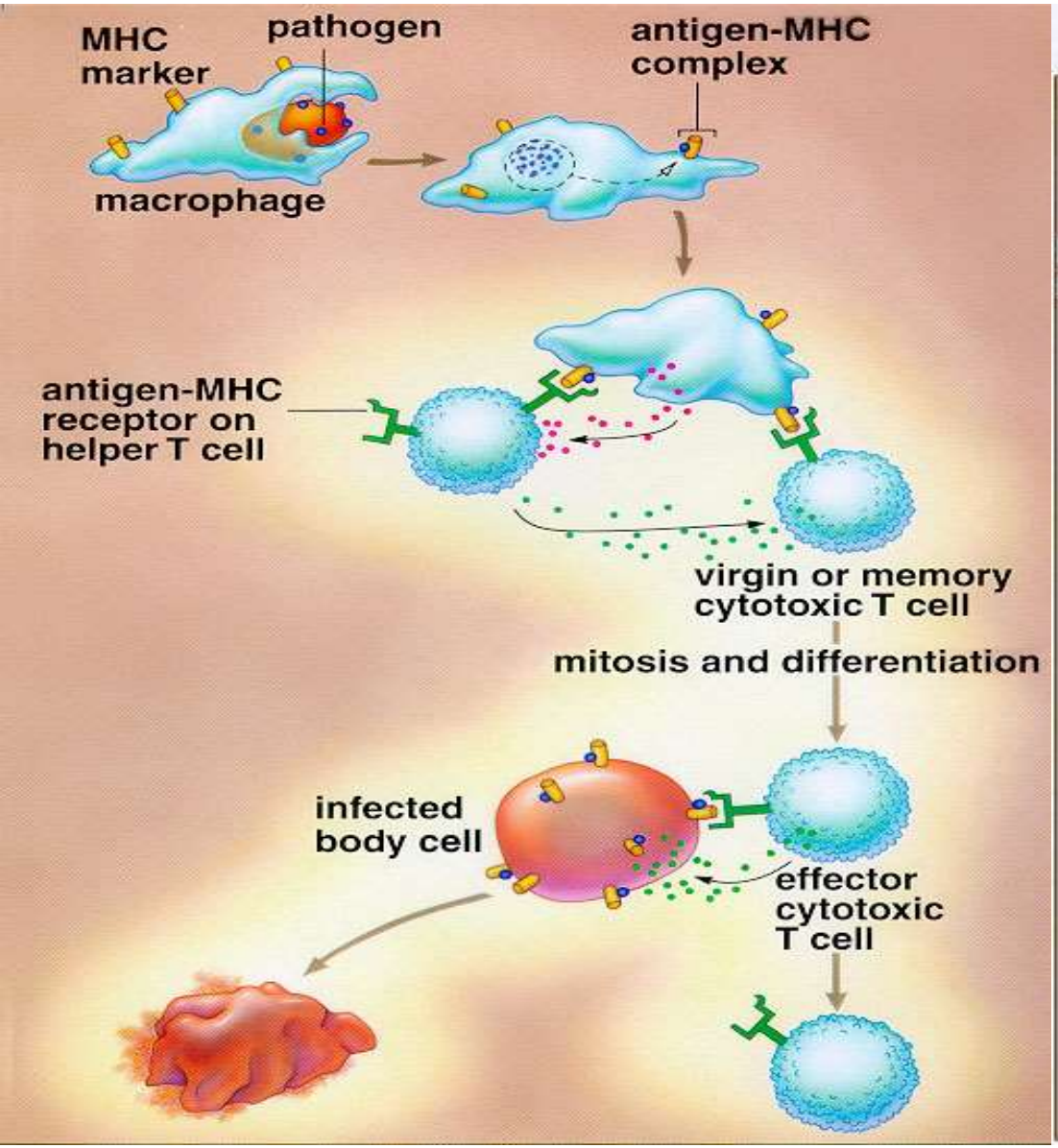
Major histocompatibility complex

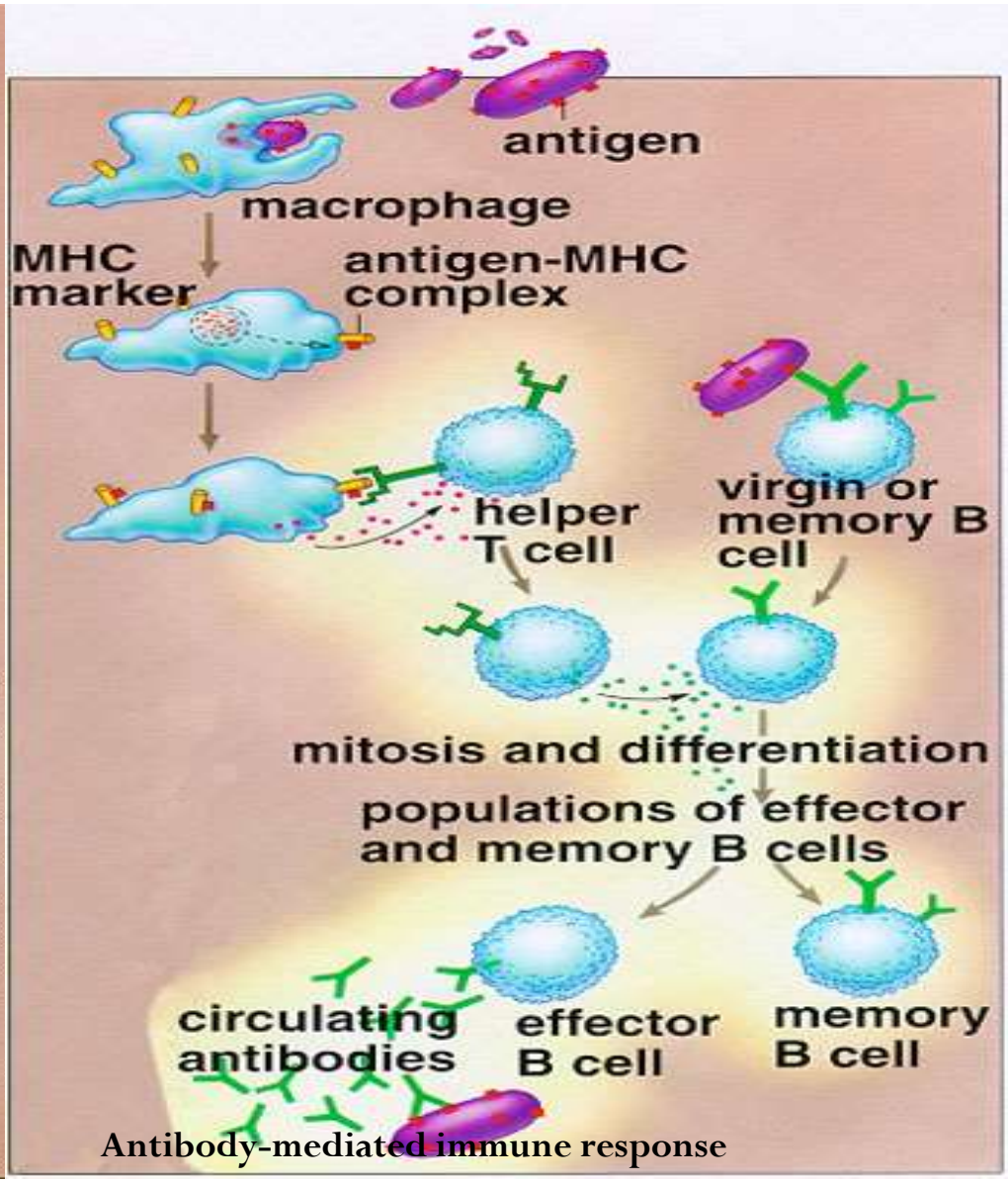


Self-Antigens: MHC Proteins

Are coded for by genes of the major histocompatibility complex (MHC) and are unique to an individual

- Our cells are dotted with protein molecules (self-antigens) that are not antigenic to us but are strongly antigenic to others
- One type, MHC proteins, mark a cell as self
- The two classes of MHC proteins are:
  - **Class I MHC proteins – found on virtually all body cells**
  - **Class II MHC proteins – found on certain cells in the immune response**





Antibody-mediated immune response

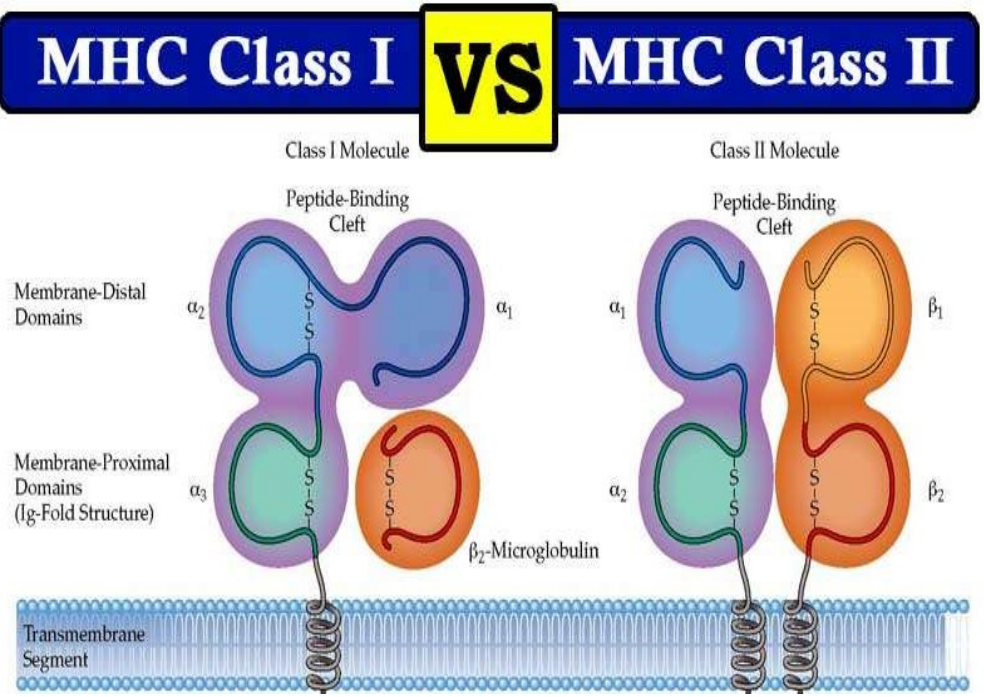
The **major histocompatibility complex =MHC**

Receptor Type	Present On	Interacts With
CD4	Lymphocytes	MHC II
CD8	Lymphocytes	MHC I
MHC I	General Body Cells	CD8
MHC II	Phagocytes	CD4

HIV infects primarily vital cells in the human immune system such as helper T cells (to be specific, $CD4^+$ T cells), macrophages, and dendritic cells

Self-Antigens: MHC Proteins=Major Histocompatibility Complex

Are coded for by genes of the major histocompatibility complex (MHC) and are unique to an individual



- Our cells are dotted with protein molecules (self-antigens) that are not antigenic to us but are strongly antigenic to others
- One type, MHC proteins, mark a cell as self
- The two classes of MHC proteins are:
  - **Class I MHC proteins – found on virtually all body cells**
  - **Class II MHC proteins – found on certain cells in the immune response**

MHC class I	MHC class II
Comprised of an MHC-encoded a chain and a b2-microglobulin chain	Comprised of MHC-encoded a and b chains
Present on most cells	Present only on antigen-presenting cells
Bind endogenous antigens synthesized in a cell	Binds exogenous antigens
Present antigen to cytotoxic T cell lymphocytes	Present antigen to helper T cell lymphocytes
Bind CD8 adhesion molecules on cytotoxic T cells	Bind CD4 adhesion molecules on helper T cells
Presence of foreign or over-abundant antigens targets cell for destruction	Presence of foreign antigens induces antibody production, and attracts immune cells to area of infection

Class-I vs. Class-II MHC molecule

Feature	Class I MHC	Class II MHC
Polypeptide chains	a (44–47 kD) b_2-Microglobulin (12 kD)	a (32–34 kD) b (29–32 kD)
Locations of polymorphic residues	a1 and a2 domains	a1 and b1 domains
Binding site for T cell coreceptor	a3 region binds CD8	b2 region binds CD4
Size of peptide-binding cleft	Accommodates peptides of 8-11 residues	Accommodates peptides of 10-30 residues or more
Nomenclature		
Human	HLA-A, HLA-B, HLA-C	HLA-DR, HLA-DQ, HLA-DP
Mouse	H-2K, H-2D, H-2L	I-A, I-E

Abbreviations: HLA, human leukocyte antigen; MHC, major histocompatibility complex

HLA VERSUS MHC

Human Leukocyte Antigen

HLA	MHC
A gene complex encoding the major histocompatibility complex (MHC) proteins in humans	A set of cell surface proteins essential for the acquired immune system to recognize foreign molecules in vertebrates, which in turn determines histocompatibilit
Form of MHC complex that occurs in humans	Occurs in all vertebrates
Class I HLA genes are HLA-A, HLA-B, and HLA-C and class II HLA genes are HLA-D	Three classes of MHC complex are Class I, II, and III

B Lymphocytes (B cells)

- B cells are a type of **adaptive immune cell** that **recognizes antigens** and produces **antibodies**, forming the basis of **humoral immunity**.

◆ Origin & Maturation:

•Develop and mature in **bone marrow**

•Activated in **secondary lymphoid organs** (e.g., lymph nodes, spleen)

◆ Function:

•Differentiate into:

- **Plasma cells** → secrete antibodies (IgM, IgG, IgA, IgE, IgD)
- **Memory B cells** → rapid response on re-exposure

◆ Antigen Recognition:

•Recognize **native (unprocessed)** antigens via **B cell receptors (BCR)**

◆ CD Markers:

•**CD19**, **CD20**, **CD21**, **CD79**

Stage	Location	Event
Origin	Bone marrow	Derived from hematopoietic stem cells
Maturation	Bone marrow	Rearrangement of **immunoglobulin (Ig) genes** → express **B cell receptor (BCR)**
Naïve B cells	Blood/lymphoid tissues	Travel to lymphoid organs to encounter antigen

Marker	Function
CD19, CD20, CD21	Surface markers (targeted in therapy e.g. rituximab → CD20)
CD40	Co-stimulation with T helper cells (CD40–CD40L interaction)
MHC Class II	Present antigen to CD4+ T cells
Surface IgM, IgD	Antigen receptors (BCR) in naïve B cells

B Lymphocytes (B cells)

Function of B Cells

1.Antigen Recognition

1. BCR binds to **intact (native)** antigen directly (no need for MHC).

2.Antigen Presentation

1. **Internalizes antigen, processes it, and presents via MHC II to CD4+ T helper cells.**

3.Activation

1. Requires 2 signals:
    1. BCR + antigen
    2. CD40 (on B cell) + CD40L (on Th cell) + cytokines

4.Differentiation

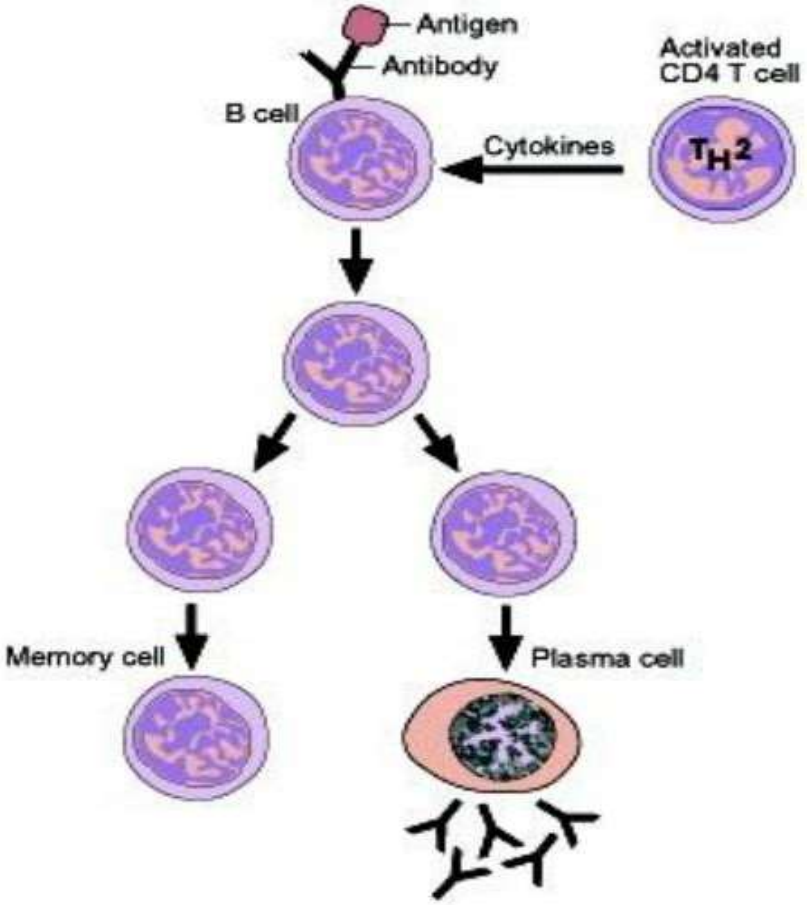
1. **Plasma cells: Produce and secrete antibodies (IgM, IgG, IgA, IgE).**
2. **Memory B cells: Long-lived cells for rapid response upon re-exposure.**

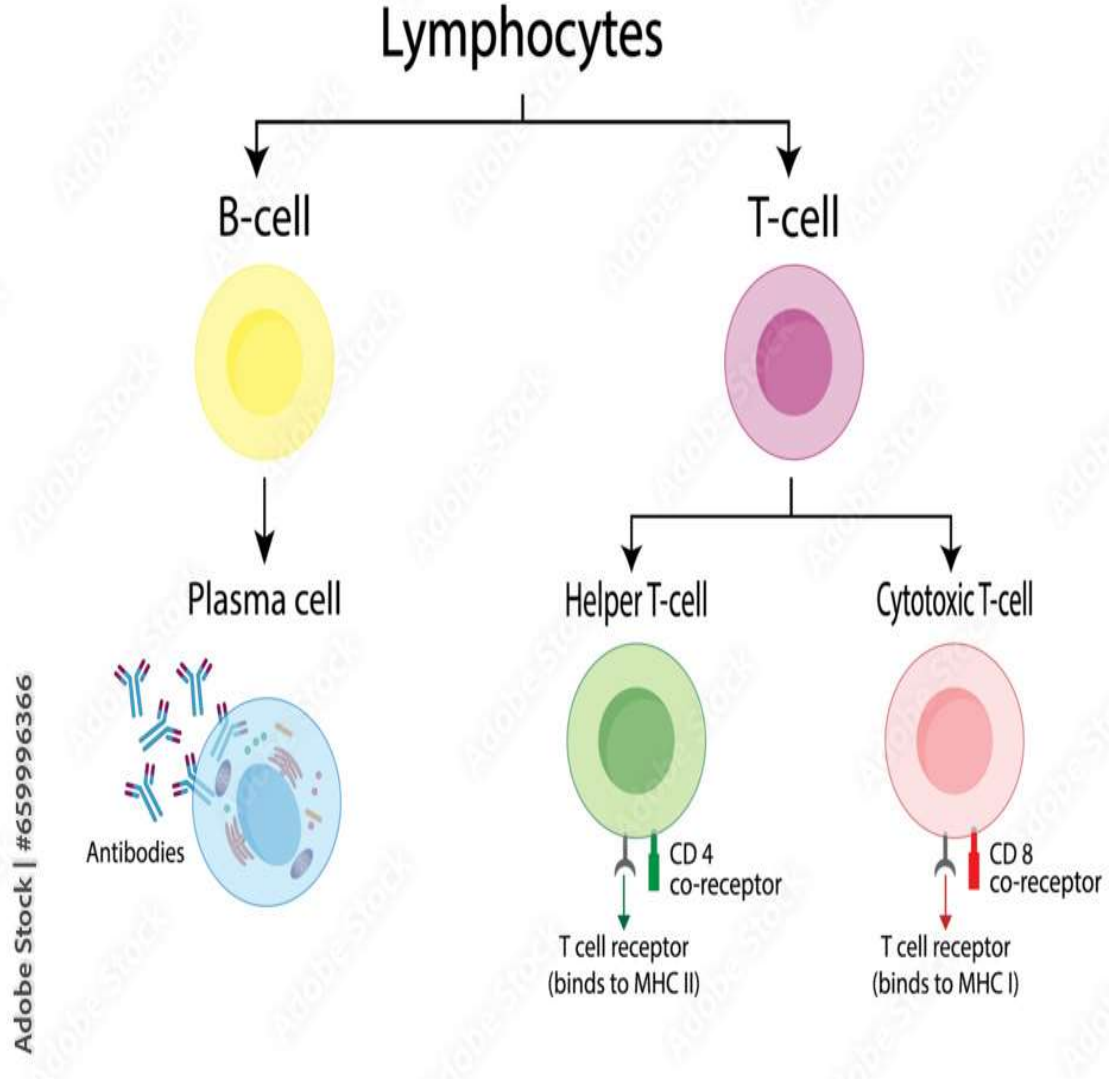
- **"B cells see whole bugs, T cells see tiny bits."**
- B cells recognize **intact antigen**. T cells need **processed peptides** via **MHC**.
- "B for Bone marrow, Bugs (intact), and Building antibodies"

Antibodies Produced

Antibody	Function	Location
IgM	First antibody made; pentameric; complement activation	Blood
IgG	Most abundant; crosses placenta	Blood, tissues
IgA	Mucosal protection	Secretions (saliva, tears, GI)
IgE	Allergy, parasite defense	Tissues (bound to mast cells)
IgD	Function unclear; marker of naïve B cells	Blood, B cell surface

B -Lymphocytes





Natural Killer (NK) Cells

- **Can lyse and kill cancer cells and virus-infected cells**
- **Are a small, distinct group of large granular lymphocytes**
- **React nonspecifically and eliminate cancerous and virus-infected cells**
- **Secrete potent chemicals that enhance the inflammatory response**
  - Form in bone marrow, circulate in blood, and accumulate in secondary lymphatic structures
    - Perform **immune surveillance—**patrol the body, detect unhealthy cells

Function:

•Kill virus-infected and tumor cells **without prior sensitization**

•Part of **innate immunity**

•Release **perforin and granzymes**

•Kill their target cells by releasing perforins and other cytolytic chemicals

Unique Features:

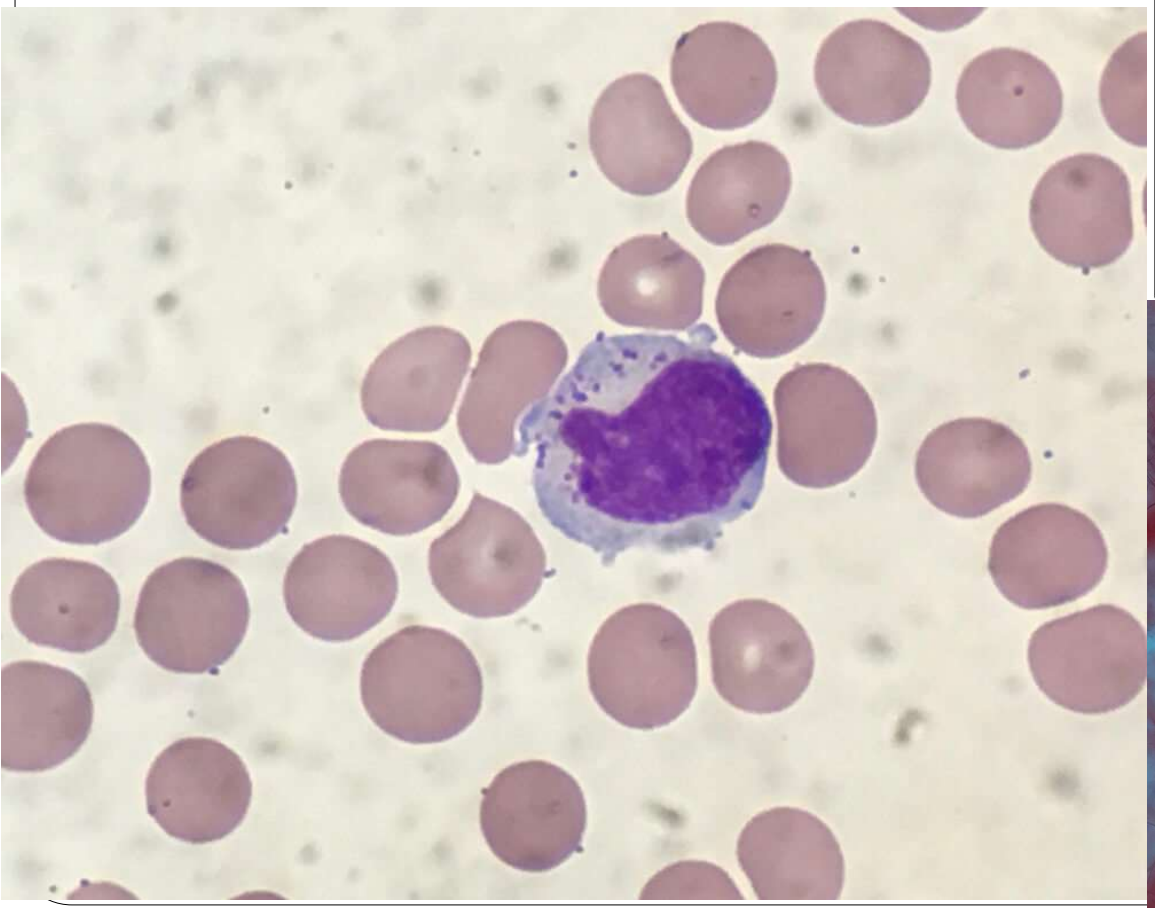
•Recognize cells lacking MHC I (often downregulated in tumors/viruses)

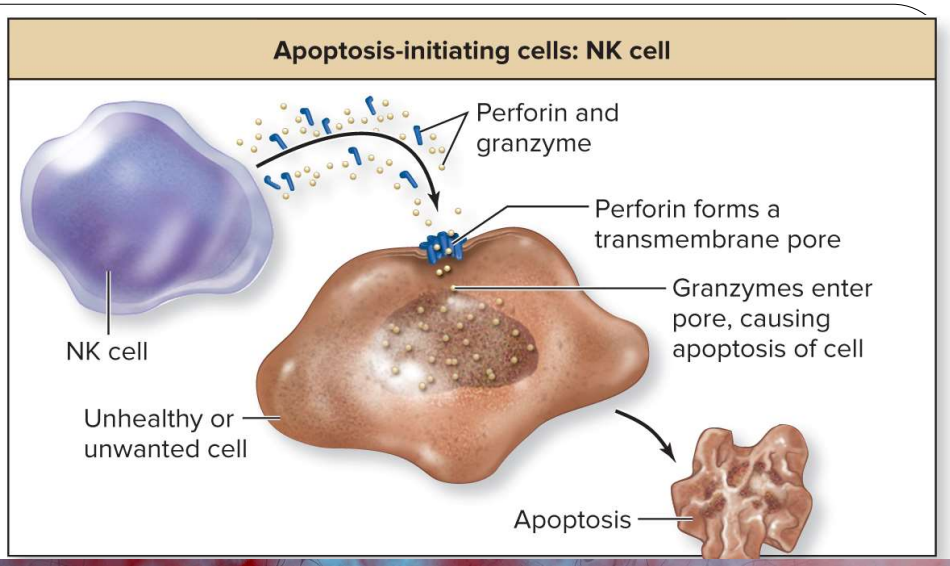
•No antigen-specific receptors like BCR or TCR

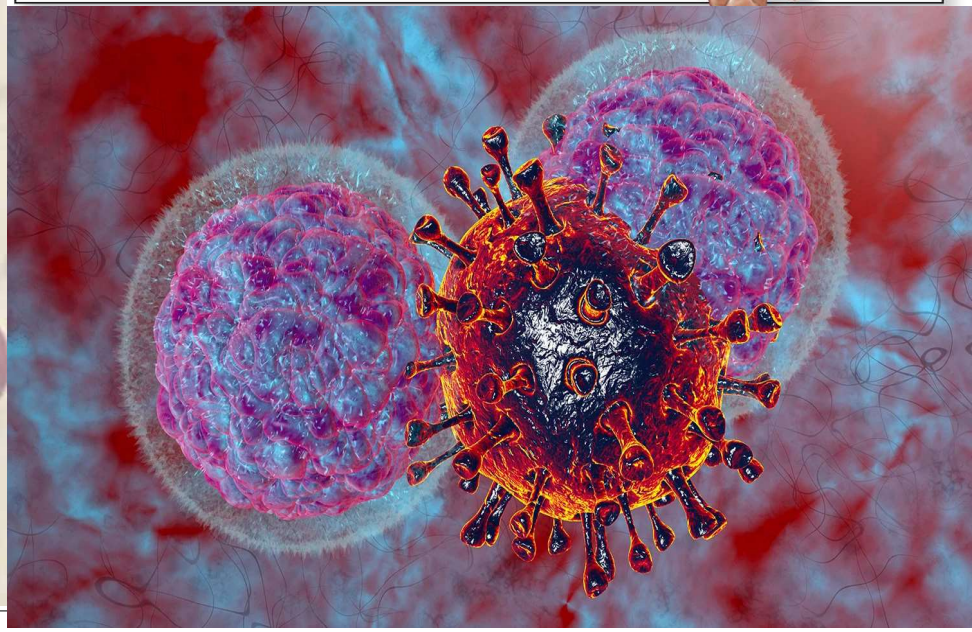
Surface Markers:

•CD16, CD56

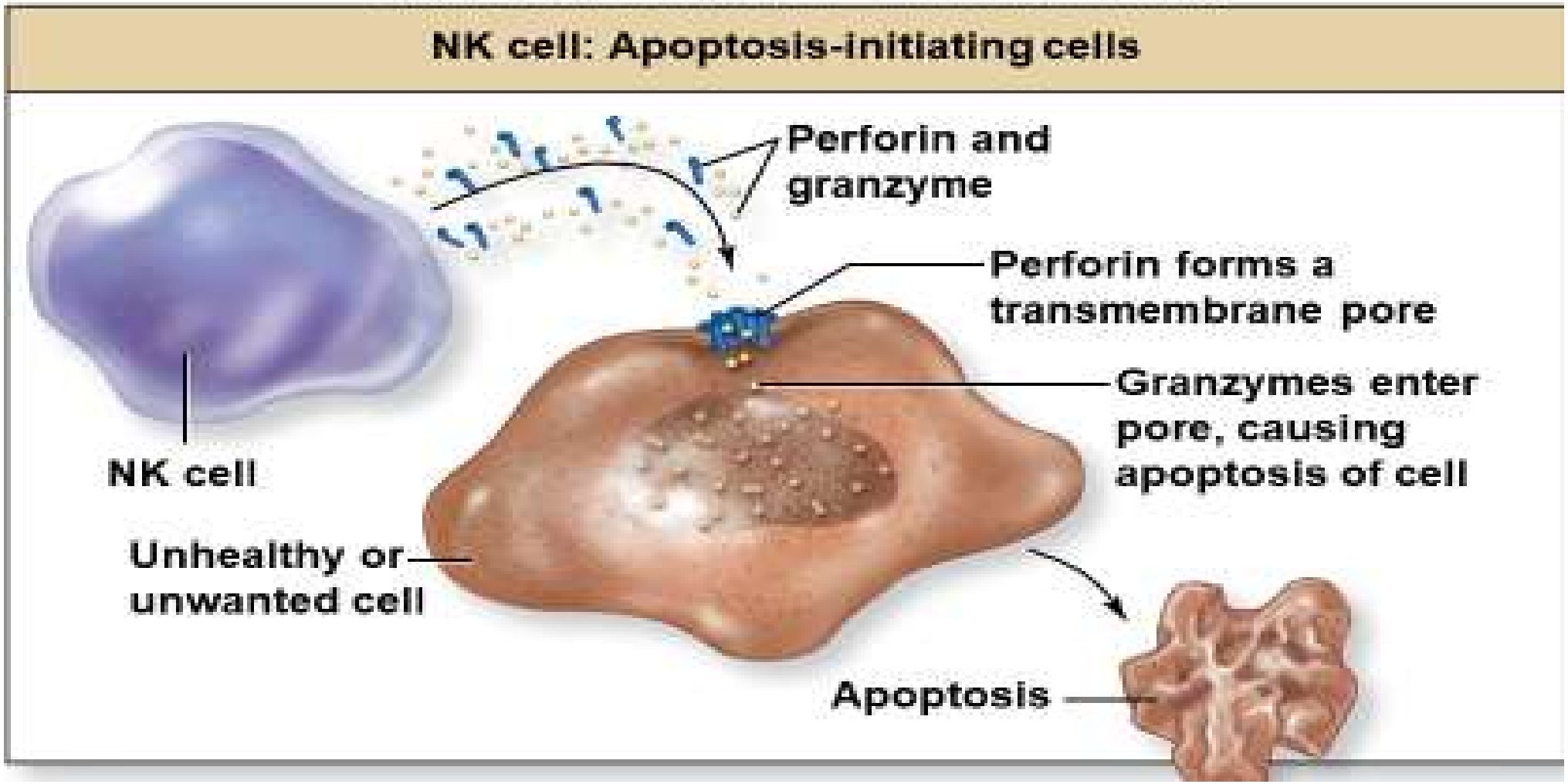
Apoptosis-Initiating Cells: NK Cell







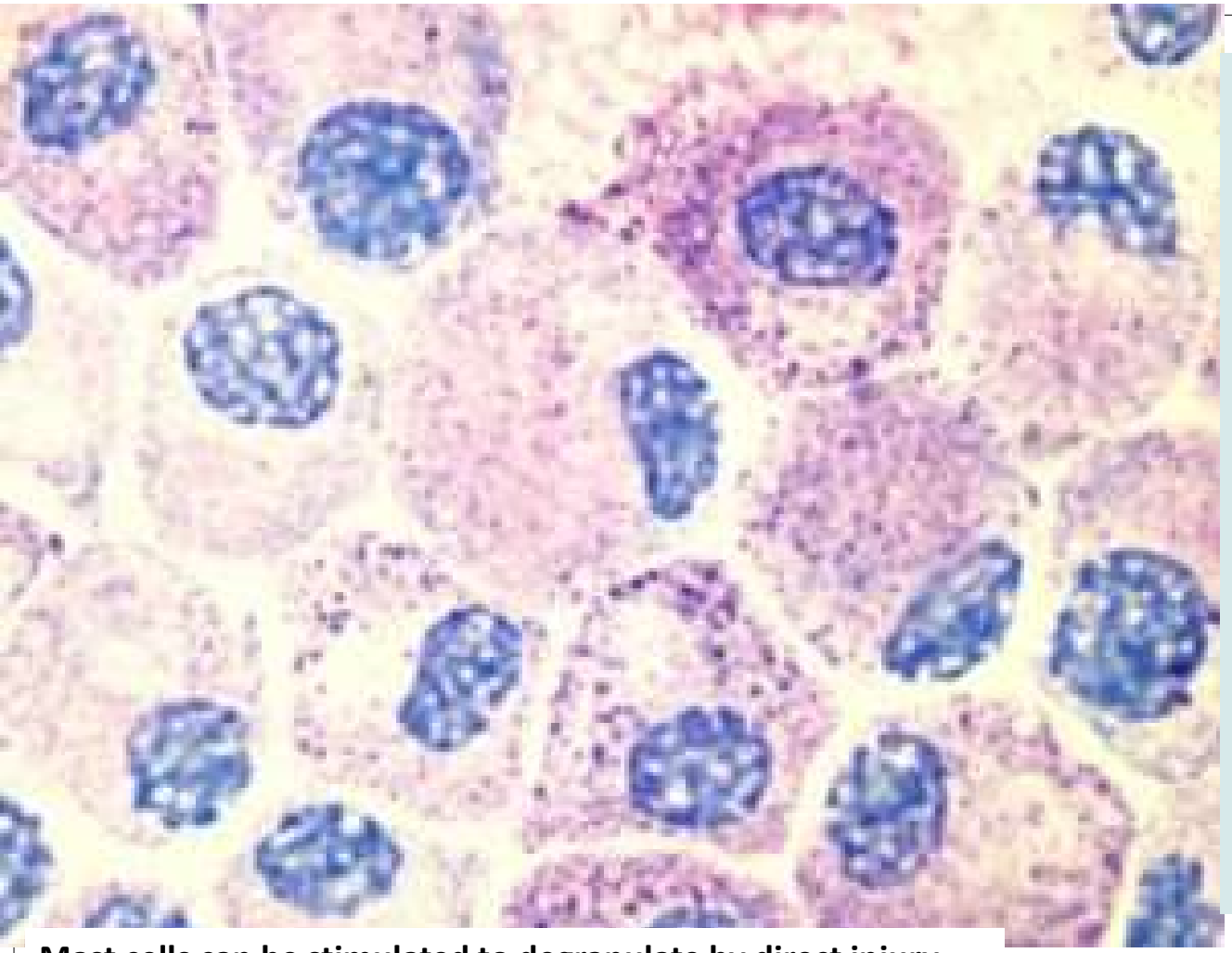
NK Cell: Apoptosis-Initiating Cells



	Types of Lymphocytes	
Cell Type	**Function**	**Type of Antigen Response**
T-LYMPHOCYTE		
Helper T-lymphocyte	Initiates and oversees the immune response	Responds to a single antigen
Cytotoxic T-lymphocyte	Directly kills foreign cells; must be activated by a helper T-lymphocyte first	Responds to a single antigen
Memory T-lymphocyte	A type of cytotoxic T-lymphocyte that has already killed; patrols the body looking for the same antigen again	Responds to a single antigen
Suppressor T-lymphocyte	Helps "turn off" the immune response once it has been activated	Responds to a single antigen
B-LYMPHOCYTE		
Plasma cell	Produces and secretes antibodies	Responds to a single antigen
Memory B-lymphocyte	Remembers an initial antigen attack and mounts a faster, more efficient response should the same antigen type attack again	Responds to a single antigen
NK (NATURAL KILLER) CELL		
NK (natural killer) cell	Kills a wide variety of infected and cancerous cells	Responds to multiple antigens

Summary of Nonspecific Body Defenses (*continued*)

CATEGORY/ASSOCIATED ELEMENTS	PROTECTIVE MECHANISM
SECOND LINE OF DEFENSE: INNATE, CELLULAR AND CHEMICAL DEFENSES	
Phagocytes	Engulf and destroy pathogens that breach surface membrane barriers; macrophages also contribute to immune response
Natural killer (NK) cells	Promote apoptosis (cell suicide) by direct cell attack against virus-infected or cancerous body cells; do not require specific antigen recognition; do not exhibit a memory response
Inflammatory response	Prevents spread of injurious agents to adjacent tissues, disposes of pathogens and dead tissue cells, and promotes tissue repair; chemical mediators released attract phagocytes (and immunocompetent cells) to the area
Antimicrobial proteins	
▪ Interferons (α, β, γ)	Proteins released by virus-infected cells and certain lymphocytes that protect uninfected tissue cells from viral takeover; mobilize immune system
▪ Complement	Lyses microorganisms, enhances phagocytosis by opsonization, and intensifies inflammatory and immune responses
Fever	Systemic response initiated by pyrogens; high body temperature inhibits microbial multiplication and enhances body repair processes



Mast cells can be stimulated to degranulate by direct injury (e.g. physical or chemical), cross-linking of Immunoglobulin E (IgE) receptors, or by activated complement proteins

A **mast cell** (or *mastocyte*)

- is a resident cell of several types of tissues and contains many granules rich in histamine and heparin.
- Although best known for their role in **allergy and anaphylaxis**,
- Mast cells play an important protective role as well,being intimately involved in **wound healing and defense against pathogens**

- Prominent near the boundaries between the outside world and the internal milieu, such as the
  - **skin**
  - **mucosa of the lungs and digestive tract**
  - **as well as in the mouth**
  - **conjunctiva and nose**

Basophils / Mast Cells

These cells are filled with mediators of inflammation:

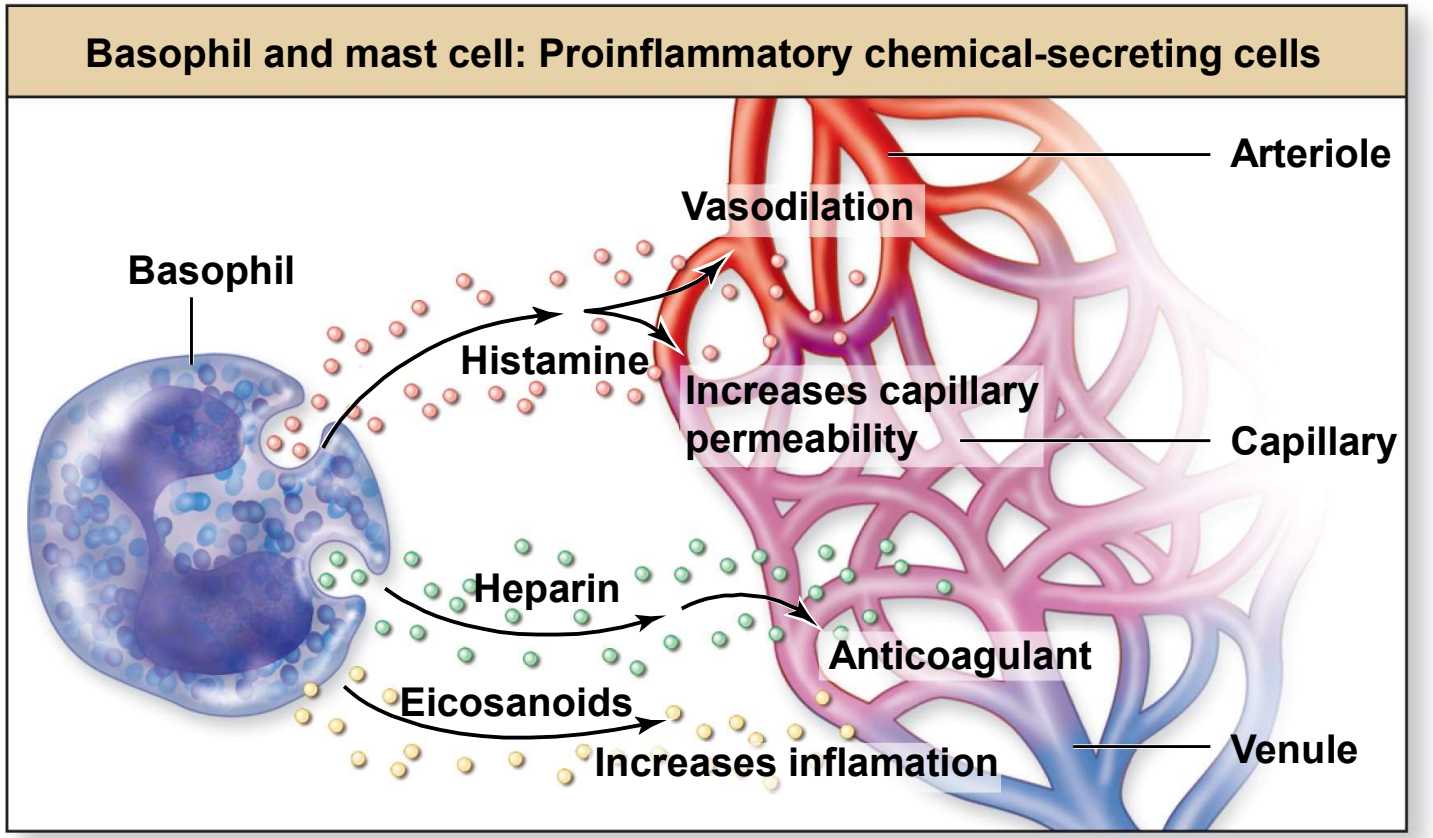
- **histamine** - causes vasodilation (blood vessels dialate) and bronchoconstriction (because it causes smooth muscles to constrict)

  heparin - inhibits blood coagulation

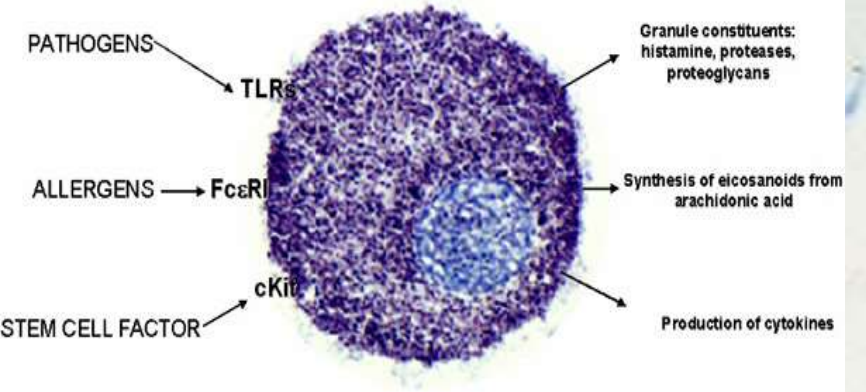
  leukotrienes - prolonged constriction of smooth muscles, pain

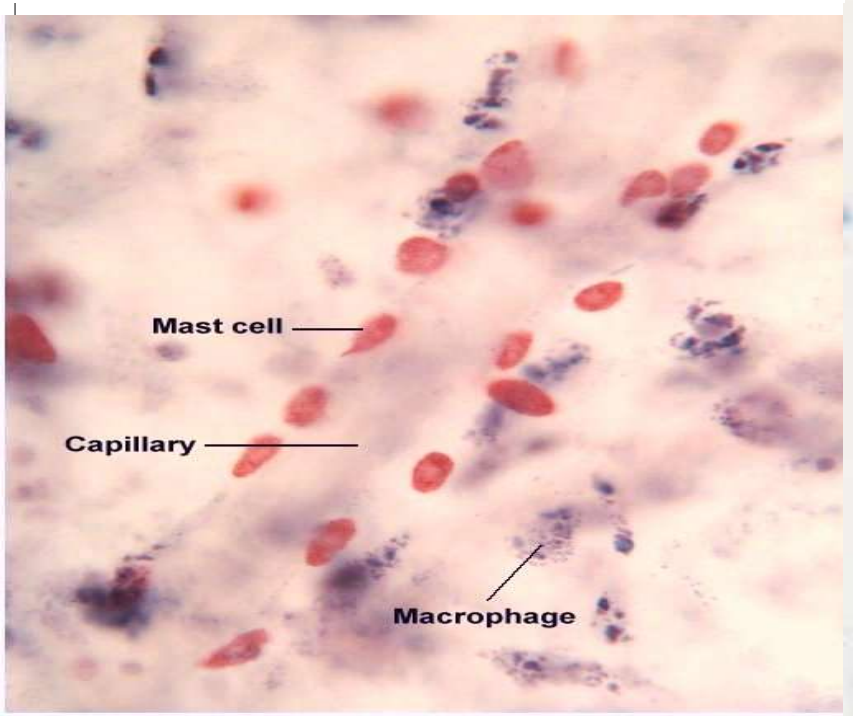
  prostaglandins - smooth muscle constriction and vasodilation, pain

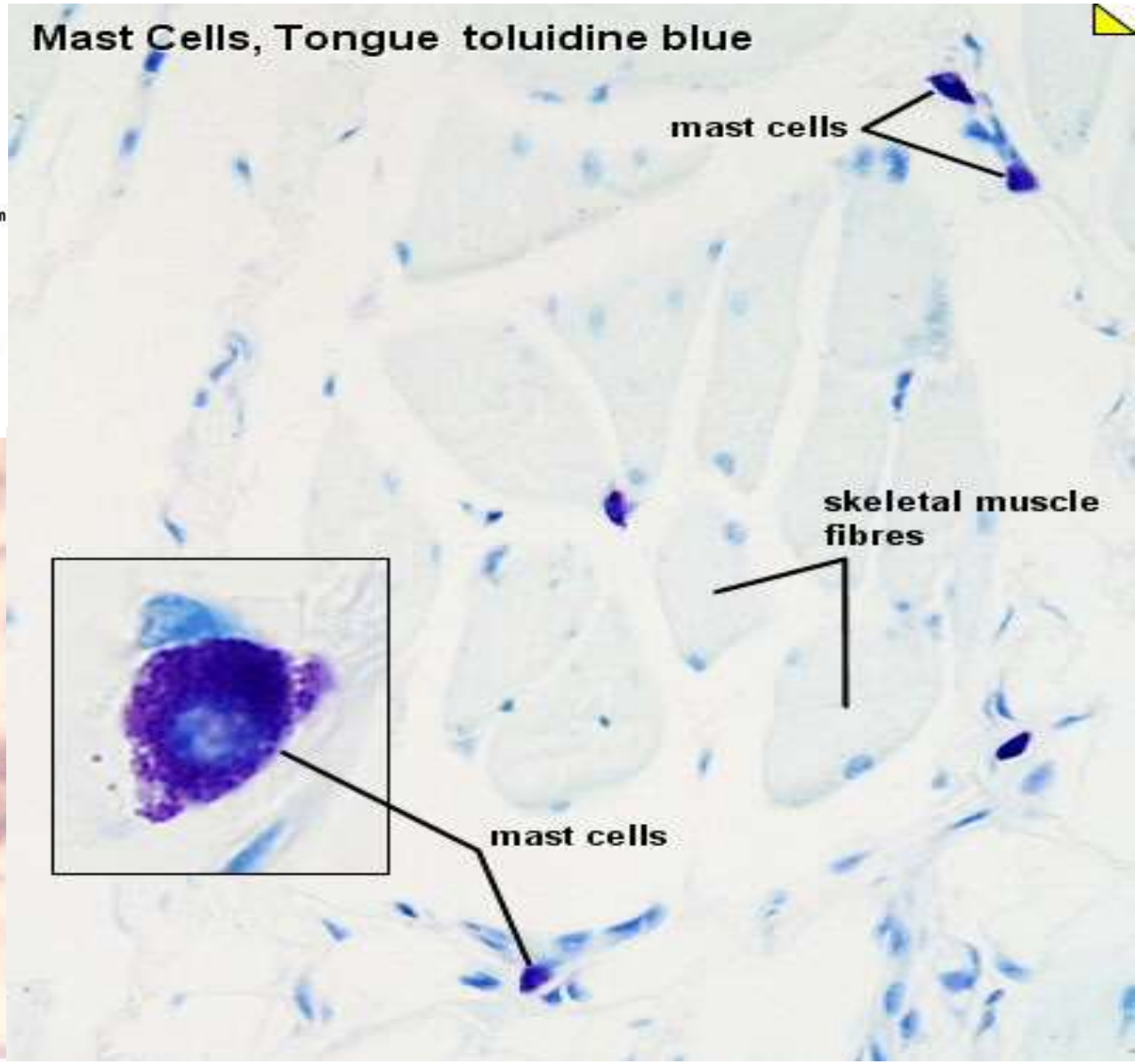
Basophil and Mast Cell: Proinflammatory Chemical-Secreting Cells



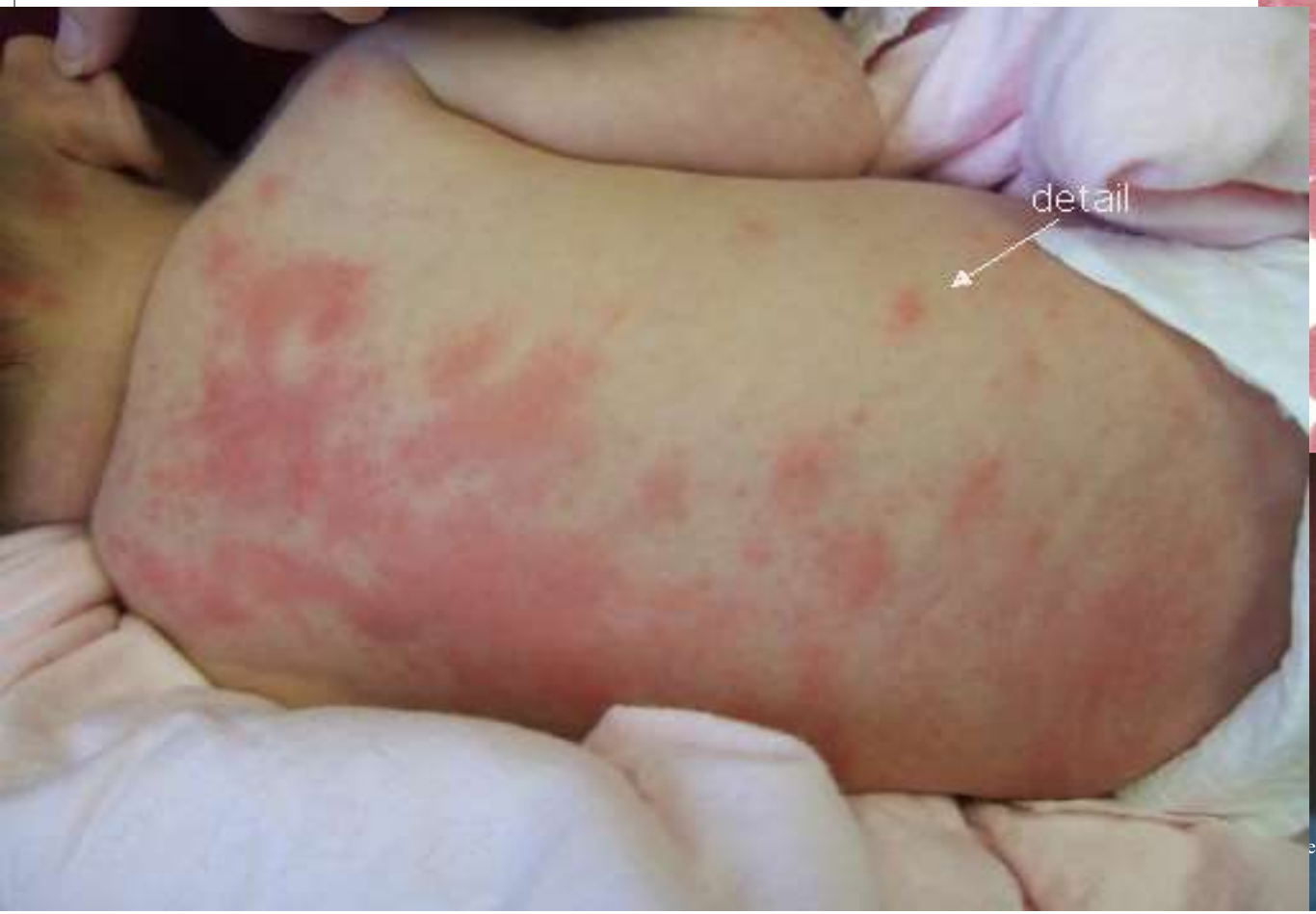
(b)

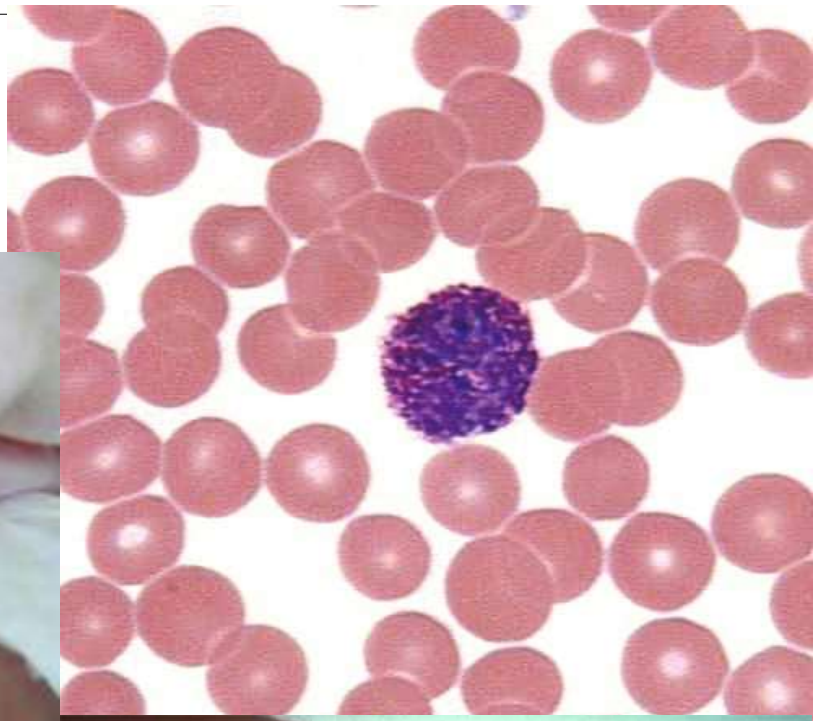

PATHOGENS
TLRs
ALLERGENS
FcεRI
cKit
STEM CELL FACTOR
Granule constituents: histamine, proteases, proteoglycans
Synthesis of eicosanoids from arachidonic acid
Production of cytokines

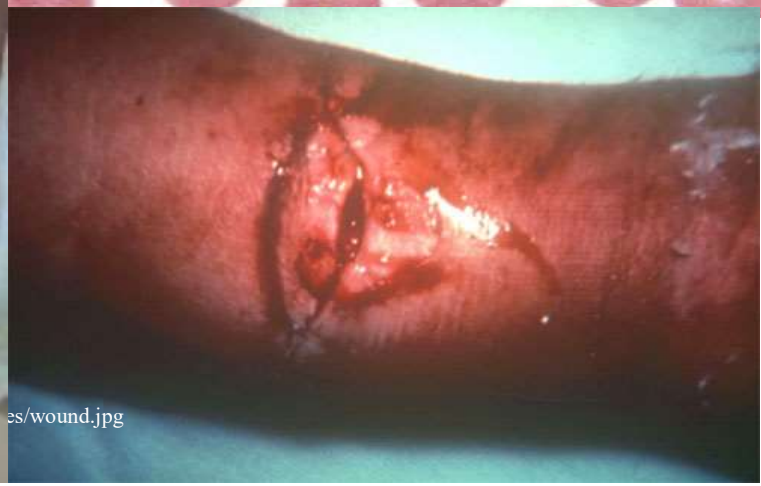

Mast cell
Capillary
Macrophage

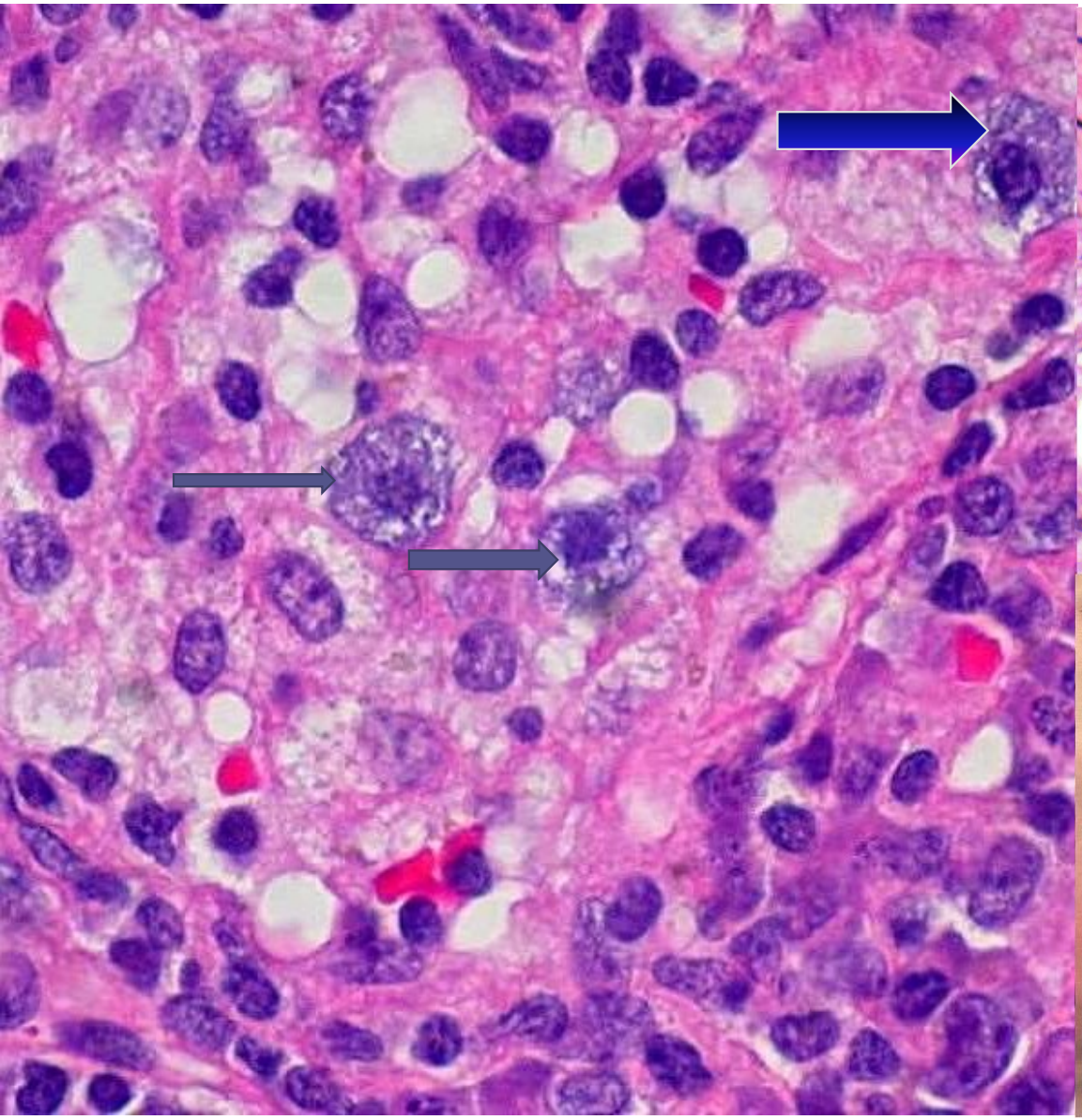

Mast Cells, Tongue toluidine blue
mast cells
skeletal muscle fibres
mast cells

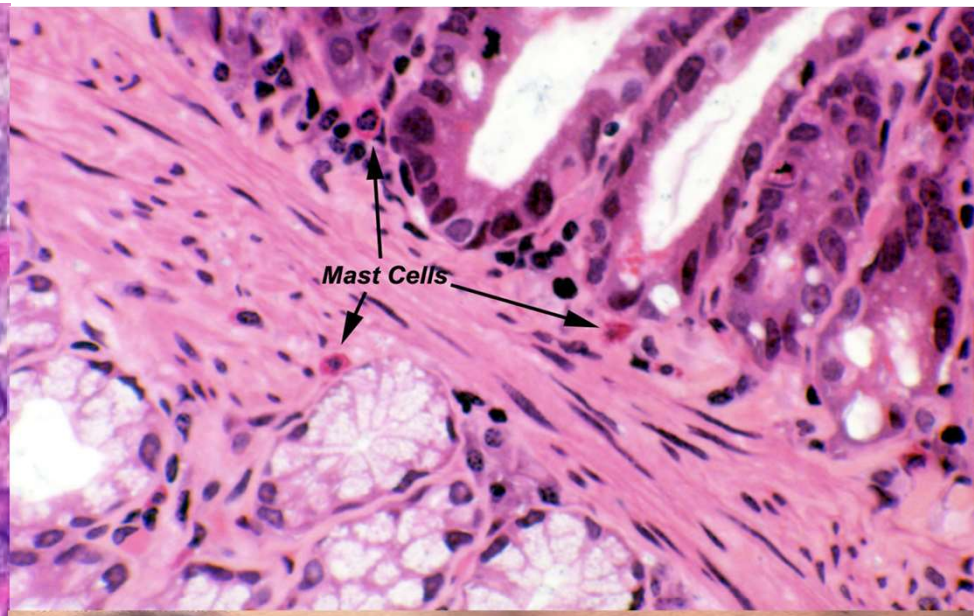
- Mast cells /basophils
  - release histamine that dilates blood vessels
  - causes redness [erythema], swelling [edema], and heat

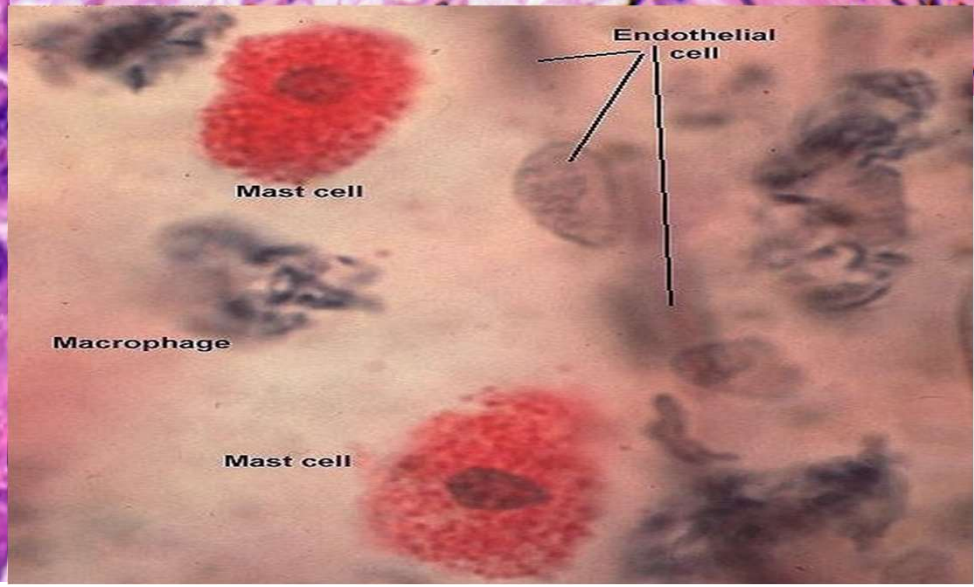









Mast Cells


Endothelial cell
Mast cell
Macrophage
Mast cell

Nonspecific Internal Defenses: Cells

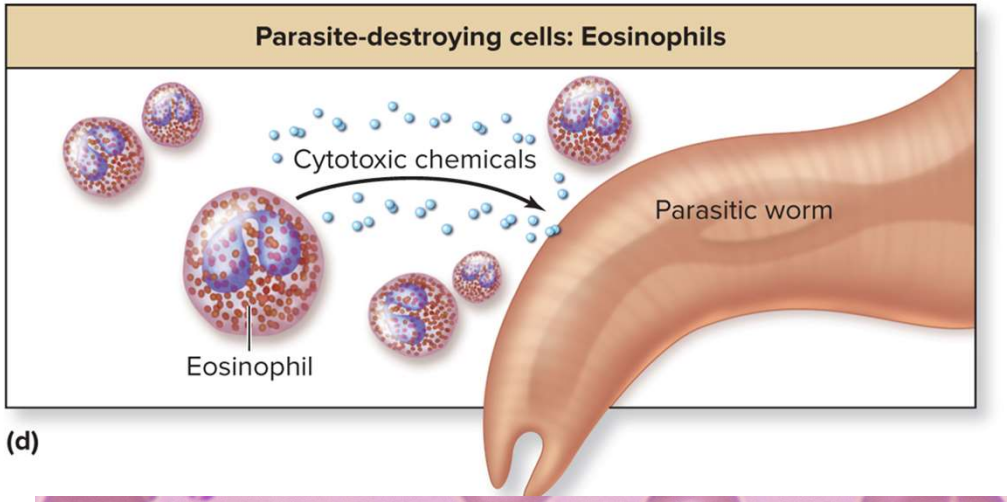
Eosinophils

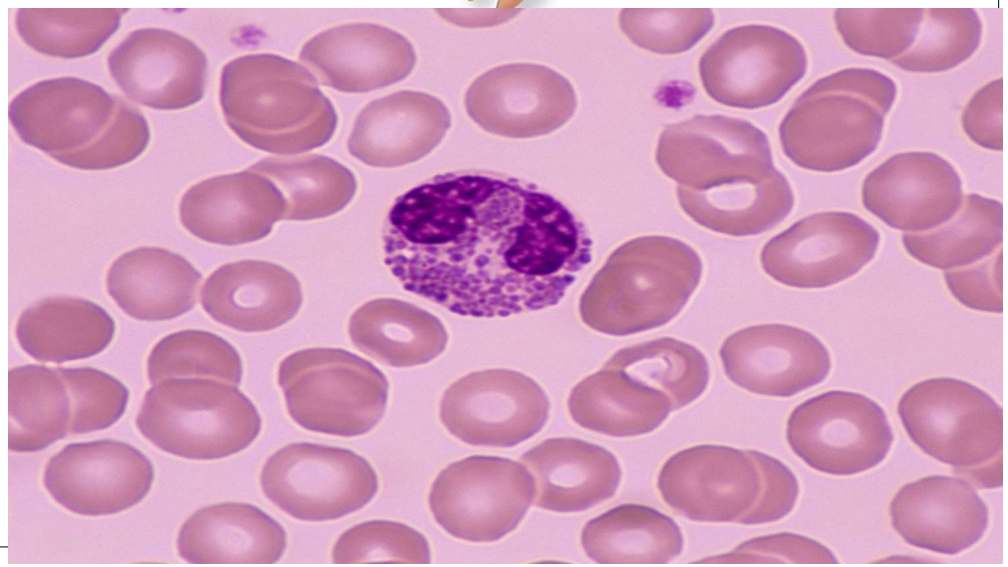
Eosinophils attack multicellular parasites

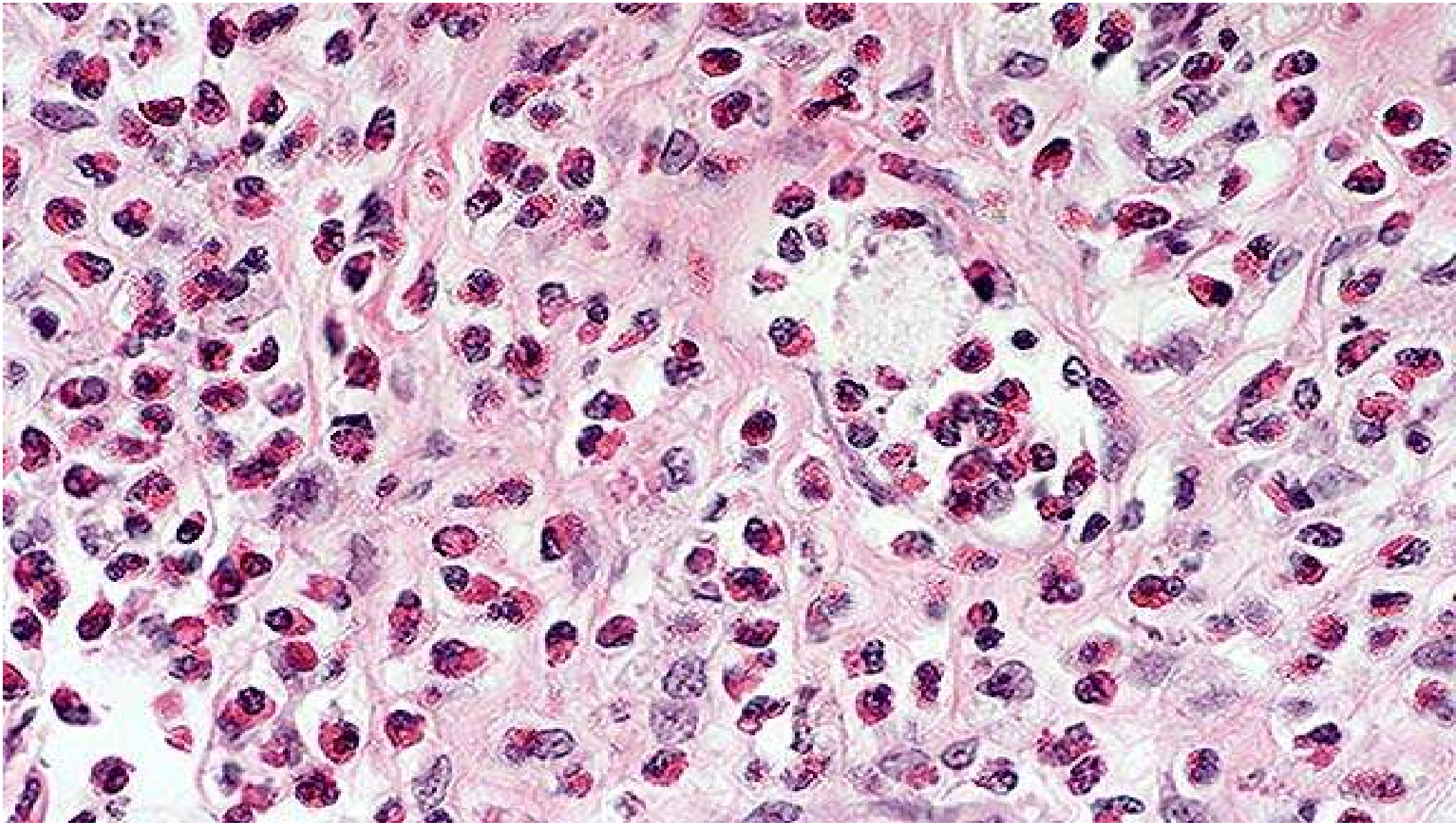
- Degranulate, release enzymes and other toxic substances
  - Can release proteins that form transmembrane pores in parasite's cells
- Participate in immune responses of allergy and asthma
- Engage in phagocytosis of antigen-antibody complexes

Cells of innate immune system recognize microbes as foreign because of receptors

- Pattern recognition receptors (toll-like receptors) on cell surface bind to patterns on microbe surface

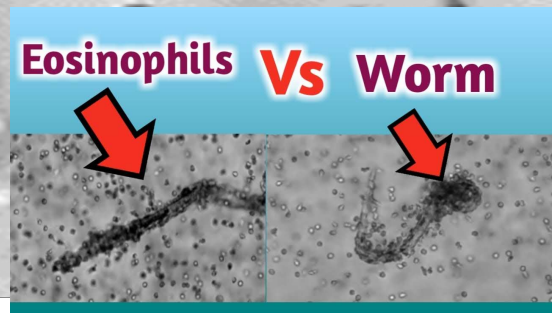


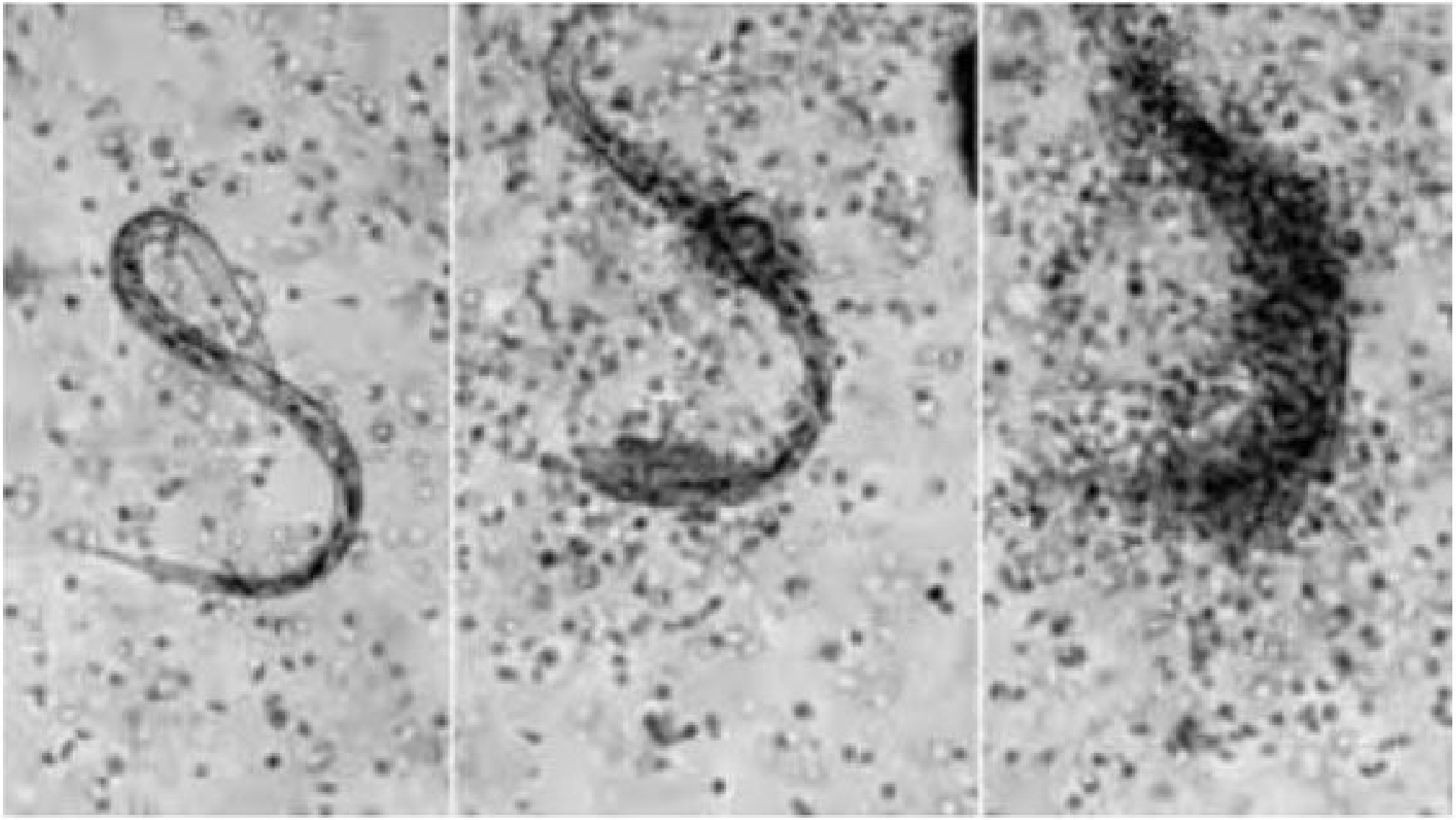




https://www.youtube.com/watch?v=wDvxLSA6kN4&ab_channel=AhmedRamzy

EOSINOPHIL EATING A PARASITE





Cells of Immune Response

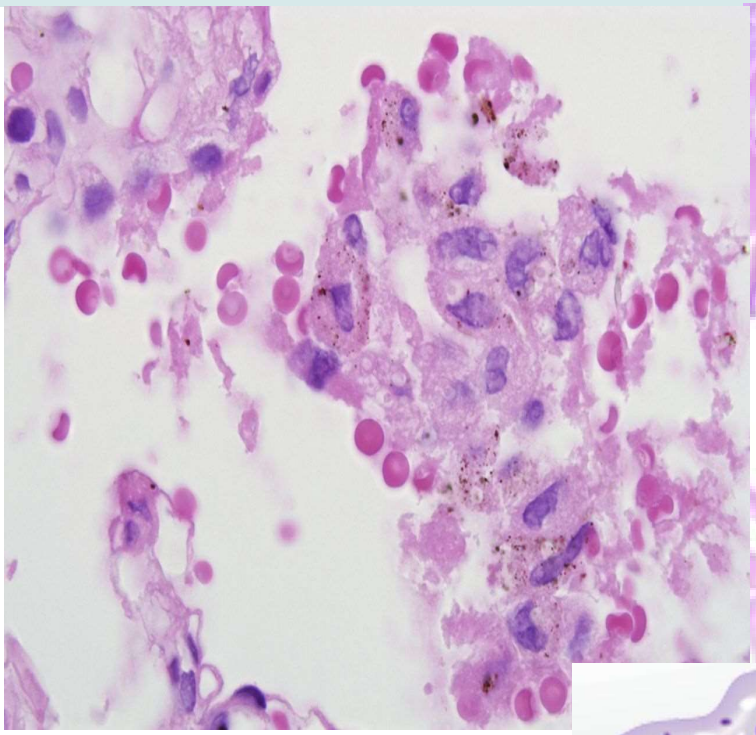
Non hematopoietic cells:

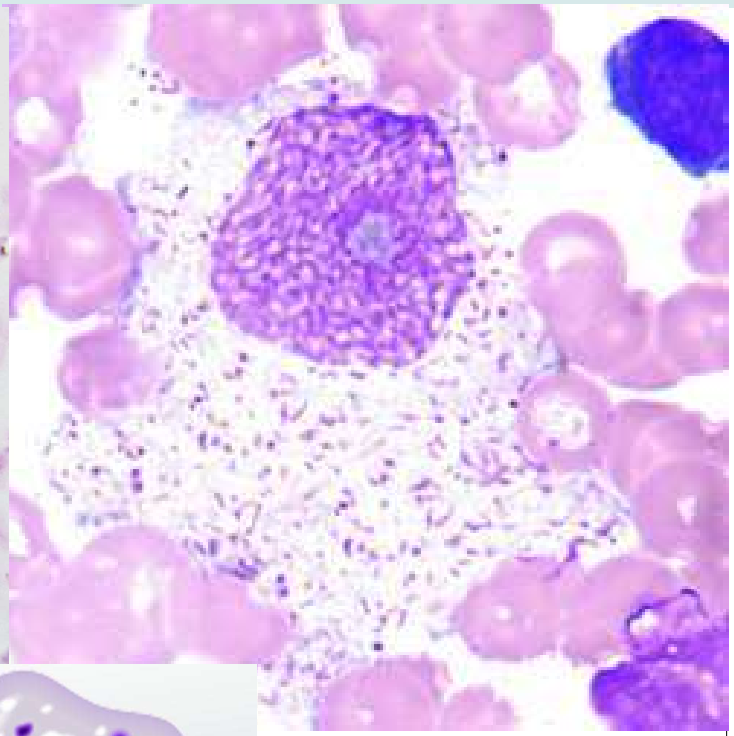
- **Dentritic cells**
- **Astrocytes and**
- **Endothelial cells**

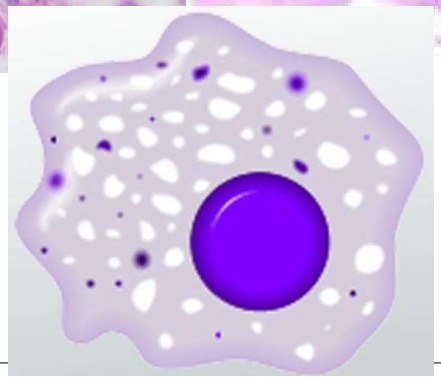
Function : antigen presentation

MACROPHAGES

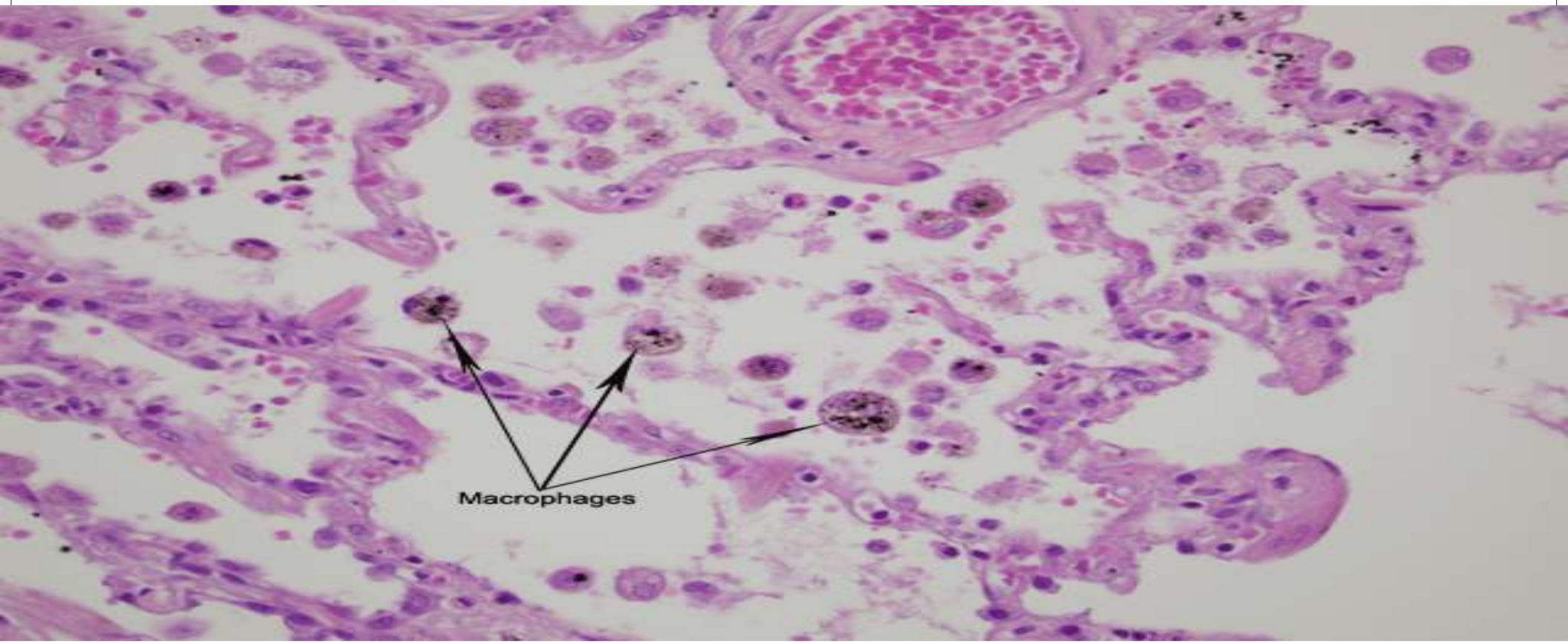
- DUST CELLS: LUNG
- MICROGLIA: BRAIN
- KUPPFLER CELLS: LIVER
- RES CELLS: SPLEEN
- DENDRITIC CELLS: LYMPH NODES
- OSTEOCLASTS: BONE
- MESANGIAL CELLS: KIDNEYS
- M CELLS: PEYER'S PATCH
- LANGHERAN'S CELLS: SKIN
- MONOCYTES: BLOOD
- **CONNECTIVE TISSUES:**
  - EPITHELIOIDS CELLS
  - GIANT CELLS
  - HISTIOCYTES.







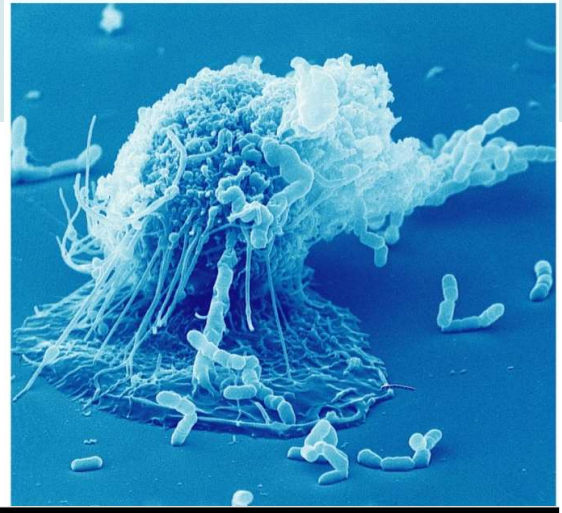
INTERFERON MEDIATED THE CHANGES OF THE MACROPHAGES [MONOCYTES].



Mechanisms

Innate defenses → Internal defenses

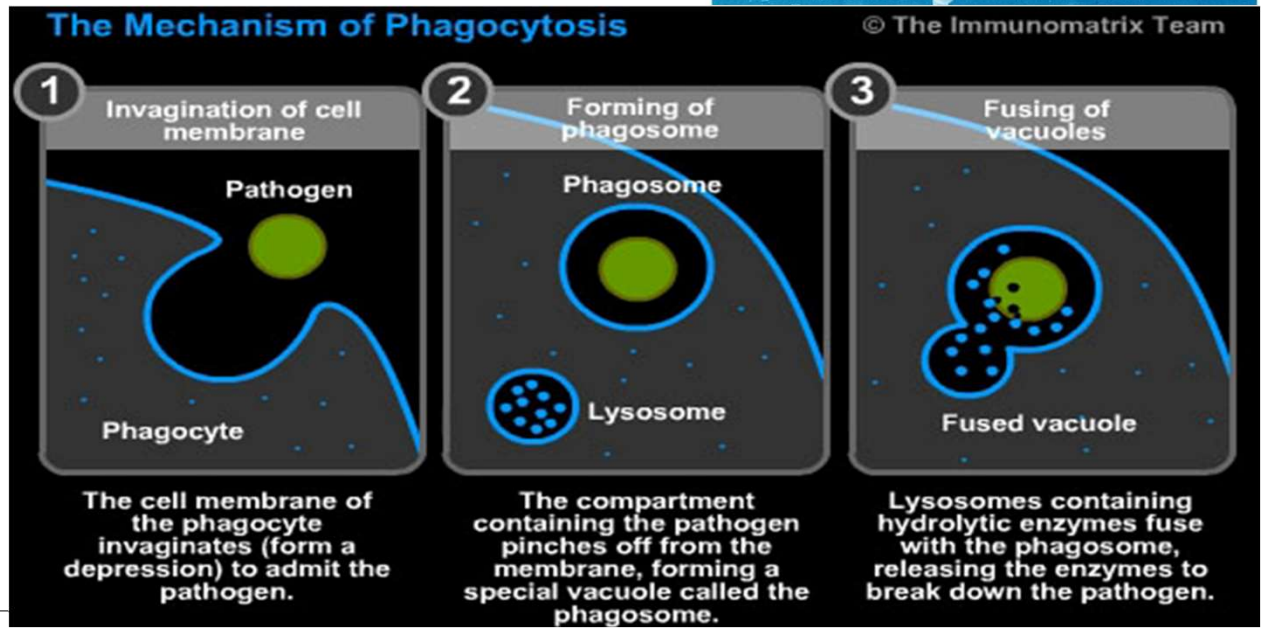
Phagocytes

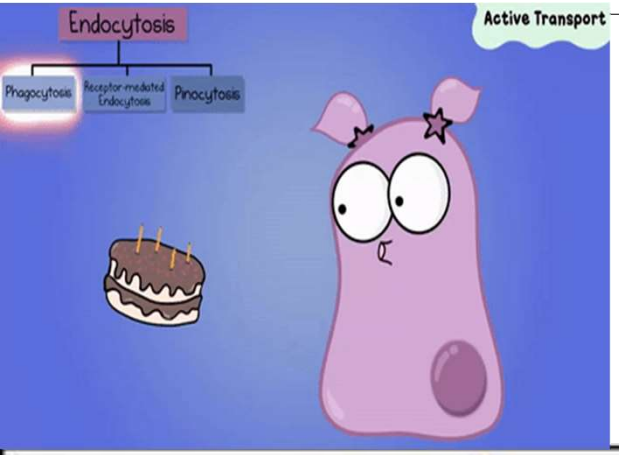


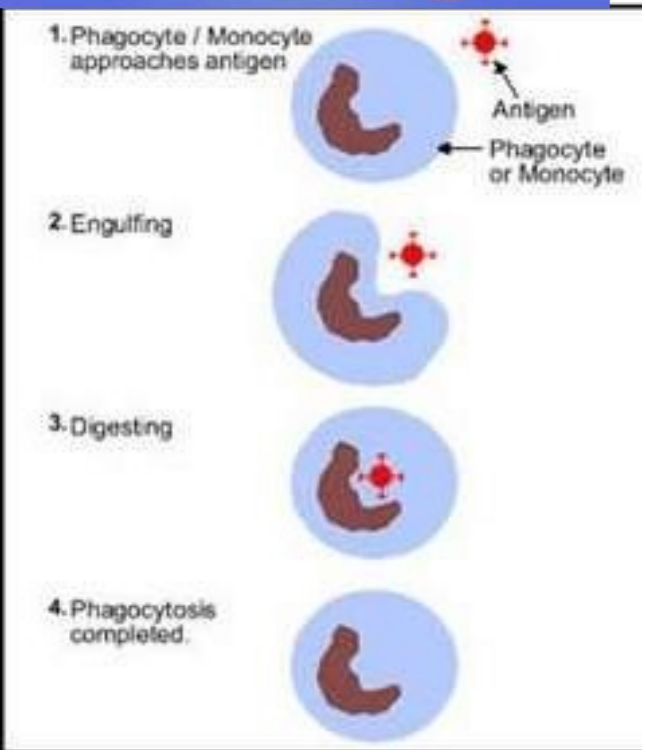
- **Macrophages are the chief phagocytic cells**
- Free macrophages wander throughout a region in search of cellular debris
- Kupffer cells (liver) and microglia (brain) are fixed macrophages
- **Neutrophils** become phagocytic when encountering infectious material
- **Eosinophils** are weakly phagocytic against parasitic worms
- **Mast cells** bind and ingest a wide range of bacteria

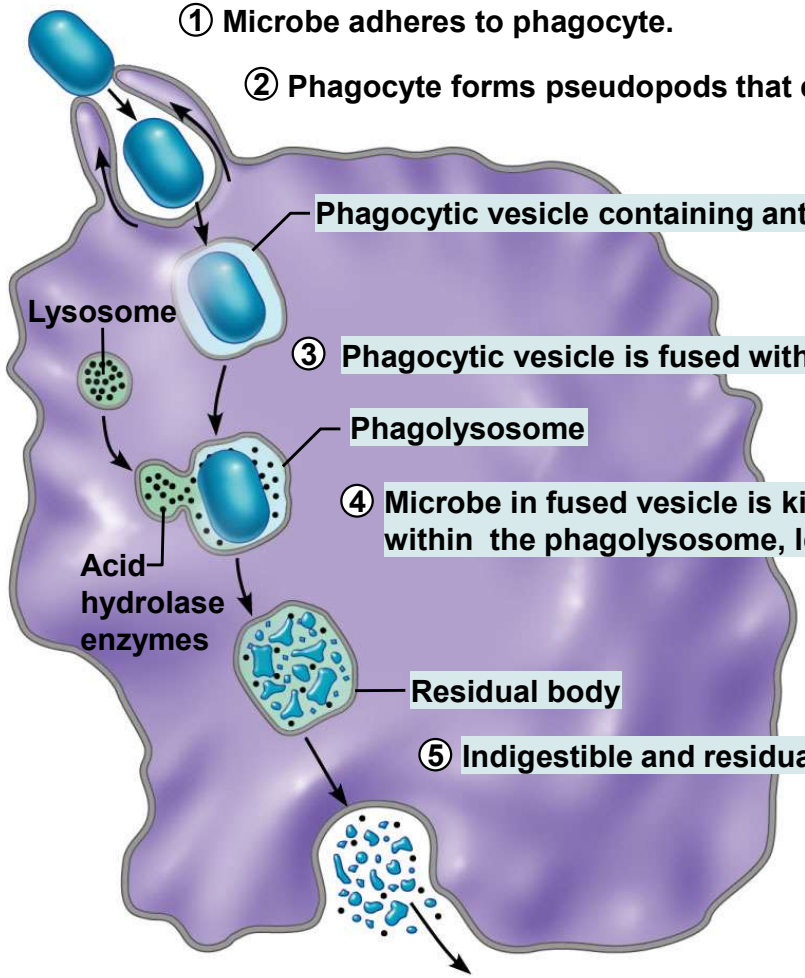
Mechanism of Phagocytosis

- 1/ Microbes **adhere** to the phagocyte
- **2/Pseudopods engulf** the particle (antigen) into a phagosome
- **3/Phagosomes fuse with a lysosome to form a phagolysosome**
- 4/Invaders in the phagolysosome are **digested by proteolytic enzymes**
- 5/Indigestible and residual material is removed by exocytosis

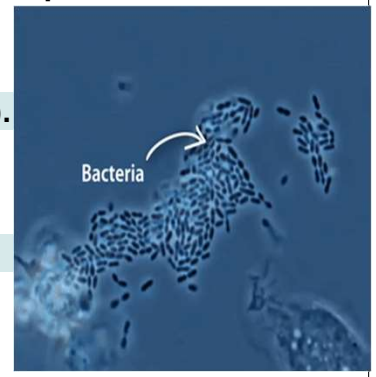


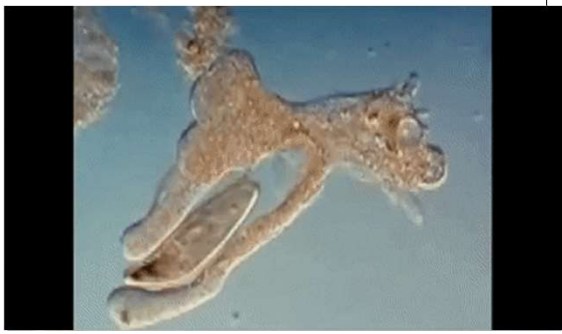

Endocytosis
Active Transport
Phagocytosis
Receptor-mediated Endocytosis
Pinocytosis

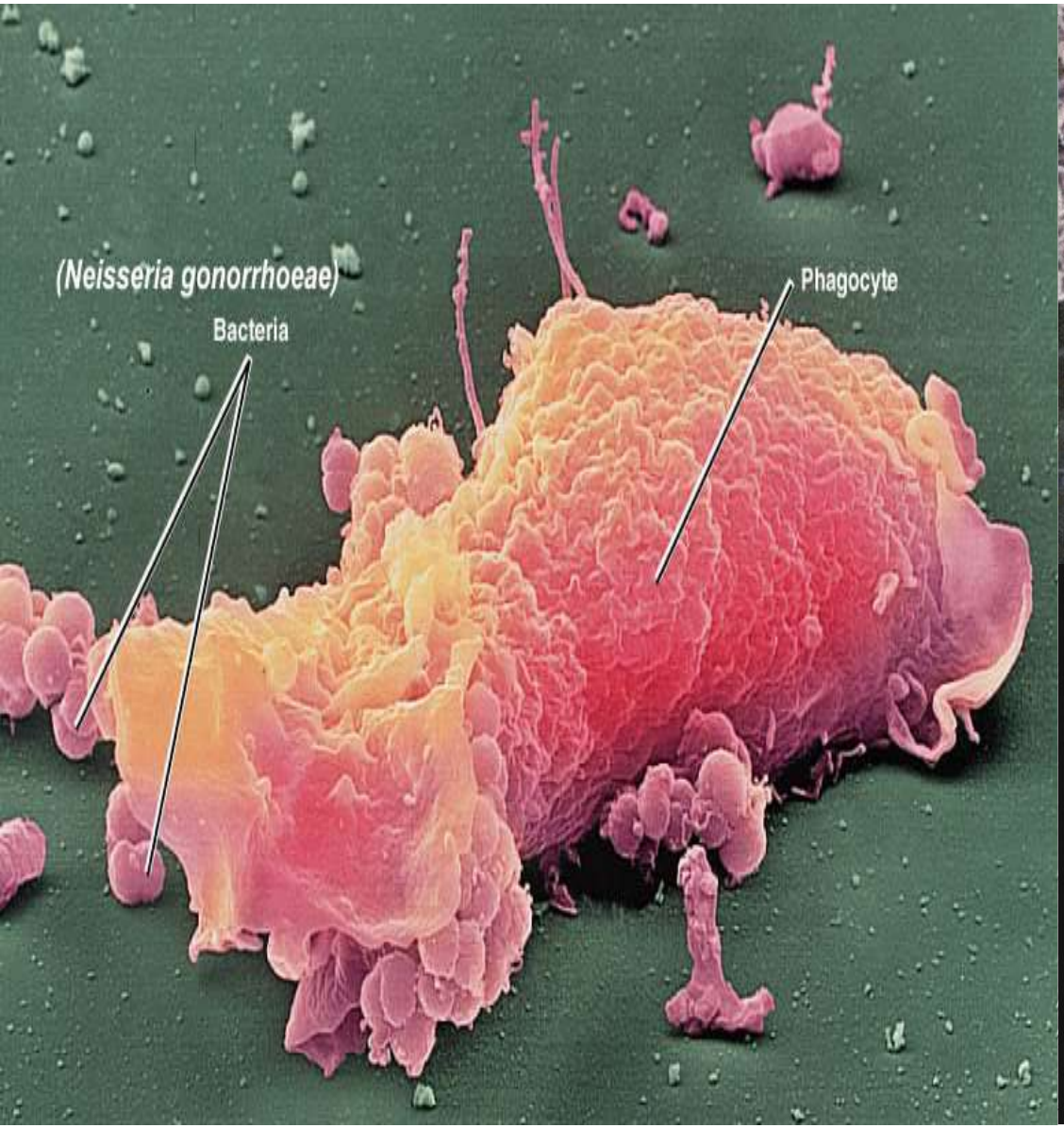

1. Phagocyte / Monocyte approaches antigen
Antigen
Phagocyte or Monocyte
2. Engulfing
3. Digesting
4. Phagocytosis completed

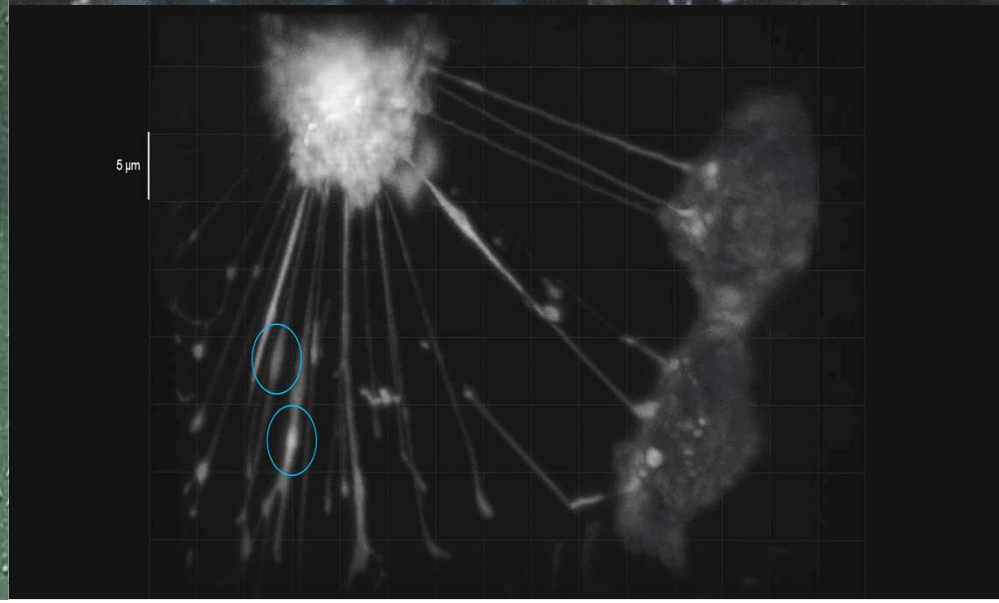

① Microbe adheres to phagocyte.
② Phagocyte forms pseudopods that eventually engulf the particle.
Phagocytic vesicle containing antigen (phagosome).
Lysosome
③ Phagocytic vesicle is fused with a lysosome.
Phagolysosome
④ Microbe in fused vesicle is killed and digested by lysosomal enzymes within the phagolysosome, leaving a residual body.
Acid hydrolase enzymes
Residual body
⑤ Indigestible and residual material is removed by exocytosis.

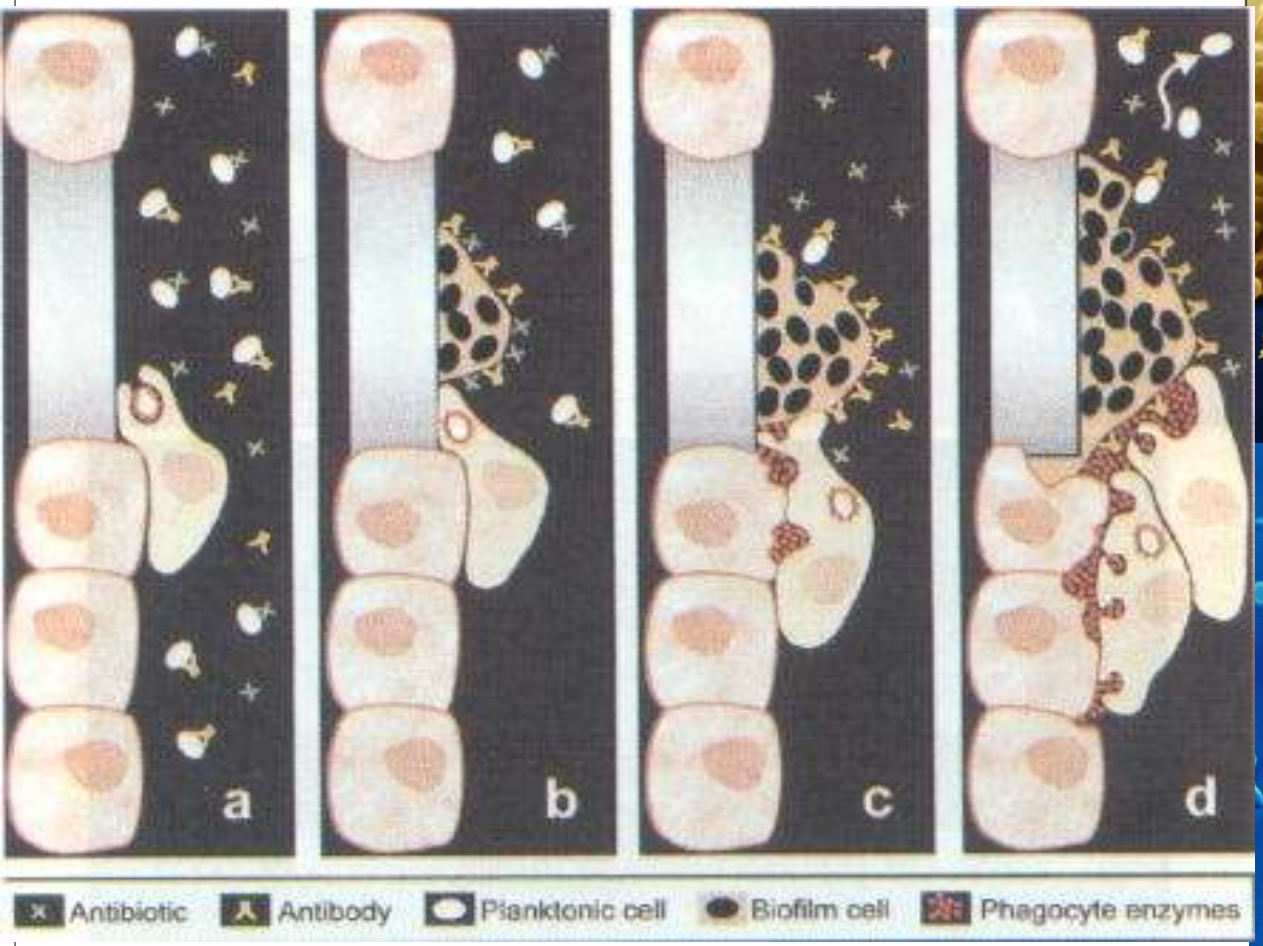
(b)

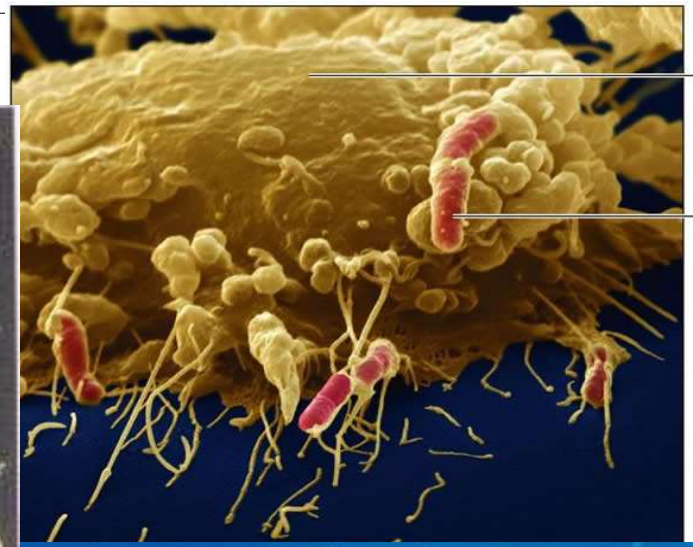

Bacteria

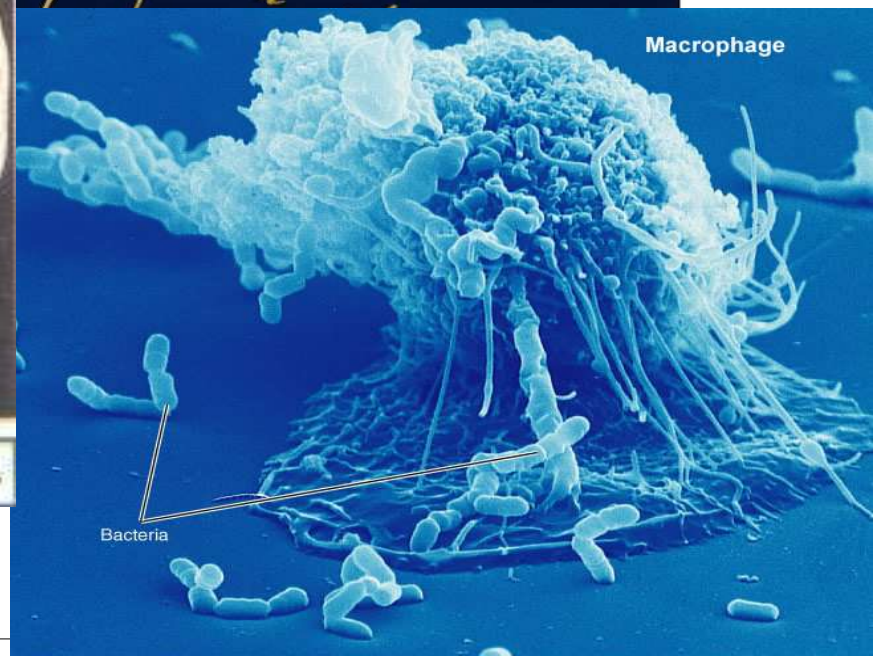



(Neisseria gonorrhoeae)
Bacteria
Phagocyte


5 µm


a
b
c
d
Antibiotic
Antibody
Planktonic cell
Biofilm cell
Phagocyte enzymes


Macrophage
Bacterium


Macrophage
Bacteria

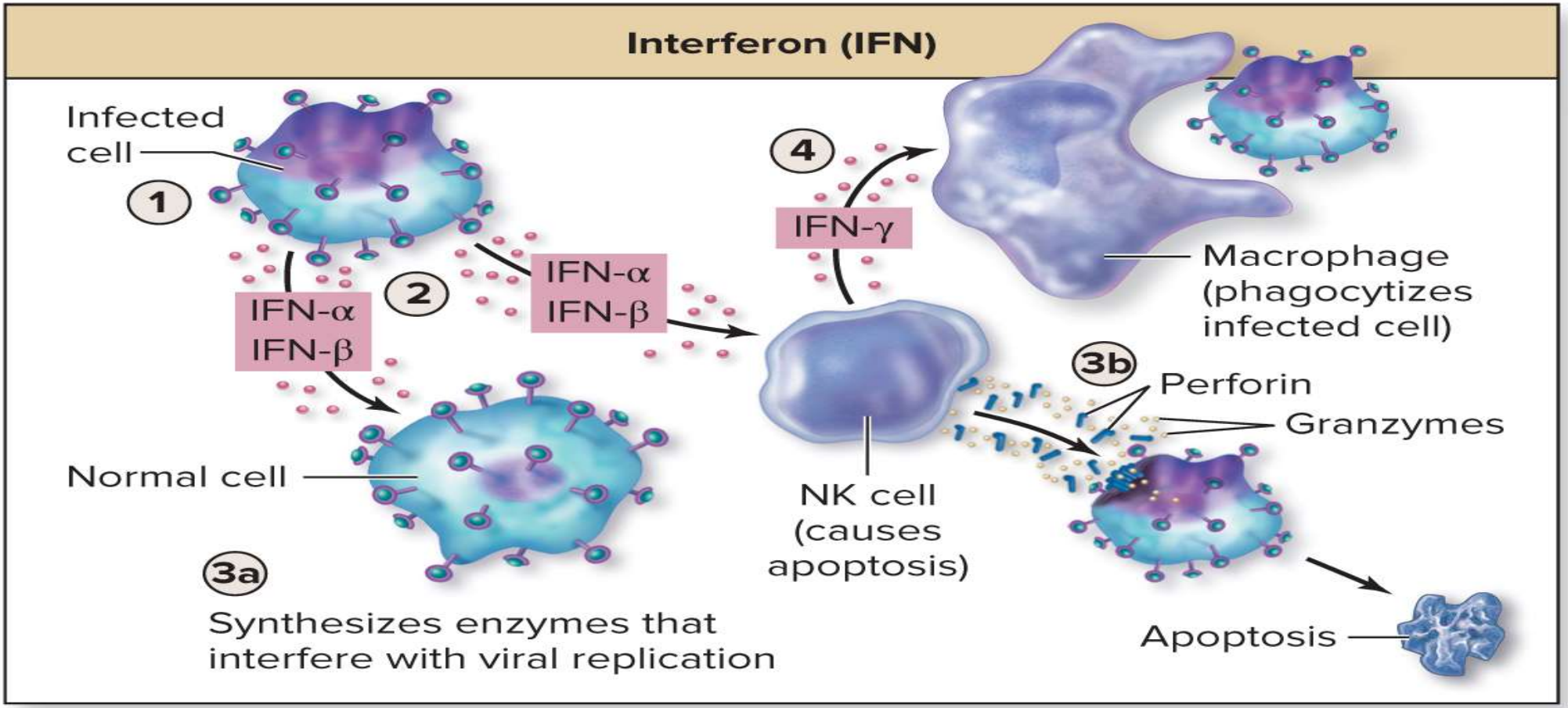
Nonspecific Internal Defenses: Antimicrobial Proteins[1]

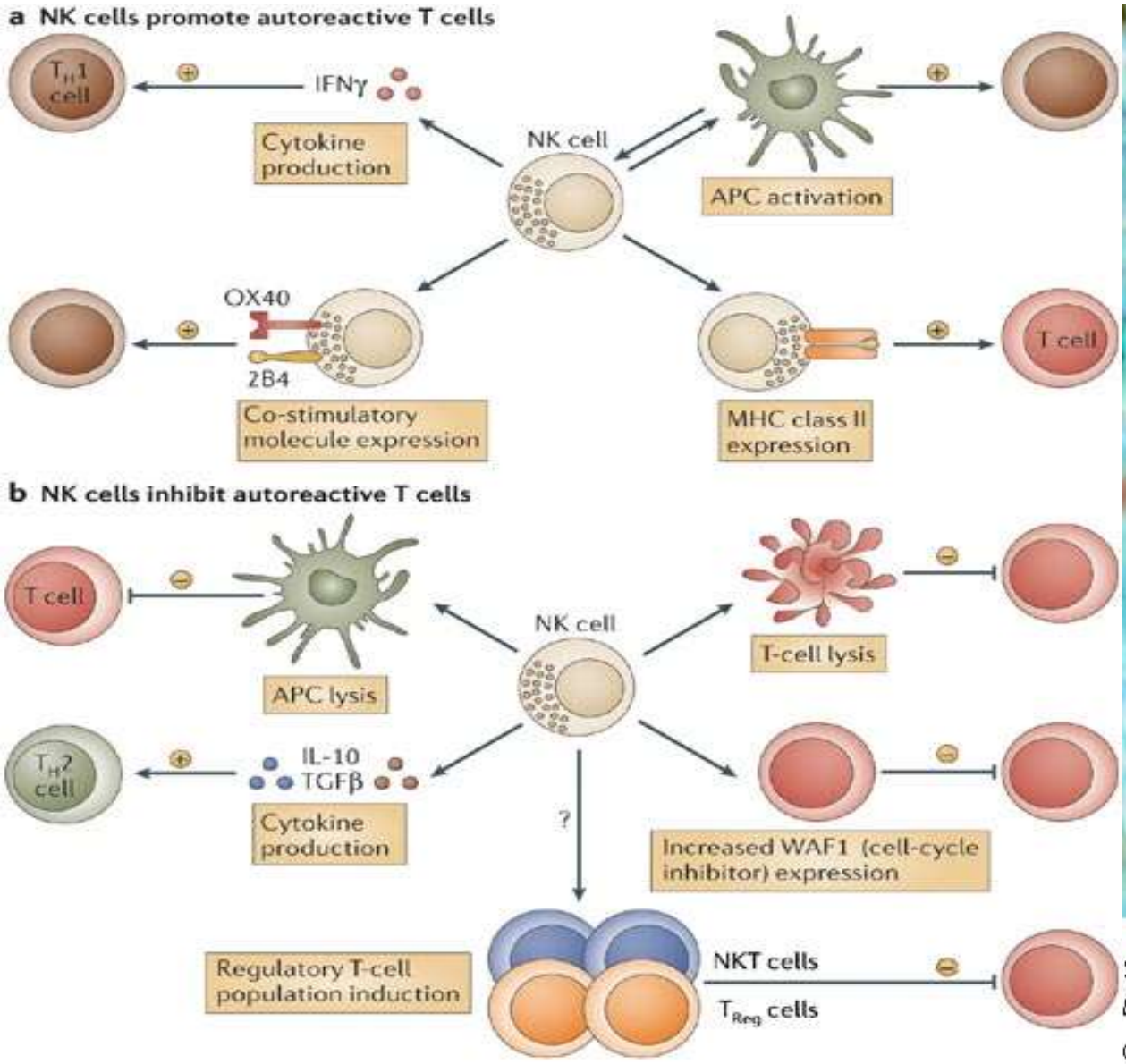
Antimicrobial proteins are molecules that function against microbes

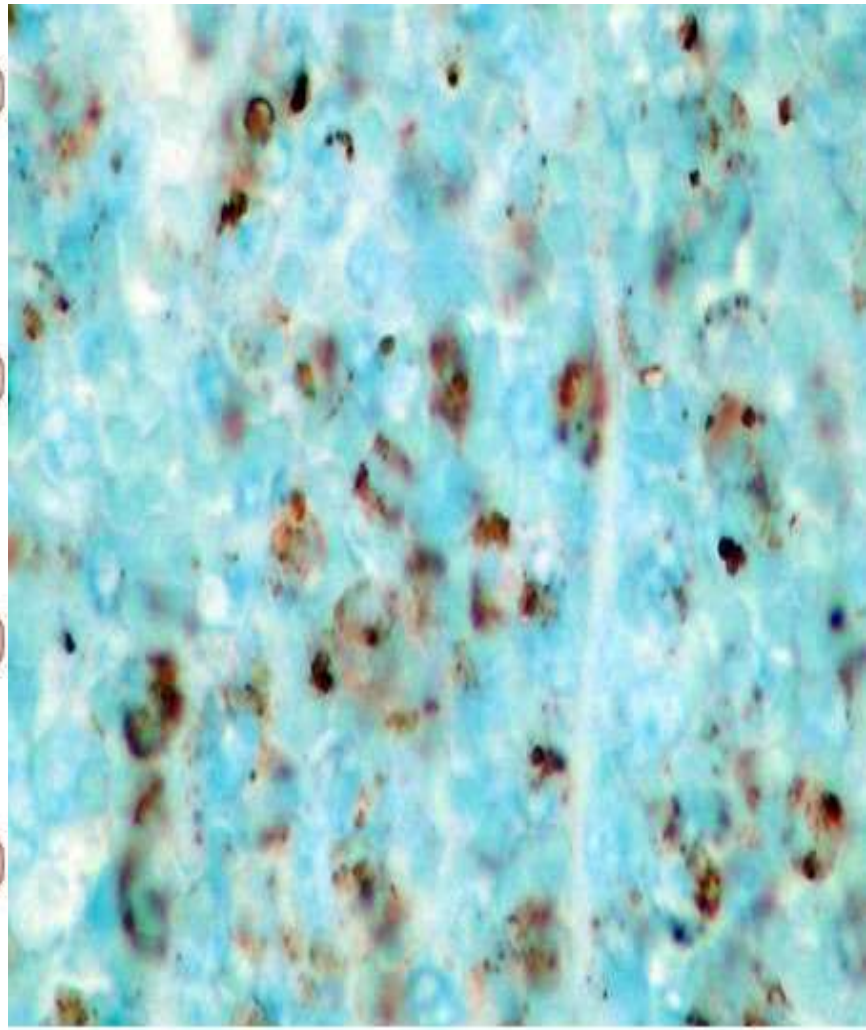
Interferons: a class of cytokines that nonspecifically impedes viral spread

- IFN-α and IFN-β produced by leukocytes and virus-infected cells
  - Bind to neighboring cells and prevent their infection
    - Trigger synthesis of enzymes that destroy viral nucleic acids, inhibit synthesis of viral proteins
  - **Stimulate NK cells to destroy virus-infected cells**
- IFN-g produced by T-lymphocytes and NK cells
  - Stimulates macrophages to destroy virus-infected cells

Effects of Interferon







Source: Lichtman MA, Shafer MS, Felgar RE, Wang N: *Lichtman's Atlas of Hematology*: http://www.accessmedicine.com

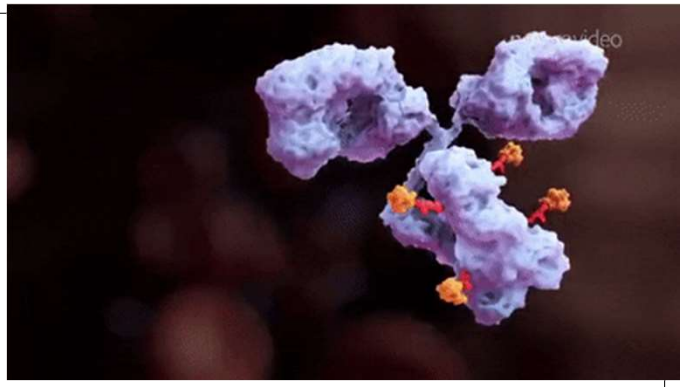
Cells and Molecules of the Adaptive Immune Response

ELEMENT	FUNCTION IN IMMUNE RESPONSE
CELLS	
B cell	Lymphocyte that matures in bone marrow. Induced to replicate by antigen binding, usually followed by helper T cell interactions in lymphoid tissues. Its progeny (clone members) form memory cells and plasma cells
Plasma cell	Antibody-producing "machine"; produces huge numbers of antibodies (immunoglobulins) with the same antigen specificity. Specialized B cell clone descendant
Helper T cell (T_H)	A CD4 T cell that is central to both humoral and cellular immunity. After binding with a specific antigen presented by an APC, it stimulates production of cytotoxic T cells and B cells to help fight invader, activates macrophages, and acts both directly and indirectly by releasing cytokines
Cytotoxic T cell (T_C)	A CD8 cell; also called a cytolytic (CTL) T cell. Activated by antigen presented by an antigen-presenting cell, often with helper T cell involvement. Its specialty is killing virus-invaded body cells and cancer cells; also involved in rejection of foreign tissue grafts
Regulatory T cell (T_{Reg})	Formerly called suppressor T cell; slows or stops activity of immune system. Thought to be important in controlling autoimmune diseases; likely several different populations exist
Memory cell	Descendant of activated B cell or any class of T cell; generated during initial immune response (primary response); may exist in body for years after, enabling it to respond quickly and efficiently to subsequent infections or meetings with same antigen
Antigen-presenting cell (APC)	Any of several cell types (dendritic cell, macrophage, B cell) that engulfs and digests antigens that it encounters, presenting parts of them on its plasma membrane (bound to an MHC protein) for recognition by T cells bearing receptors for same antigen. This function, antigen presentation, is essential for normal cell-mediated responses. Macrophages also release chemicals (cytokines) that activate T cells

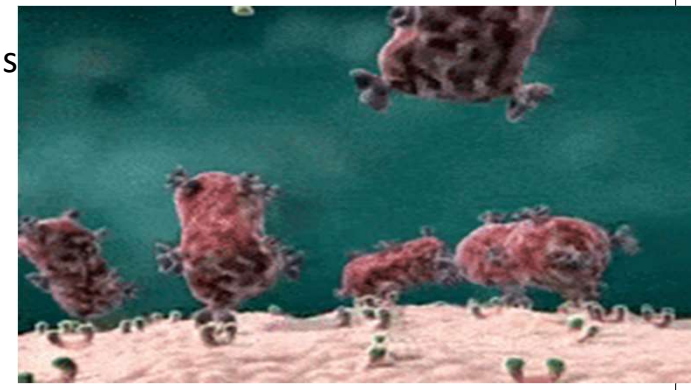
- **HUMORAL RESPONSE**

- **The humoral immune response is mediated by antibody molecules that are secreted by plasma cells.**
  - **BLOOD [BLOOD TESTING, HEMOCULTURE]**
  - **B CELLS, NEUTROPHILS**

This type of immunity is essential for defending against extracellular pathogens such as bacteria, viruses, and toxins.



- **CELL MEDIATED RESPONSE**
  - **TISSUE [BIOPSY]**
  - **T CELLS,**
  - **MACROPHAGES**



- The cell-mediated immune response is a crucial aspect of the adaptive immune system, primarily involving T cells that recognize and respond to antigens presented by infected or altered cells.
- This type of immunity is essential for combating intracellular pathogens such as viruses and some bacteria, as well as for tumor surveillance and transplant rejection.

Key Components of the Humoral Immune Response

1.B Cells

1. **Role:** Recognize specific antigens, differentiate into plasma cells, and produce antibodies.
2. **Types:** Naive B cells, plasma cells, and memory B cells.

2.Helper T Cells (CD4+ T Cells)

1. **Role:** Provide necessary signals to B cells for activation and differentiation through direct cell contact and cytokine secretion.

3.Antibodies

1. **Role:** Bind to specific antigens to neutralize pathogens, mark them for destruction by other immune cells, or activate complement pathways.
2. **Types:** IgM, IgG, IgA, IgE, and IgD, each with distinct functions and locations in the body.

Key Components of the Cell-Mediated Response

1.Antigen-Presenting Cells (APCs)

1. **Role:** Capture, process, and present antigens on their surface using major histocompatibility complex (MHC) molecules.
2. **Types: Dendritic cells, macrophages, and B cells are primary APCs.**

2.T Cells

1. **Types: Include CD4+ T helper cells and CD8+ cytotoxic T cells.**
2. **Functions:** Recognize antigens presented by APCs and orchestrate the immune response.

Importance of the Humoral Immune Response

1.Defense Against Extracellular Pathogens: Essential for neutralizing and eliminating pathogens and toxins in the extracellular environment.

2.Long-Term Immunity: Memory B cells provide rapid and robust responses upon re-exposure to the same antigen, forming the basis of immunological memory.

3.Vaccine Efficacy: Many vaccines work by stimulating the humoral immune response to produce protective antibodies.

Importance of the Cell-Mediated Immune Response

1.Combating Intracellular Pathogens: Crucial for eliminating cells infected with viruses and some bacteria that hide within host cells, where antibodies cannot reach them.

2.Tumor Surveillance: Helps recognize and destroy cancer cells that express abnormal antigens.

3.Transplant Rejection: Mediates the rejection of transplanted tissues and organs by recognizing foreign MHC molecules.

4.Autoimmune Regulation: Prevents autoimmune diseases by maintaining self-tolerance through regulatory mechanisms.

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**

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

Cell Mediated Immunity (CMI)

* **Host defenses against extracellular infection are mediated by:**
  - **Antibody**
  - **Complement**
  - **Macrophages**

* **Intercellular infections are mediates by CMI**

* **CMI are responsible for:**
  - **Resistance to intracellular pathogens**
  - **Resistance to fungal and protozoal infections**
  - **Resistance to tumors**

* **CMI may play a role in some harmful conditions:**
  - **Hypersensitivity reactions type IV (contact dermatitis)**
  - **Graft rejection**
  - **Autoimmune diseases**
* **Cell mediated cytotoxicity mediated by:**
  - **T-cytotoxic cells cells**
  - **Natural killer cells**
  - **Activated macrophages**

T-lymphocytes:

- Antigen specific cells carrying CD3 complex, CD4, CD8
- Dominant blood lymphocytes (70%)
- Produce cytokines
- **Activation of other cells (Th CD4)**
- **Suppressors for others (Ts CD8)**

B-lymphocytes:

- **Antigen specific cells with surface receptor**
- **Less common lymphocytes (20%)**
- **Responsible for antibody production**

* **NK, K cells:**
  - **Not antigen specific**
  - **Carry Fc receptors , NK-target cell receptor**

The **humoral immune response**

- is the arm of the **adaptive immune system** that defends against **extracellular pathogens (e.g., bacteria, viruses in blood/fluids)** through the production of **antibodies** by **B lymphocytes**.

- 🧠 **"Humoral" = "fluid"** → Think antibodies circulating in body **fluids** (plasma, lymph, mucosa).

Feature	Description
Primary cell	**B lymphocytes**
Main effector molecules	**Antibodies (IgG, IgA, IgM, IgE, IgD)**
Helper cell	**$CD4^+$ T helper cells (especially Th2 subtype)**
Target	**Extracellular pathogens** (e.g., bacteria, toxins, viruses before cell entry)
Location	**Blood, lymph, mucosal secretions**

STEPS OF HUMORAL IMMUNE RESPONSE

1.Antigen Recognition

1. **Naive B cells** bind antigen via surface **B cell receptor (BCR)** (membrane-bound IgM or IgD).

2.Antigen Processing & Presentation

1. B cell internalizes antigen, processes it, and presents it on **MHC II**.

3.T Cell Help

1. **$CD4^+$ T helper cells** recognize MHC II-antigen complex.
2. They secrete **cytokines (e.g., IL-4, IL-5, IL-6)** to stimulate B cells.

4.B Cell Activation & Clonal Expansion

1. B cells proliferate and differentiate into:
    1. **Plasma cells** → secrete antibodies.
    2. **Memory B cells** → long-term protection.

5.Antibody Secretion

1. **Plasma cells** secrete specific antibodies:
    1. **IgM** (initial response)
    2. **IgG** (long-term protection, opsonization)
    3. **IgA** (mucosal immunity)
    4. **IgE** (parasites, allergies)

Effector Functions of Antibodies:

- **Neutralization** – block pathogen entry/toxins.
- **Opsonization** – enhance phagocytosis.
- **Complement activation** – leads to pathogen lysis.

Cell-Mediated Immunity (CMI)

The **cell-mediated immune response** is a branch of the **adaptive immune system** that **does not involve antibodies**, but instead **uses T cells to identify and destroy infected or abnormal cells**.

Feature	Description
🧠 **Main Cells Involved**	T lymphocytes ($CD4^+$ helper T cells and $CD8^+$ cytotoxic T cells)
🎯 **Target**	**Intracellular pathogens** (viruses, some bacteria, fungi), tumor cells, transplanted cells
❌ **Antibodies involved?**	No (this is what distinguishes it from **humoral immunity**)

Steps of the Cell-Mediated Response

1. Antigen Presentation

- **Dendritic cells**, macrophages, and B cells (APCs) present **processed antigen** via:
  - **MHC class I** → to $CD8^+$ T cells
  - **MHC class II** → to $CD4^+$ T cells

"Cell-Mediated = Cytotoxic + CD Cells"

2. T Cell Activation

- Requires 2 signals:
  - Signal 1: TCR binds MHC–peptide complex
  - Signal 2: Co-stimulation (e.g., CD28–B7 interaction)
- Leads to **clonal expansion and differentiation**.

T Cell Type	Function	Key Cytokines
$CD8^+$ Cytotoxic T Cells	Kill virus-infected or cancerous cells via perforin + granzymes	IL-2 (from $CD4^+$ T cells)
$CD4^+$ Th1 Cells	Activate macrophages, promote phagocytosis	IFN-γ
$CD4^+$ Th17 Cells	Recruit neutrophils, promote inflammation	IL-17
Tregs	Suppress immune response	IL-10, TGF-β

Disease / Scenario	Cell-Mediated Role
Tuberculosis	Granuloma formation by Th1-mediated macrophage activation
Viral infections (e.g., HIV, EBV)	$CD8^+$ T cells kill infected cells
Organ rejection	$CD8^+$ T cells recognize non-self MHC and destroy transplanted cells
Cancer immunotherapy	Checkpoint inhibitors unleash $CD8^+$ T cells against tumors
Type IV Hypersensitivity	Delayed-type (e.g., PPD test, contact dermatitis) mediated by **Th1/$CD8^+$T cells**

A patient with tuberculosis shows granulomatous inflammation on lung biopsy. Which of the following immune mechanisms is most responsible for this response?

A. B cell production of IgM antibodies
B. Complement activation by immune complexes
C. Activation of macrophages by Th1 cells
D. $CD8^+$ T cell perforin-mediated killing
E. Mast cell degranulation by IgE

✅ **Correct Answer: C. Activation of macrophages by Th1 cells**

🧠 This is classic **cell-mediated immunity** via Th1 cells producing **IFN-γ**, leading to macrophage activation and granuloma formation.

Feature	Cell-Mediated Immunity (CMI)	Humoral Immunity
Main Cells	T lymphocytes ($CD4^+$, $CD8^+$)	B lymphocytes (→ Plasma cells)
Effectors	Cytotoxic T cells, activated macrophages	Antibodies (IgG, IgA, IgM, etc.)
Target Pathogens	**Intracellular** (viruses, TB, fungi, some protozoa, tumor cells)	**Extracellular** (bacteria, toxins, free viruses)
Activation	TCR binds to **MHC-peptide complex** on APC	BCR binds directly to antigen (with $CD4^+$ T cell help for class switching)
Response Type	Killing of infected cells, macrophage activation	Neutralization, opsonization, complement activation
Diagnostic Test Clues	PPD test, organ rejection, viral cytotoxicity	Serum antibody titers, ELISA, agglutination tests
Hypersensitivity Type	**Type IV** (Delayed-type)	**Types I, II, III**

Mnemonic:

"T for Touch" (Cell-mediated = T cells touch infected cells to kill)

"B for Blood" (Humoral = B cells → antibodies circulate in blood)

Functions of APCs

1.Antigen Processing: APCs process antigens (foreign substances) by **engulfing and breaking them down into smaller fragments.**

2.Antigen Presentation: They present these antigen fragments on their cell surface bound to major histocompatibility complex (MHC) molecules. This presentation is **crucial for the activation of T cells.**

3.T Cell Activation: APCs interact with T cells, providing the necessary signals for their activation and differentiation. This interaction is essential for the **adaptive immune response**.

4.Immune Regulation: APCs help regulate the immune response by **determining the type of immune response** (e.g., activating different T helper cell subsets).

Importance in Immunity

- **Initiating Adaptive Immunity:** APCs are essential for initiating adaptive immune responses, as they present antigens to T cells, triggering their activation and proliferation.
- **Determining Immune Response:** The type of APC, the nature of the antigen, and the context of antigen presentation (e.g., presence of danger signals) influence the nature of the immune response (e.g., cytotoxic, helper, or regulatory T cell responses).
- **Immune Regulation:** APCs help maintain immune tolerance and prevent autoimmune responses by regulating T cell activation and differentiation.

Types of APCs

1.Dendritic Cells (DCs)

1. **Location:** Found in tissues that are in contact with the external environment, such as the skin (Langerhans cells) and mucosal surfaces.
2. **Function:** Highly efficient at antigen capture, processing, and presentation. They migrate to lymph nodes to activate T cells.
3. **Significance:** Considered the most potent APCs, crucial for initiating primary immune responses.

2.Macrophages

1. **Location:** Found throughout the body, particularly in tissues like the lungs, liver (Kupffer cells), spleen, and lymph nodes.
2. **Function:** Engulf and digest pathogens, dead cells, and debris. They present antigens to T cells and secrete cytokines to modulate the immune response.
3. **Significance:** Important for both innate and adaptive immunity, helping to clear infections and stimulate T cells.

3.B Cells

1. **Location:** Found in the blood, spleen, and lymph nodes.
2. **Function:** Besides producing antibodies, B cells can present antigens to helper T cells, especially in the context of secondary immune responses.
3. **Significance:** Link between humoral immunity (antibody production) and cell-mediated immunity (T cell activation).

4.Other Cells with APC Capabilities

1. **Function:** Other cells, like endothelial cells and certain epithelial cells, can present antigens under specific conditions, although they are not professional APCs.
2. **Significance:** These cells can contribute to immune responses, particularly in localized tissues.

Mechanism of Antigen Presentation

1.Antigen Uptake: APCs capture antigens through phagocytosis, endocytosis, or pinocytosis.

2.Antigen Processing: The captured antigens are processed within the APC, broken down into peptide fragments.

3.MHC Binding: The peptide fragments are loaded onto MHC molecules (MHC class I or II).

4.Antigen Presentation: The MHC-peptide complexes are transported to the cell surface of the APC.

5.T Cell Interaction: T cells recognize the antigen-MHC complex via their T cell receptors (TCRs). This interaction, along with co-stimulatory signals provided by the APC, activates the T cells.

What are the cells of adaptive immunity?

T-lymphocytes and B-lymphocytes

Q: A patient with chronic hepatitis B infection shows a dense lymphocytic infiltrate in liver biopsy with hepatocyte apoptosis. Which immune mechanism is most likely responsible?

A. IgG-mediated opsonization
B. $CD8^+$ T cell cytotoxicity
C. Mast cell degranulation
D. Complement C3 activation
E. B cell IgM production

✅ **Correct Answer: B. $CD8^+$ T cell cytotoxicity**
🧠 This is **cell-mediated immunity**, targeting **virus-infected hepatocytes**.

Primary Location of Immune Cells

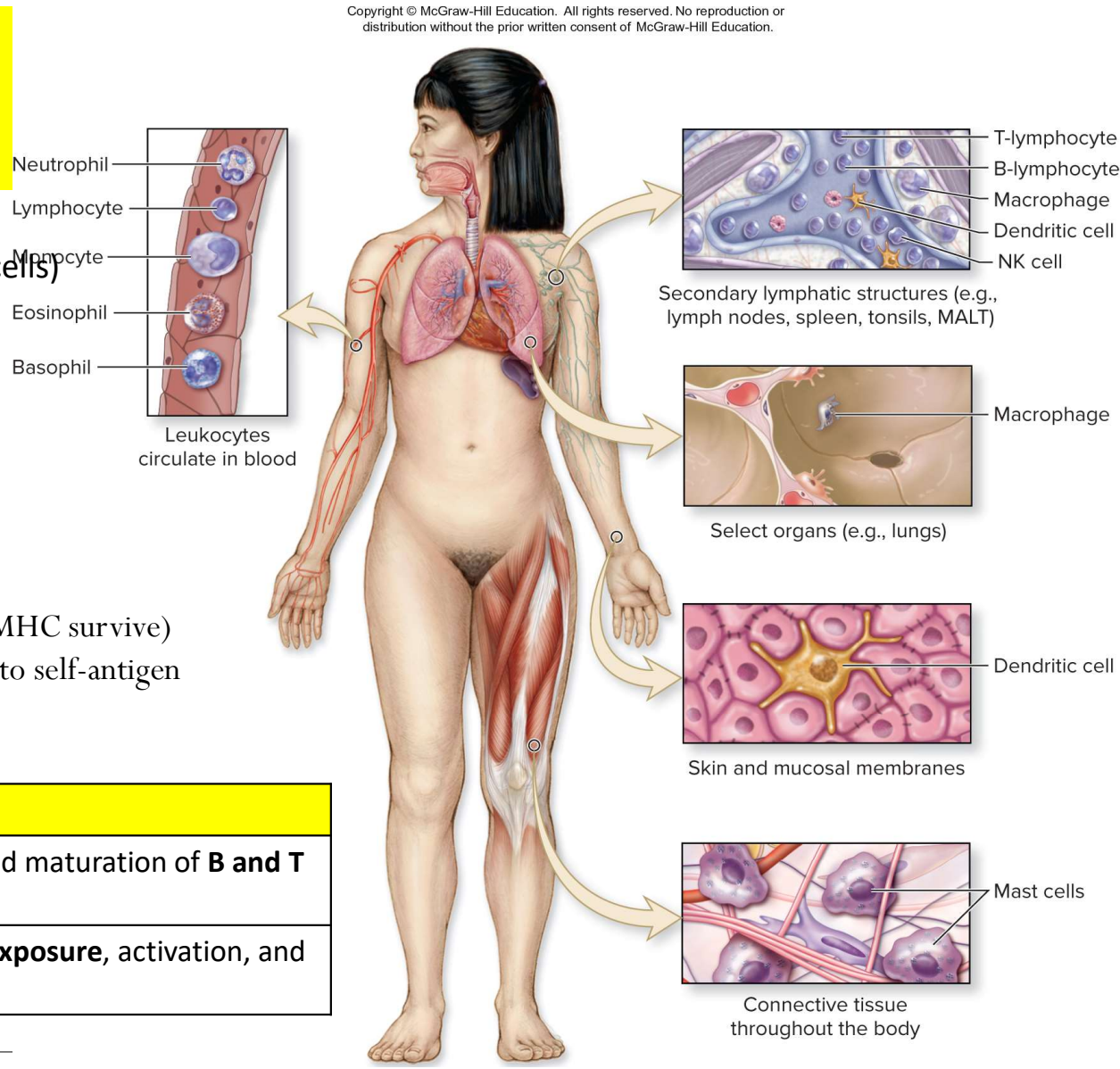
Bone Marrow

- **Function**: Hematopoiesis (production of all blood cells)
- **Immune Role**:
  - Origin of **all immune cells**
  - **B cells mature** here (in humans)
  - Source of immature **T cell precursors**

Thymus

- **Function**: Maturation of **T lymphocytes**
- **Location**: Anterior mediastinum
- **Immune Role**:
  - **Positive selection** (T cells that recognize self-MHC survive)
  - **Negative selection** (T cells that react strongly to self-antigen undergo apoptosis)

Category	Organs	Function
Primary (Central)	**Bone marrow, Thymus**	Development and maturation of **B and T cells**
Secondary (Peripheral)	**Lymph nodes, Spleen, MALT**	Site of **antigen exposure**, activation, and proliferation



Secondary Lymphoid Organs

1. Lymph Nodes

- **Function**: Filter lymph from tissues
- **Key Sites**:
  - **Cortex**: B cells in follicles
  - **Paracortex**: T cells
  - **Medulla**: Plasma cells and macrophages
- **Clinical Relevance**:
  - Swollen nodes = immune activation
  - Paracortex underdeveloped in DiGeorge Syndrome

2. Spleen

- **Function**: Filters **blood**, responds to blood-borne antigens
- **Key Zones**:
  - **White pulp**: lymphoid tissue (B and T zones)
  - **Red pulp**: RBC destruction, macrophage activity
- **Clinical Relevance**:
  - Asplenic patients (e.g., post-splenectomy, sickle cell) are at risk for **encapsulated bacteria** (e.g., *S. pneumoniae*, *H. influenzae*, *N. meningitidis*)

3. MALT (Mucosa-Associated Lymphoid Tissue)

- Includes:
  - **Peyer's patches** (ileum)
  - **Tonsils**
  - **Appendix**
  - Bronchus and nasal-associated lymphoid tissue
- **Function**: Protect mucosal surfaces
- **Special Feature**: **IgA secretion** for mucosal defense

Other Immune Cell Locations

Cell Type	Primary Locations
Macrophages	All tissues (Kupffer cells – liver, microglia – brain)
Dendritic Cells	Skin (Langerhans), mucosa, lymph nodes
Plasma Cells	Bone marrow, medulla of lymph nodes, lamina propria
NK Cells	Circulate in blood, accumulate in tissues
T and B Memory Cells	Circulate in blood, lymphoid organs, and peripheral tissues

Immunity: Two Intrinsic Defense Systems

- **Innate (nonspecific) system responds quickly and consists of:[3 line of defense]**
  - **First line of defense – skin and mucosa prevent entry of microorganisms**
  - **Second line of defense – antimicrobial proteins, phagocytes, and other cells**
    - **Inhibit spread of invaders throughout the body**
    - **Inflammation is its most important mechanism**

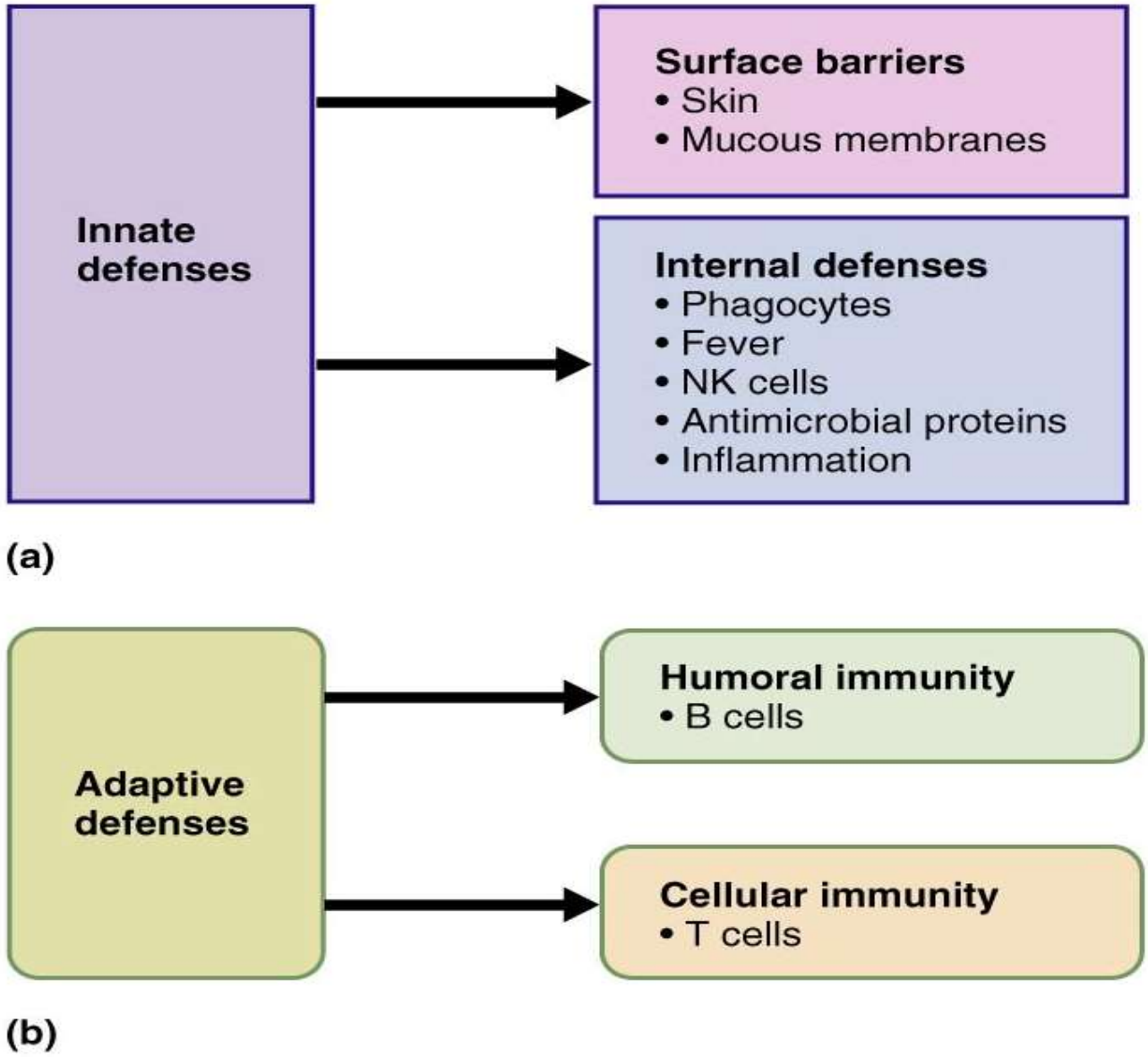
•Adaptive (specific) defense system

•Third line of defense – mounts attack against particular foreign substances

Takes longer to react than the innate system

Works in conjunction with the innate system

Innate and Adaptive Defenses



Outline of the Immune System		
Innate Immunity	1st Line of Defense	Skin
		Mucus
		Secretions
	2nd Line of Defense	Phagocytic Cells
		Antimicrobial Proteins
		Other tissues which participate in inflammatory responses
Adaptive Immunity	3rd Line of Defense	Lymphocytes
		Antibodies
Acquired Immunity	Vaccines / Immunotherapies	Attenuated Viruses
		Killed Viruses
		Toxoid Vaccines
		Component Vaccines

Mechanical, Physical and Chemical Barriers

What are the examples of Physiologic and Chemical Barriers at the skin and mucous membranes?

- **Acid pH -- this also relates to the stomach Hydrolytic enzymes Proteolytic enzymes**
- **Interferon refers to a group of proteins that can help prevent the spread of viruses. There is one special one called gamma-interferon -- this one is a cytokine produced by T_H cells.**
- **Complement is a term that refers to a group of serum proteins that are normally found "inactive" in the serum.**
- **Antibody-antigen reactions and the cell walls of certain microorganisms can "activate" complement. When this happens the active components can destroy cells in the area of complement activation.**
- **Mucous producing membrane together with cilia help eliminate organisms = mucociliary escalator**

Surface Barriers

- **Skin, mucous membranes, and their secretions make up the first line of defense**
- **Keratin in the skin:**
  - **Presents a physical barrier to most microorganisms**
  - **Is resistant to weak acids and bases, bacterial enzymes, and toxins**
- **Mucosae provide similar mechanical barriers**

Skin

- **Tough**, no bacteria can penetrate unaided.
- **Dry** (most skin infections take place in the wetter areas).
- **Acid** (approximately pH 5), Low temperature, Skin cells are constantly shedding, high salt content.
- **Lysozyme** in the pores.
- **Resident microflora**.
- Skin Associated Lymphoid Tissue

Epithelial Chemical Barriers

- Epithelial membranes produce protective chemicals that destroy microorganisms
  - **Skin acidity** (pH of 3 to 5) inhibits bacterial growth
  - **Sebum** contains chemicals toxic to bacteria
  - **Stomach mucosae** secrete concentrated HCl and protein-digesting enzymes
  - **Saliva and lacrimal fluid** contain lysozyme
  - **Mucus** traps microorganisms that enter the digestive and respiratory systems

Mucous Epithelia

- **GI**
- **Respiratory**
- **Urogenital**
- **Eyes**

- These areas are warm and wet.
- They are sites of **secretion** and/or **absorption** and therefore cannot be thick like the skin.

- **mucus - contains polysaccharides and proteins which trap organisms.**
- **Ciliated cells and parastalsis and cough reflex moves trapped organisms out. (ie.: Muco-ciliary escalator in the lungs.)**
- **Lots of lysozyme and lactoferrin (an enzyme that binds iron and keeps it away from microorganisms).**

Respiratory Tract Mucosae

- **Mucus-coated hairs in the nose trap inhaled particles**
- **Mucosa of the upper respiratory tract is ciliated**
  - **Cilia sweep dust- and bacteria-laden mucus away from lower respiratory passages**

Attributes of Selected areas

- **Mouth** - rich resident normal flora -- these help to keep the bad guys out.
- **Lungs** - sterile if not compromised Otherwise this is a vulnerable area. If organisms get down into the alveolar area they have easy access to the blood. Mucociliary escalator is very important
- **Stomach** - Low pH is an important barrier
- **Small Intestine** - Paneth cells in the crypts produce lysozyme and **defensins** (these are small proteins which inhibit bacterial growth).
- **Urethra** - flow of urine important.
- **Female Genitalia** - microflora very important. Mucus plug in the cervix important in preventing movement of microbes into the uterus.

Summary of Nonspecific Body Defenses

CATEGORY/ASSOCIATED ELEMENTS	PROTECTIVE MECHANISM
FIRST LINE OF DEFENSE: SURFACE MEMBRANE BARRIERS	
Intact skin epidermis	Forms mechanical barrier that prevents entry of pathogens and other harmful substances into body
▪ Acid mantle	Skin secretions (perspiration and sebum) make epidermal surface acidic, which inhibits bacterial growth; sebum also contains bactericidal chemicals
▪ Keratin	Provides resistance against acids, alkalis, and bacterial enzymes
Intact mucous membranes	Form mechanical barrier that prevents entry of pathogens
▪ Mucus	Traps microorganisms in respiratory and digestive tracts
▪ Nasal hairs	Filter and trap microorganisms in nasal passages
▪ Cilia	Propel debris-laden mucus away from lower respiratory passages
▪ Gastric juice	Contains concentrated hydrochloric acid and protein-digesting enzymes that destroy pathogens in stomach
▪ Acid mantle of vagina	Inhibits growth of most bacteria and fungi in female reproductive tract
▪ Lacrimal secretion (tears); saliva	Continuously lubricate and cleanse eyes (tears) and oral cavity (saliva); contain lysozyme, an enzyme that destroys microorganisms
▪ Urine	Normally acid pH inhibits bacterial growth; cleanses the lower urinary tract as it flushes from the body

Table 21.2.1

Key Components of Innate Immunity

1.Physical and Chemical Barriers

1. **Skin:** Acts as a physical barrier to prevent pathogen entry.
2. **Mucous Membranes:** Line the respiratory, gastrointestinal, and urogenital tracts; trap pathogens in mucus.
3. **Secretions:** Such as saliva, tears, and gastric acid, contain antimicrobial substances (e.g., lysozyme, defensins).

2.Cellular Components

1. **Phagocytes:**
    1. **Neutrophils:** First responders to infection, engulf and destroy pathogens.
    2. **Macrophages:** Engulf pathogens and dead cells, secrete cytokines to recruit other immune cells.
2. **Dendritic Cells:** Capture antigens and present them to T cells, bridging innate and adaptive immunity.
3. **Natural Killer (NK) Cells:** Destroy infected or cancerous cells by inducing apoptosis.
4. **Mast Cells and Basophils:** Release histamine and other mediators in response to infection, contributing to inflammation.

3.Soluble Mediators

1. **Cytokines:** Proteins that modulate the immune response by promoting inflammation, recruiting immune cells, and activating adaptive immunity.
2. **Chemokines:** Attract immune cells to the site of infection.
3. **Complement System:** A group of proteins that enhance phagocytosis, lyse pathogens, and promote inflammation.

Overview of the Immune System

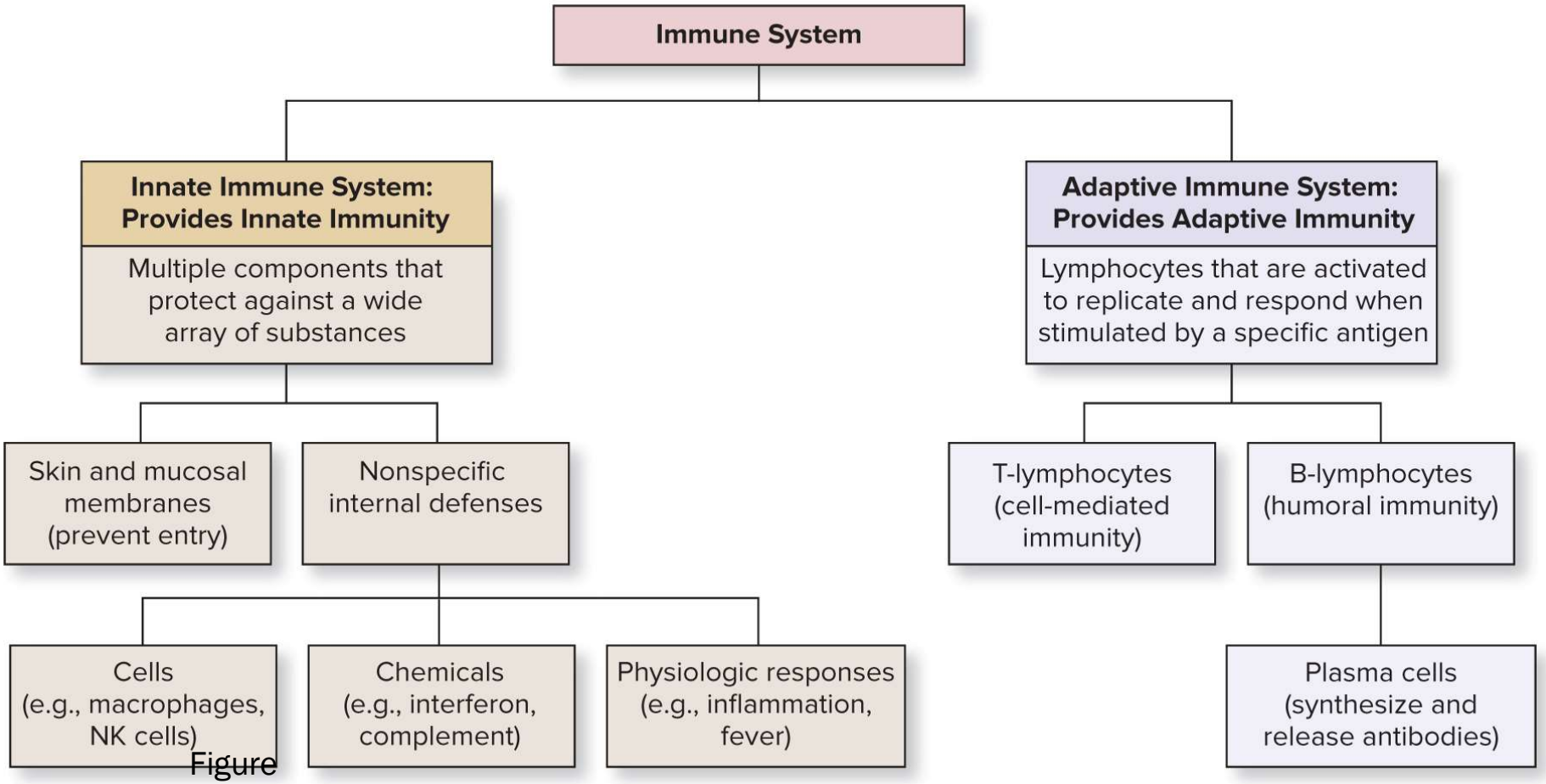
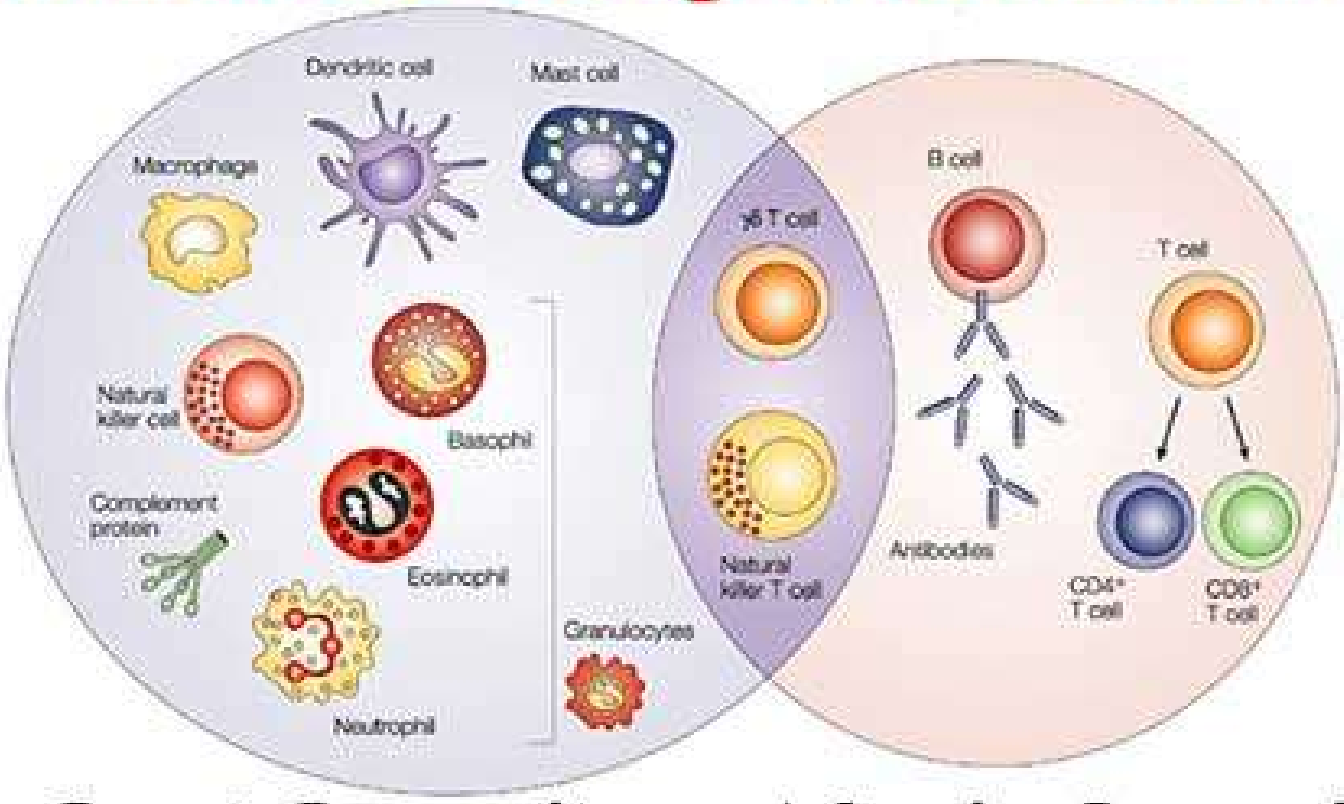


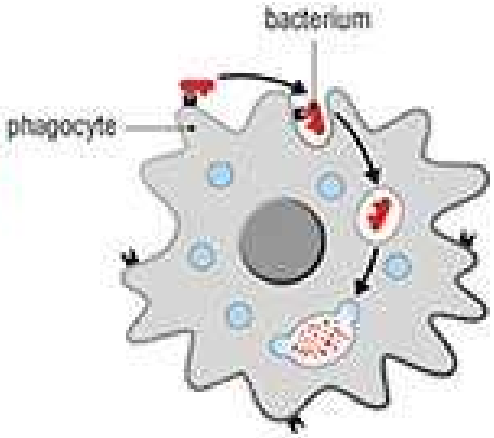
Figure 22.2

Difference between

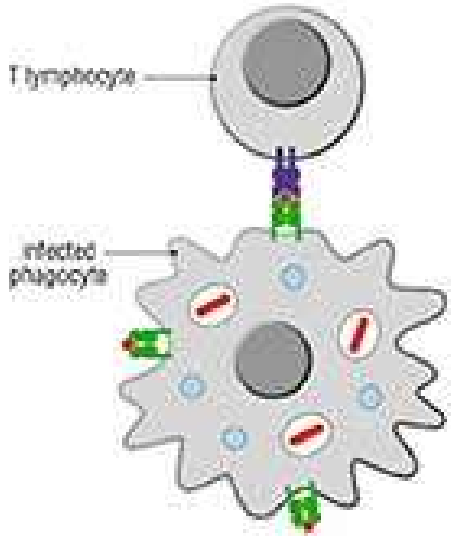
Innate and Adaptive Immunity



Innate Immunity **Adaptive Immunity**



VS

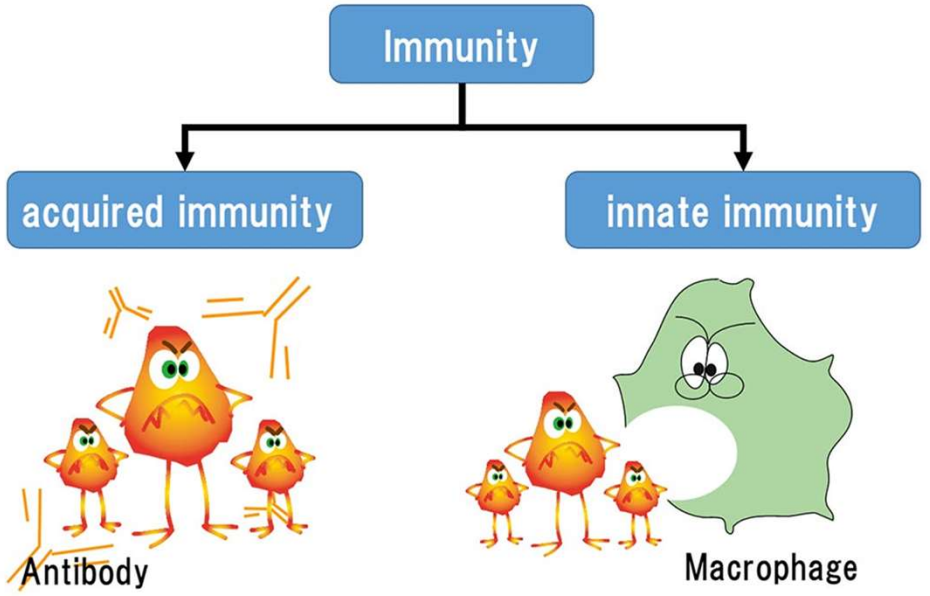


Nature Reviews | Cancer

Comparison of Innate Immunity and Adaptive Immunity

Two types of immunity differ based on

- Cells involved
- Specificity of cell response
- Mechanisms of eliminating harmful substances
- Amount of time for response



Although innate and adaptive immunities are distinct, they work together in body defense

🧱 **“Innate = Immediate & Inflexible”**
🎯 **“Adaptive = Accurate & Acquired”**

Think of it as the body's **front-line, primitive army**.
Like a **trained sniper** that remembers each target.

Feature	Innate Immunity	Adaptive Immunity
Response Time	Immediate (minutes to hours)	Delayed (days to weeks on first exposure)
Specificity	**Non-specific**, recognizes broad patterns (PAMPs)	**Highly specific**, recognizes unique antigens
Memory	No memory (same response each time)	Has **memory** (faster, stronger secondary response)
Key Cells	Neutrophils, macrophages, dendritic cells, NK cells, mast cells	**T cells ($CD4^+$, $CD8^+$), B cells (plasma cells)**
Recognition Molecules	PRRs (Pattern Recognition Receptors, e.g., TLRs)	TCRs and BCRs (antigen-specific receptors)
Pathogen Targets	Broad: bacteria, fungi, viruses, parasites	Targeted: antigen-specific, both intra/extracellular
Inflammation	Strong initiator of inflammation	Modulates and fine-tunes inflammation
Barriers	Skin, mucosa, pH, enzymes (lysozyme), complement	None physical; relies on clonal expansion of lymphocytes
Activation Requirement	Always ready; no prior exposure needed	Requires **antigen exposure and activation**

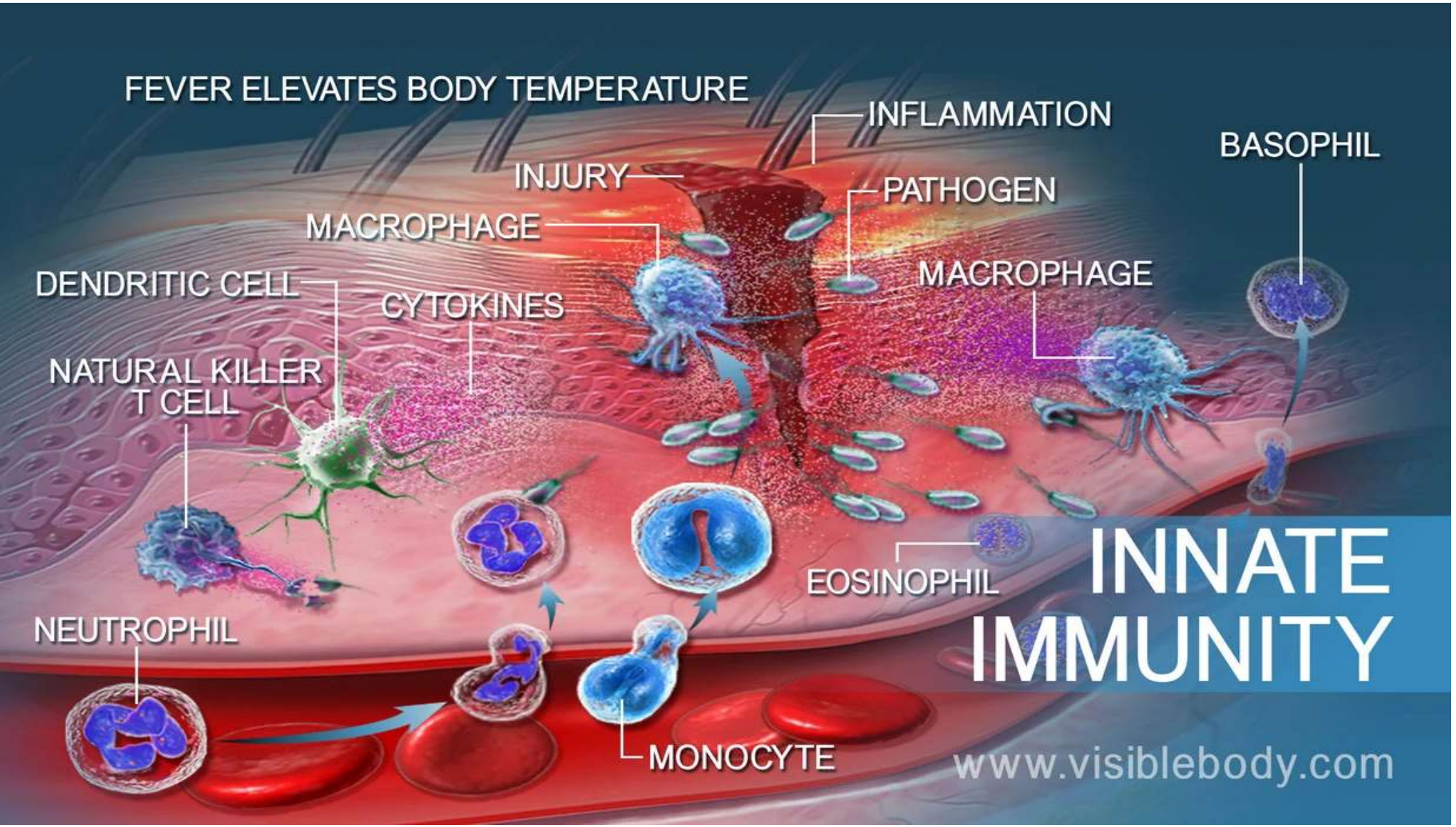
Innate Immunity: Preventing Entry

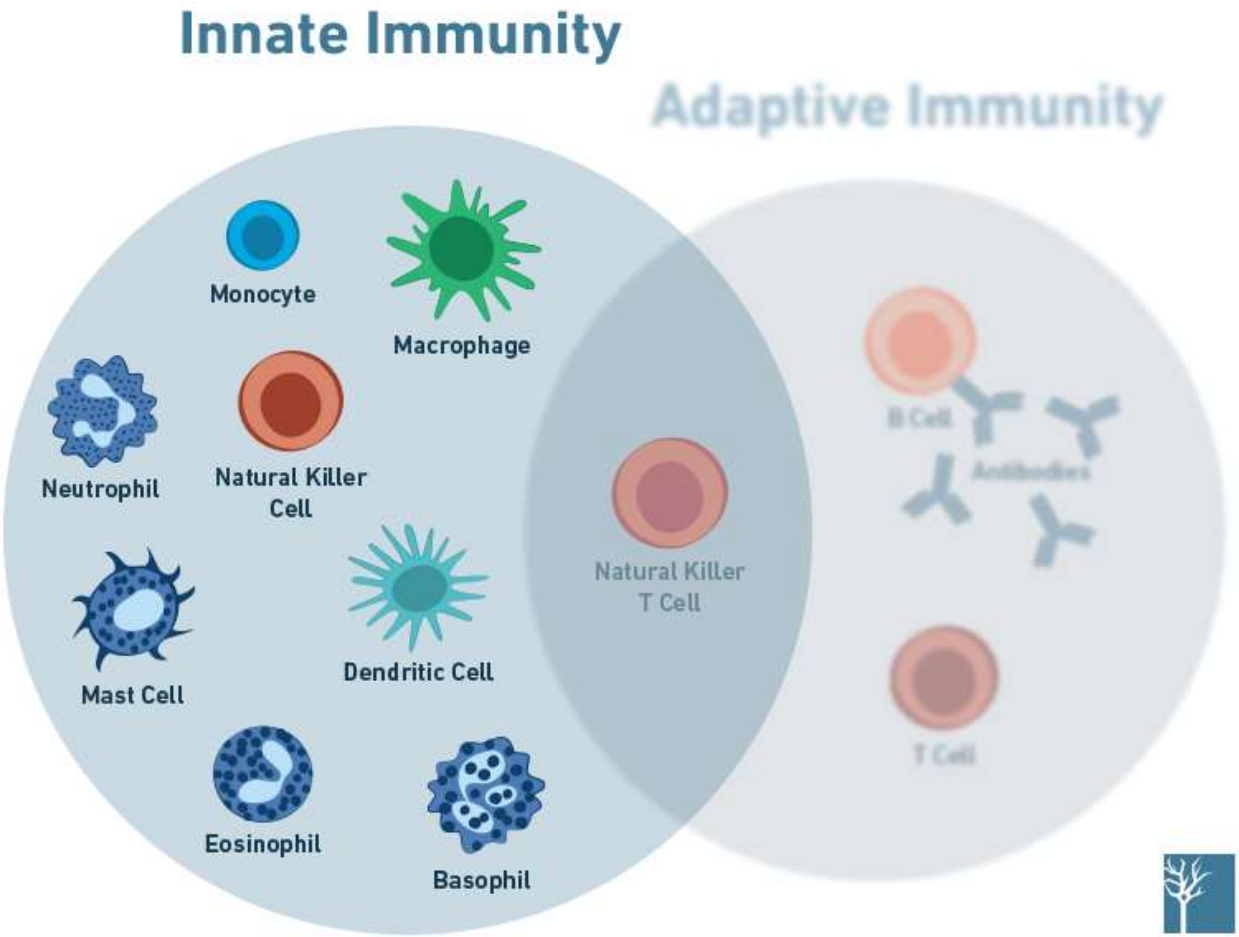
What positive role is played by nonpathogenic microorganisms on the skin and mucous membranes?

They help prevent the growth of pathogenic organisms.

Feature	Innate Immunity
Speed	Immediate (minutes to hours)
Specificity	Non-specific (PAMPs/DAMPs)
Memory	None
Response Type	General inflammation, phagocytosis
Cell Types	Macrophages, neutrophils, NK cells, dendritic cells, eosinophils, basophils
Barriers	Skin, mucous membranes, enzymes, acids

- Innate immunity is the first line of defense against infections and is characterized by **its rapid response to pathogens.**
- Unlike adaptive immunity, **innate immunity does not require prior exposure to a pathogen to be effective**.
- It is non-specific and recognizes a broad range of pathogens through **pattern recognition receptors (PRRs).**


FEVER ELEVATES BODY TEMPERATURE
INFLAMMATION
BASOPHIL
INJURY
PATHOGEN
MACROPHAGE
MACROPHAGE
DENDRITIC CELL
CYTOKINES
NATURAL KILLER T CELL
EOSINOPHIL
INNATE IMMUNITY
NEUTROPHIL
MONOCYTE
www.visiblebody.com



Cell Signaling TECHNOLOGY®

Innate Immune System (there is more but….

1. Physical & Chemical Barriers

- **Skin** – tight junctions, acidic pH, antimicrobial peptides (defensins)
- **Mucosa** – mucus, lysozyme (in saliva/tears), cilia
- **Gastric acid** – kills ingested microbes

2. Cellular Defenses

Cell Type	Function
Neutrophils	Fastest responders; phagocytose & kill microbes
Macrophages	Phagocytosis, antigen presentation, cytokine release
Dendritic Cells	Bridge innate & adaptive immunity; professional APCs
NK Cells	Kill virus-infected and tumor cells lacking MHC I
Eosinophils	Kill parasites, trigger allergic response
Basophils/Mast Cells	Histamine release (allergies, inflammation)

Complement System

- Activated by 3 pathways: **Classical**, **Alternative**, **Lectin**
- Key effects:
  - **Opsonization (C3b)**
  - **Inflammation (C3a, C5a)**
  - **Membrane Attack Complex (C5b–C9)** → lysis of microbes

Complex Biological Responses of Innate Immunity

. Pattern Recognition & Activation

•Innate cells recognize **Pathogen-Associated Molecular Patterns (PAMPs)**

Inflammatory Response

•**Goal:** Recruit immune cells to site of infection/damage.

Key Steps:

1.Vasodilation & vascular permeability → redness, swelling

2.Endothelial activation → expression of adhesion molecules (ICAM, VCAM)

3.Leukocyte recruitment → rolling, adhesion, transmigration (via integrins)

Mediators:

•Histamine (from mast cells)

•Prostaglandins, leukotrienes

•Cytokines: **IL-1, IL-6, TNF-α**

3. Phagocytosis & Killing

•**Neutrophils & macrophages** ingest and kill microbes via:

- **ROS (reactive oxygen species)**
- **Nitric oxide**
- **Lysosomal enzymes**

Clinical Tie-in:

•**Chronic Granulomatous Disease** = NADPH oxidase deficiency → recurrent infections with catalase-positive organisms.

4. Complement System Activation

•3 pathways: **Classical**, **Alternative**, and **Lectin**

•Functions:

- **Opsonization** (C3b)
- **Chemotaxis** (C5a)
- **Cell lysis via MAC** (C5b–C9)

Clinical Tie-in:

•**C3 deficiency** → recurrent bacterial infections

•**C5–C9 (MAC) deficiency** → susceptibility to *Neisseria* infections

Complex Biological Responses of Innate Immunity

Cytokine	Source	Function
IL-1, IL-6, TNF-α	Macrophages	Fever, acute phase response, endothelial activation
IL-8	Macrophages	Neutrophil chemotaxis
IFN-α/β	Viral-infected cells	Antiviral state in neighboring cells
IL-12	Macrophages	Activates NK cells and promotes Th1 response

6. Natural Killer (NK) Cell Activity

•Kill **virus-infected or tumor cells** lacking **MHC I**

•Activated by **IL-12, IFN-α/β**

•Release **perforin and granzymes** → apoptosis

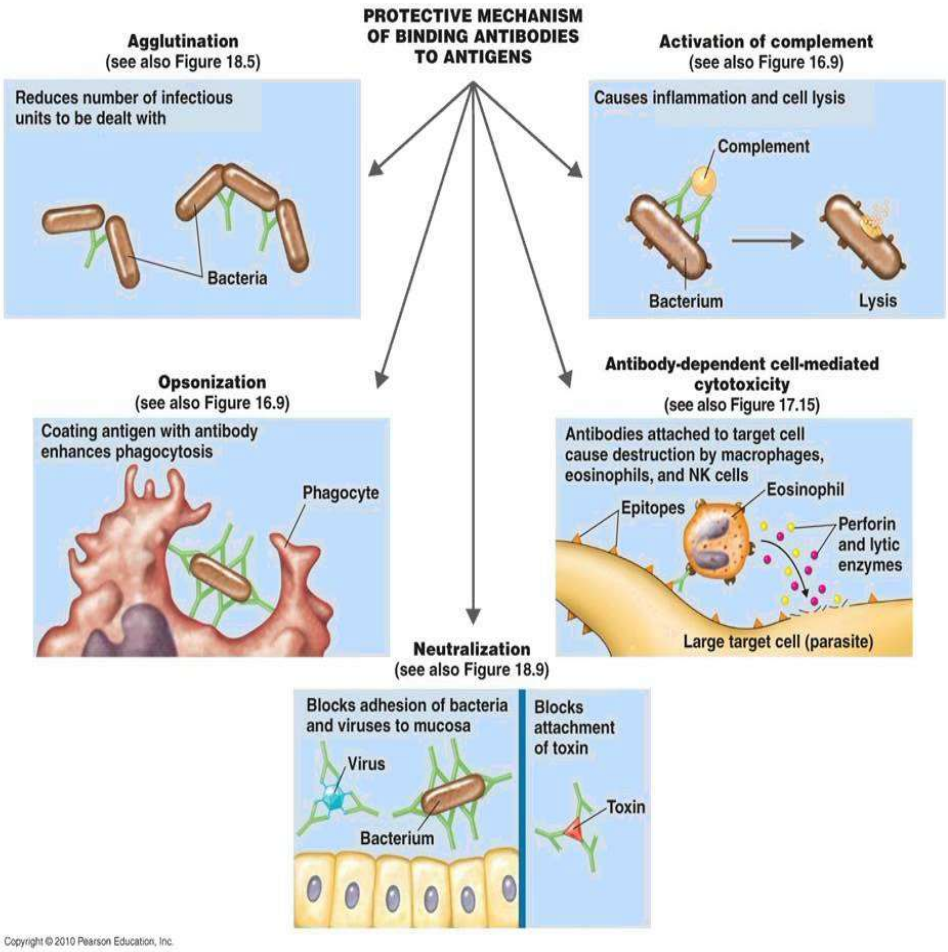
🧠 **Key Mnemonic:**

"NK = No Klas I" — NK cells kill cells **without MHC class I**

Cells and Chemicals

Antigen-Antibody Binding and its Results

- Agglutination – antibodies cause antigens to clump together and fall out of solution
- Opsonization – antigen is coated with antibodies to enhance digestion by phagocytic cells
- Neutralization – antibodies inactivate microbes by blocking their attachment to host cells
- Activation of complement



Adaptive Immunity

- **Adaptive immunity** is the **antigen-specific** arm of the immune system.
- Responsible for long-term protection and immunological memory.
- It includes **humoral** (B-cell-mediated) and **cell-mediated** (T-cell-mediated) immunity.

Feature	Adaptive Immunity
Specificity	Highly specific for unique antigens
Memory	Yes – faster, stronger upon re-exposure
Diversity	Millions of antigen receptors
Clonal Expansion	Upon antigen encounter
Delayed Onset	Takes days to develop (primary response)

Two Arms of Adaptive Immunity

Clinical Application:

- **Vaccines** aim to elicit antibody production.
- **Agammaglobulinemia**: No B cells → recurrent bacterial infections.

1/Humoral Immunity (B cells)

Feature	Description
Cells involved	B cells → Plasma cells → **Antibodies**
Antigens targeted	**Extracellular pathogens** (bacteria, toxins)
Key immunoglobulins	IgM (first), IgG (most abundant), IgA (mucosa), IgE (parasites/allergy), IgD
Function	Neutralization, opsonization, complement activation

2/Cell-Mediated Immunity (T cells)

Cell Type	Function
CD4+ (Helper T)	Activate B cells, macrophages, and cytotoxic T cells via **cytokines**
CD8+ (Cytotoxic T)	Kill virus-infected or cancerous cells via perforin/granzyme
Regulatory T cells (Tregs)	Suppress autoimmunity, maintain tolerance

Antigen Presentation	MHC Class
To **CD4+ T cells**	MHC II (extracellular antigens)
To **CD8+ T cells**	MHC I (intracellular antigens, e.g. viruses)

Major Phases of Adaptive Immune Response

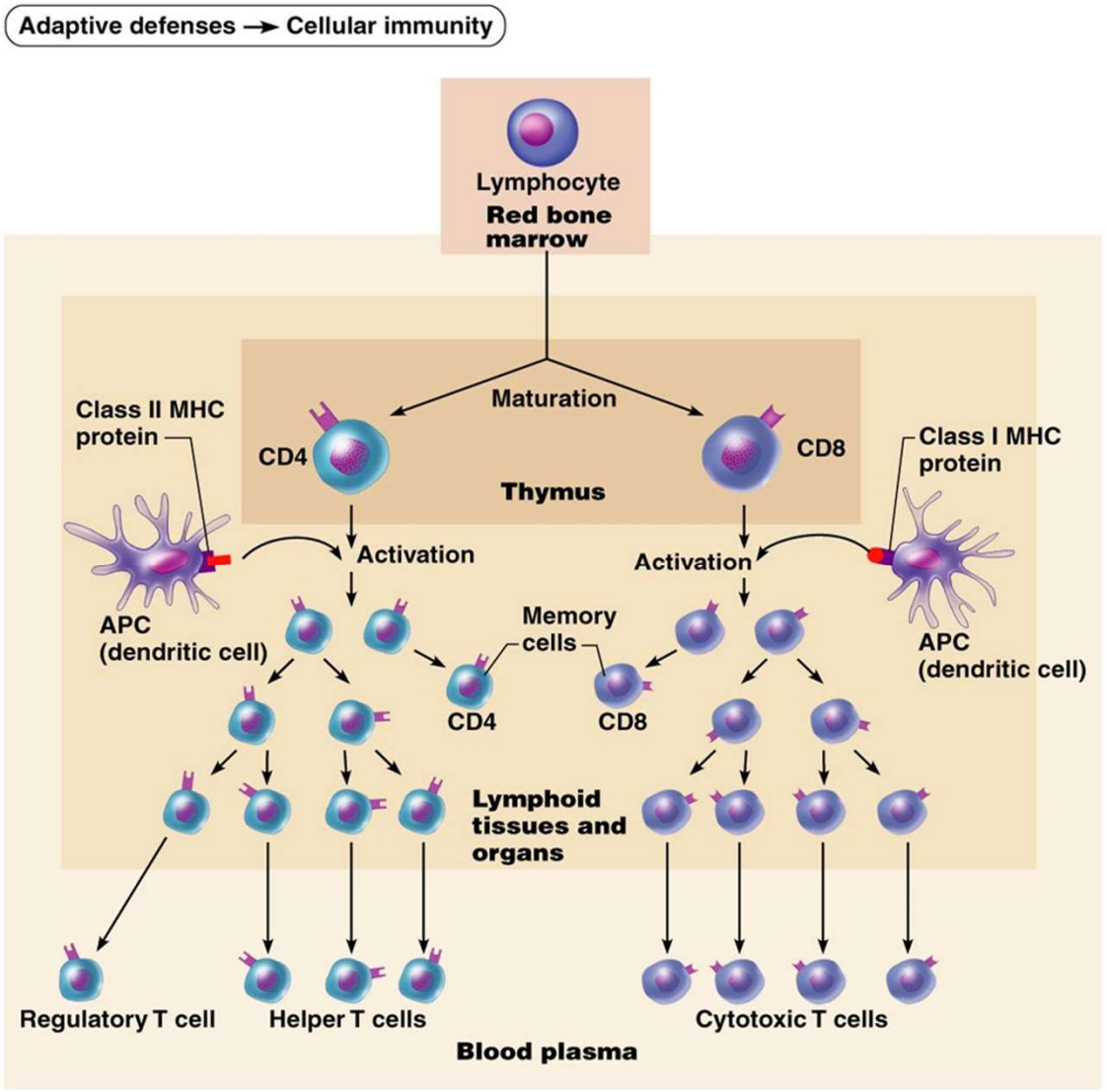
1. **Recognition** – BCRs or TCRs bind antigen.
2. **Activation** – Co-stimulation (e.g., CD28-B7) + cytokines.
3. **Proliferation** – Clonal expansion.
4. **Differentiation** – Into effector or memory cells.
5. **Resolution / Memory** – Immune memory established.

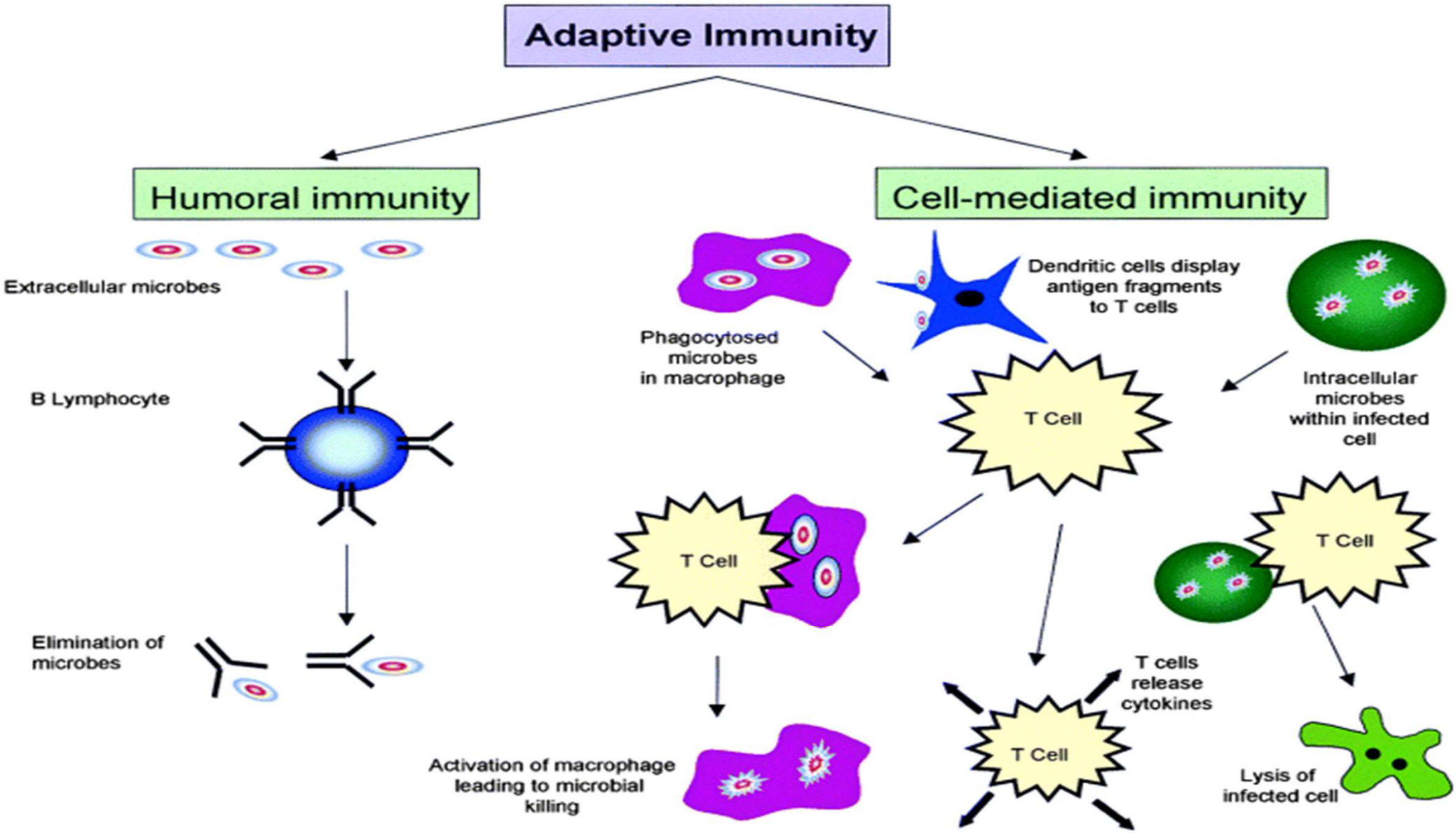
T cells = "Taught" (need APCs)

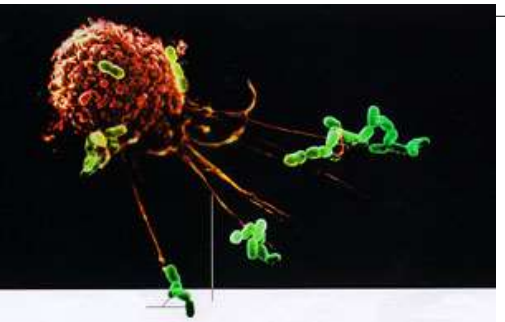
- CD4+ = Teachers (Help others)
  CD8+ = Terminators (Kill infected cells)

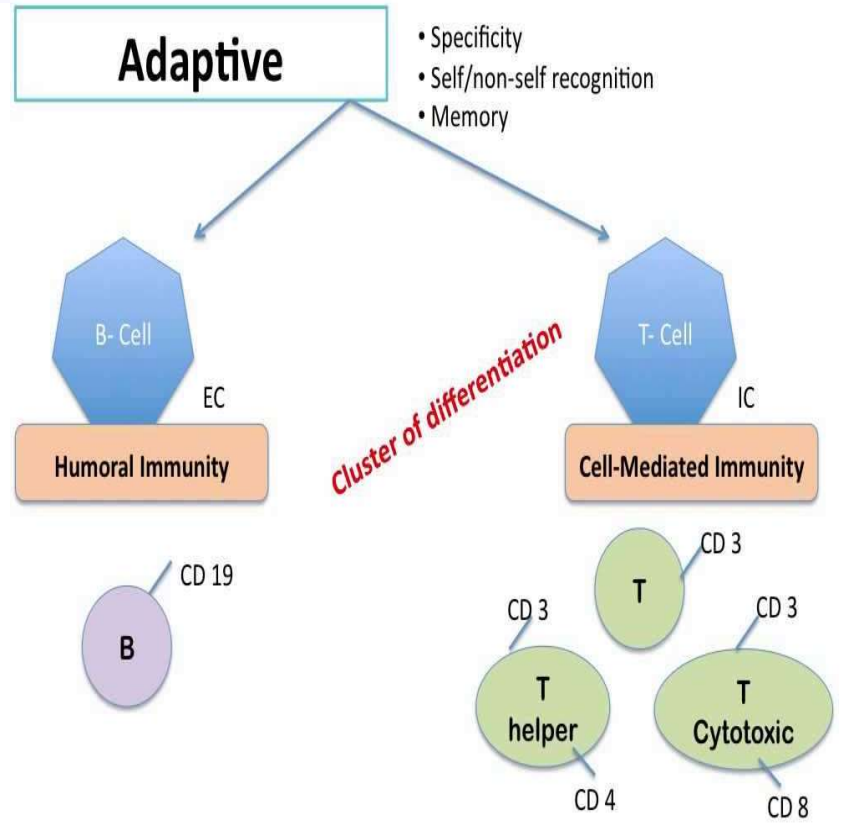
B cells = "Bookworms"

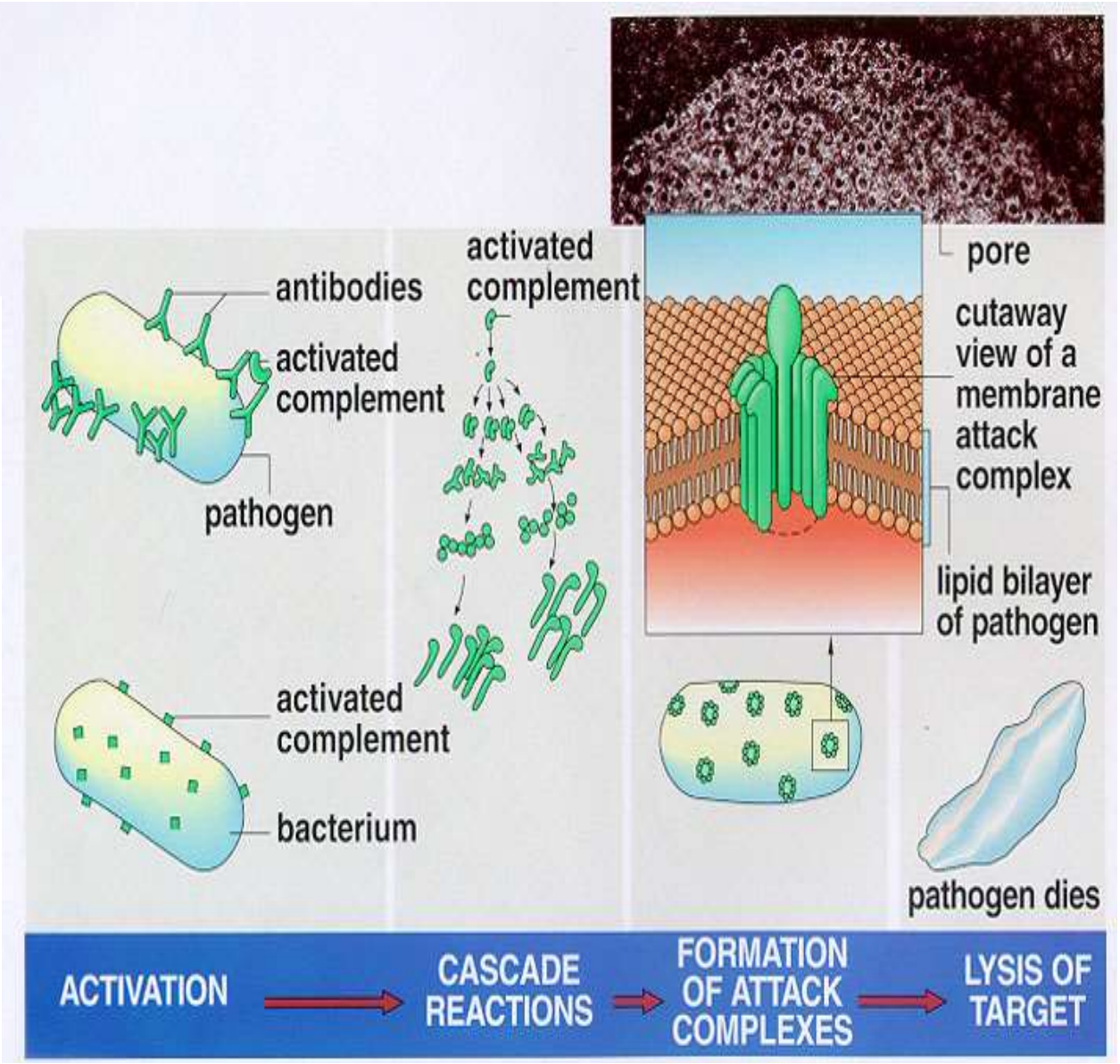
- Make antibodies from their notes (plasma cells)

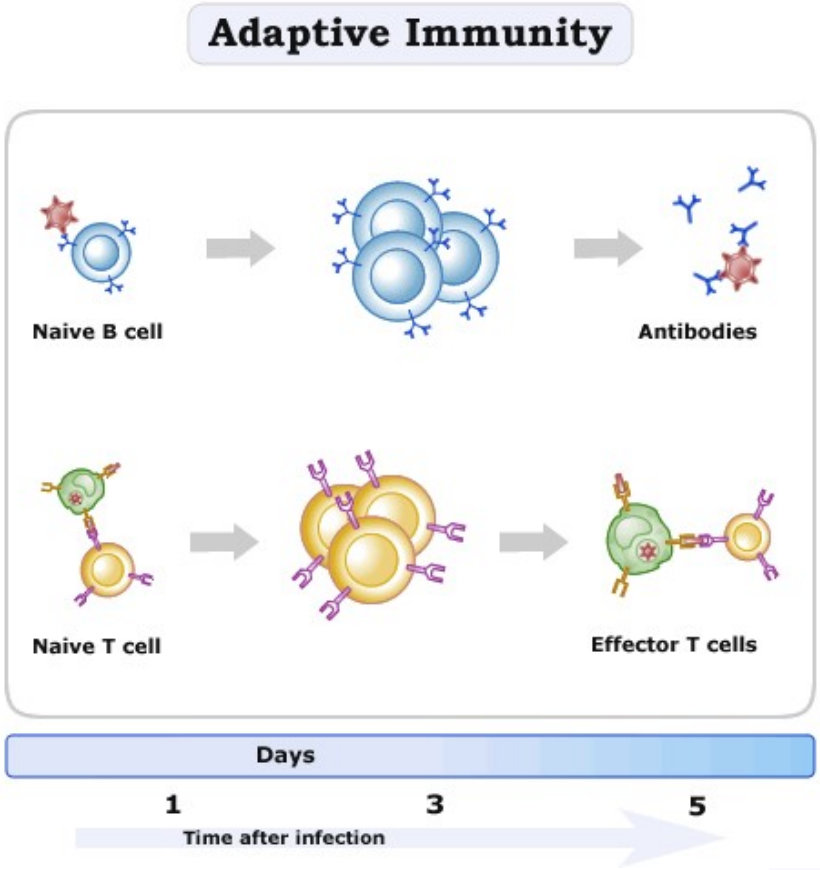


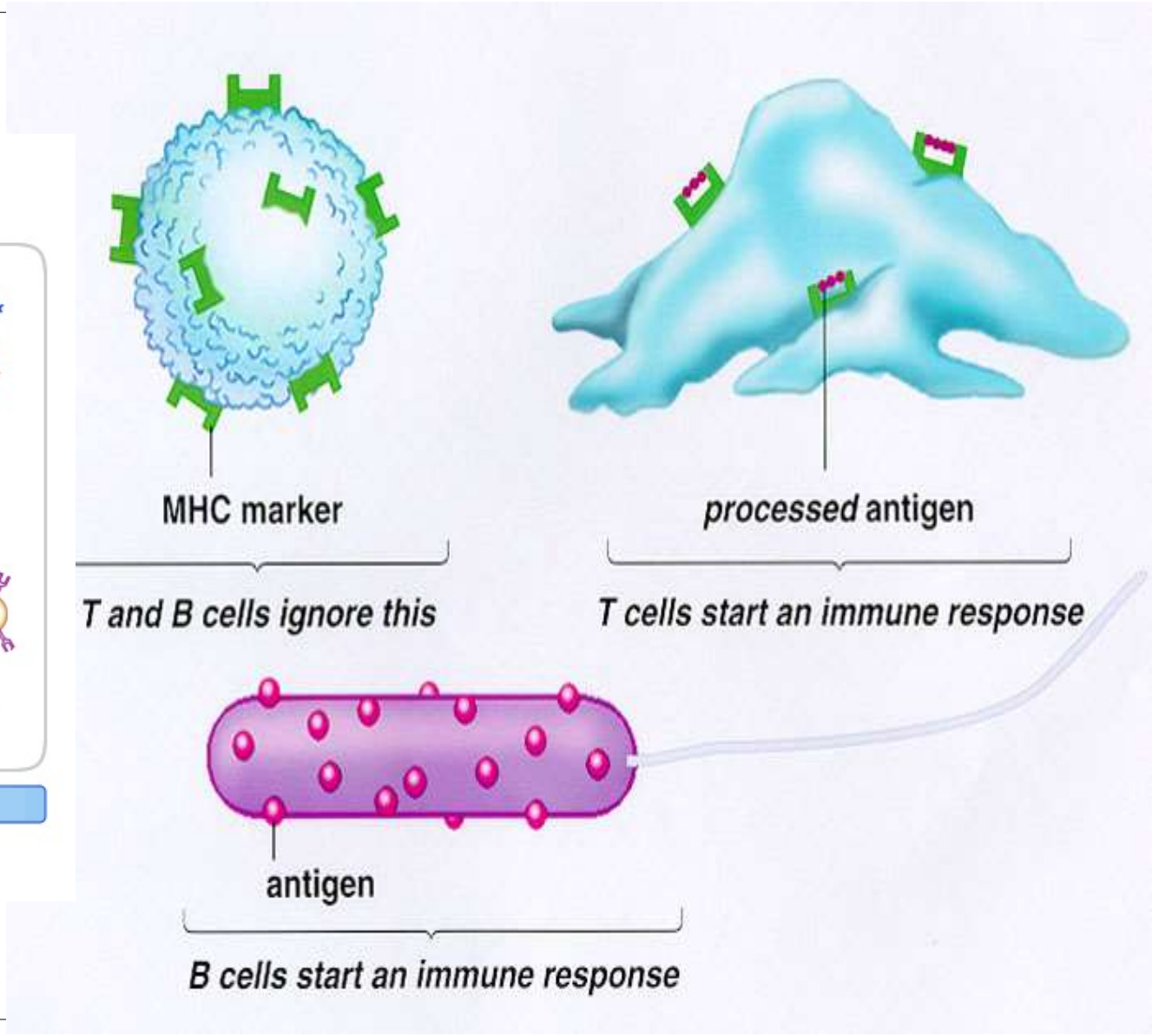

Adaptive Immunity
Humoral immunity
Cell-mediated immunity
Extracellular microbes
B Lymphocyte
Elimination of microbes
Phagocytosed microbes in macrophage
Dendritic cells display antigen fragments to T cells
Intracellular microbes within infected cell
T Cell
T Cell
T Cell
T Cell
T cells release cytokines
Activation of macrophage leading to microbial killing
Lysis of infected cell




Adaptive
• Specificity
• Self/non-self recognition
• Memory
B- Cell
EC
Humoral Immunity
Cluster of differentiation
T- Cell
IC
Cell-Mediated Immunity
CD 19
B
CD 3
T
CD 3
CD 3
T
helper
CD 4
T
Cytotoxic
CD 8


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


Adaptive Immunity
Naive B cell
Antibodies
Naive T cell
Effector T cells
Days
1
3
5
Time after infection


MHC marker
processed antigen
T and B cells ignore this
T cells start an immune response
antigen
B cells start an immune response

ADAPTIVE IMMUNE SYSTEM

T-lymphocytes

- T-cytotoxic → Cytoyoxic

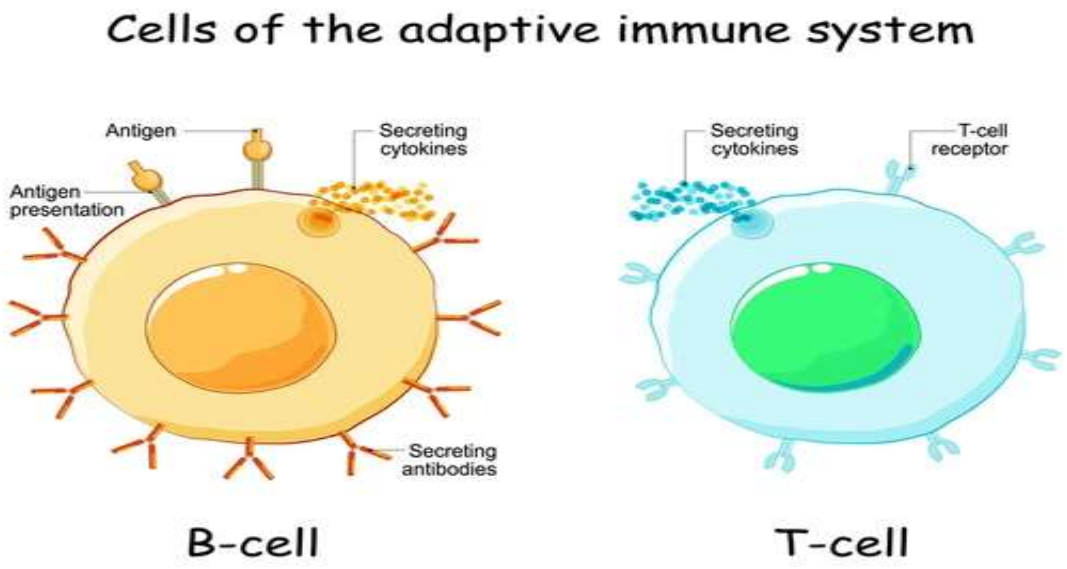
B-lymphocytes

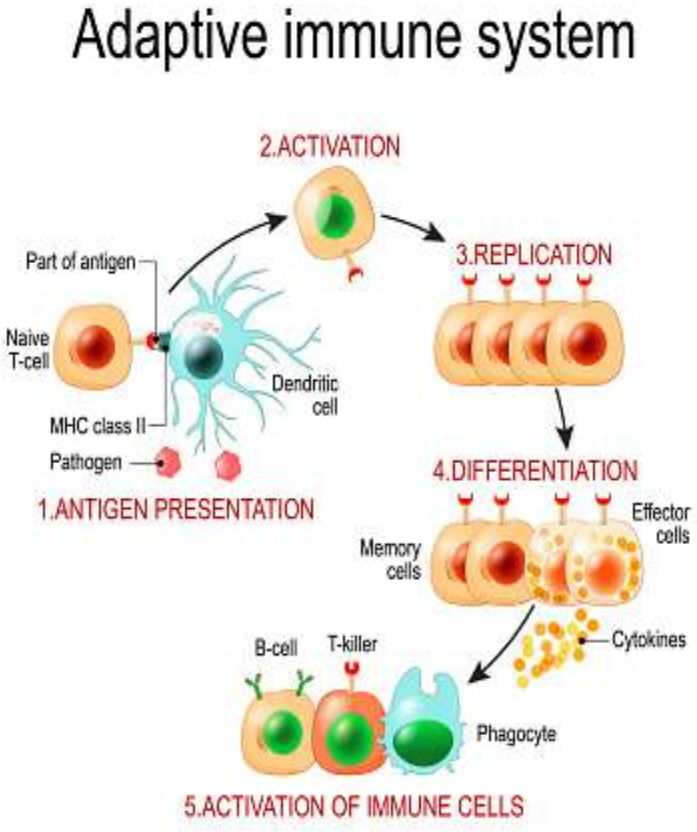
- Plasma cells → Antibodies

Response takes 7 to 10 days

Adaptive Immune System

- T and B Lymphocytes
- Highly specific for pathogen
- Response improves with repeated exposure
- Memory
- Life-long immunity





Acquired (Adaptive) Immunity

- Passive acquired immunity involves **direct transfer of pre-formed antibodies** to a person,
- providing **immediate, short-term protection without activation of the immune system**.

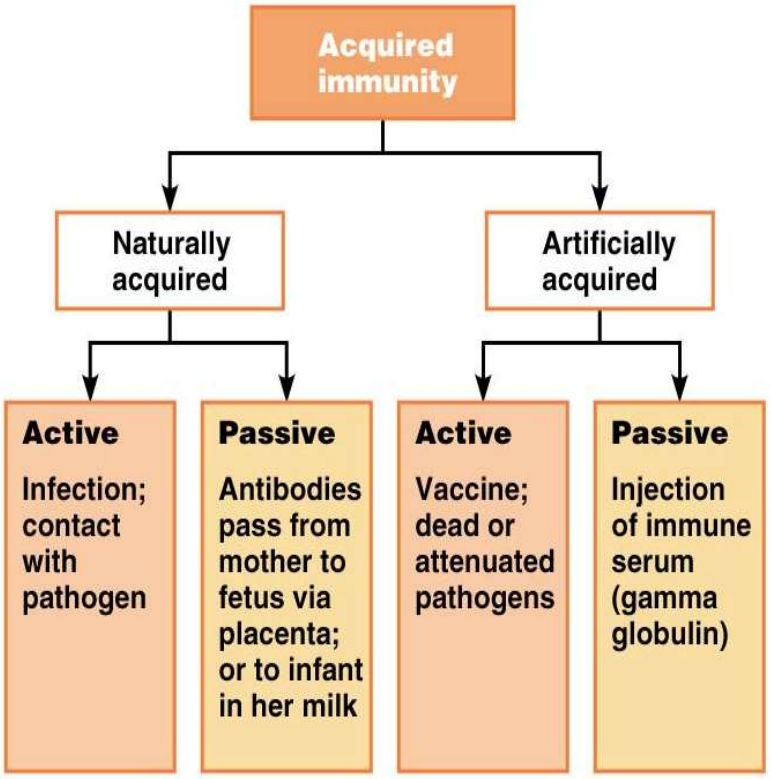
I- Passive acquired immunity

a-Naturally passive acquired immunity

Antibodies are passed through placenta to the fetus

b- Artificially passive acquired immunity

The injection of alredy prepared antibodies, such as gamma globulin (short-term immunization)



Acquired (Adaptive) Immunity

Feature	Description
Type of Immunity	Adaptive (but *passively received*)
Onset	Immediate
Memory	✖ None
Duration	Short-lived (weeks to months)
Involves	Antibodies only (no activation of B/T cells)

Passive Acquired Immunity

Mechanism

1. **Antibodies already produced** in another person/animal
2. **Transferred to recipient** (placenta, breast milk, or injection)
3. **Immediate protection** against specific antigens
4. **No memory** → protection wanes as antibodies degrade

Type	Description	Example
Natural Passive Immunity	Transfer from mother to baby	IgG across placenta; IgA in breast milk
Artificial Passive Immunity	Injection of antibodies	Rabies immune globulin, tetanus immune globulin, anti-venom

Situation	Type	Purpose
Maternal IgG to fetus	Natural	Protects newborn for ~6 months
Rho(D) immune globulin	Artificial	Prevents hemolytic disease of the newborn
HBV exposure + HBIG	Artificial	Immediate post-exposure protection
Snake bite antivenom	Artificial	Neutralizes venom toxins rapidly

Acquired Or Adaptive Immunity

II- Active acquired immunity

- Active acquired immunity is immunity that develops **after exposure to an antigen**, leading to **an immune response with memory**.
- It involves **activation of B and T lymphocytes**, antibody production, and **long-term protection**.

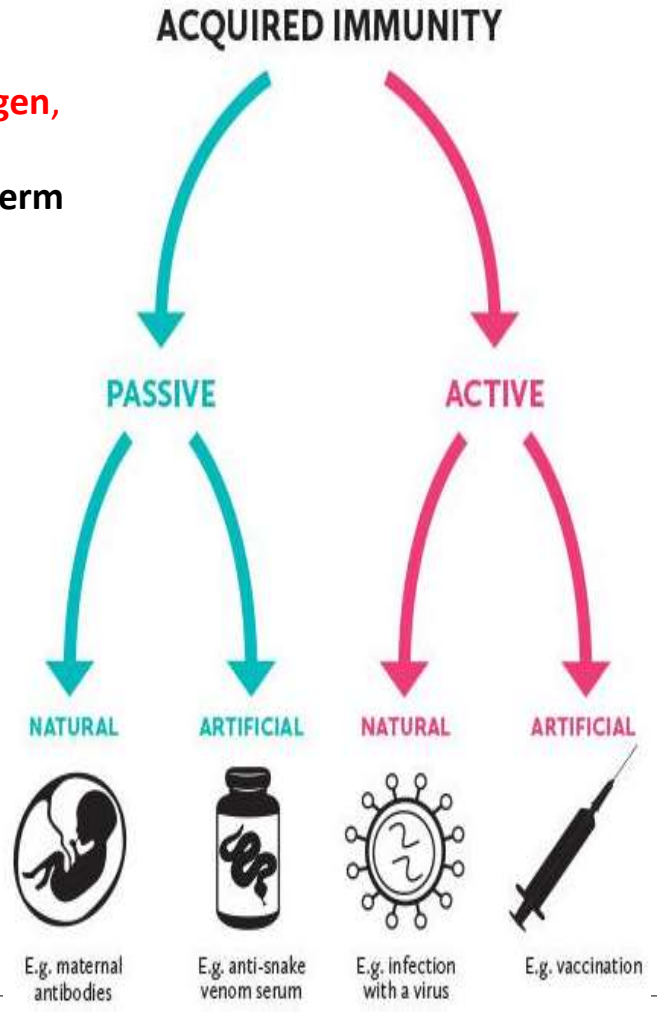
a-Natural active acquired immunity :

- Following clinical or subclinical infections
- measles or mumps, in which immunity is long lasting

b- Artificial active acquired immunity :

- Following vaccination with live or killed infectious agents or their products

Type	Description	Example
Natural Active Immunity	Acquired through **natural infection**	Recovering from measles, COVID-19
Artificial Active Immunity	Acquired through **vaccination**	MMR vaccine, Hepatitis B vaccine



II- Active acquired immunity

Mechanism

1. **Antigen Exposure** (infection or vaccine)
2. **Antigen Processing & Presentation** (via APCs to T cells)
3. **Activation of B and/or T cells**
4. **Clonal Expansion**
5. **Antibody production (B cells)** and/or **Cytotoxic activity (T cells)**
6. **Formation of memory cells** for faster response upon re-exposure

Condition	Importance of Active Immunity
Herd Immunity	Relies on population-level active immunity via vaccination
Immunocompromised patients	May not mount effective active response (e.g., HIV, chemotherapy)
Booster doses	Reactivate immune memory (e.g., Tdap, COVID boosters)

Situation	Type of Active Immunity	Notes
Child recovers from chickenpox	Natural	Memory prevents reinfection
Patient receives tetanus toxoid vaccine	Artificial	Booster needed every 10 years
COVID-19 infection or mRNA vaccine	Both exist	May produce neutralizing antibodies and memory cells

Active vs Passive Immunity

Active = Your body works (makes its own response)

Passive = Preformed antibodies given (e.g., IVIG, maternal IgG)

"Active = Action by the body"

You get the germ or the shot → your body **acts** → you get memory.

Condition	Dominant Arm Affected
Sepsis	Overactivation of **innate immunity** (TLRs, cytokine storm)
HIV/AIDS	Failure of **adaptive immunity** (loss of $CD4^+$ T cells)
Vaccination	Stimulates **adaptive memory** (B and T cells)
Chronic granulomatous disease	Innate defect: neutrophil oxidative burst
Agammaglobulinemia	Adaptive defect: B cells can't produce antibodies

A patient exposed to *Mycobacterium tuberculosis* develops granulomas in the lungs. Which of the following immune responses is primarily responsible for this finding?

A. Natural killer cell activation
B. Mast cell degranulation
C. Th1-mediated macrophage activation
D. Complement C3a release
E. Neutrophil extracellular trap formation

✅ **Correct Answer: C. Th1-mediated macrophage activation**

🧠 This reflects **adaptive cell-mediated immunity** — specifically, **Th1 $CD4^+$ T cells** activating macrophages with IFN-γ.

The end

- Stop complaining, it has been resumed

It can be worst