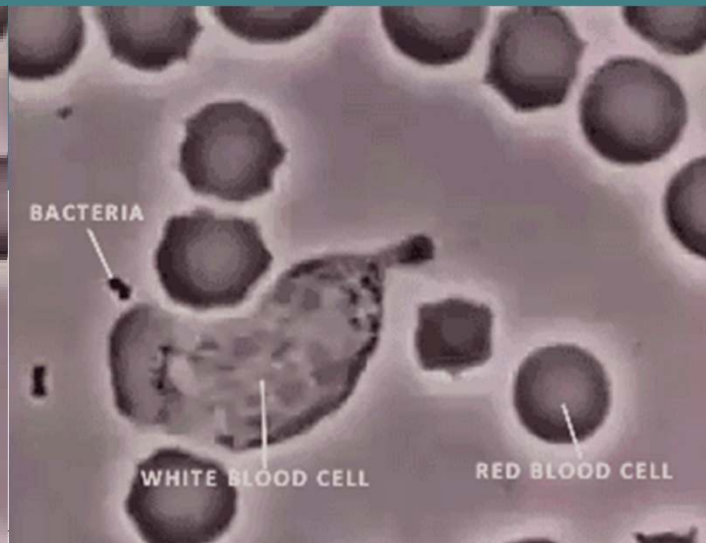
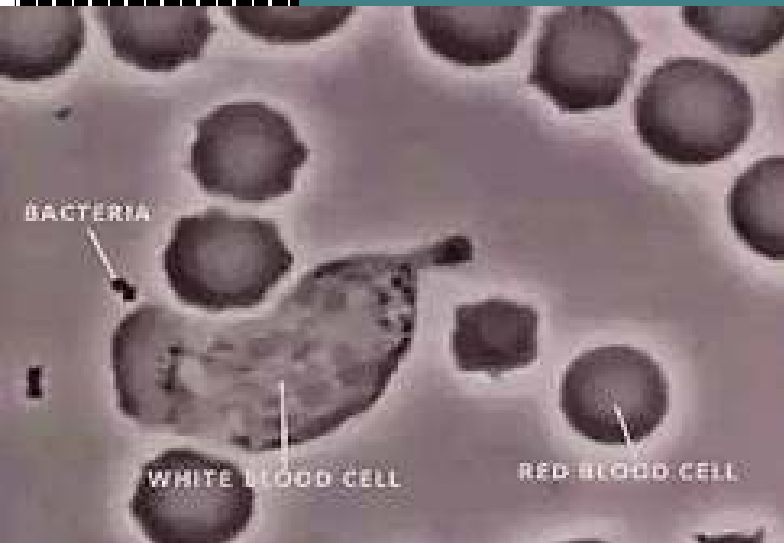


Immunology or licensed to kill

Lecture summer 2020 update

D.HAMMOUDI.MD



Generality



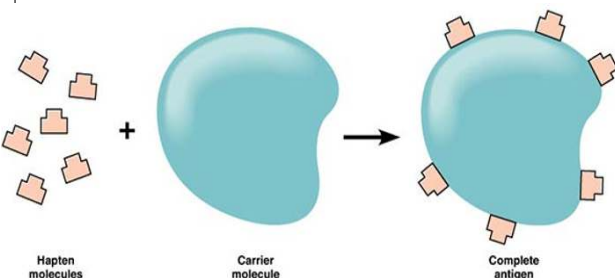
ANTIGEN: CAN BE ANYTHING, MOSTLY PROTEIN, CARDIOLIPID [ONLY LIPID]

● HAPTEN

- **TOO SMALL FOR A IMMUNE REACTION**
- 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 anesthetic gas **halothane** can cause a life-threatening hepatitis, as well as the mechanism by which **penicillin-class drugs** cause autoimmune hemolytic anemia.

● IMMUNOGEN

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



● Immunogenicity

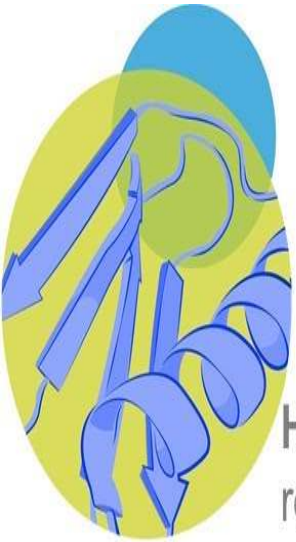
- is the ability to induce a humoral and/or cell-mediated immune response

Antigenicity

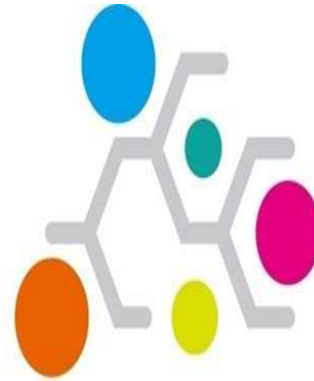
- is the **ability to combine specifically with the final products of the immune response (i.e. secreted antibodies and/or surface receptors on T-cells)**.
- Although all molecules that have the property of immunogenicity also have the property of antigenicity, the reverse is not true

● Antigen(ic) specificity

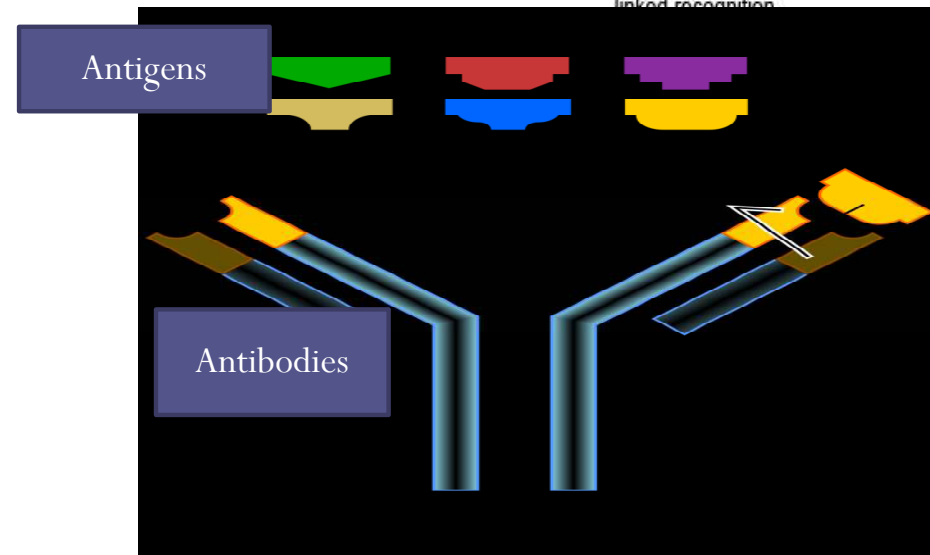
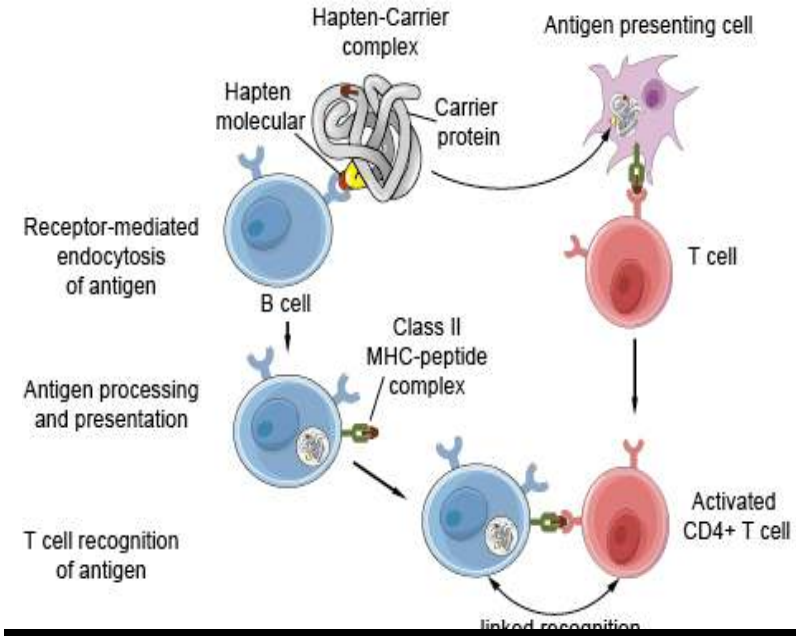
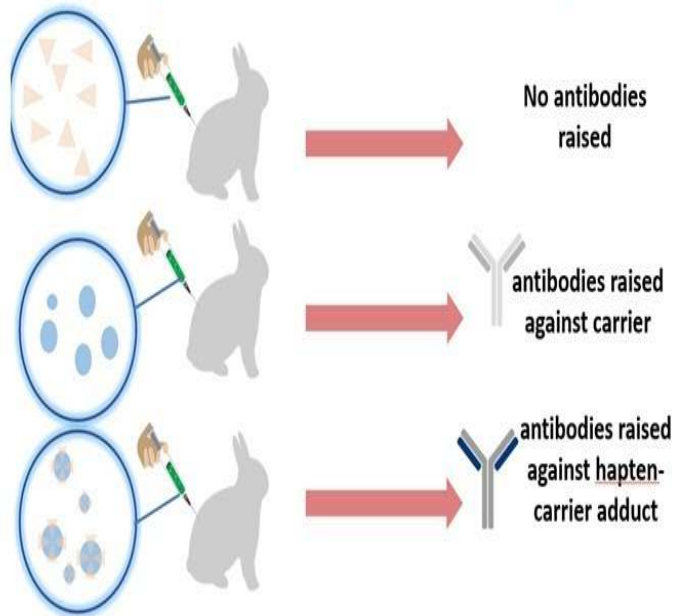
- is the **ability of the host cells to recognize an antigen specifically as a unique molecular entity and distinguish it from another with exquisite precision**



Hapten



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



ANTIGEN VERSUS IMMUNOGEN

ANTIGEN

A substance specifically bind to antibodies or a cell surface receptors of B cells and T cells

Can be either immunogenic or non-immunogenic

Not all are immunogens

Can be either proteins, polysaccharides, lipids or nucleic acids

Haptens are low-molecular-weight molecules, which bind to antibodies

IMMUNOGEN

An antigen capable of inducing an immune response

Immunogenic

All are antigens

Normally proteins and large polysaccharides

Haptens become immunogenic when binding to larger carrier molecules

Visit www.PEDIAA.com

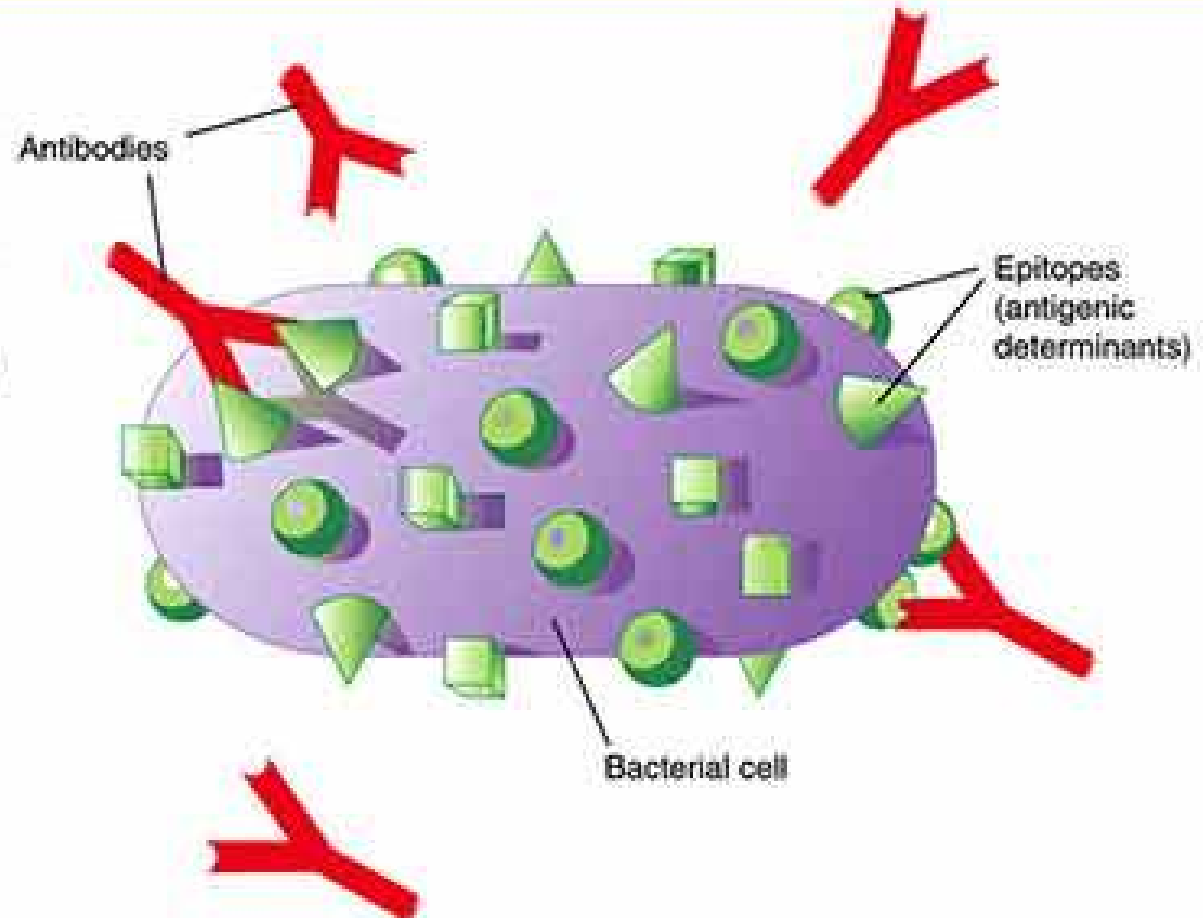
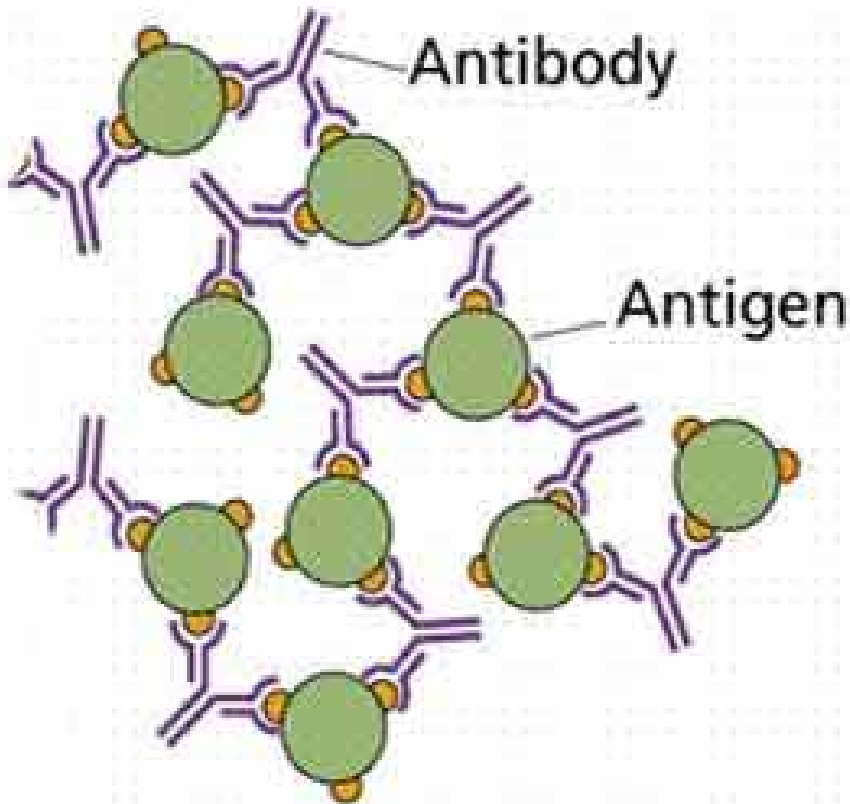
Immunogen vs Antigen

- 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

epitope (antigenic determinant)

- recognized by antibody
- recognized by T-cell receptor

Differences Between Antigen and Antibody

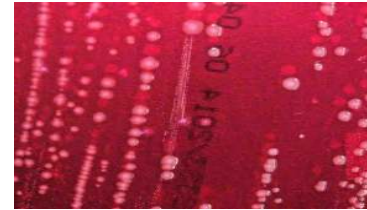


THE MOST IMMUNOGENIC BACTERIA

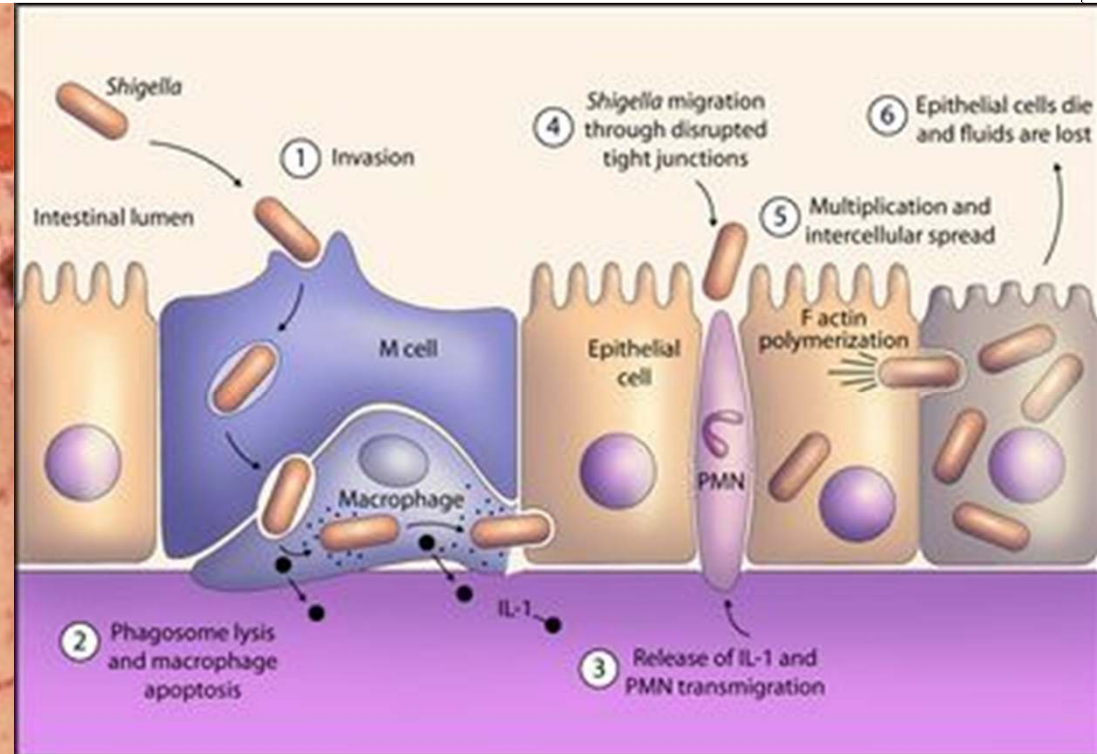
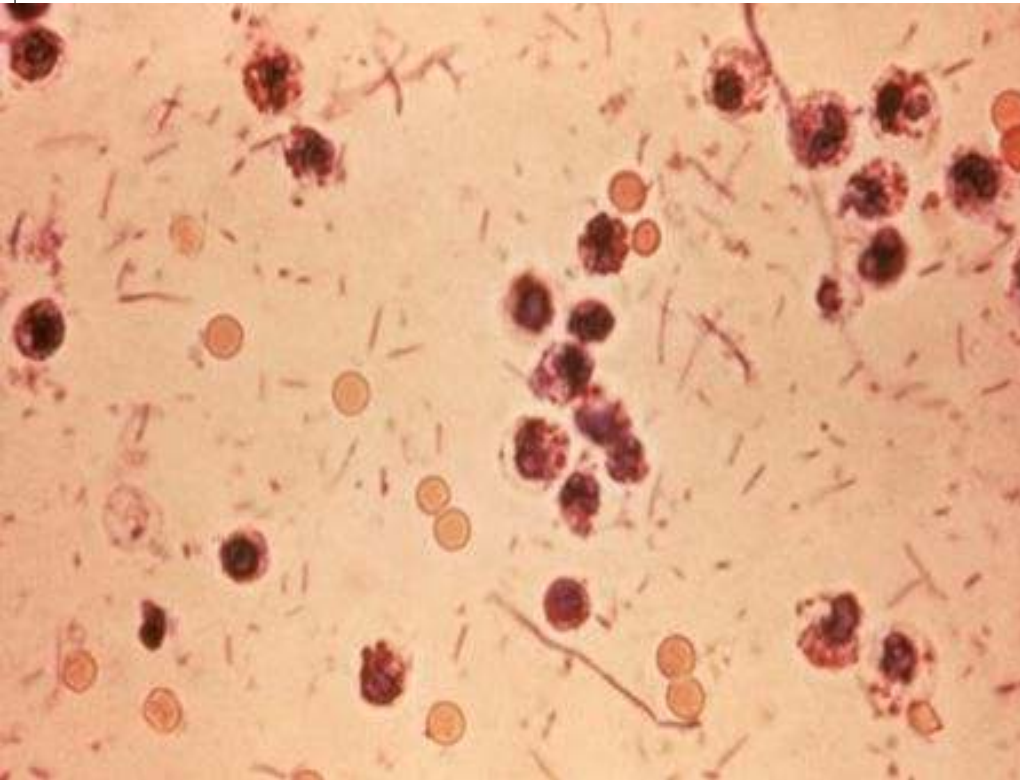


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SHIGELLA

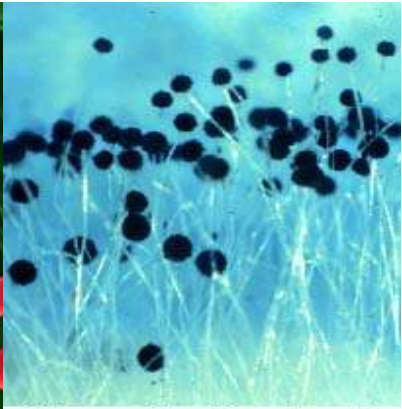
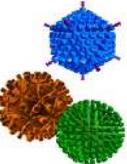


[ONLY 8 TO 10 OF THEM WILL GET YOU SICK.]



The Invaders . . .

- Bacteria
- Viruses
- parasites : protista, & worms
- Fungi
- Prion



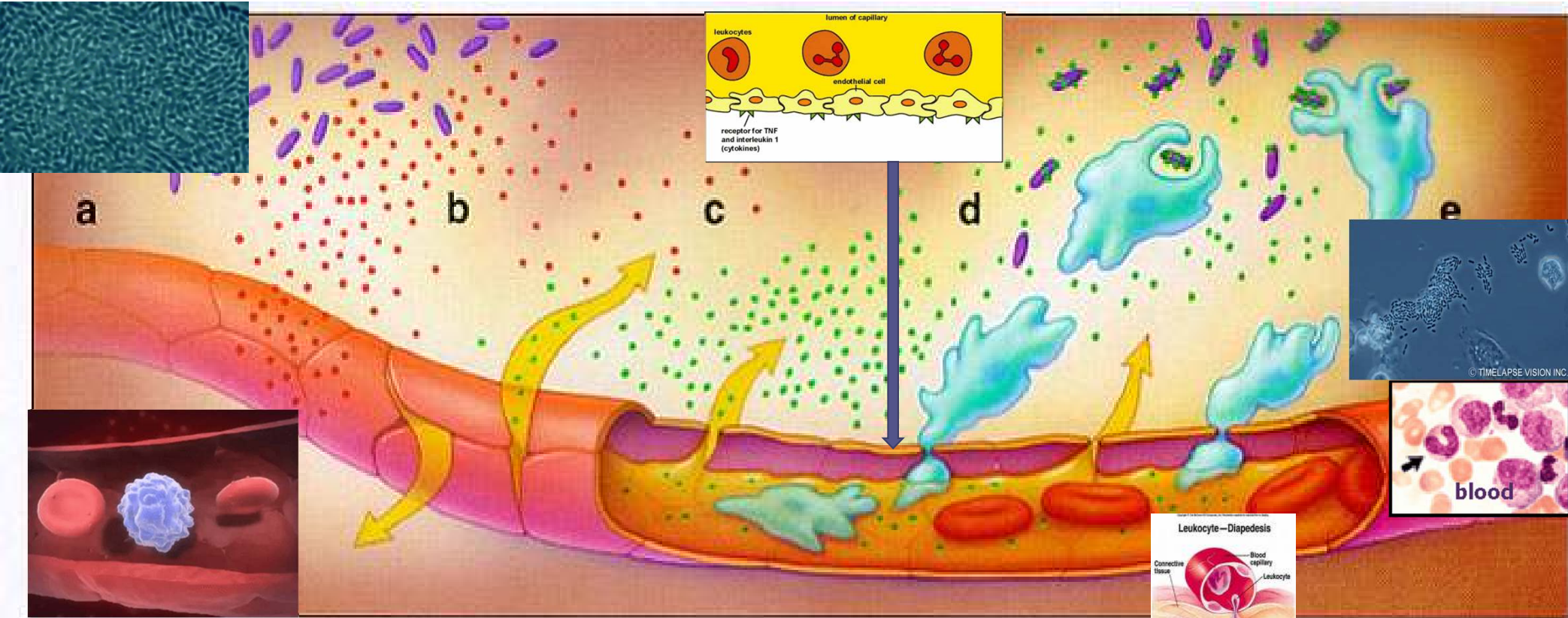
Rhizopus -black bread mold



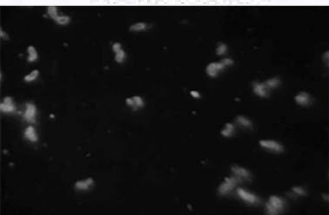
migrate out of the **mouth or nose.**



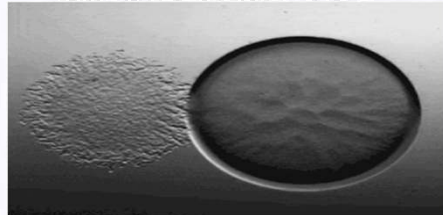
<http://www.sdnhm.org/exhibits/epidemic/teachers/background.html>



a Bacteria invade.



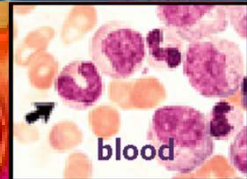
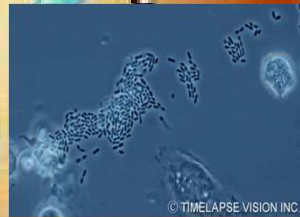
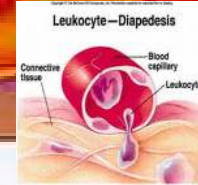
b Substances accumulate.



c The substances make plasma and proteins escape.

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

e Phagocytes engulf bacteria.



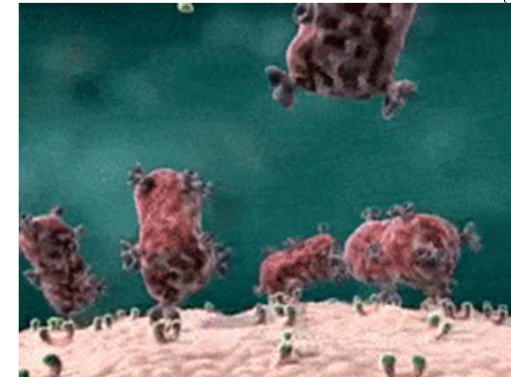
- **HUMORAL RESPONSE**

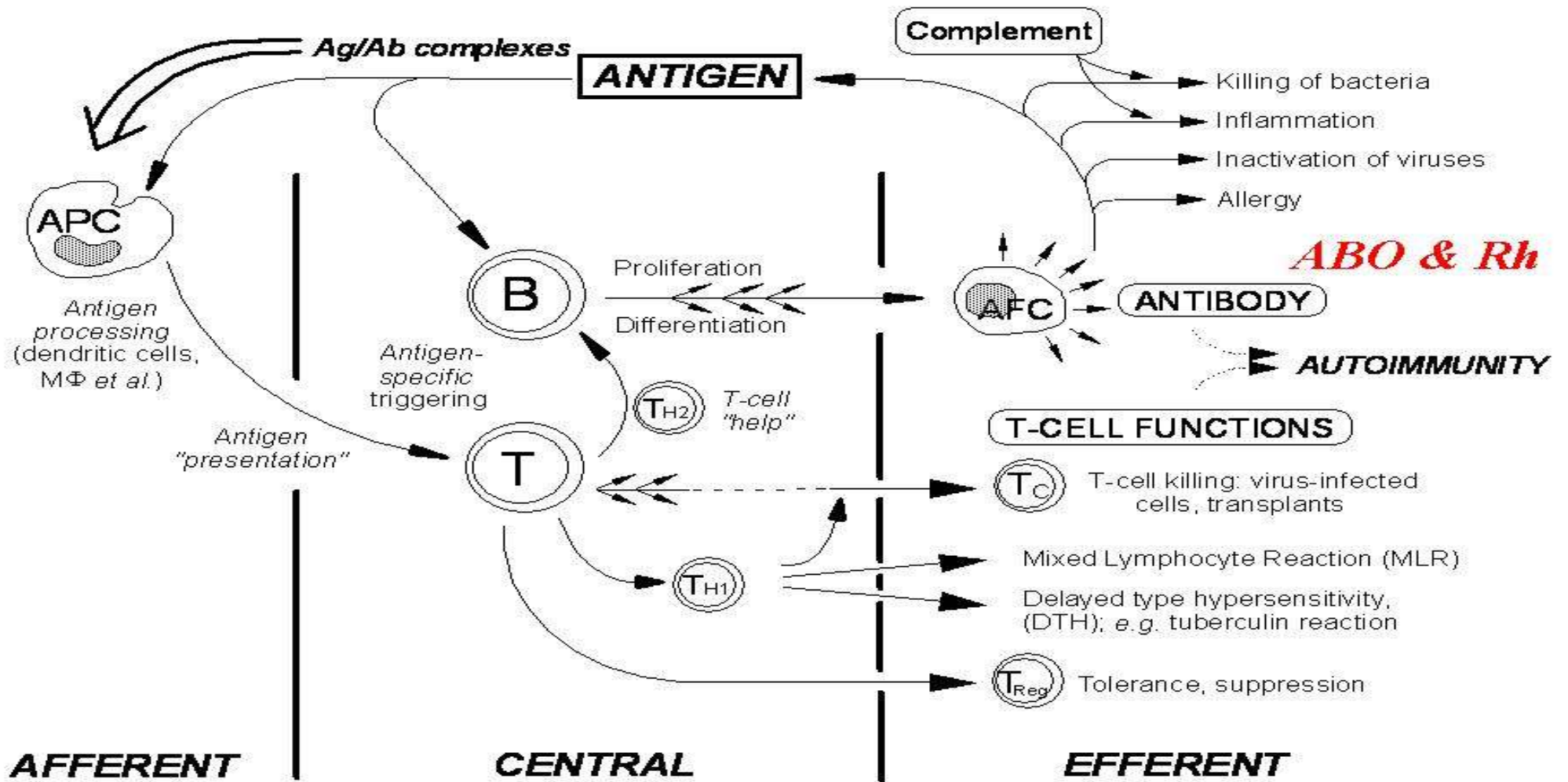
- The humoral immune response is mediated by antibody molecules secreted by plasma cells.

- BLOOD [BLOOD TESTING, HEMOCULTURE]
- B CELLS, NEUTROPHILS

- **CELL MEDIATED RESPONSE**

- TISSUE [BIOPSY]
- T CELLS,
- MACROPHAGES



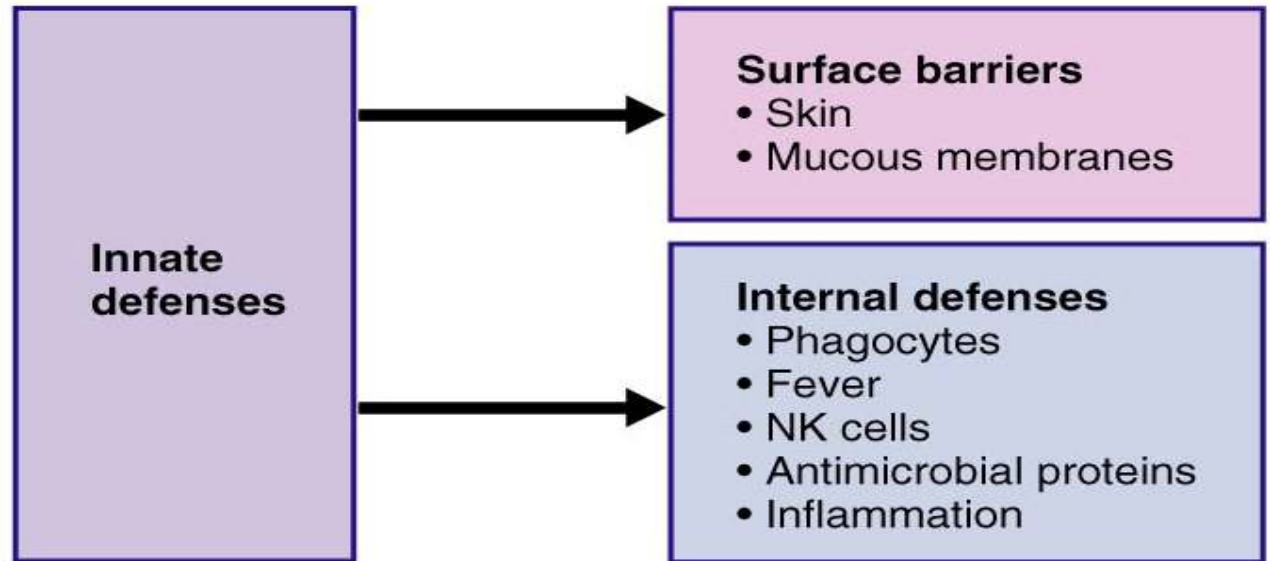


THREE "LIMBS" OF THE IMMUNE RESPONSE

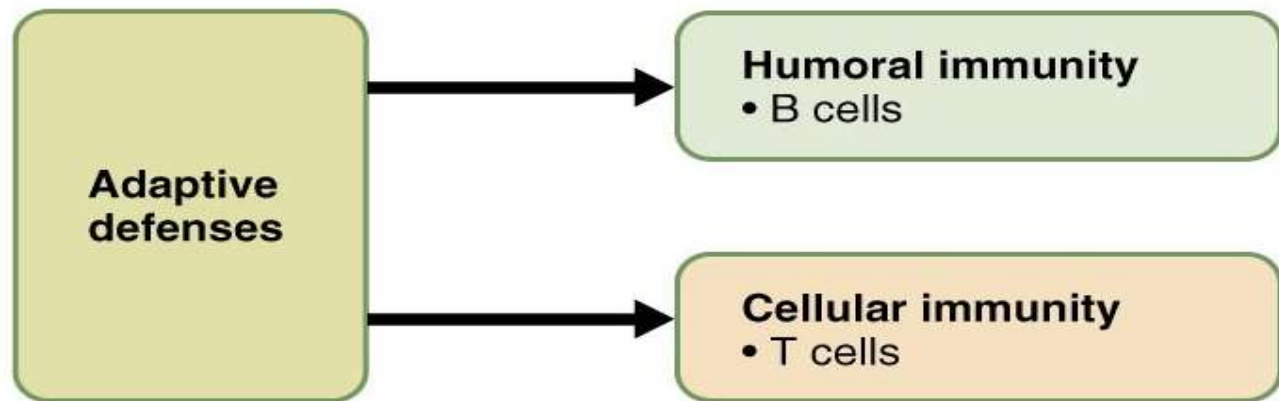
Immunity: Two Intrinsic Defense Systems

- Innate (nonspecific) system responds quickly and consists of:
 - **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



(a)

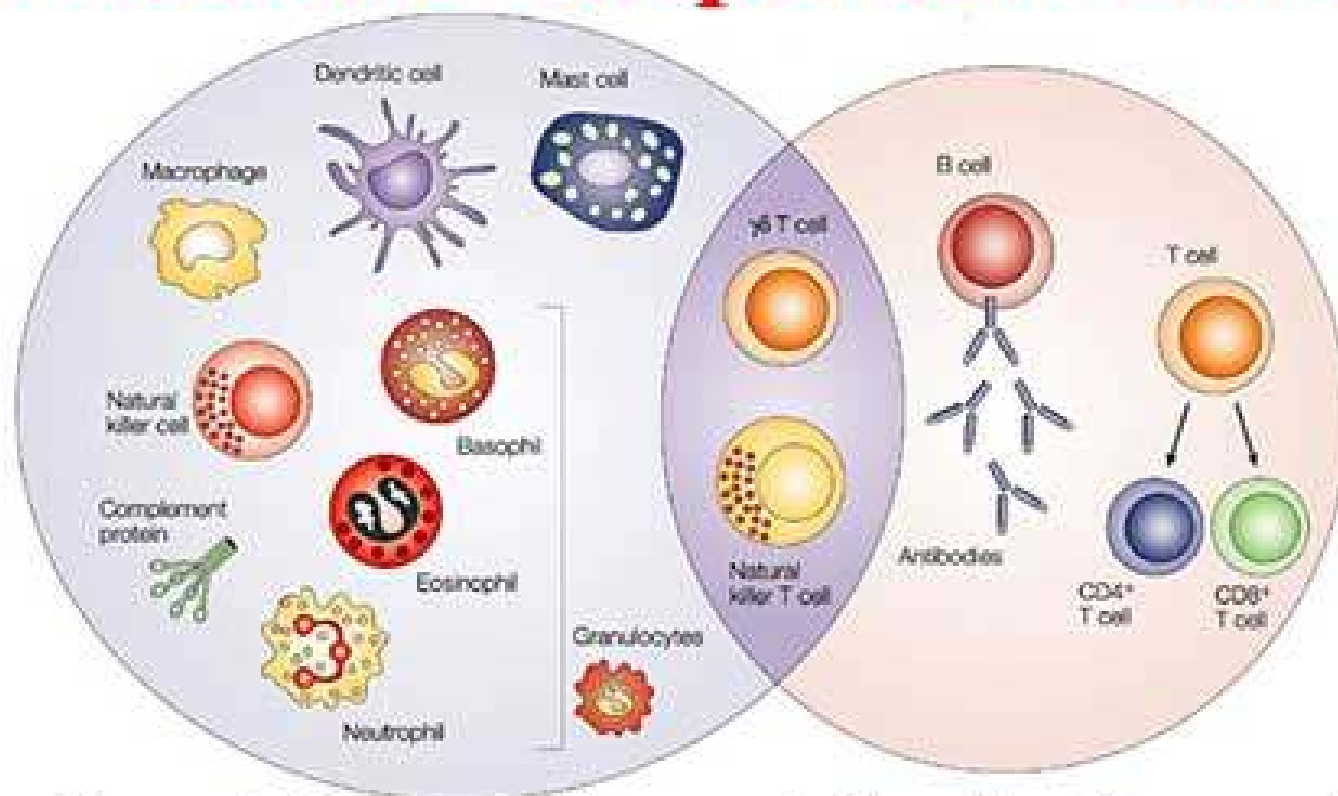


(b)

Outline of the Immune System

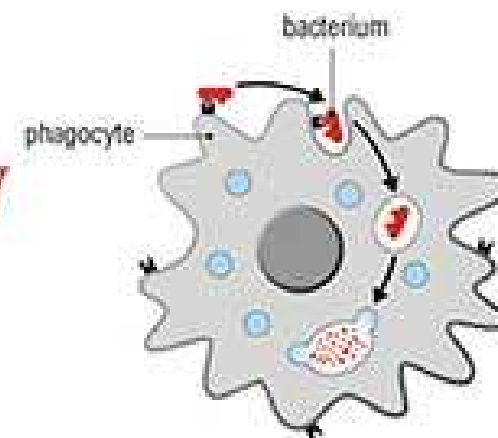
Innate Immunity	1st Line of Defense	Skin
		Mucus
		Secretions
	2nd Line of Defense	Phagocytic Cells
		Antimicrobial Proteins
		Other tissues which participate in inflammatory responses
Adaptive Immunity	3rd Line of Defense	Lymphocytes
		Antibodies
Acquired Immunity	Vaccines / Immunotherapies	Attenuated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

Difference between Innate and Adaptive Immunity

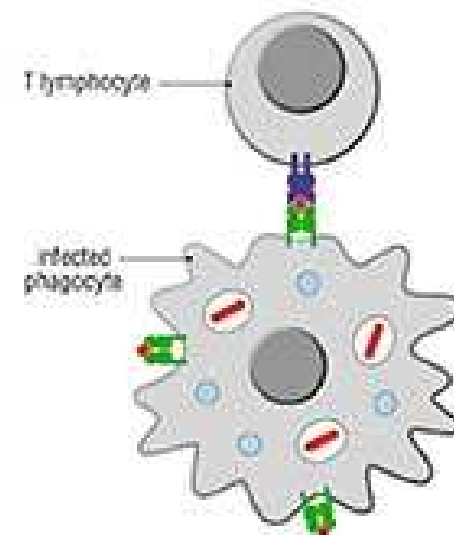


Innate Immunity

Adaptive Immunity



VS



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

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.

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

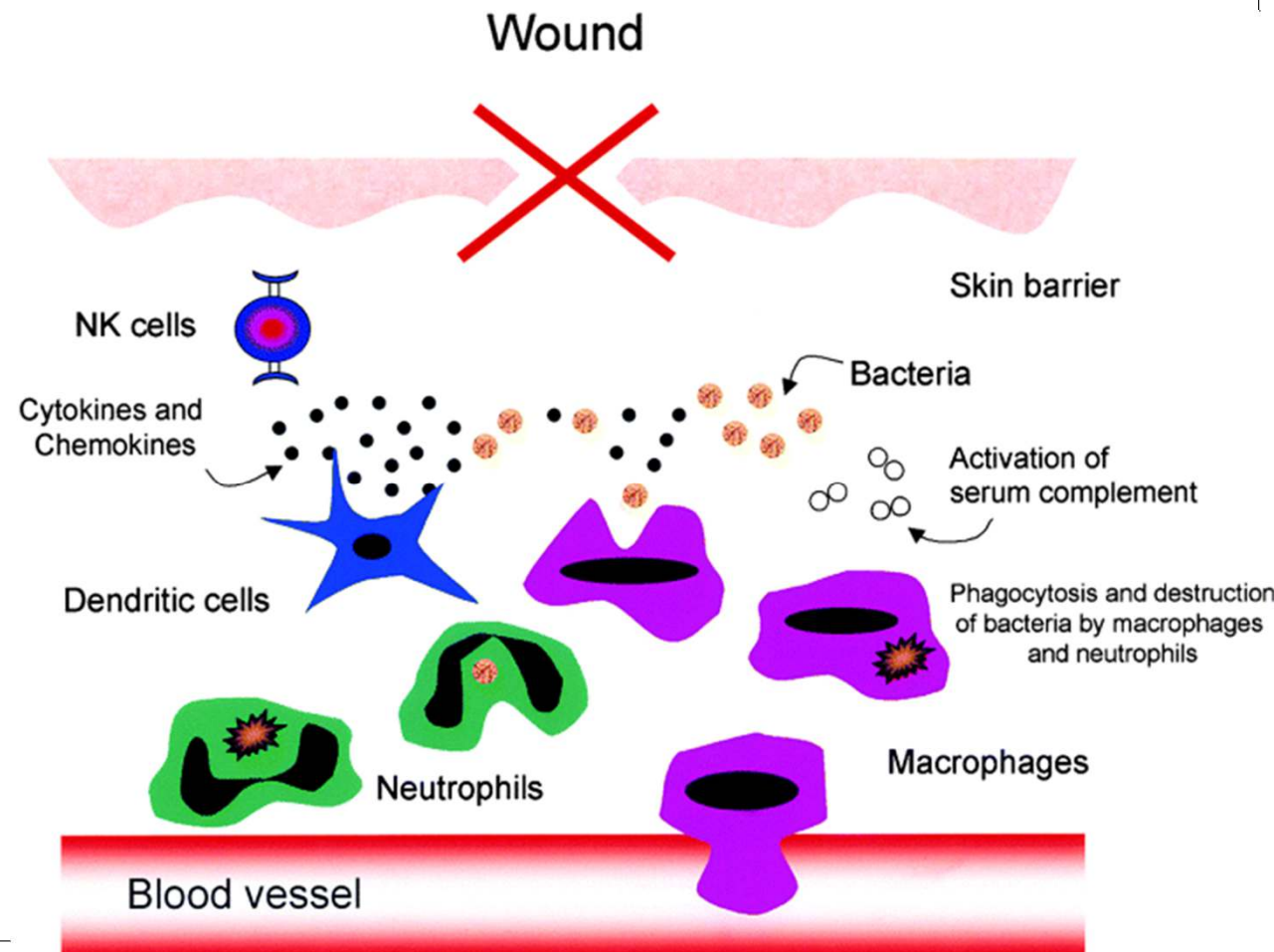
FIRST LINE OF DEFENSE: SURFACE MEMBRANE BARRIERS

Intact skin epidermis	Forms mechanical barrier that prevents entry of pathogens and other harmful substances into body
<ul style="list-style-type: none"> ▪ Acid mantle ▪ Keratin 	<p>Skin secretions (perspiration and sebum) make epidermal surface acidic, which inhibits bacterial growth; sebum also contains bactericidal chemicals</p> <p>Provides resistance against acids, alkalis, and bacterial enzymes</p>
Intact mucous membranes	Form mechanical barrier that prevents entry of pathogens
<ul style="list-style-type: none"> ▪ Mucus ▪ Nasal hairs ▪ Cilia ▪ Gastric juice ▪ Acid mantle of vagina ▪ Lacrimal secretion (tears); saliva ▪ Urine 	<p>Traps microorganisms in respiratory and digestive tracts</p> <p>Filter and trap microorganisms in nasal passages</p> <p>Propel debris-laden mucus away from lower respiratory passages</p> <p>Contains concentrated hydrochloric acid and protein-digesting enzymes that destroy pathogens in stomach</p> <p>Inhibits growth of most bacteria and fungi in female reproductive tract</p> <p>Continuously lubricate and cleanse eyes (tears) and oral cavity (saliva); contain lysozyme, an enzyme that destroys microorganisms</p> <p>Normally acid pH inhibits bacterial growth; cleanses the lower urinary tract as it flushes from the body</p>

Complex Biological Responses of Innate Immunity

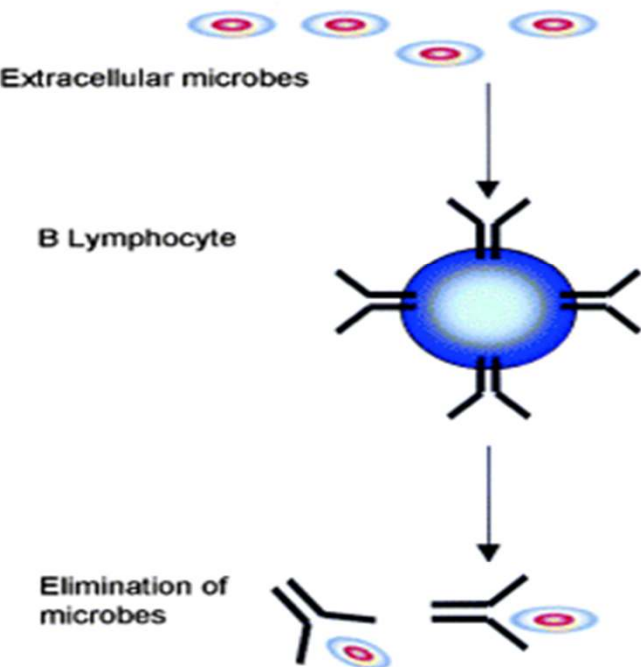
Complex biological responses include:

- **Phagocytosis**
- **Complement Activation**
- **Inflammation and Fever**
- **Interferon**

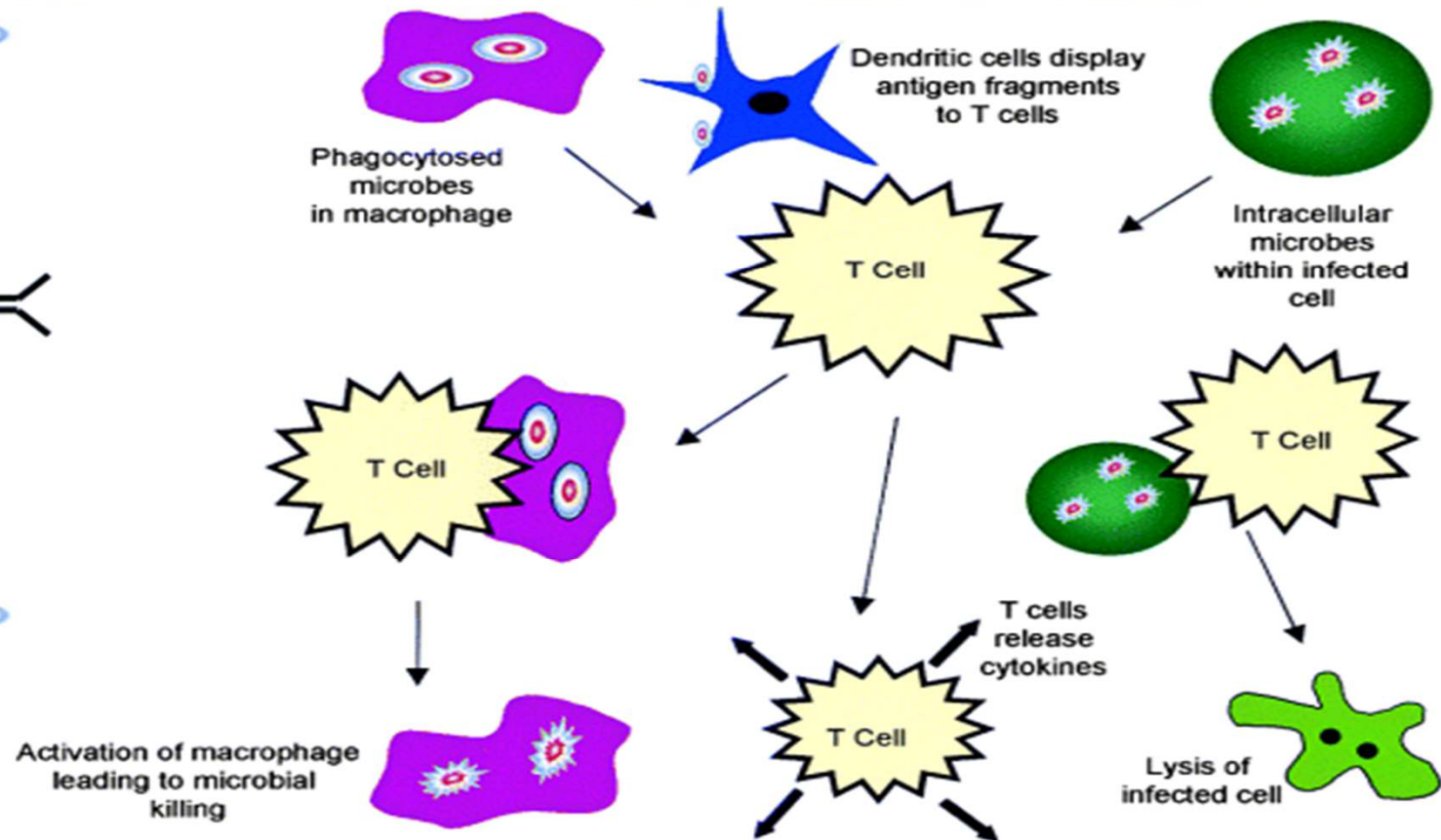


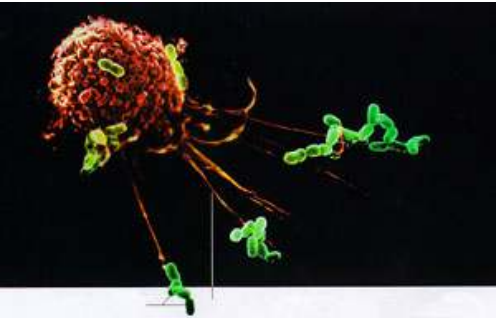
Adaptive Immunity

Humoral immunity



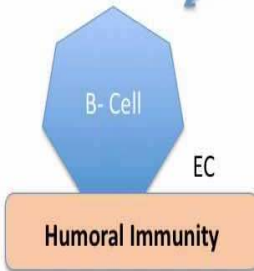
Cell-mediated immunity



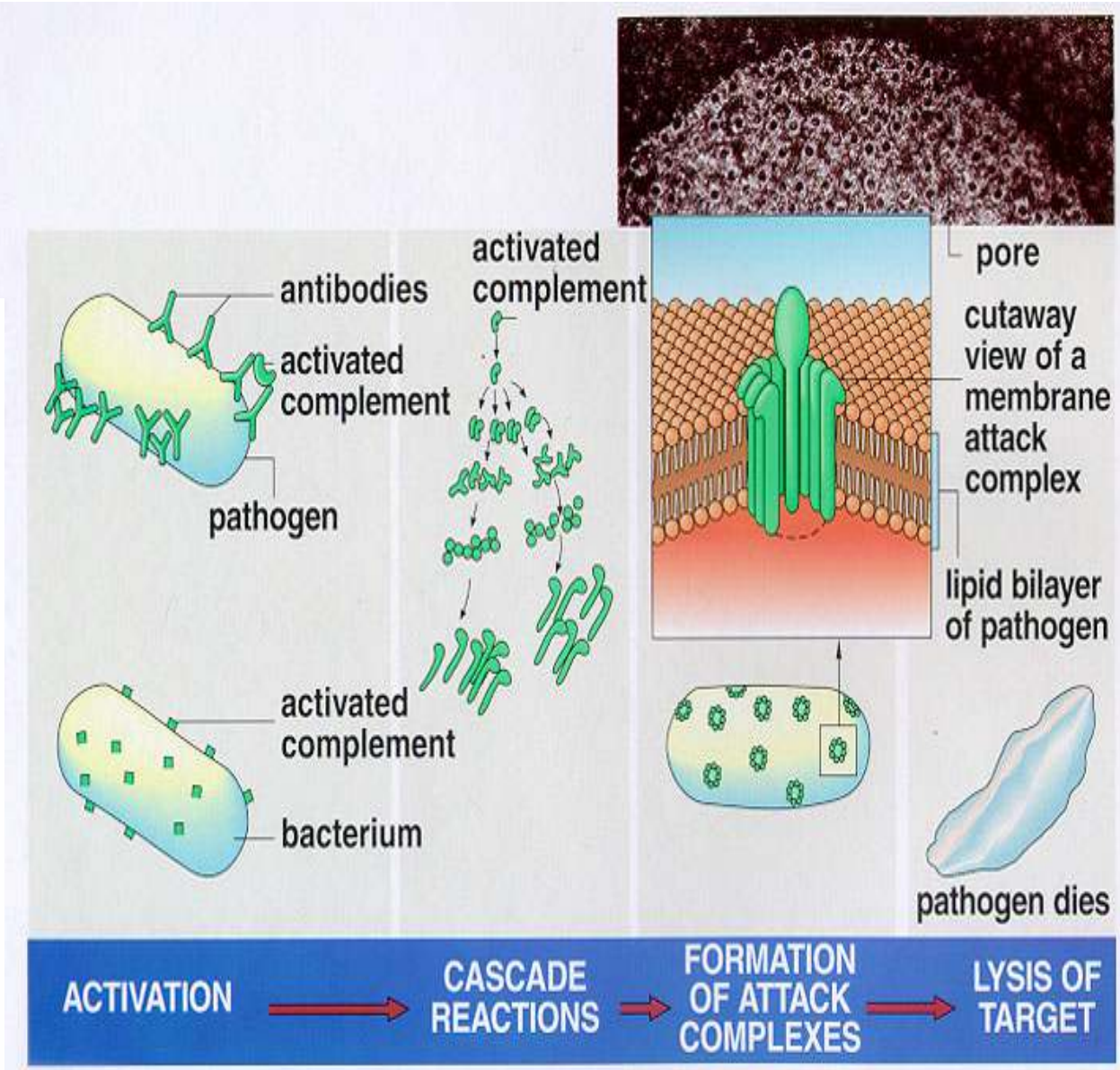
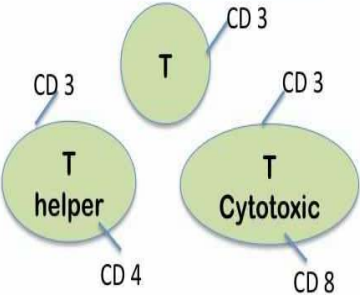
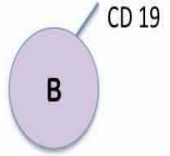
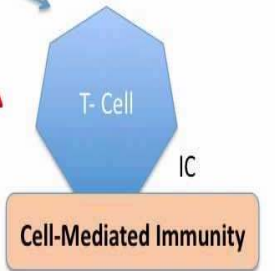


Adaptive

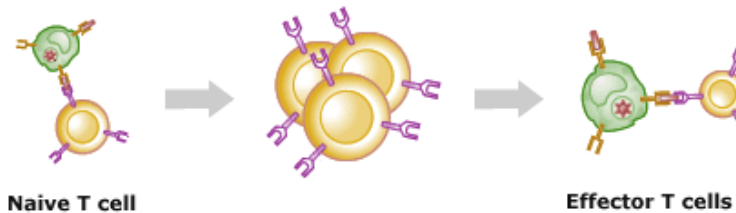
- Specificity
- Self/non-self recognition
- Memory



Cluster of differentiation



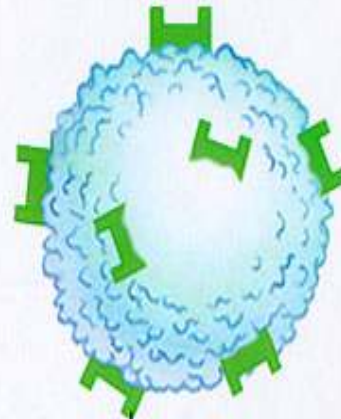
Adaptive Immunity



Days

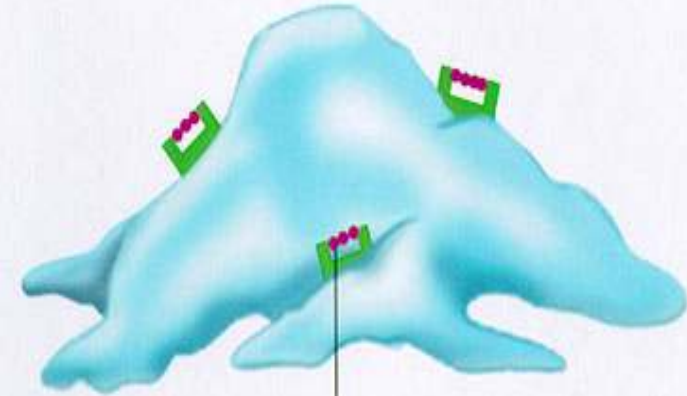
1 3 5

Time after infection



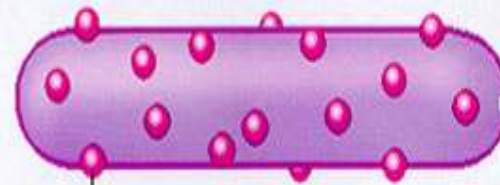
MHC marker

T and B cells ignore this



processed antigen

T cells start an immune response



antigen

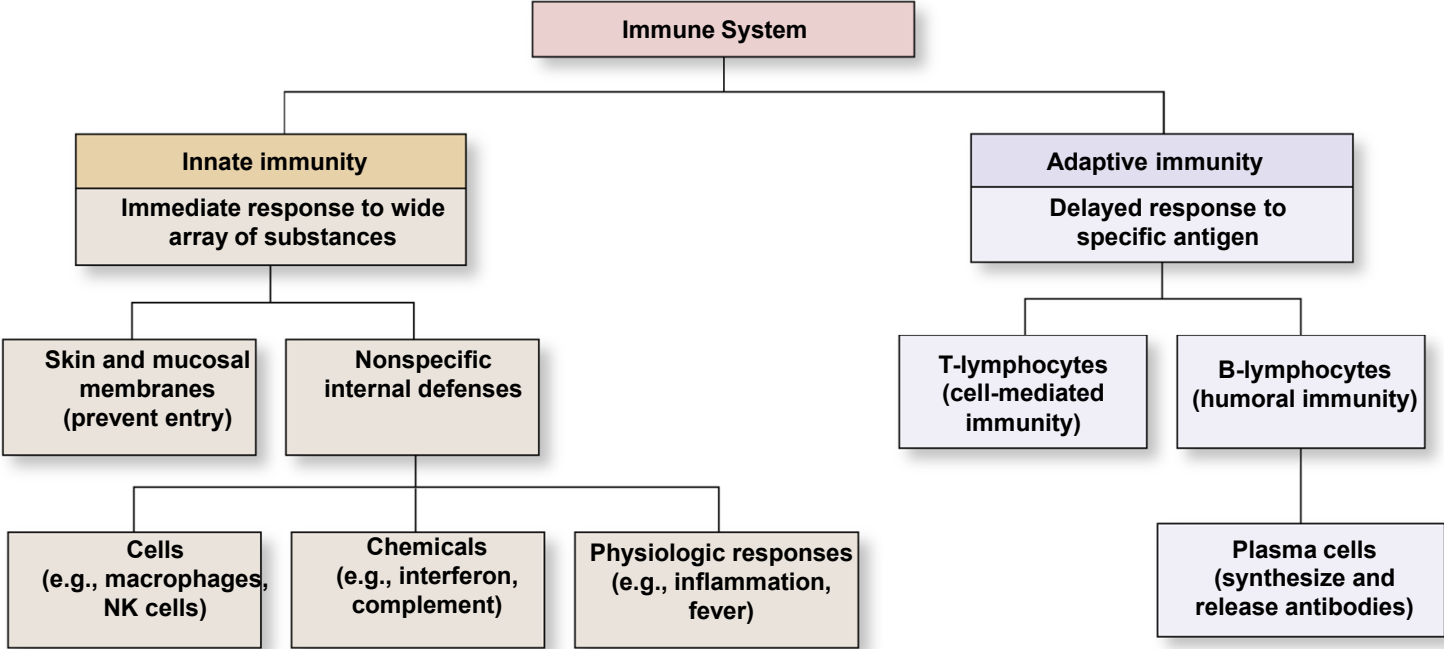
B cells start an immune response

What are the cells of adaptive immunity?

T-lymphocytes and B-lymphocytes

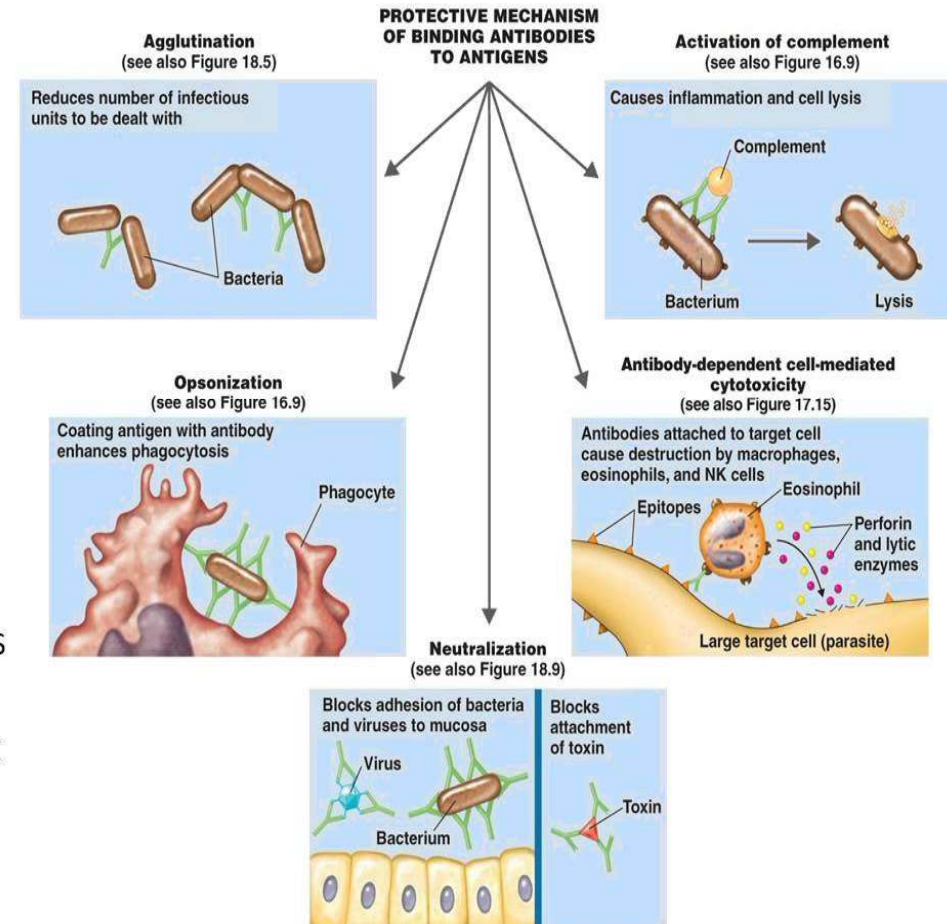
Overview of the Immune System

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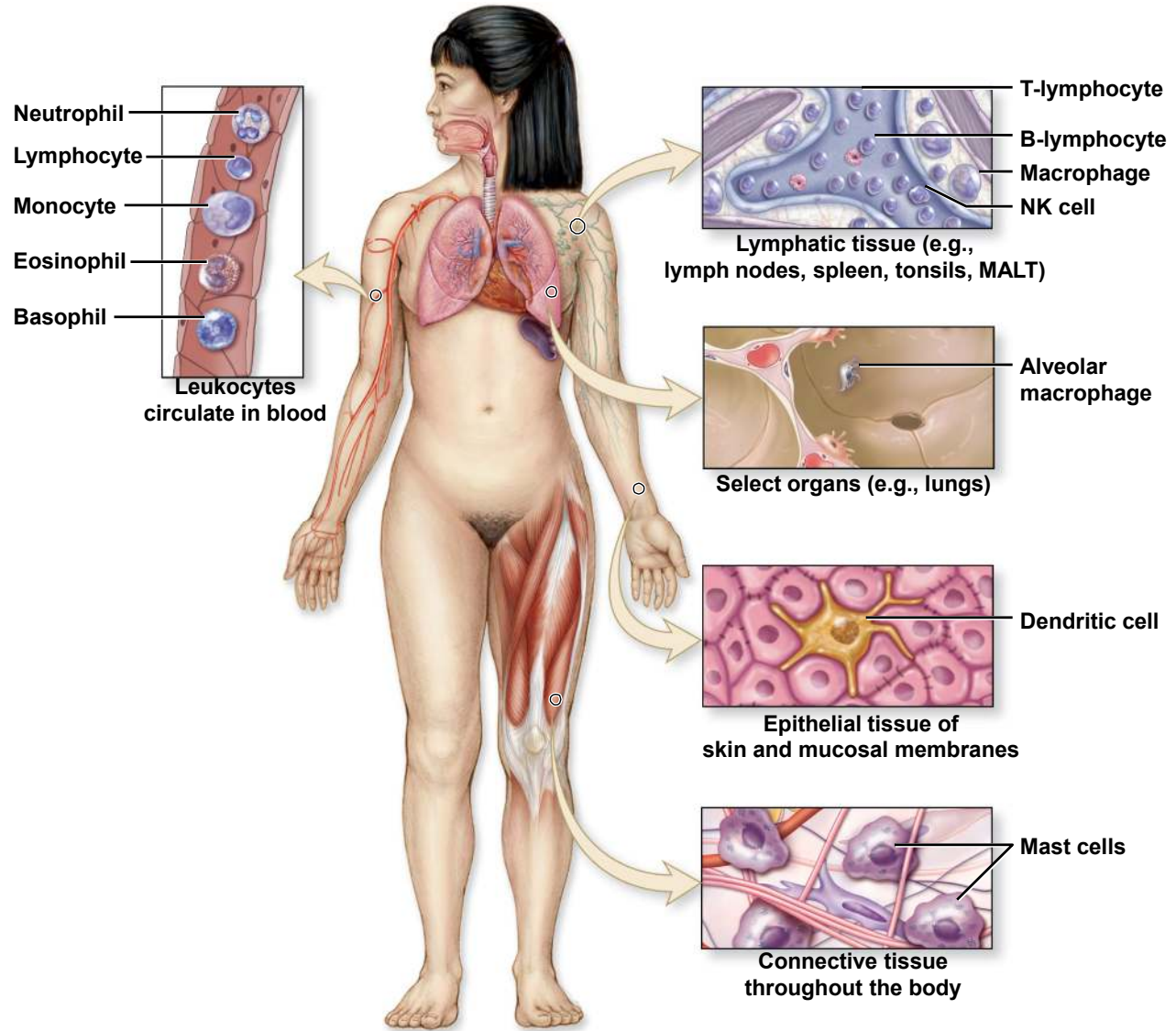
Antigen-Antibody Binding and its Results

- 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



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Cells and Chemicals



Primary Location of Immune Cells)

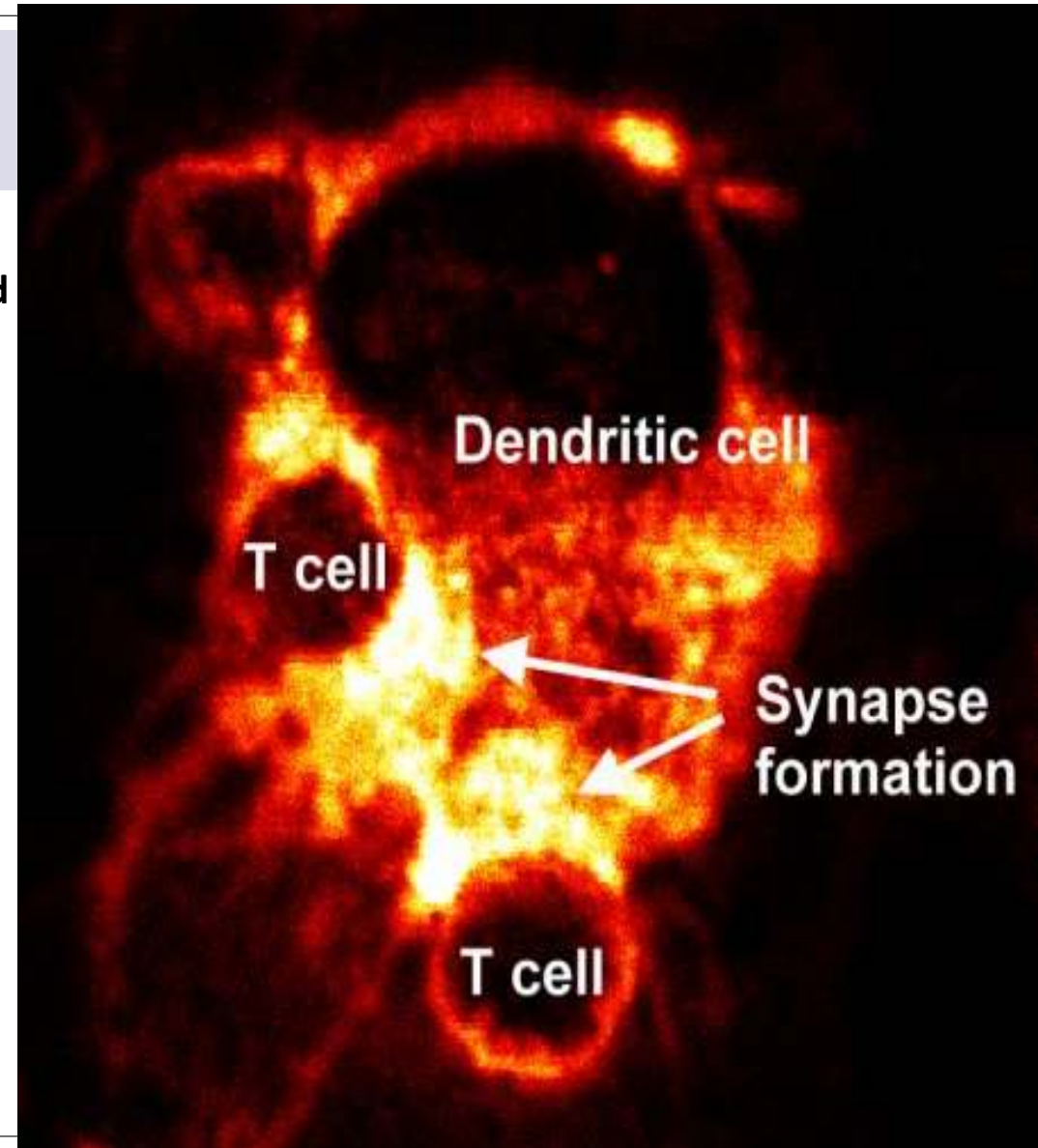
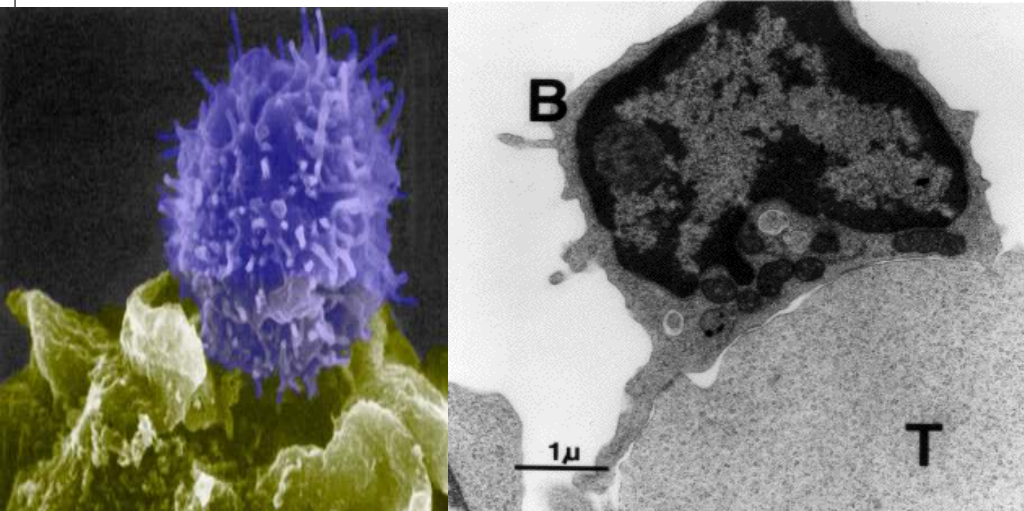
Overview of the Immune System: Immune Cells and Their Locations

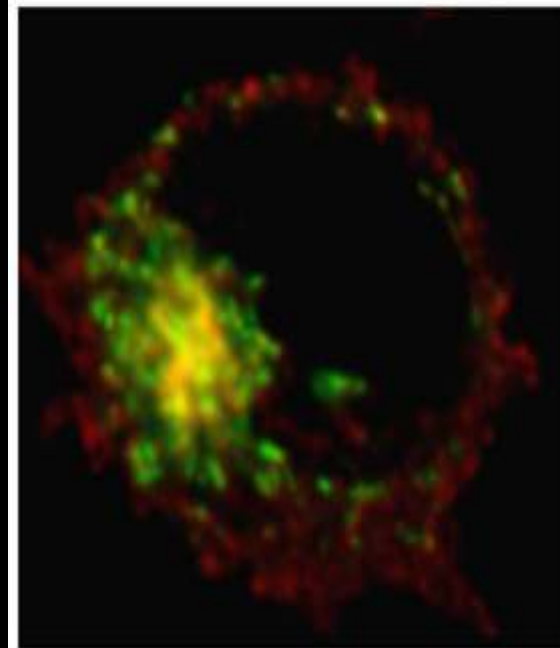
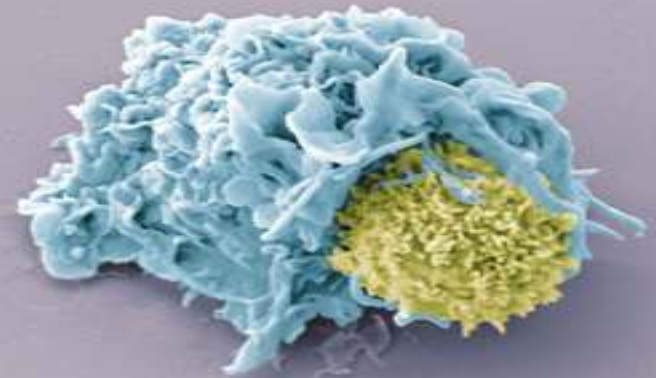
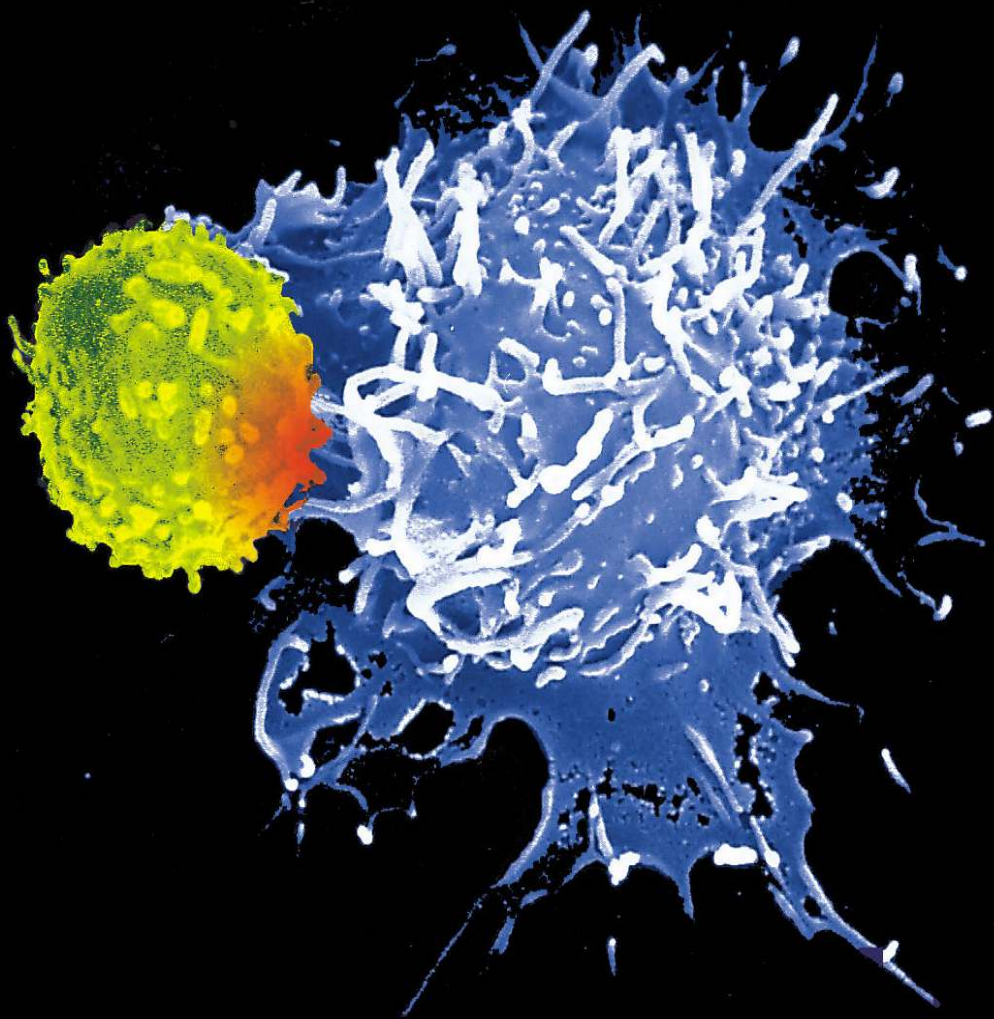
What types of immune cells are housed in lymphatic tissue? What two types of immune cells are located in the skin and mucosal membranes?

T- and B-lymphocytes, macrophages, NK cells
dendritic and mast cells

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 colocalization of both proteins

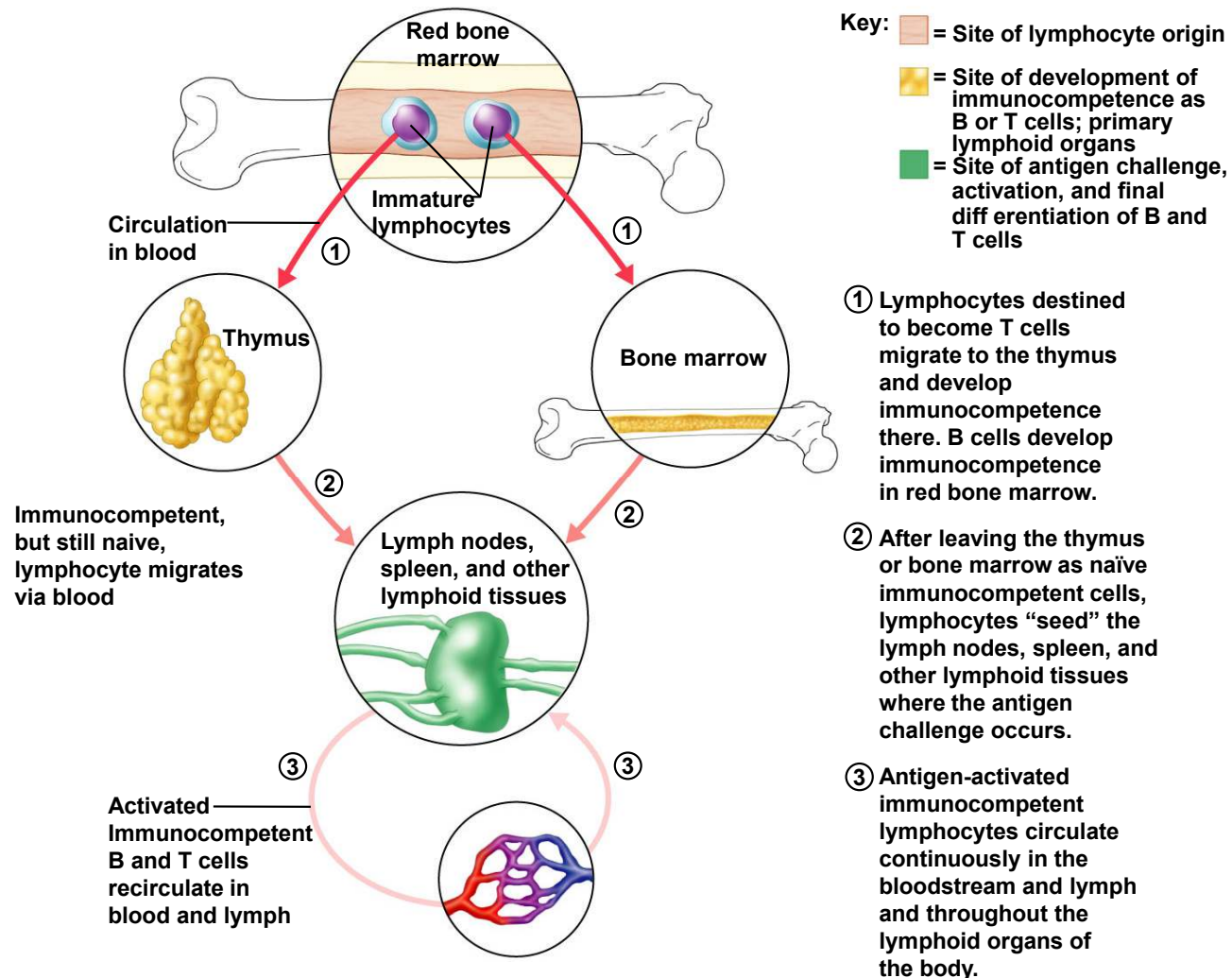


Figure 21.8

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		
Cytokines		

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**

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**

Lymphocytes

- 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**

The Cells of the Immune Response

T cells: Lymphocytes that regulate response

- *Cytotoxic T cells*: destroy specific targeted cells
- *Helper T cells*: stimulate immune responses
- *Suppressor T cells*: stop immune response
- *Memory T cells*: provide future immunity

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

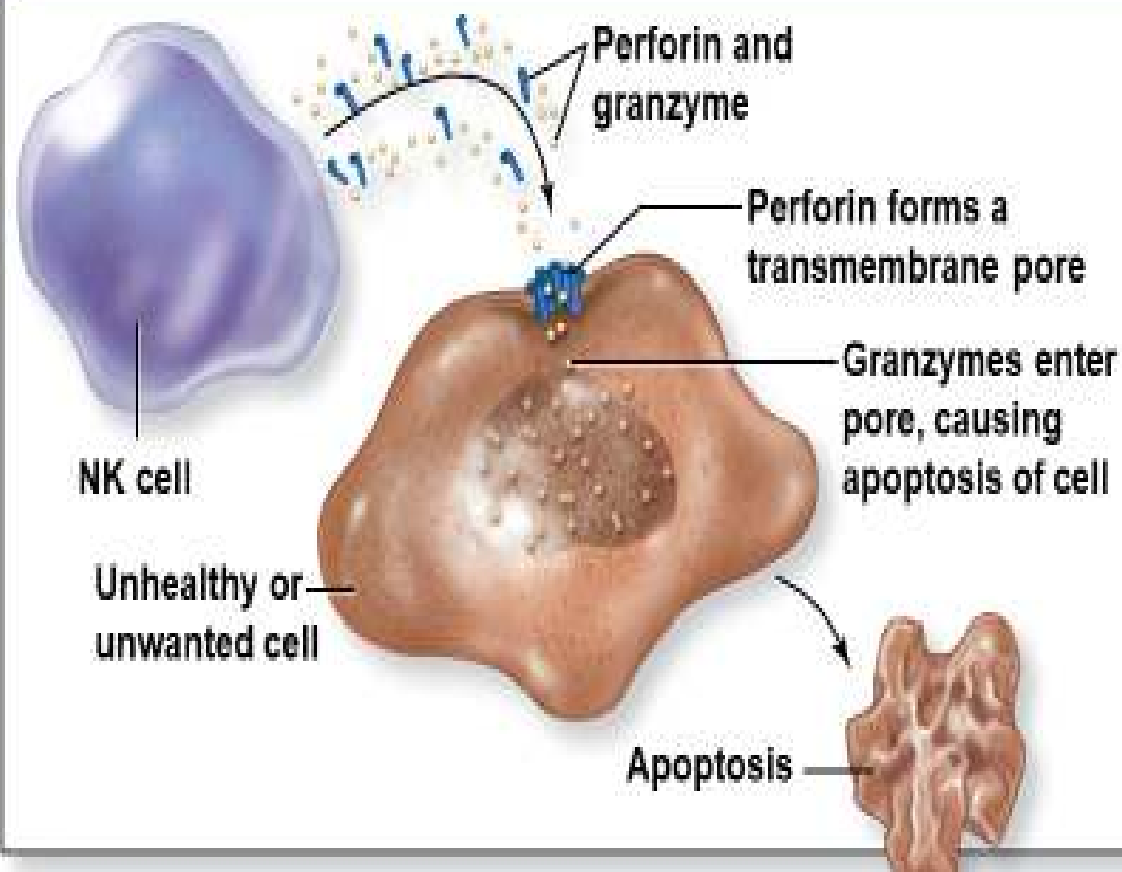
SECOND LINE OF DEFENSE: INNATE, CELLULAR AND CHEMICAL DEFENSES

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 <ul style="list-style-type: none">▪ Interferons (α, β, γ)▪ Complement	Proteins released by virus-infected cells and certain lymphocytes that protect uninfected tissue cells from viral takeover; mobilize immune system 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

NK Cell: Apoptosis-Initiating Cells

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NK cell: Apoptosis-initiating cells



Natural killer cells

Destroy wide variety of unwanted cells
virus- and bacteria-infected cells,
tumor cells, cells of transplanted
tissue

Formed in bone marrow and circulate
in blood

Accumulate in secondary lymphatic
structures

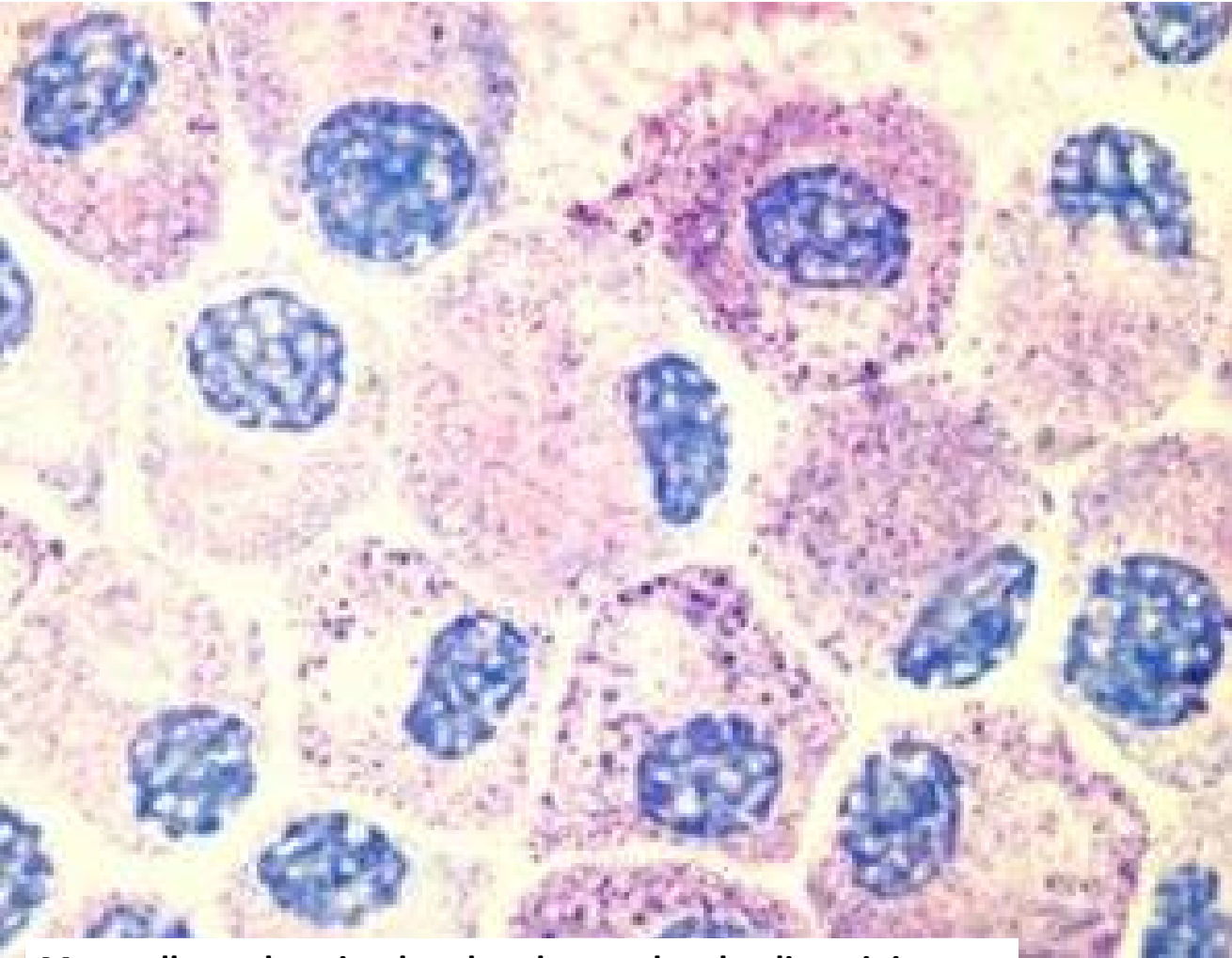
Patrol the body detecting unhealthy
cells

termed **immune surveillance**

Destroy unhealthy cells by releasing
cytotoxic chemicals

include perforin, forming
transmembrane pore in unwanted cells
include granzymes, initiating
apoptosis

Apoptosis, form of cellular death



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**

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

Basophils / Mast Cells

These cells are filled with mediators of inflammation:

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

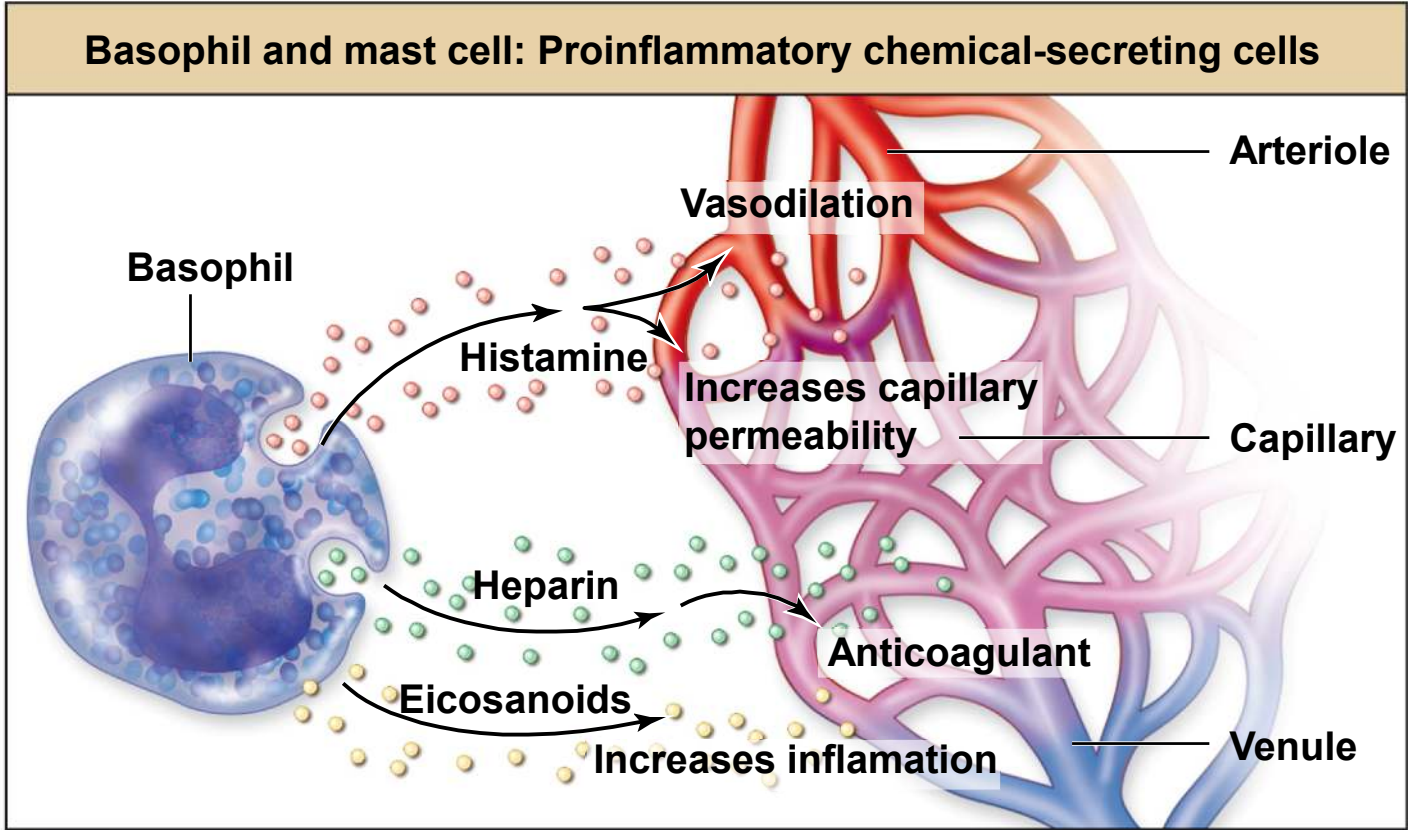
heparin - inhibits blood coagulation

leukotrienes - prolonged constriction of smooth muscles, pain

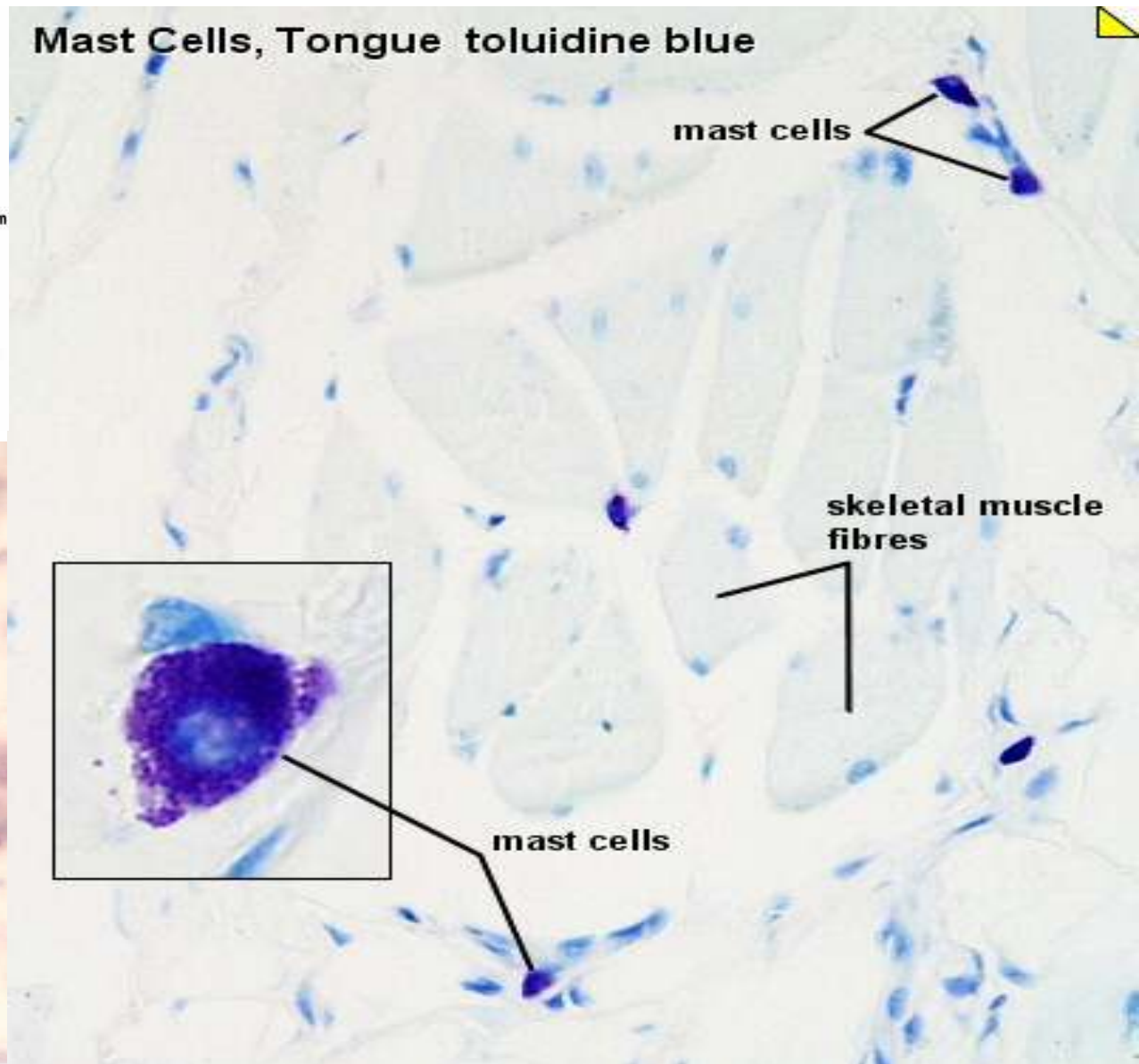
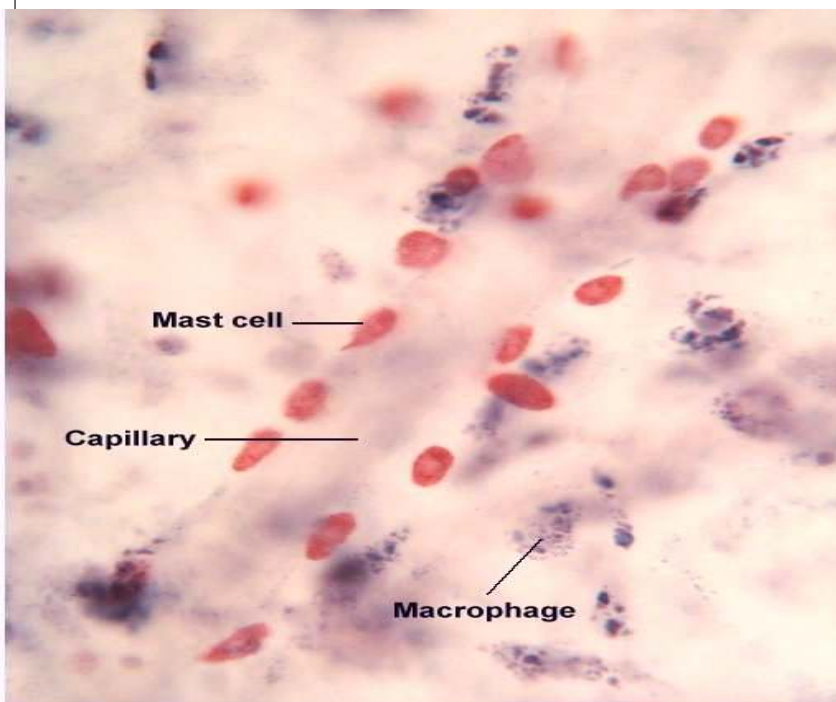
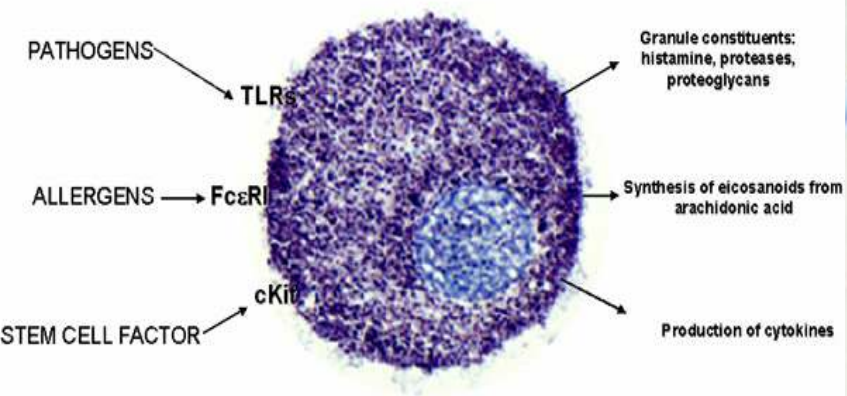
prostaglandins - smooth muscle constriction and vasodilation, pain

Basophil and Mast Cell: Proinflammatory Chemical-Secreting Cells

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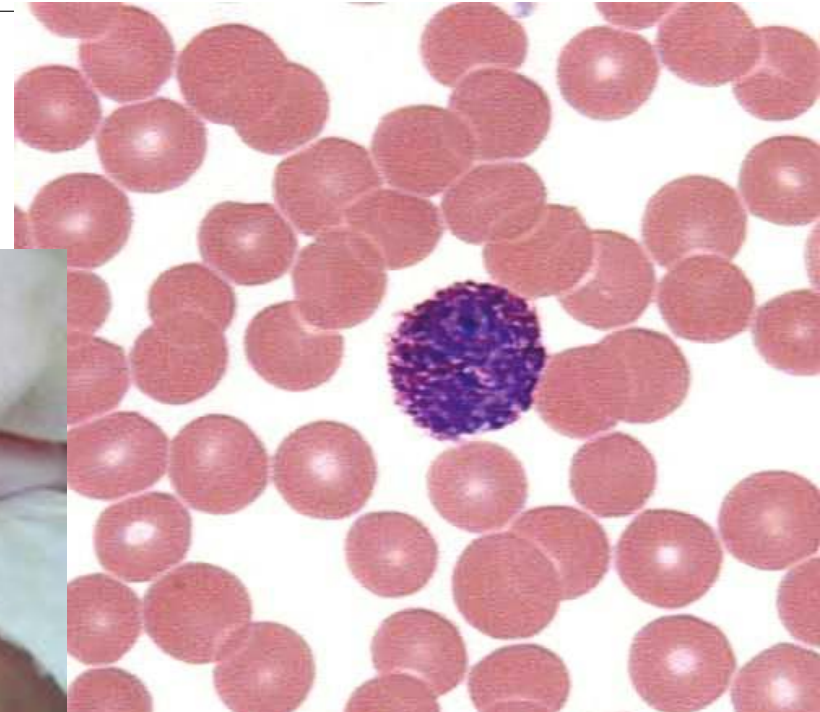


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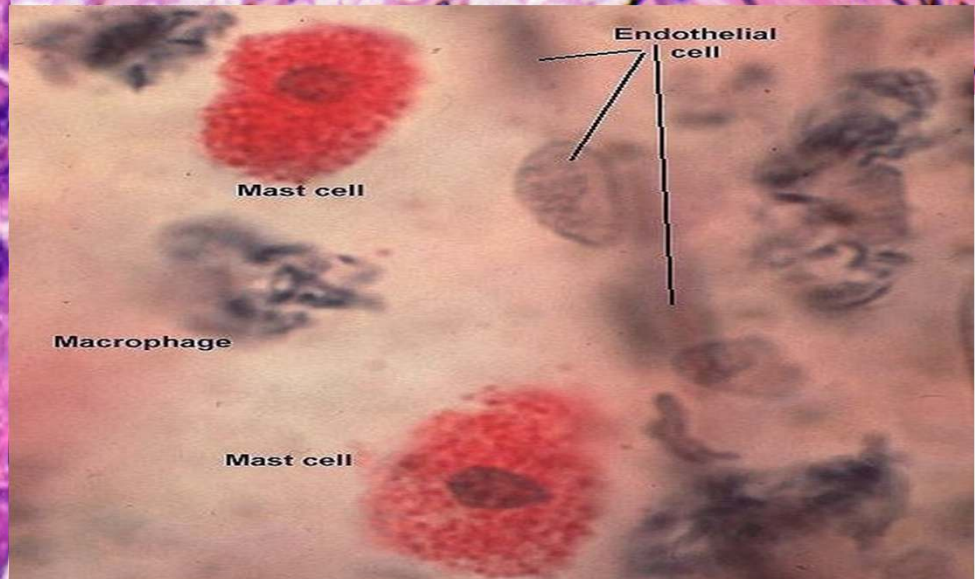
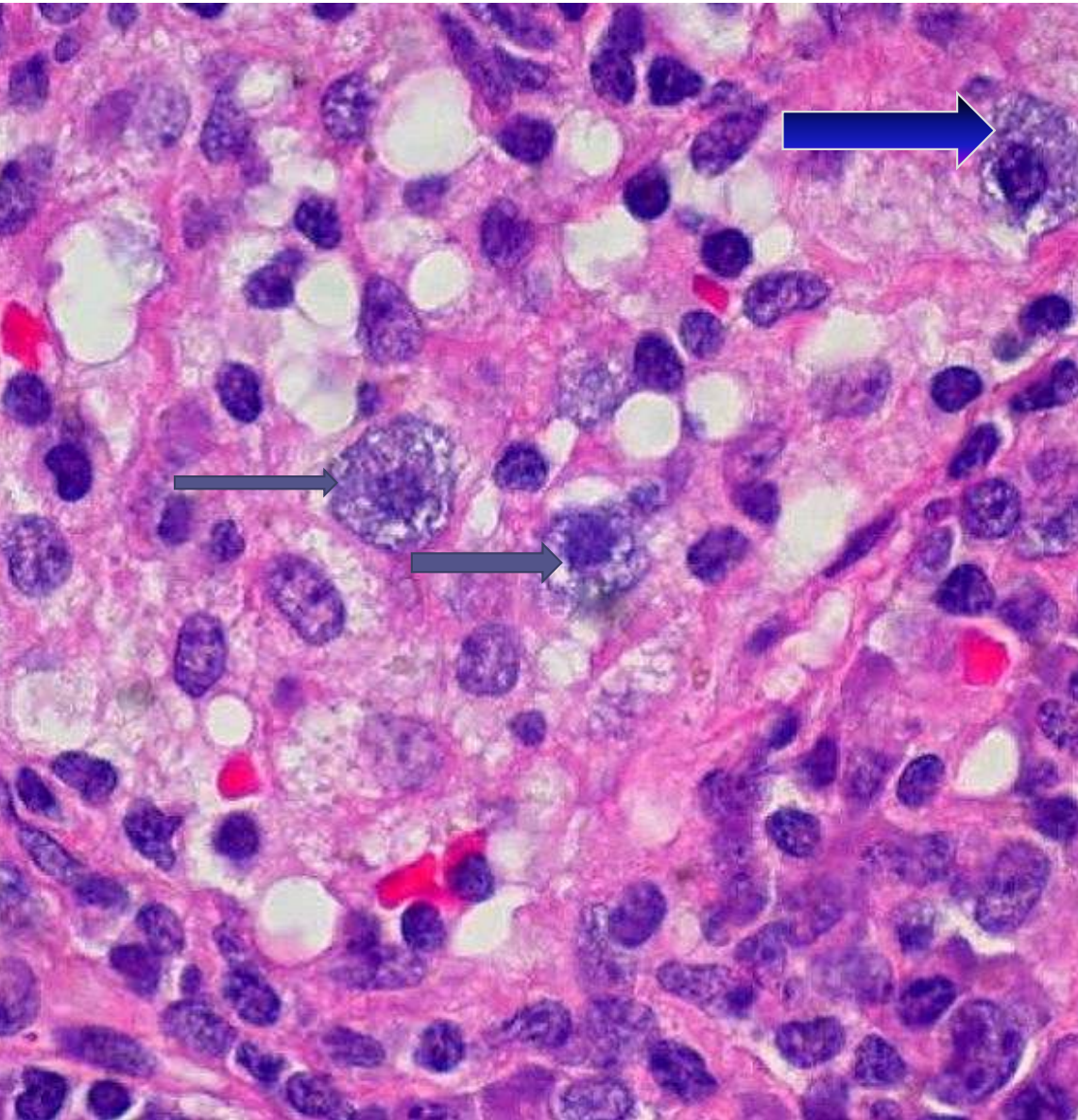


- Mast cells / basophils

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



es/wound.jpg



Cells of Immune Response

Non hematopoietic cells:

- **Dendritic cells**
- **Astrocytes and**
- **Endothelial cells**

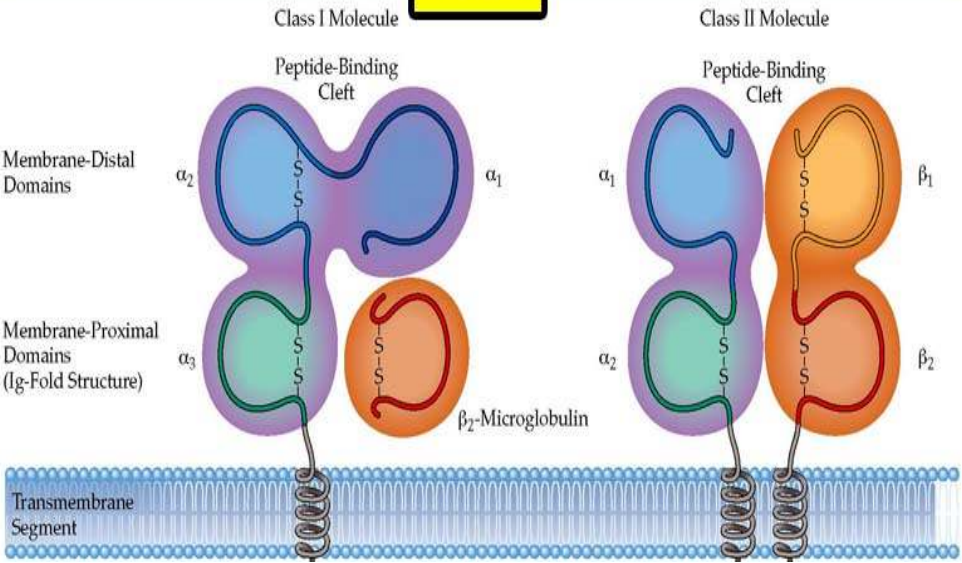
Function : antigen presentation

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:

MHC Class I VS MHC Class II



- 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

Comprised of an MHC-encoded α chain and a β 2-microglobulin chain

Present on most cells

Bind endogenous antigens synthesized in a cell

Present antigen to cytotoxic T cell lymphocytes

Bind CD8 adhesion molecules on cytotoxic T cells

Presence of foreign or over-abundant antigens targets cell for destruction

MHC class II

Comprised of MHC-encoded α and β chains

Present only on antigen-presenting cells

Binds exogenous antigens

Present antigen to helper T cell lymphocytes

Bind CD4 adhesion molecules on helper T cells

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

HLA

A gene complex encoding the major histocompatibility complex (MHC) proteins in humans

Form of MHC complex that occurs in humans

Class I HLA genes are HLA-A, HLA-B, and HLA-C and class II HLA genes are HLA-D

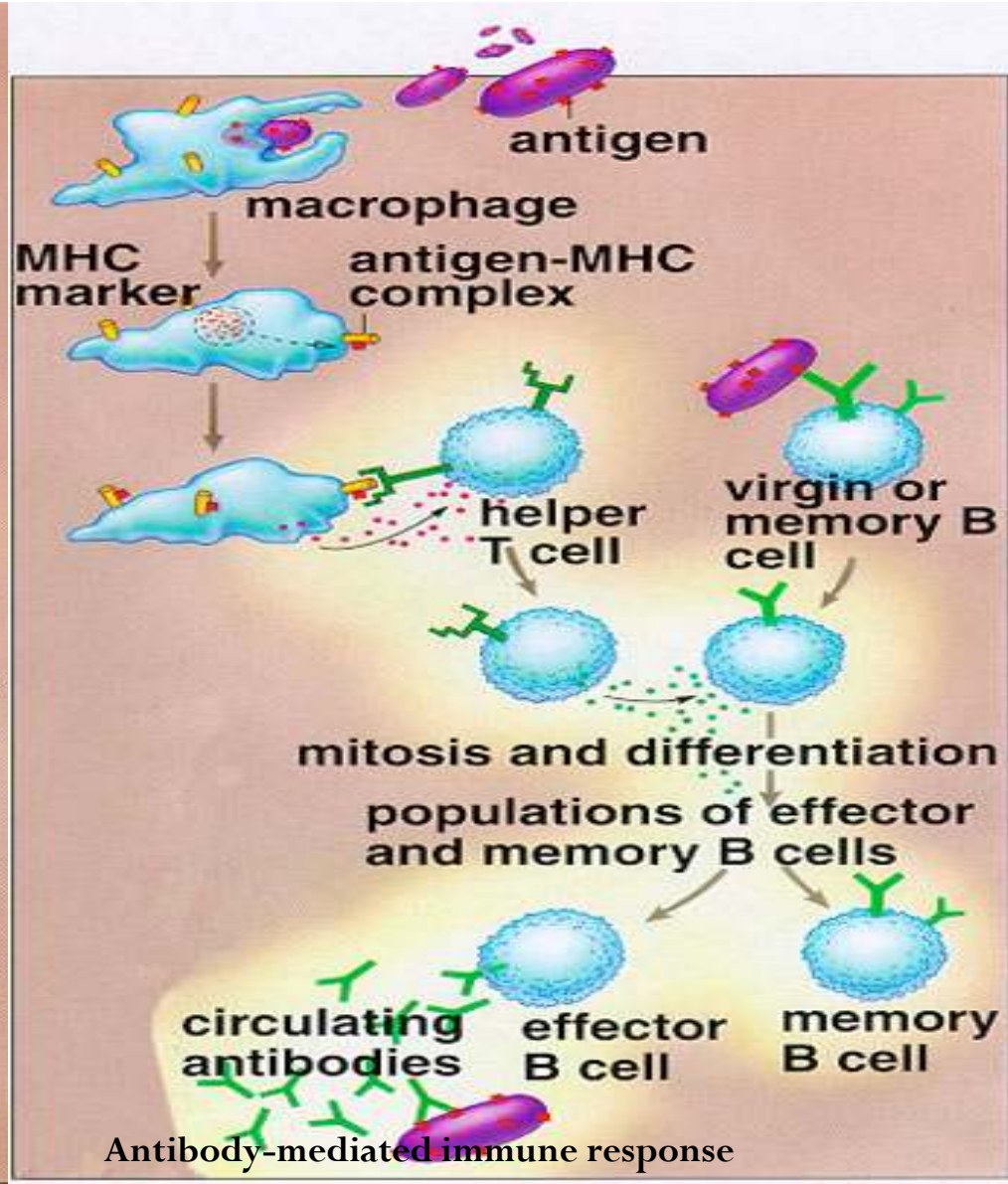
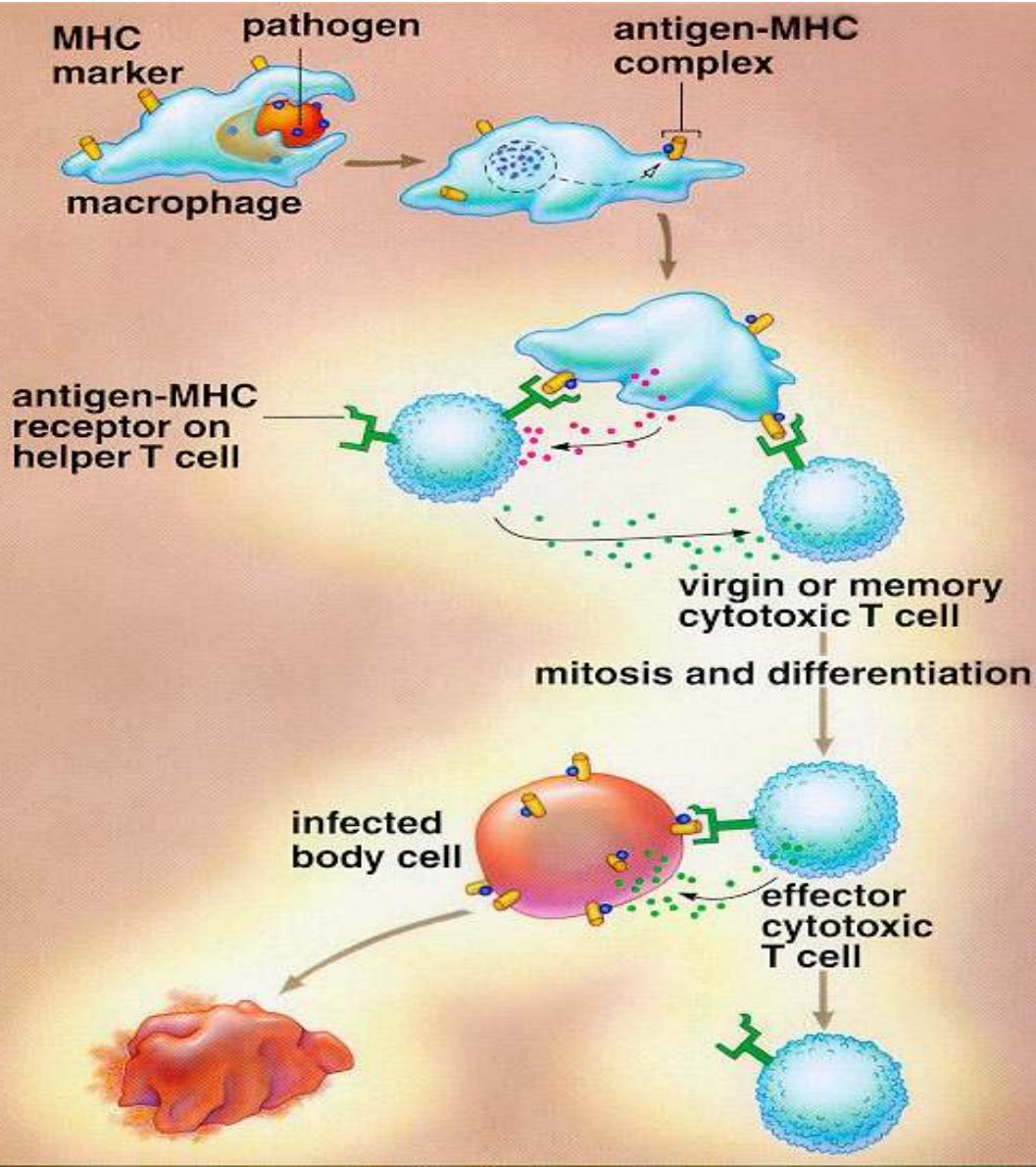
MHC

A set of cell surface proteins essential for the acquired immune system to recognize foreign molecules in vertebrates, which in turn determines histocompatibility

Occurs in all vertebrates

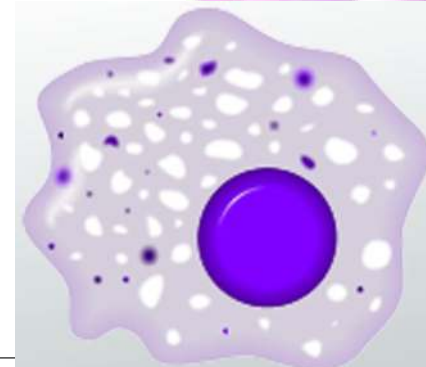
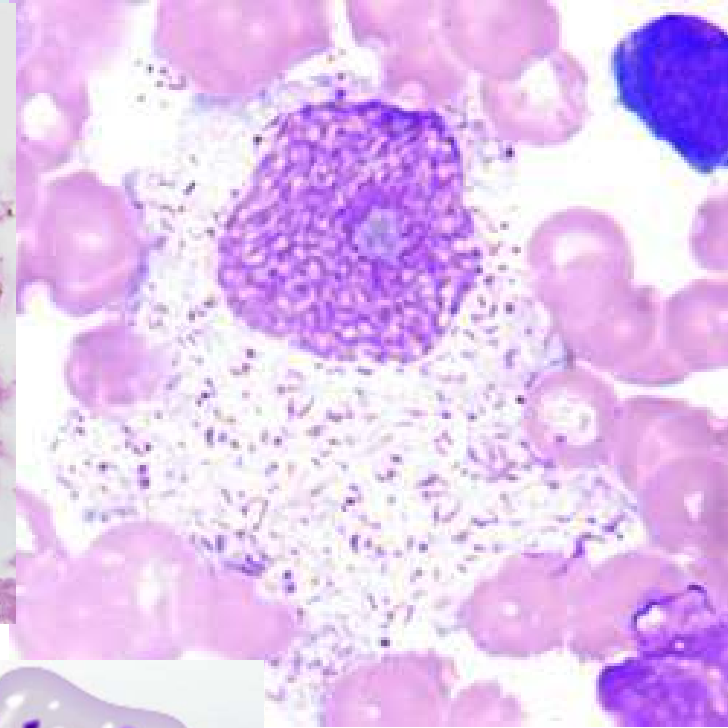
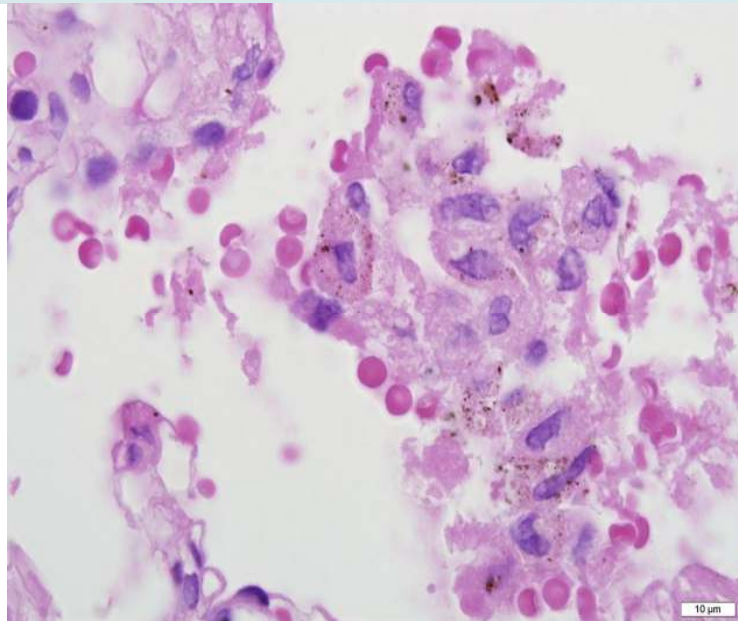
Three classes of MHC complex are Class I, II, and III

Visit www.PEDIAA.com

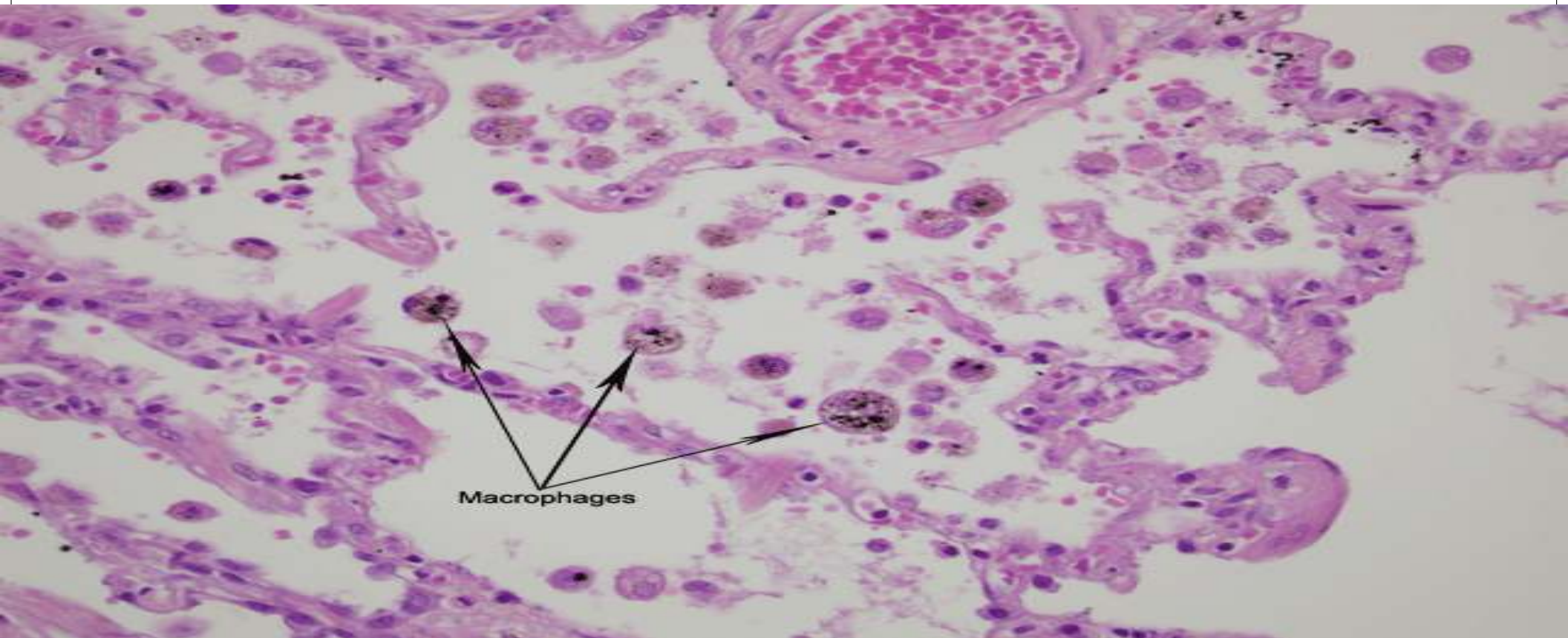


MACROPHAGES

- **DUST CELLS:** LUNG
- **MICROGLIA:** BRAIN
- **KUPFFLER 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
- **Placenta on the fetal side :** Hofbauer cells
- **CONNECTIVE TISSUES:**
 - **EPITHELIoids CELLS**
 - **GIANT CELLS**
 - **HISTIOCYTES.**



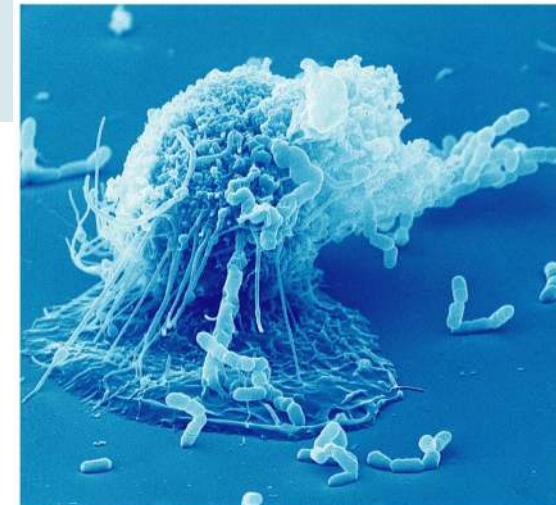
INTERFERON MEDIATED THE CHANGES OF THE MACROPHAGES [MONOCYTES].



Mechanisms

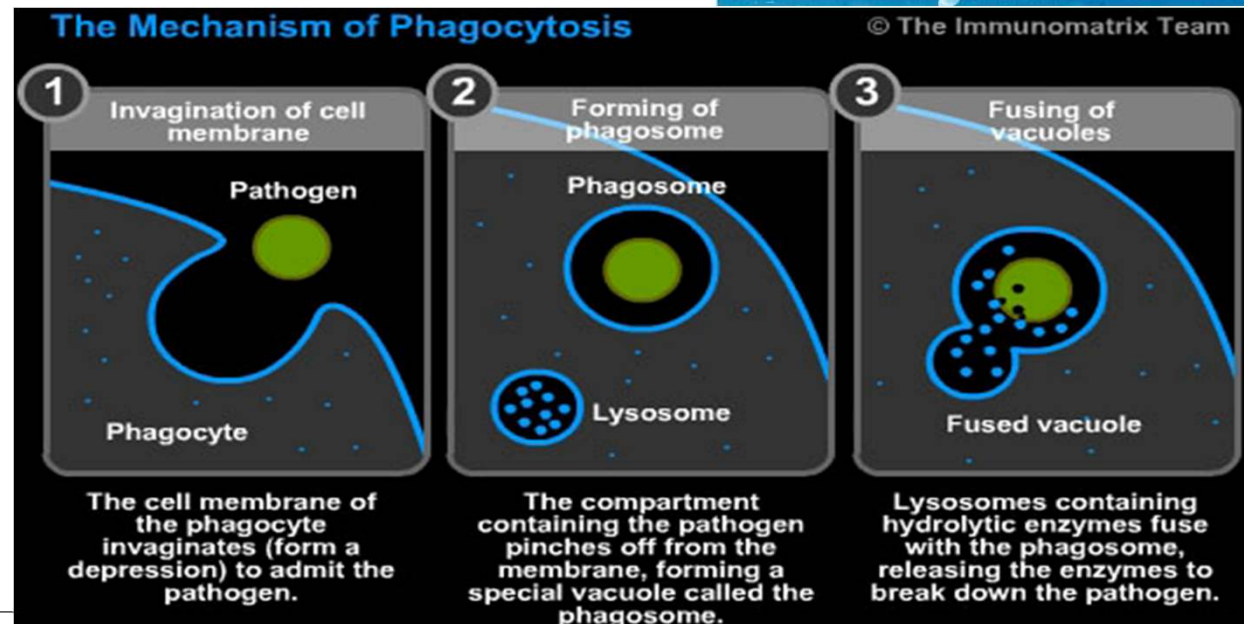
Phagocytes

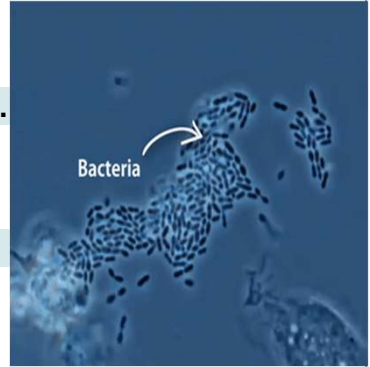
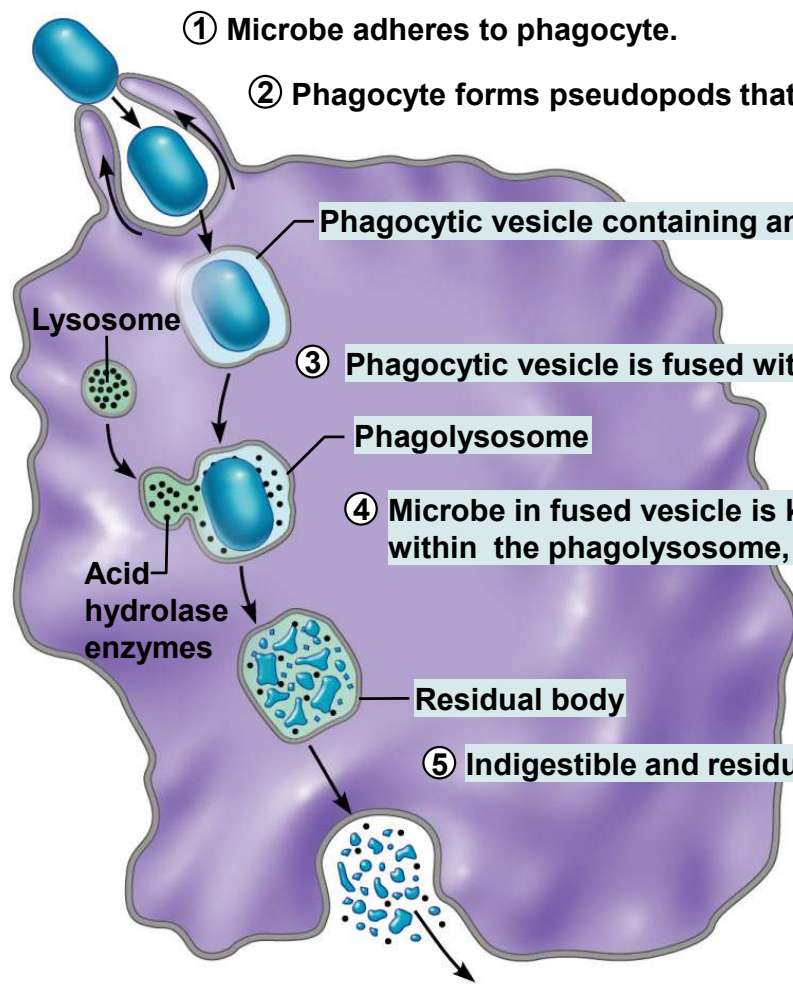
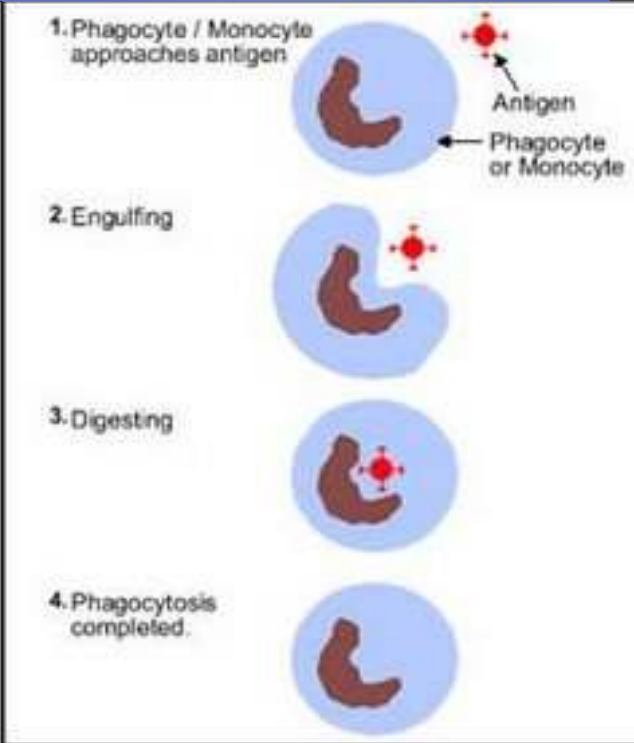
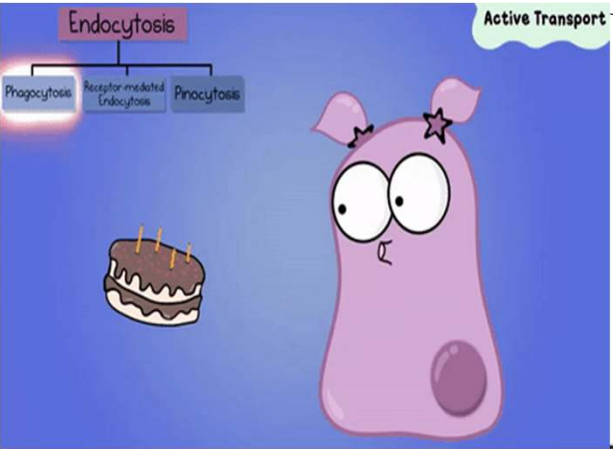
- **Macrophages are the chief phagocytic cells**
- Free macrophages wander throughout a region in search of cellular debris
- Kupffer cells (liver) and microglia (brain) are fixed macrophages
- **Neutrophils** become phagocytic when encountering infectious material
- **Eosinophils** are weakly phagocytic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



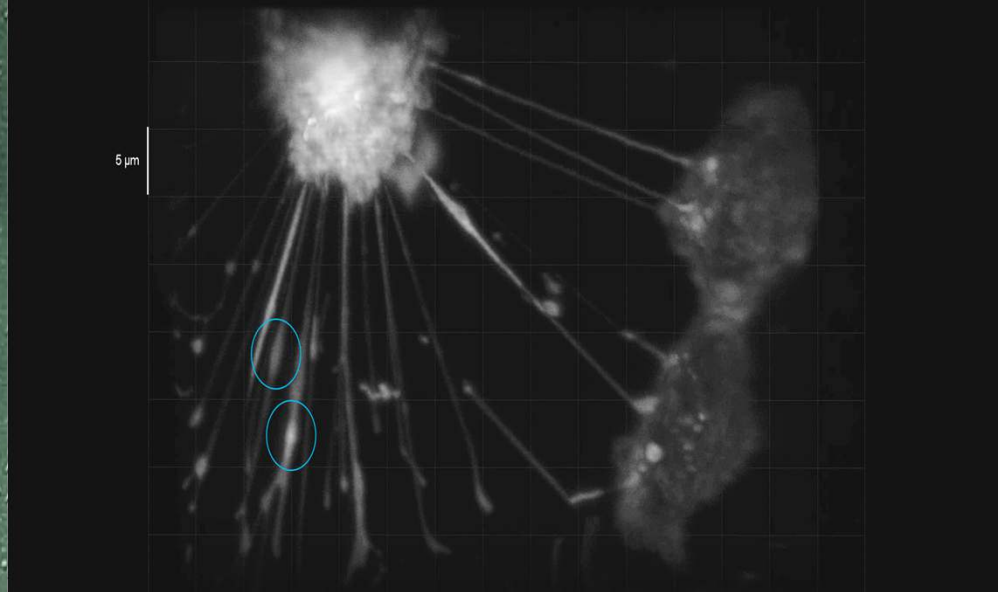
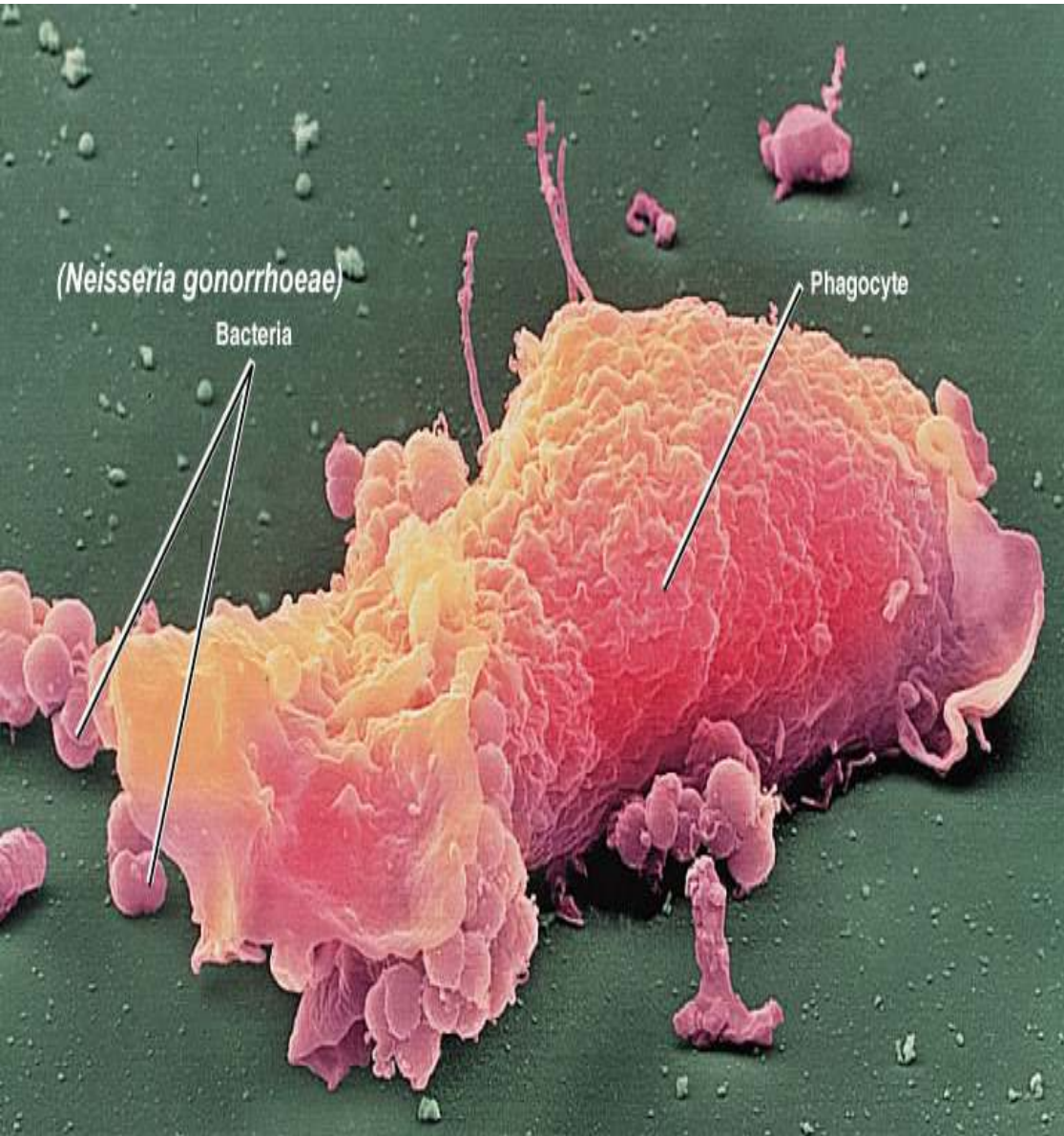
Mechanism of Phagocytosis

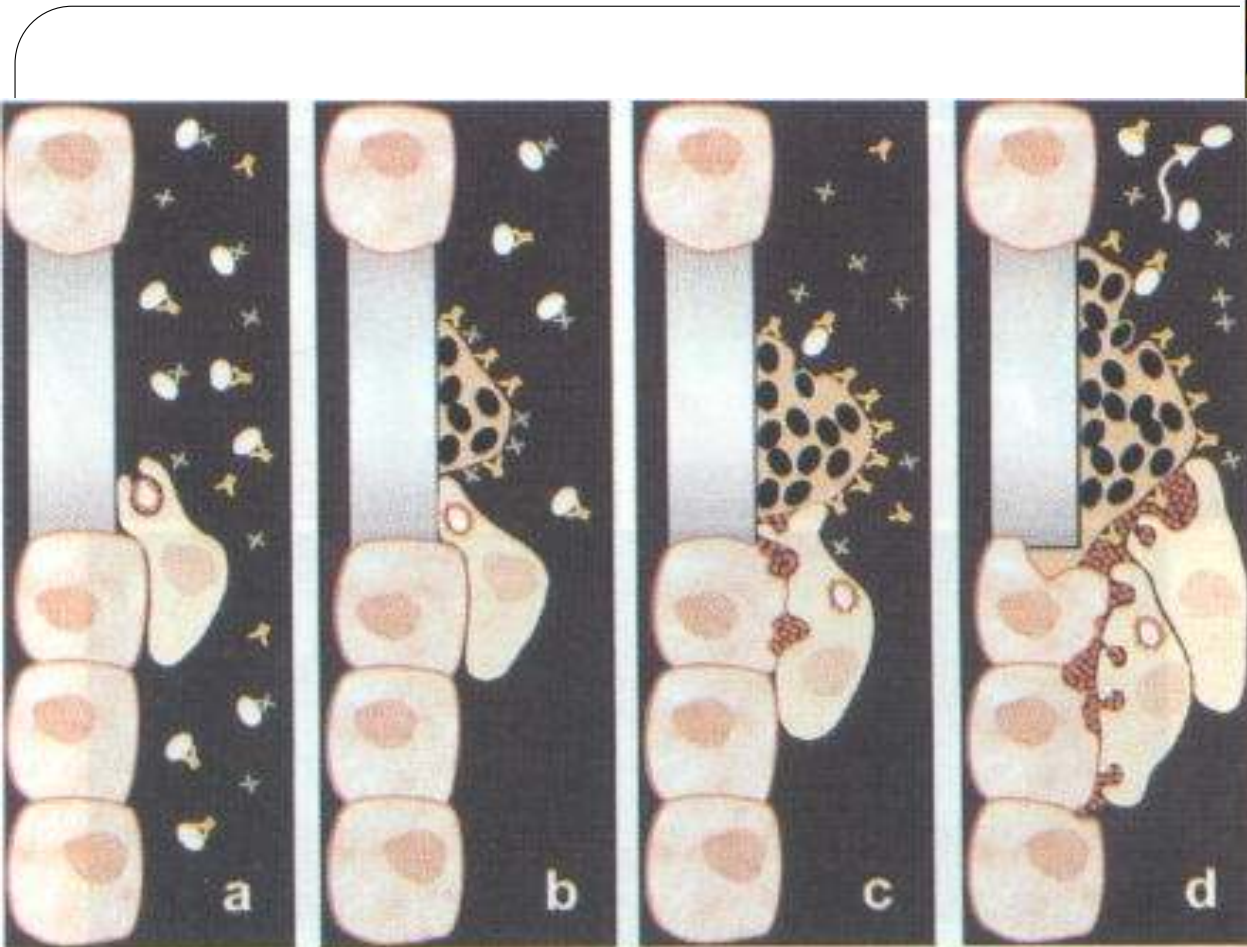
- 1/ Microbes **adhere** to the phagocyte
- **2/Pseudopods engulf** the particle (antigen) into a phagosome
- **3/Phagosomes fuse with a lysosome to form a phagolysosome**
- 4/Invaders in the phagolysosome are **digested by proteolytic enzymes**
- 5/Indigestible and residual material is removed by exocytosis



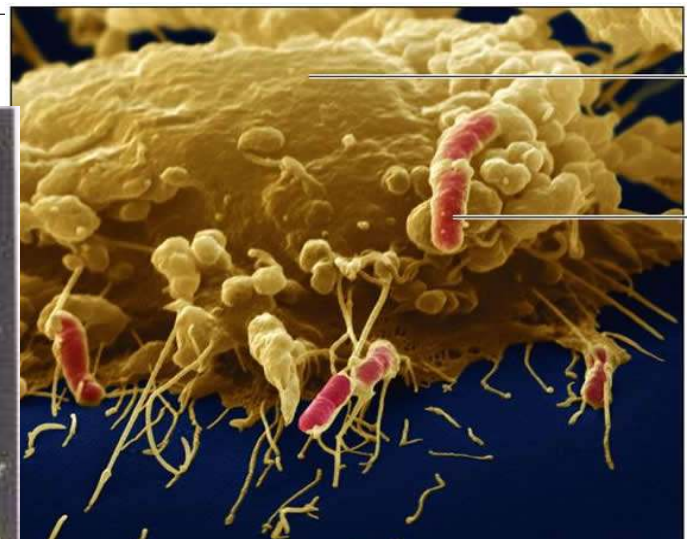


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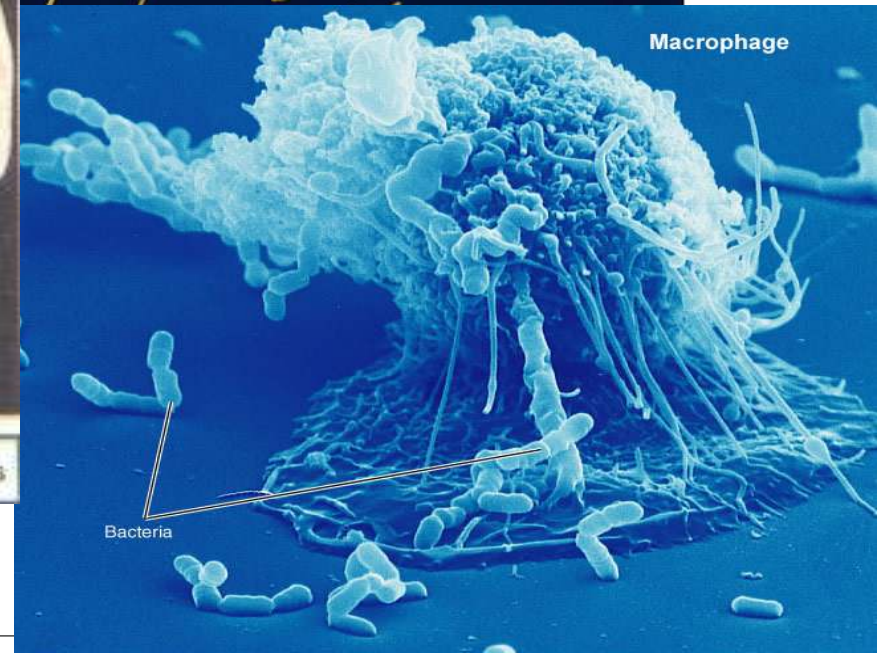




x Antibiotic A Antibody ● Planktonic cell ● Biofilm cell E Phagocyte enzymes



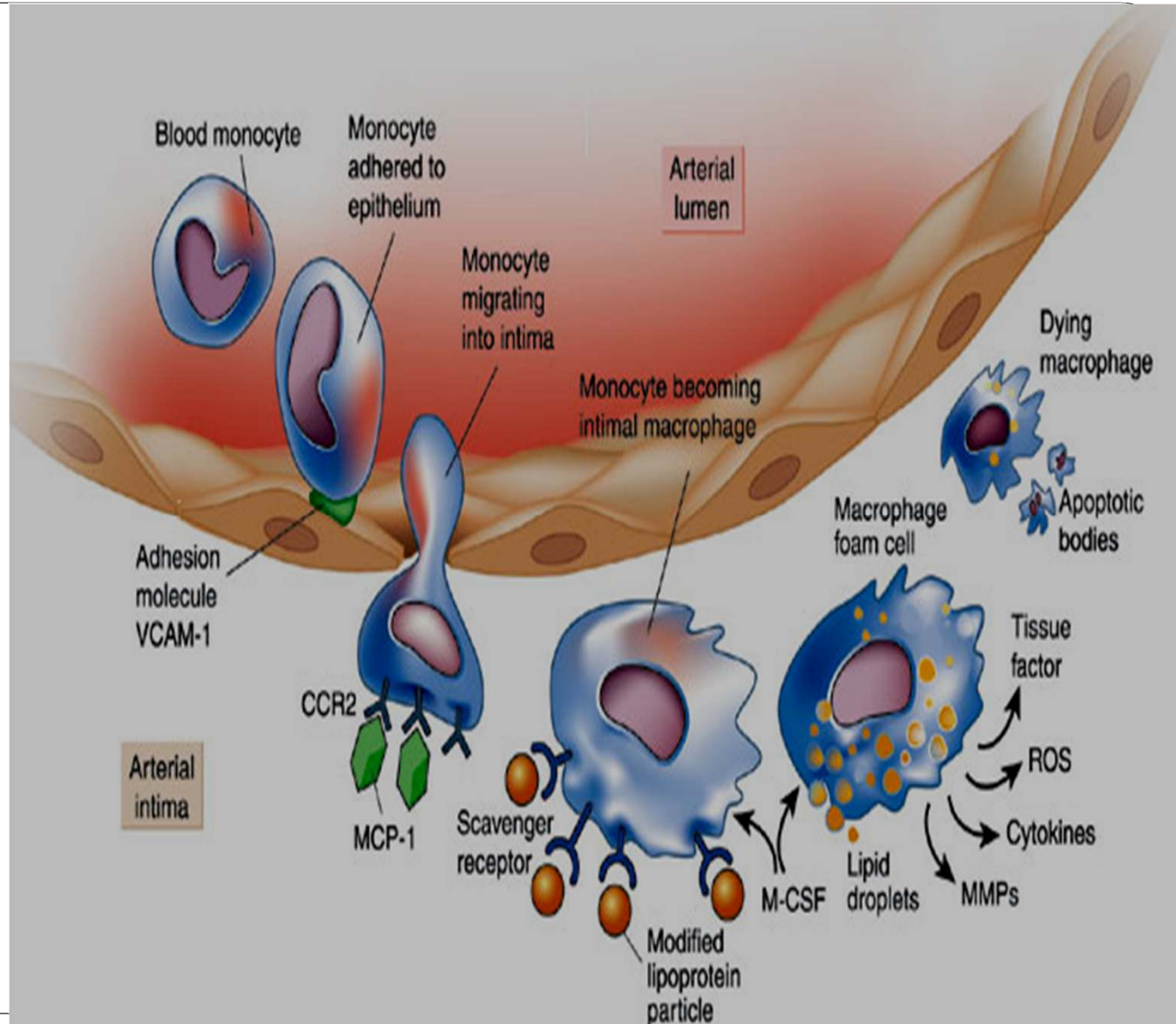
Macrophage
 Bacterium



Macrophage

Bacteria

- injury & infection
- macrophages slip between cells [extravasation] to arrive
- cytokine chemicals attract other “troops” [chemotaxis]
- histamine chemicals dilate blood vessels for easier access to injury [vasodilation]



The **major histocompatibility complex =MHC**

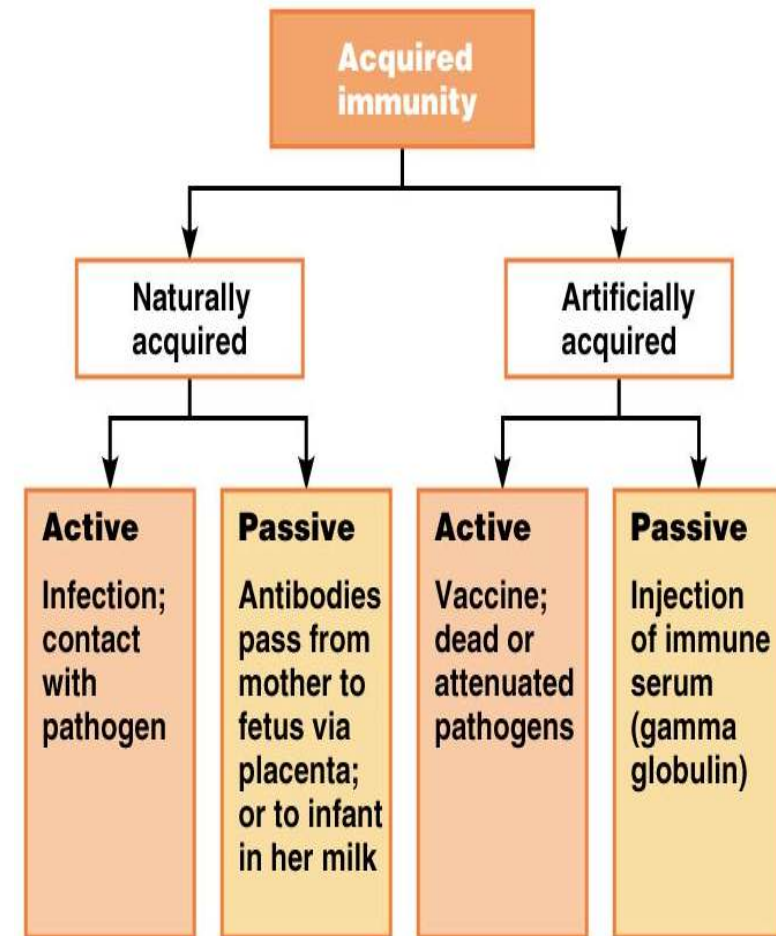
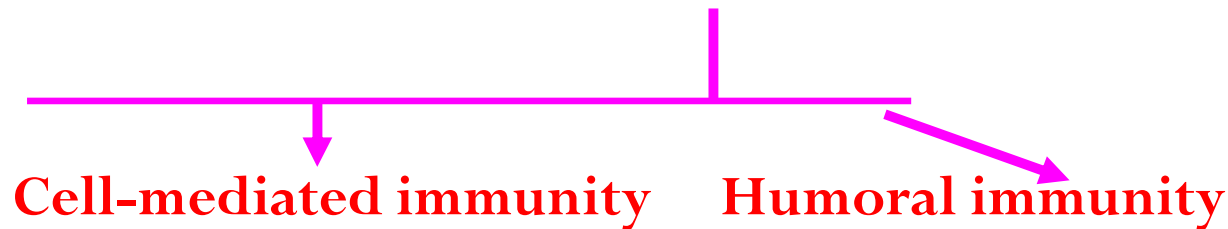
Receptor Type	Present On	Interacts With
CD4	Lymphocytes	MHC II
CD8	Lymphocytes	MHC I
MHC I	General Body Cells	CD8
MHC II	Phagocytes	CD4

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**

Acquired (Adaptive) Immunity

Defensive mechanisms include :

- 1) Innate immunity (Natural or Non specific)
- 2) Acquired immunity (Adaptive or Specific)



Acquired (specific) immunity

Two mechanisms

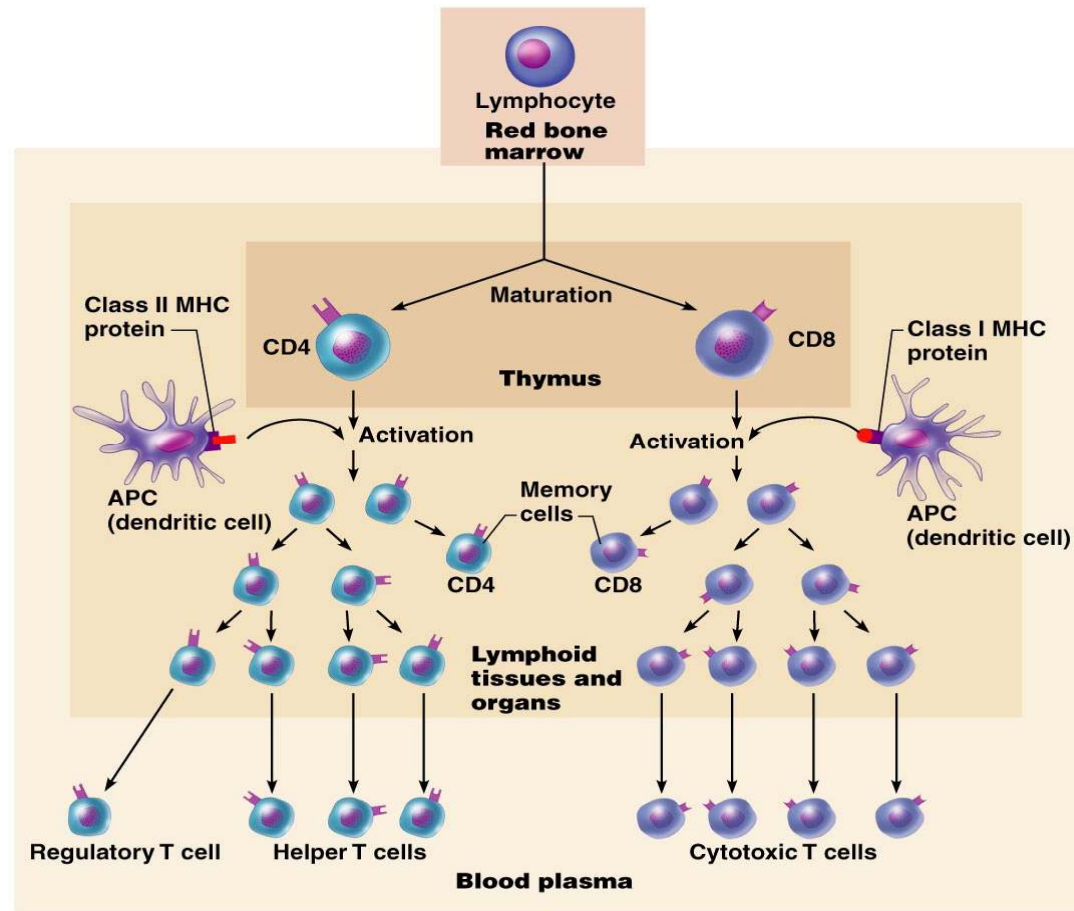
1) Humoral immune response:

- **Antibodies** are produced by **B-lymphocytes**
- These have the ability to recognize and bind specifically to antigen that induced their formation

2) The cell mediated immune response (CMI)

- It is mediated by certain types of **T-lymphocytes**
- T-lymphocytes recognize foreign material by means of **surface receptors**
- T-lymphocytes attack and destroy foreign material directly or through release of soluble mediators i.e. **cytokines**

Adaptive defenses → Cellular immunity



Acquired Or Adaptive Immunity

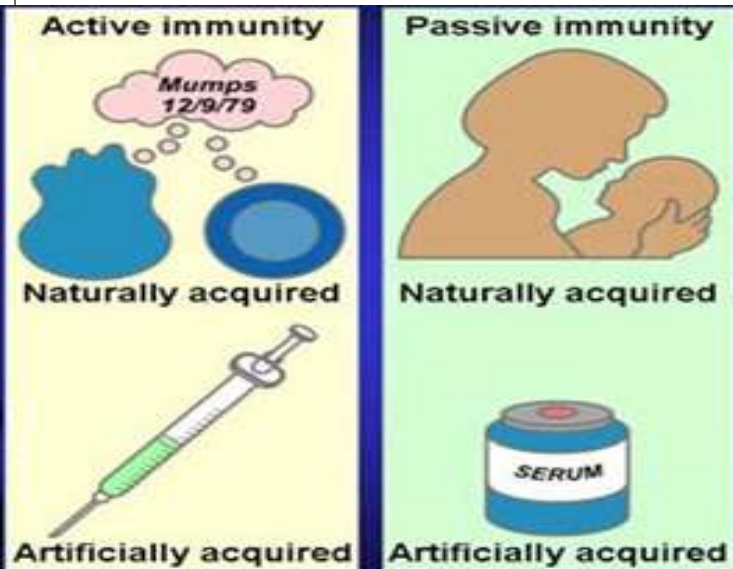
I- Passive acquired immunity

a-Naturally passive acquired immunity

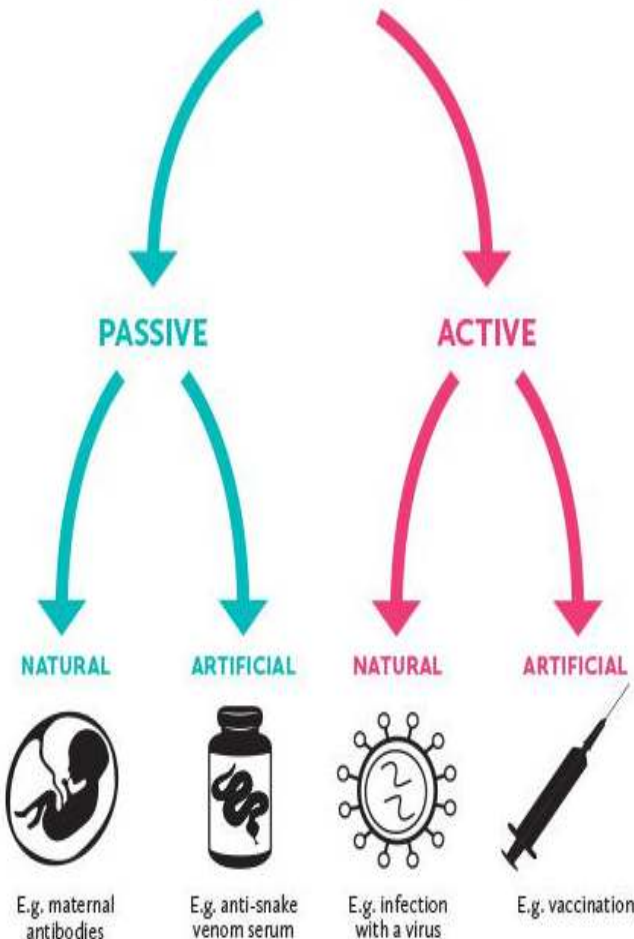
Antibodies are passed through placenta to the fetus

b- Artificially passive acquired immunity

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



ACQUIRED IMMUNITY



II- Active acquired immunity

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

Immune System

Innate/Inborn/non-specific defence mechanism

Acquired/adaptive/specific defence mechanism
Third Line of defence

External defence
First line of defence

1. **Physical barriers:** Skin, Mucus, Nasal hair, Cilia
2. **Chemical barriers:** oil and sweat by sebaceous glands, stomach acid or Low pH (gastric juice), Cerumen (earwax), lysozyme in tears and tissue fluids, vaginal bacteria producing lactic acid (low pH)

Internal defence
Second line of defence

1. **Phagocytes:** Macrophages & WBCs (neutrophils and monocytes)
2. Inflammatory reactions
3. Fever
4. Interferons
5. Complement system
6. Natural killer cells (NK cells)

Active immunity

- In contact with Antigen
- 1) **T cells:** Cytotoxic T cells+ helper T cells+ suppressor T cells+ memory T cells
 - 2) **B cells:** plasma cells+ memory B cells
 - 3) **Antigen presenting cells**=Macrophages, B cells and dendritic cells

Passive immunity

Antibodies artificially produced outside directly injected to the body
No contact with pathogen

ADAPTIVE IMMUNE SYSTEM

T-lymphocytes

T-cytotoxic → Cytotoxic

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

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 mediated 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
- 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)

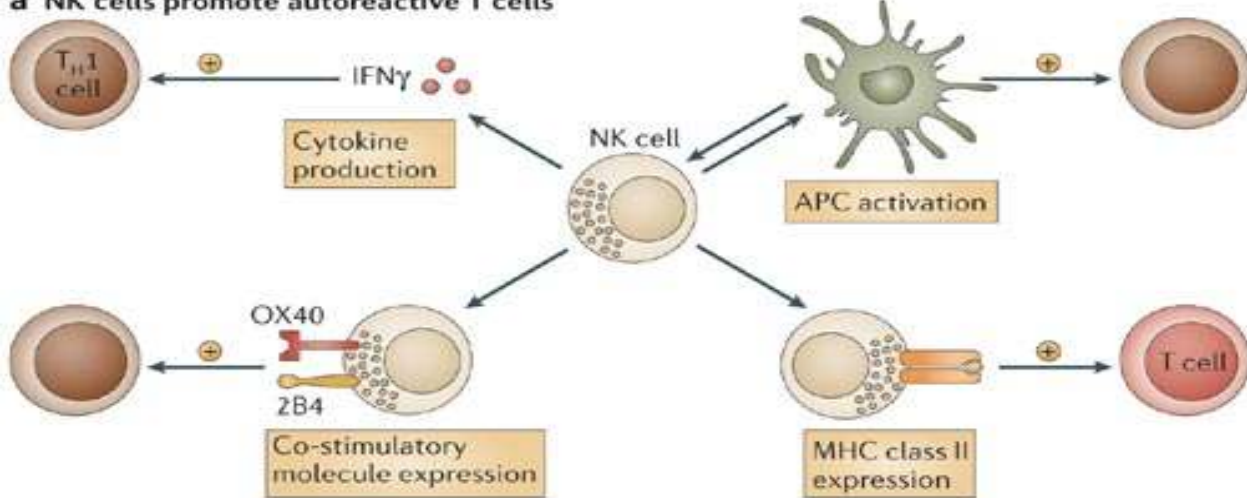
B-lymphocytes:

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

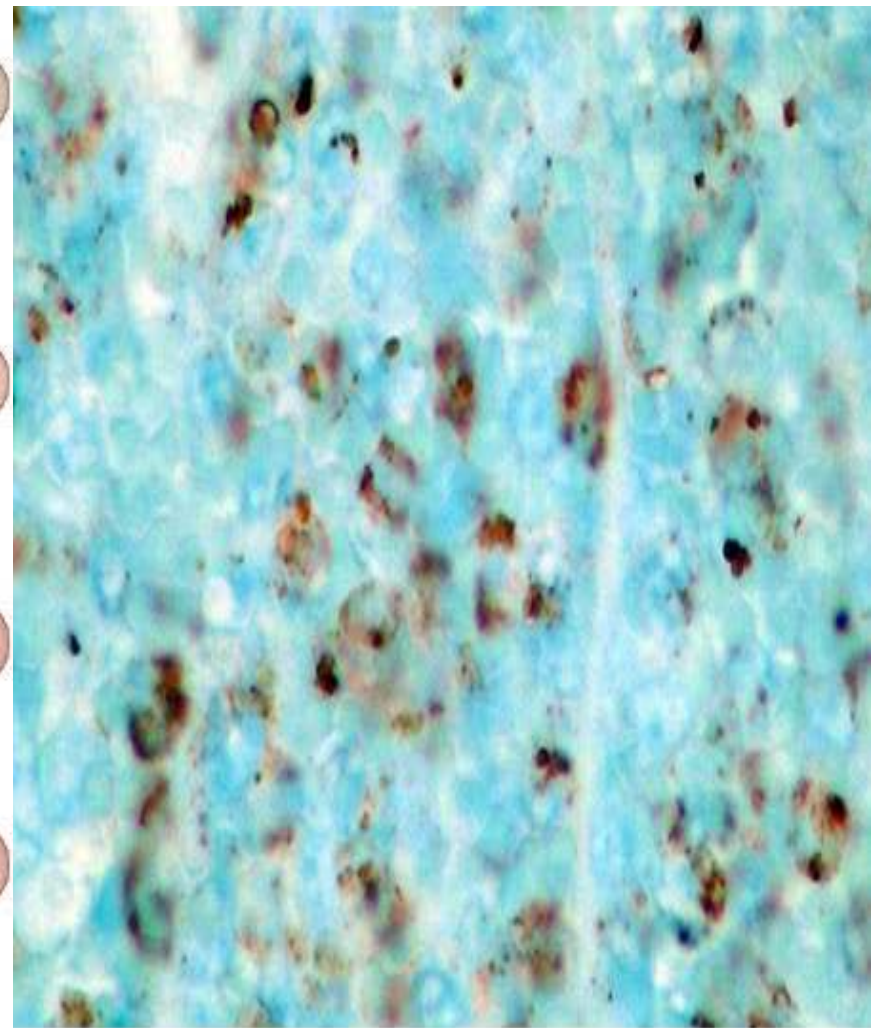
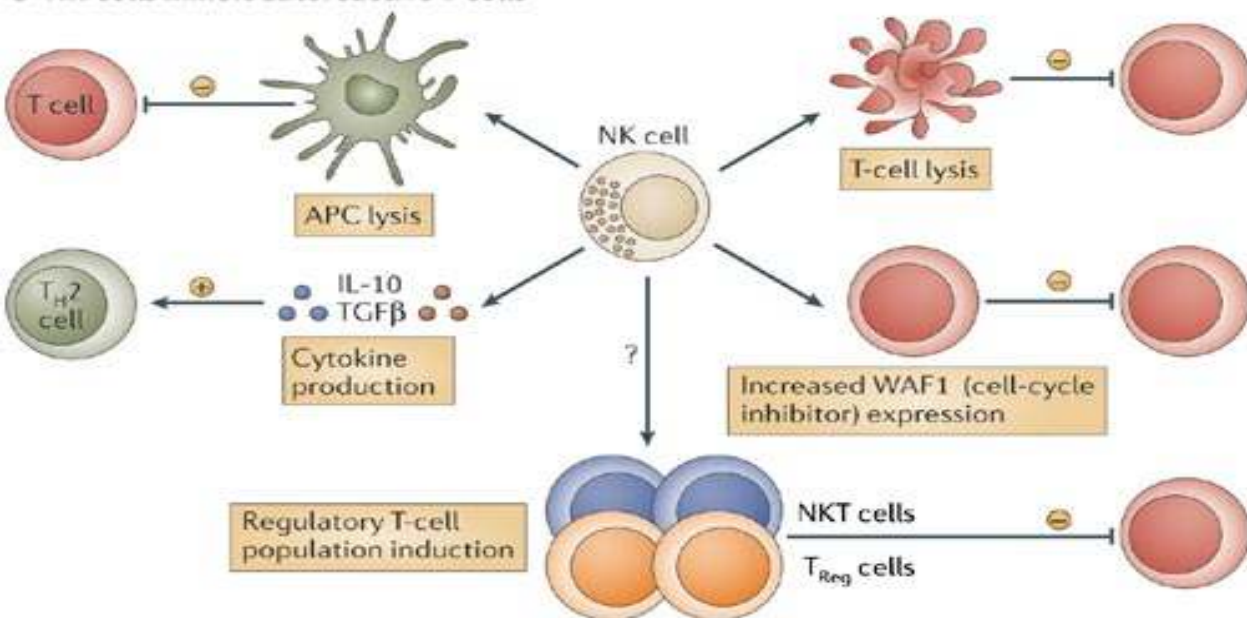
* **NK, K cells:**

- Not antigen specific
- Carry Fc receptors , NK-target cell receptor

a NK cells promote autoreactive T cells



b NK cells inhibit autoreactive T cells



Source: Lichtman MA, Shafer MS, Felgar RE, Wang N:
 Lichtman's Atlas of Hematology: <http://www.accessmedicine.com>
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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
- Kill their target cells by releasing perforins and other cytolytic chemicals
- Secrete potent chemicals that enhance the inflammatory response

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

Cytokines

• Cytokine characteristics

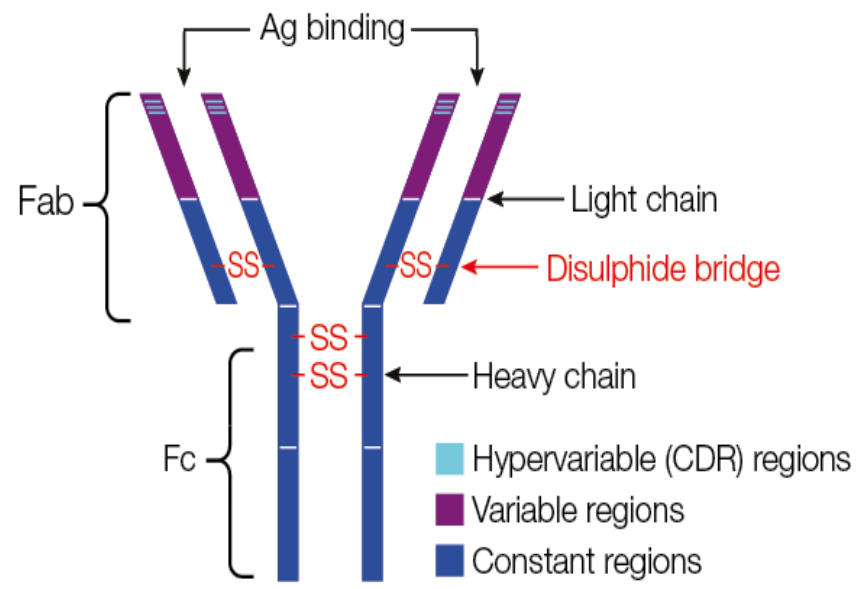
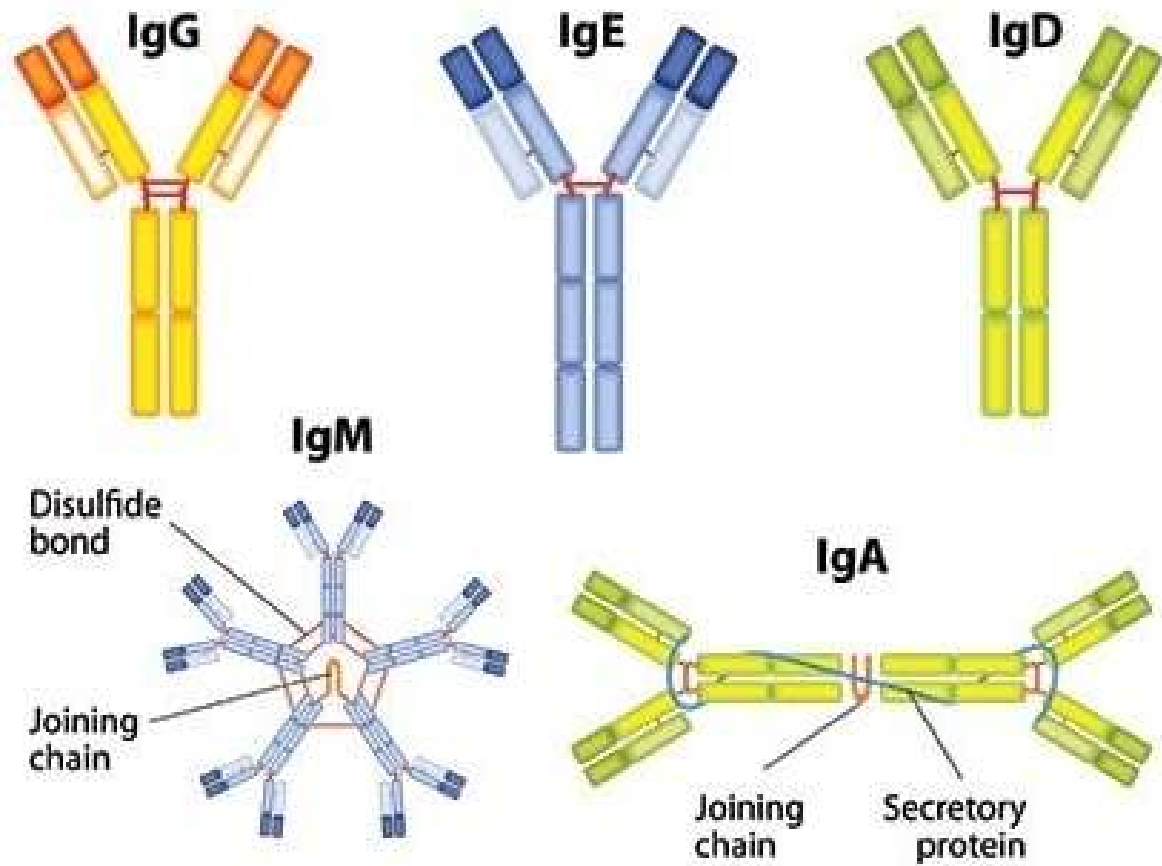
- Small soluble proteins
- Produced by cells of both innate and adaptive immune system
- Released from one cell and bind specific receptor of target cell
 - action similar to that of a hormone
 - can act on cell that released it (autocrine)
 - can act on local cells (paracrine)
 - can circulate in the 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



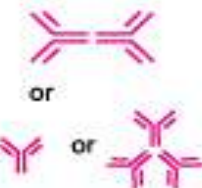



• Cytokine categories

- 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

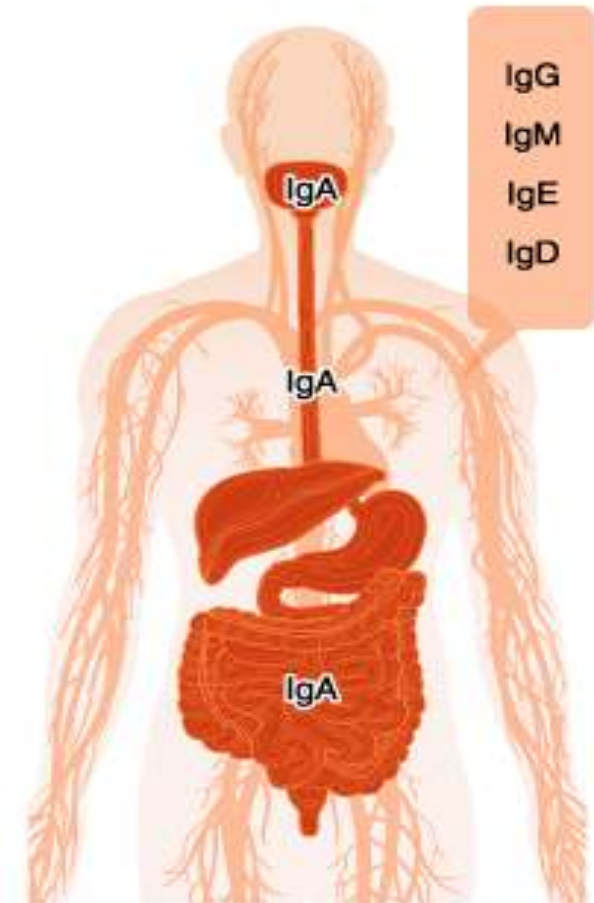


Immunoglobulins


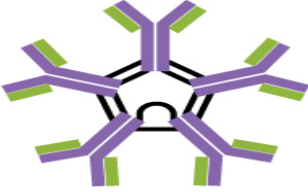



Types and characteristics of antibodies

IgG		<ul style="list-style-type: none"> • Highest opsonization and neutralization activities. • Classified into four subclasses (IgG1, IgG2, IgG3, and IgG4).
IgM		<ul style="list-style-type: none"> • Produced first upon antigen invasion. Increases transiently.
IgA	 or 	<ul style="list-style-type: none"> • Expressed in mucosal tissues. Forms dimers after secretion.
IgD		<ul style="list-style-type: none"> • Unknown function.
IgE		<ul style="list-style-type: none"> • Involved in allergy.

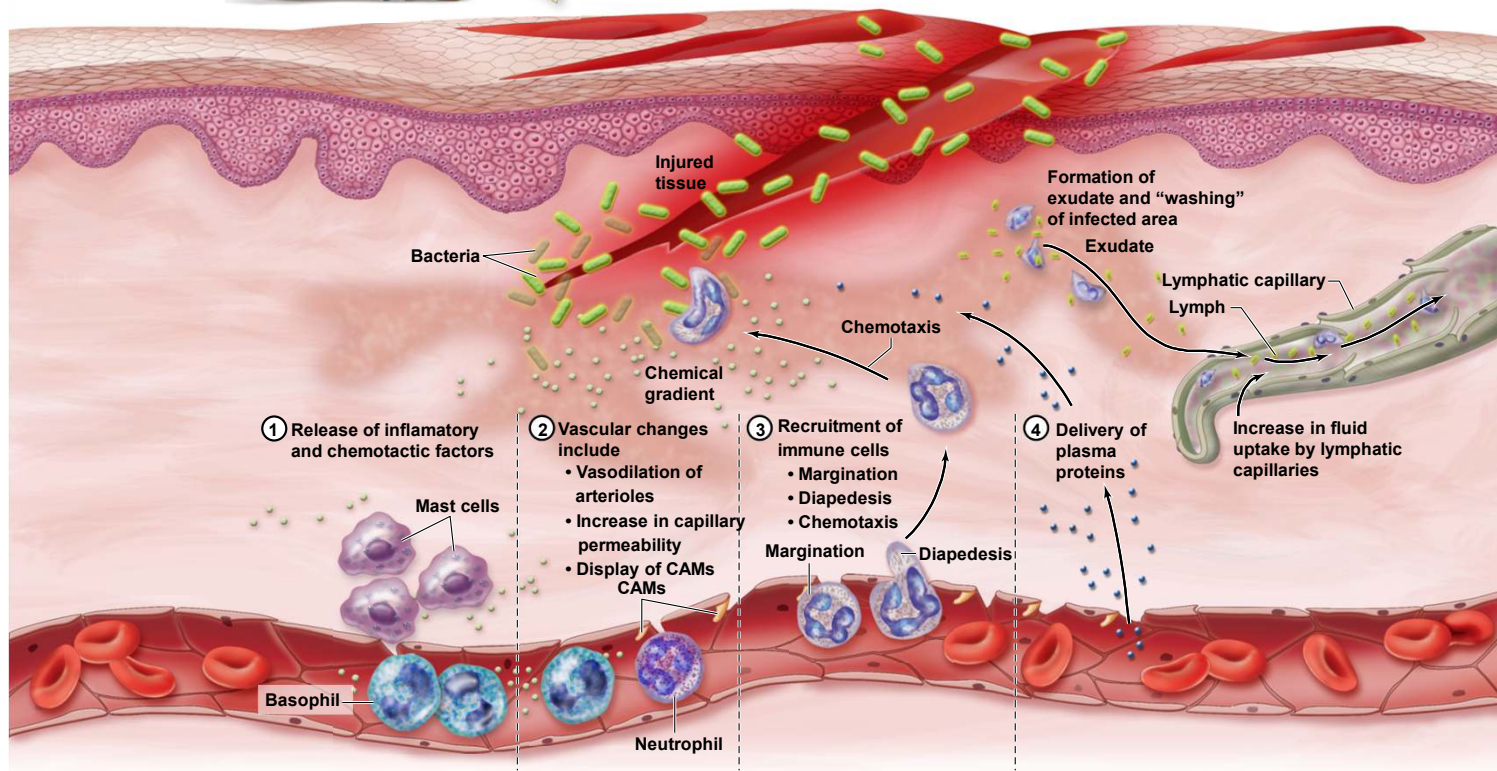
Distribution in the body



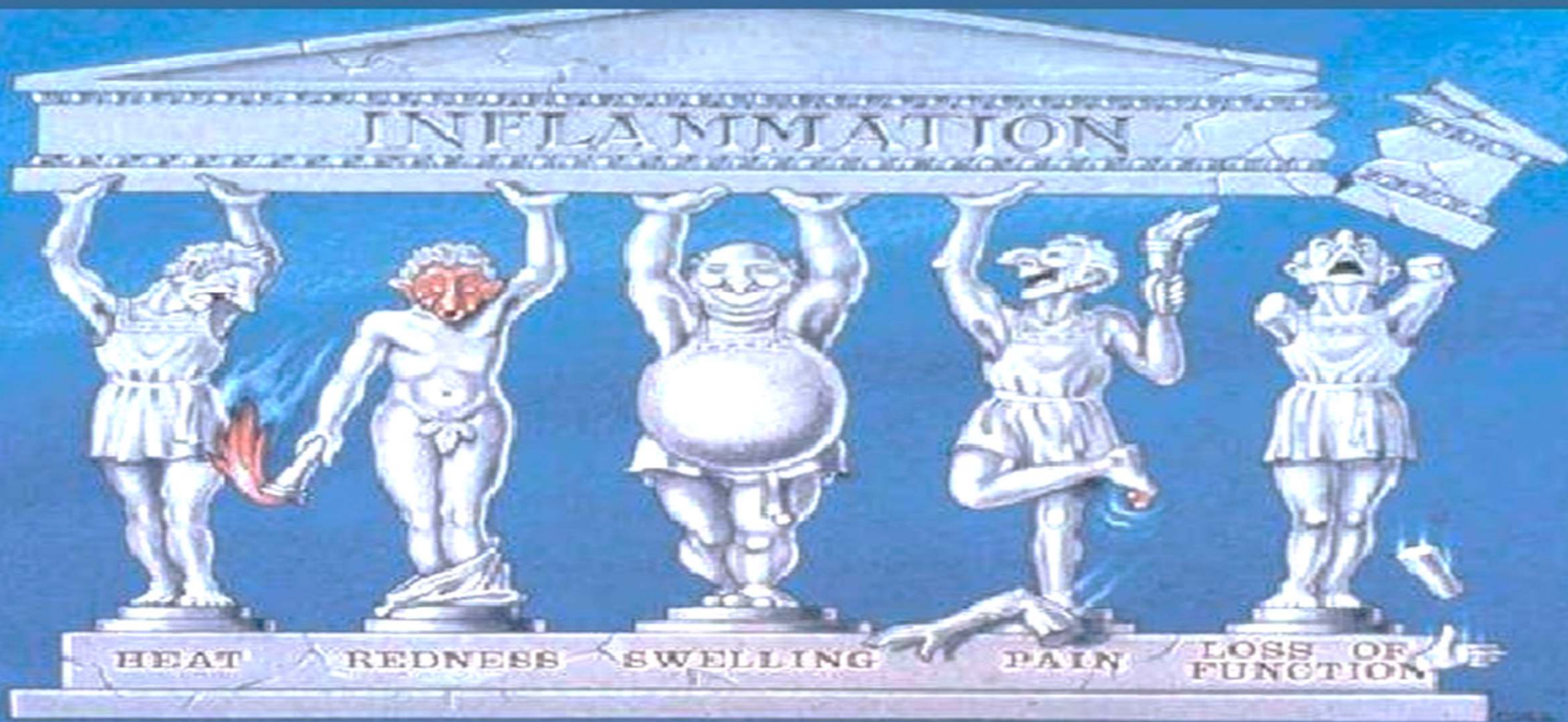
The Five Immunoglobulin (Ig) Classes

Properties	IgG monomer	IgM pentamer	Secretory IgA dimer	IgD monomer	IgE monomer
Structure			 Secretory component		
Heavy chains	γ	μ	α	δ	ϵ
Number of antigen-binding sites	2	10	4	2	2
Molecular weight (Daltons)	150,000	900,000	385,000	180,000	200,000
Percentage of total antibody in serum	80%	6%	13% (monomer)	<1%	<1%
Crosses placenta	yes	no	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to	phagocytes				mast cells and basophils
Function	Neutralization, agglutination, complement activation, opsonization, and antibody-dependent cell-mediated cytotoxicity.	Neutralization, agglutination, and complement activation. The monomer form serves as the B-cell receptor.	Neutralization and trapping of pathogens in mucus.	B-cell receptor.	Activation of basophils and mast cells against parasites and allergens.

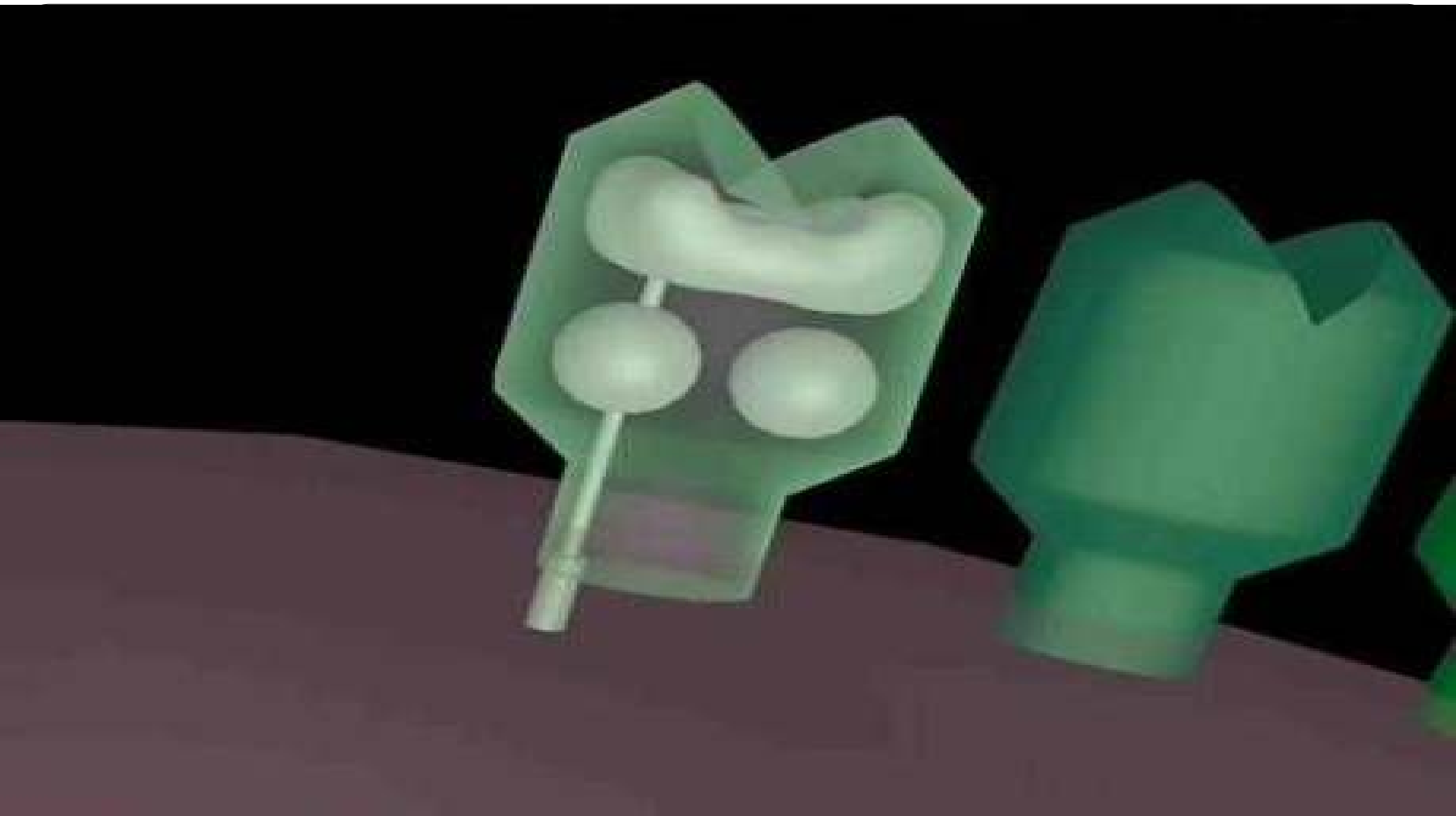
Inflammation



The Cardinal Signs of Inflammation



Hypersensitivity Types and Their Mechanisms				
	Type I	Type II	Type III	Type IV
Immune reactant	IgE	IgG or IgM	IgG and IgM	T cells
Antigen form	Soluble antigen	Cell-bound antigen	Soluble antigen	Soluble or cell-bound antigen
Mechanism of activation	Allergen-specific IgE antibodies bind to mast cells via their Fc receptor. When the specific allergen binds to the IgE, cross-linking of IgE induces degranulation of mast cells.	IgG or IgM antibody binds to cellular antigen, leading to complement activation and cell lysis. IgG can also mediate ADCC with cytotoxic T cells, natural killer cells, macrophages, and neutrophils.	Antigen-antibody complexes are deposited in tissues. Complement activation provides inflammatory mediators and recruits neutrophils. Enzymes released from neutrophils damage tissue.	T _H 1 cells secrete cytokines, which activate macrophages and cytotoxic T cells.
Examples of hypersensitivity reactions	Local and systemic anaphylaxis, seasonal hay fever, food allergies, and drug allergies	Red blood cell destruction after transfusion with mismatched blood types or during hemolytic disease of the newborn.	Post-streptococcal glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Contact dermatitis, type I diabetes mellitus, and multiple sclerosis



The end

- Stop complaining, it has been resumed



It can be worst

