

The background of the slide is a grayscale micrograph showing a dense field of small, roughly spherical cells, likely leukocytes or bacteria, with varying degrees of focus and lighting.

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INTRODUCTION **to** **IMMUNOLOGY**

2009/3

Study materials at : <http://www.zoologie.upol.cz/zam.htm>

LECTURE OVERVIEW

Basic immune terminology

- immunity, immunology, immune system
- immune response
- antigen
- immune system

Components of the immune system

- lymphoid tissues and organs
- cells of immune system
- molecules of immune system

The mechanisms of immune responses:

- innate [native, natural, non-specific] immunity
- adaptive [specific, aquire,] immunity



Ability to respond to foreign and pathological substances or tissue damage is called:

immunity

(lat. *immunitas* = protection)



Immunology – discipline

The study of all aspects of

- host's defense against infection
- response to damage tissue
- pathology response against to own cells and tissue

is called:

Immunology

Defense against infectious microbes is provided by

Immune system

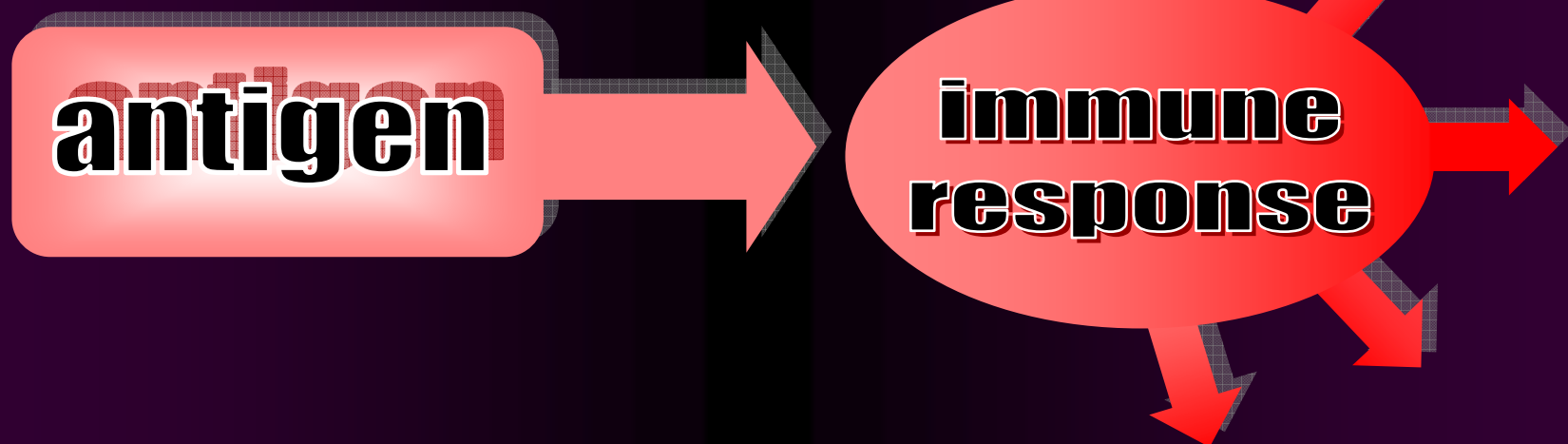
[tissues, cells and molecules involved in the host defense mechanism]

Immune response

Collective and highly coordinated response to the presence of:

- Foreign substances (infectious microbes)
- Damage or pathologically changed cells or molecules
- Tissue injury

foreign substance, pathological cells, tissue injury



ANTIGEN

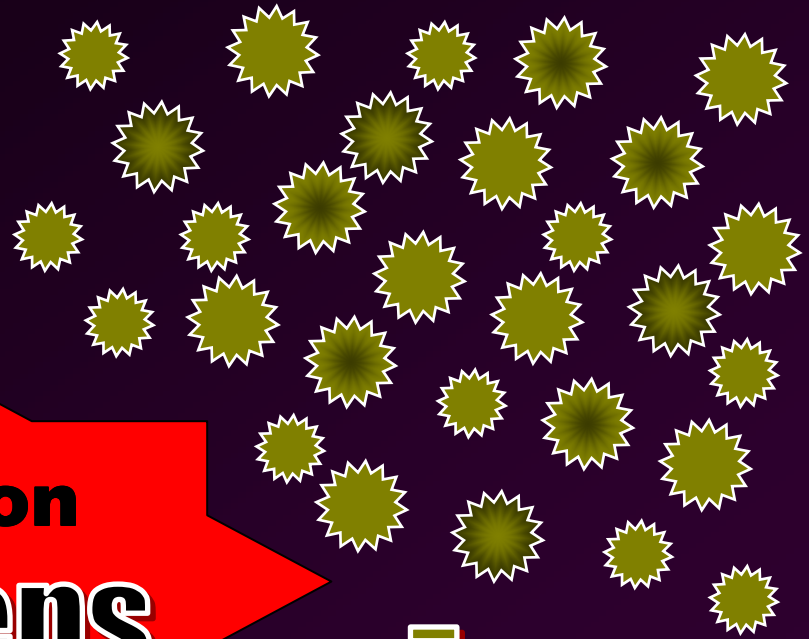
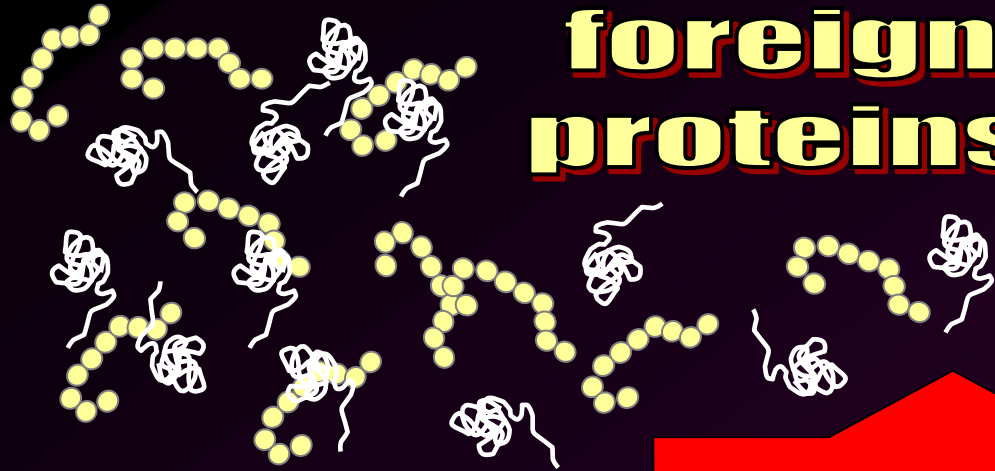
(**Antibody generator**)

Cell, molecule, substance:

- is recognized by receptors of B or T cells
- initiate adaptive immune response
(immunogenic substance)

- Typically **proteins and polysacharides** (generally any kind of molecule)
- Usually big molecules (> 10 000 dalton) but could be a short peptide too
- **exoantigen**: comes from external environment
- **endoantigen**: comes from endogenous environment

**foreign
proteins**



bacteria

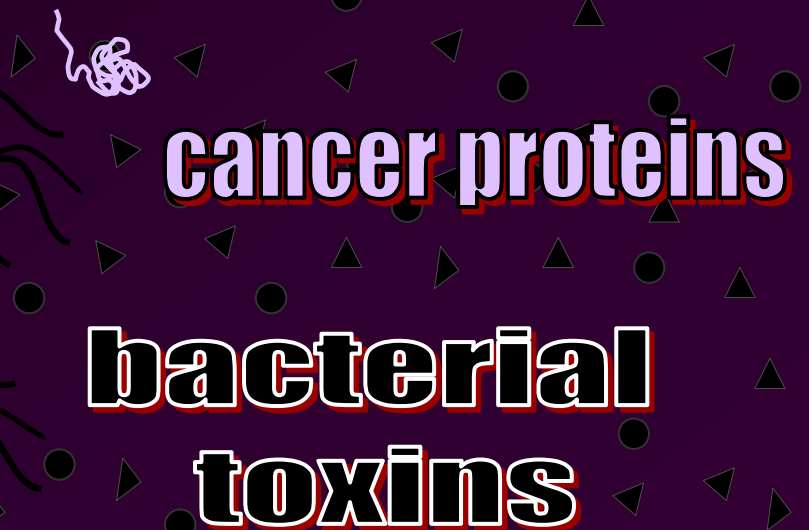


**Common
antigens**

virus

cancer proteins

**bacterial
toxins**



The key feature of the immune system

❑ **SPECIFICITY**

is ability to recognize and distinguish self and non-self molecules according to very small differences

❑ **POLYMORPHISM**

Molecules exist in many different variants

❑ **MEMORY**

Leads to an increased targeted response to specific invaders when they are encountered a second time

Immune system is one of the basic homeostatic mechanisms in the body

Immunogenetics

The study of GENETIC ASPECTS [rules], which take place during forming of immune system is calling

Imunogenetika

It is study of GENES coding highly POLYMORPHIC molecules of immune system.

TOLERANCE

SELF [own], regular cells and molecules

IMMUNE CONTROL

OWN dead, damaged or abnormal cells and molecules

Immune system can recognize:

Foreign [non-self] substances

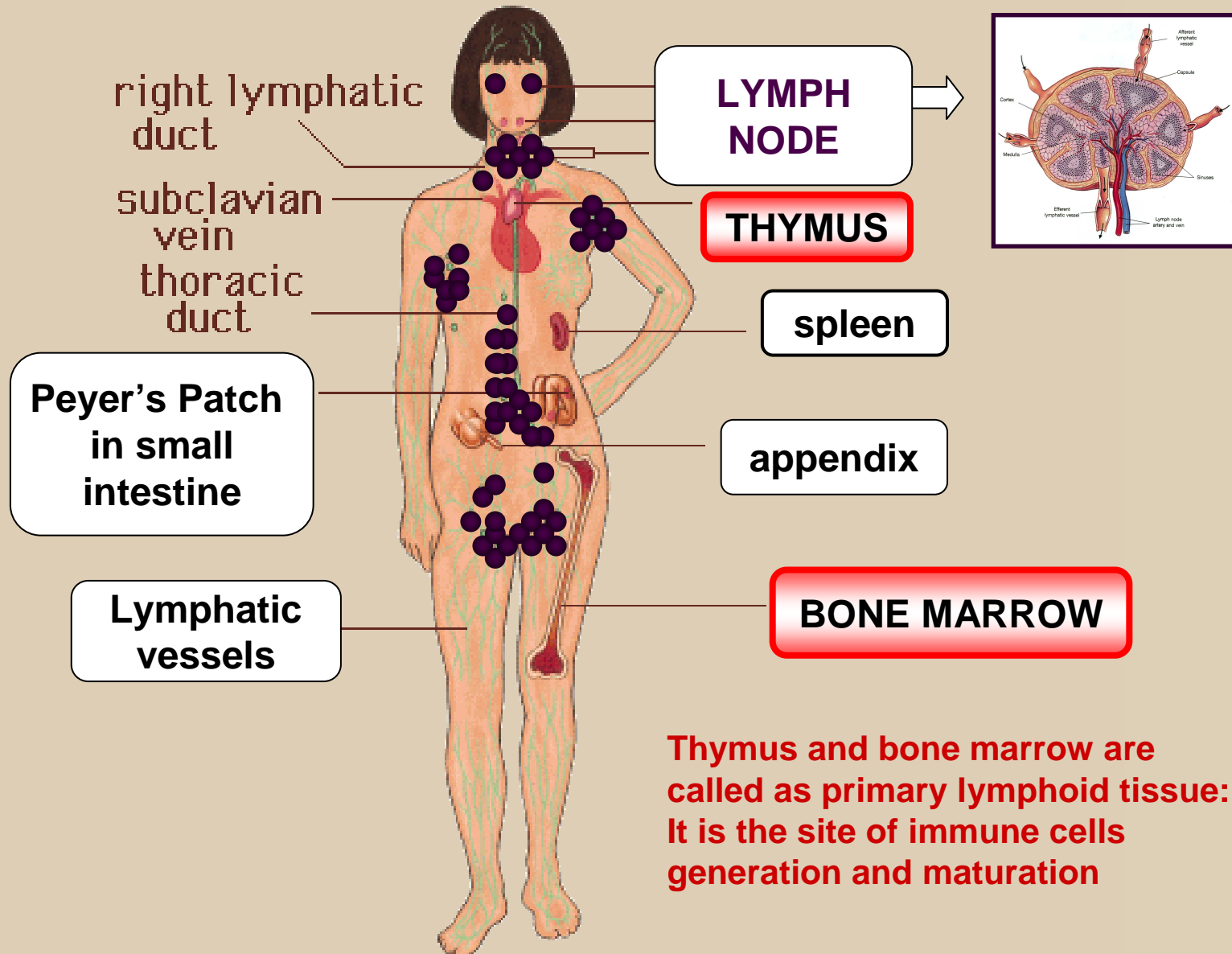
Protection against potential pathogens [disease-causing invaders]

DEFENSE

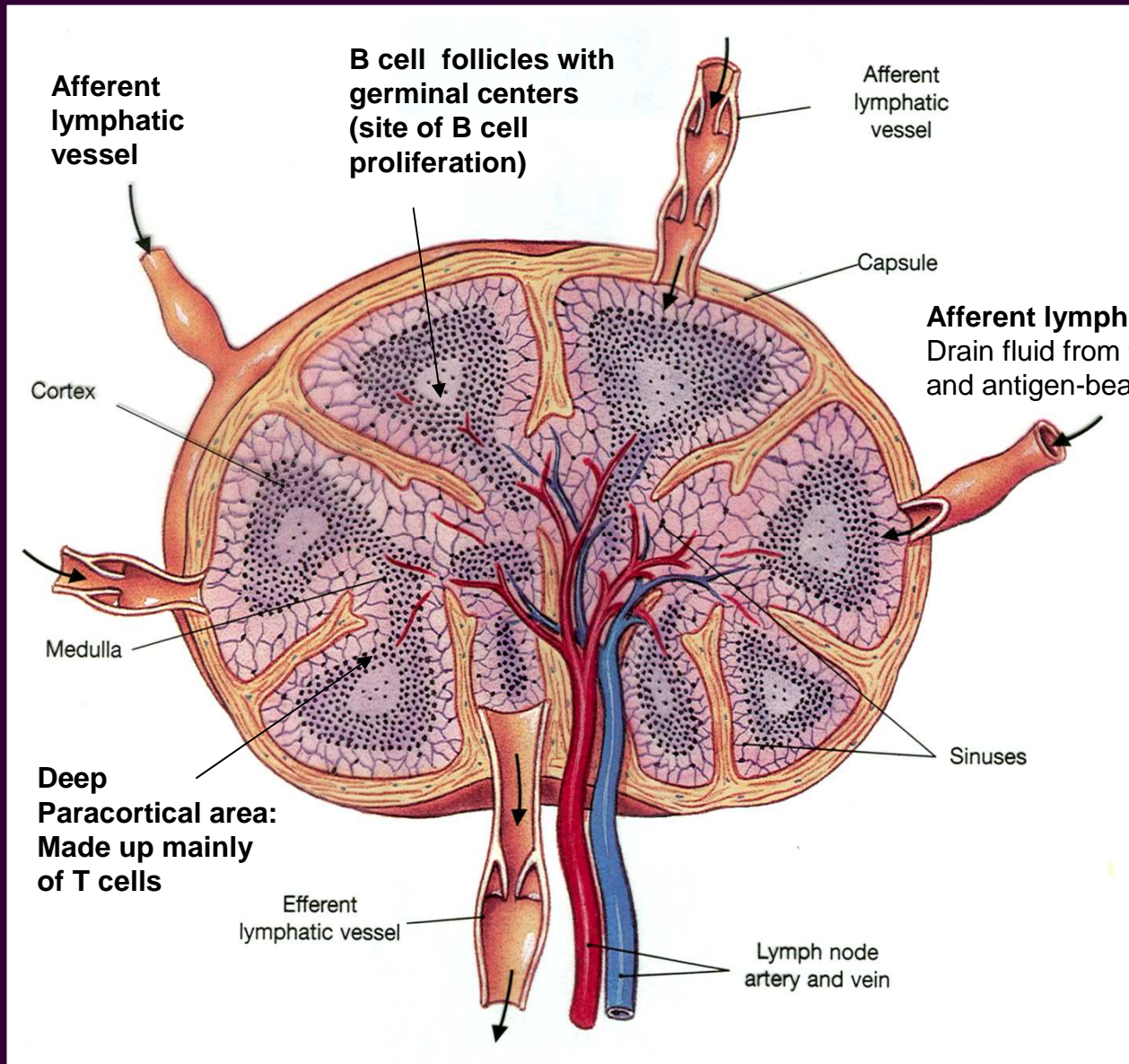
COMPONENTS of the immune system

- A. Lymphoid tissues and organs
- B. The cells of the immune system
- C. Molecules of the immune system

A: Lymphoid tissues and organs



Lymph node



- Small nodular aggregates
- Situated along lymphatic channels

• Site of initiation of adaptive immune response

• B-cell zones (follicles) contains B-cells

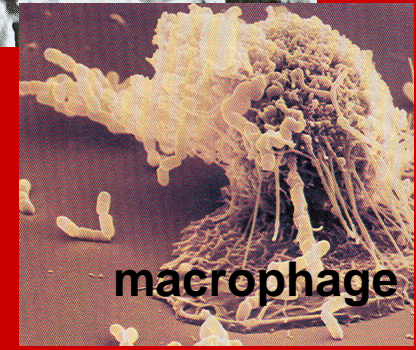
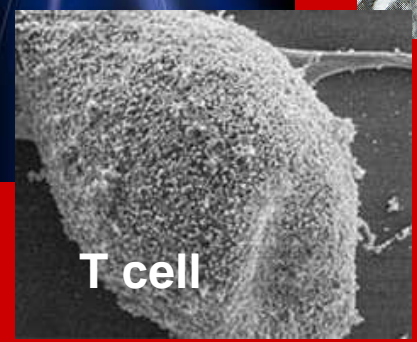
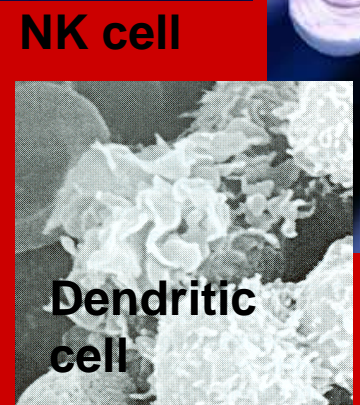
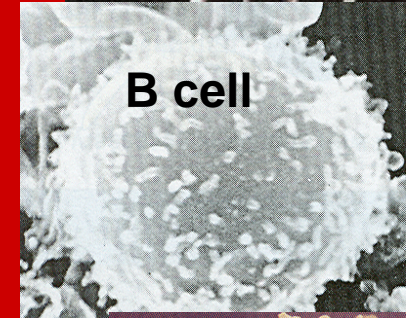
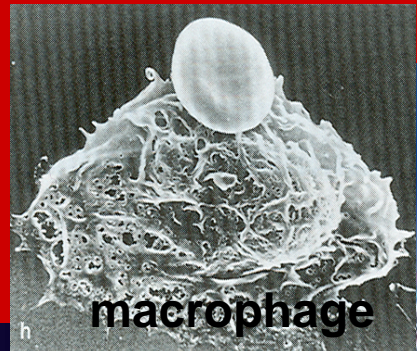
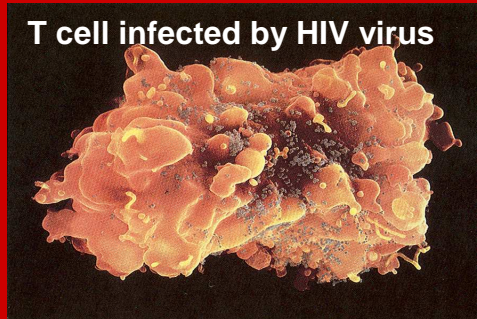
• T-cell zones (paracortical areas) diffusely surrounding B cell follicles

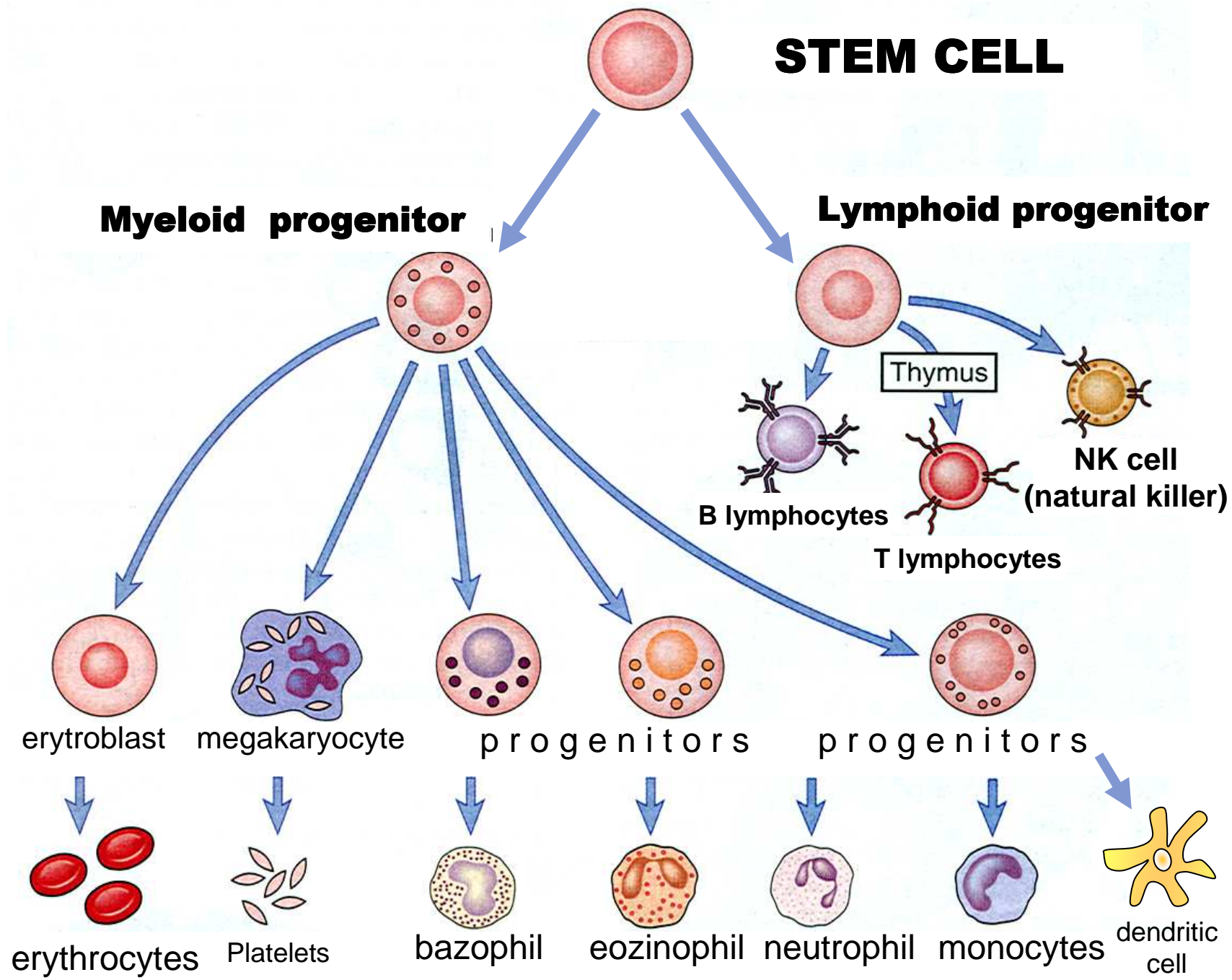
Components of the immune system

B: The cells of the immune system

White cells (in the blood stream)

Extravascular cells in the tissue



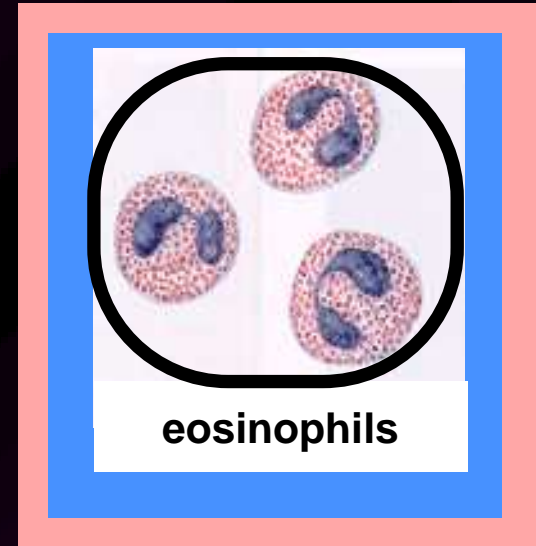


B: The category of the immune cells

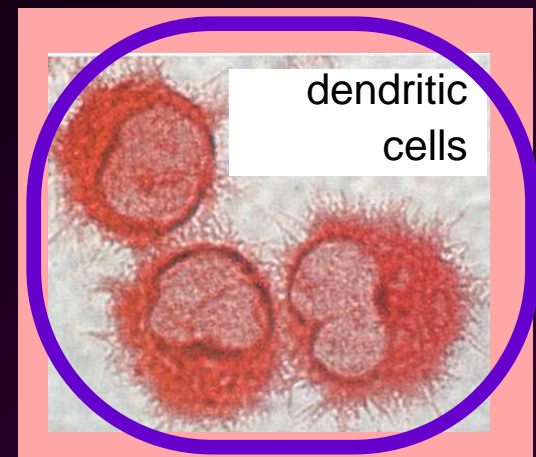
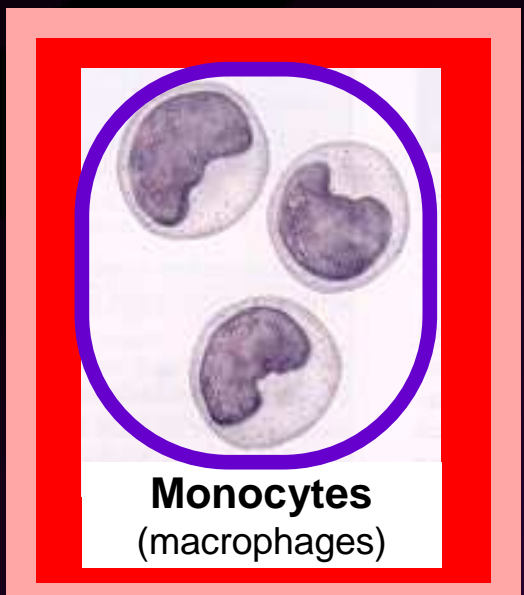
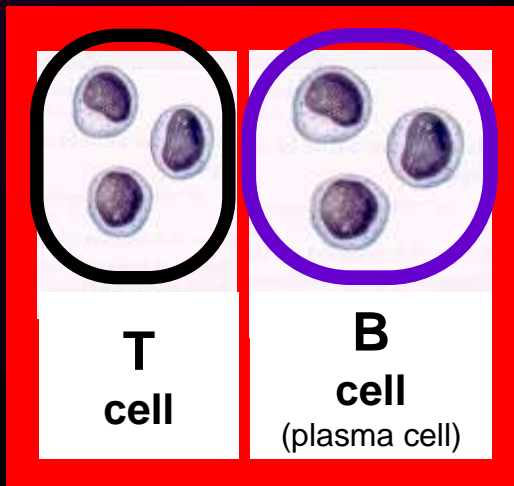
GRANULOCYTES



PHAGOCYTES



AGRANULOCYTES



CYTOTOXIC cell

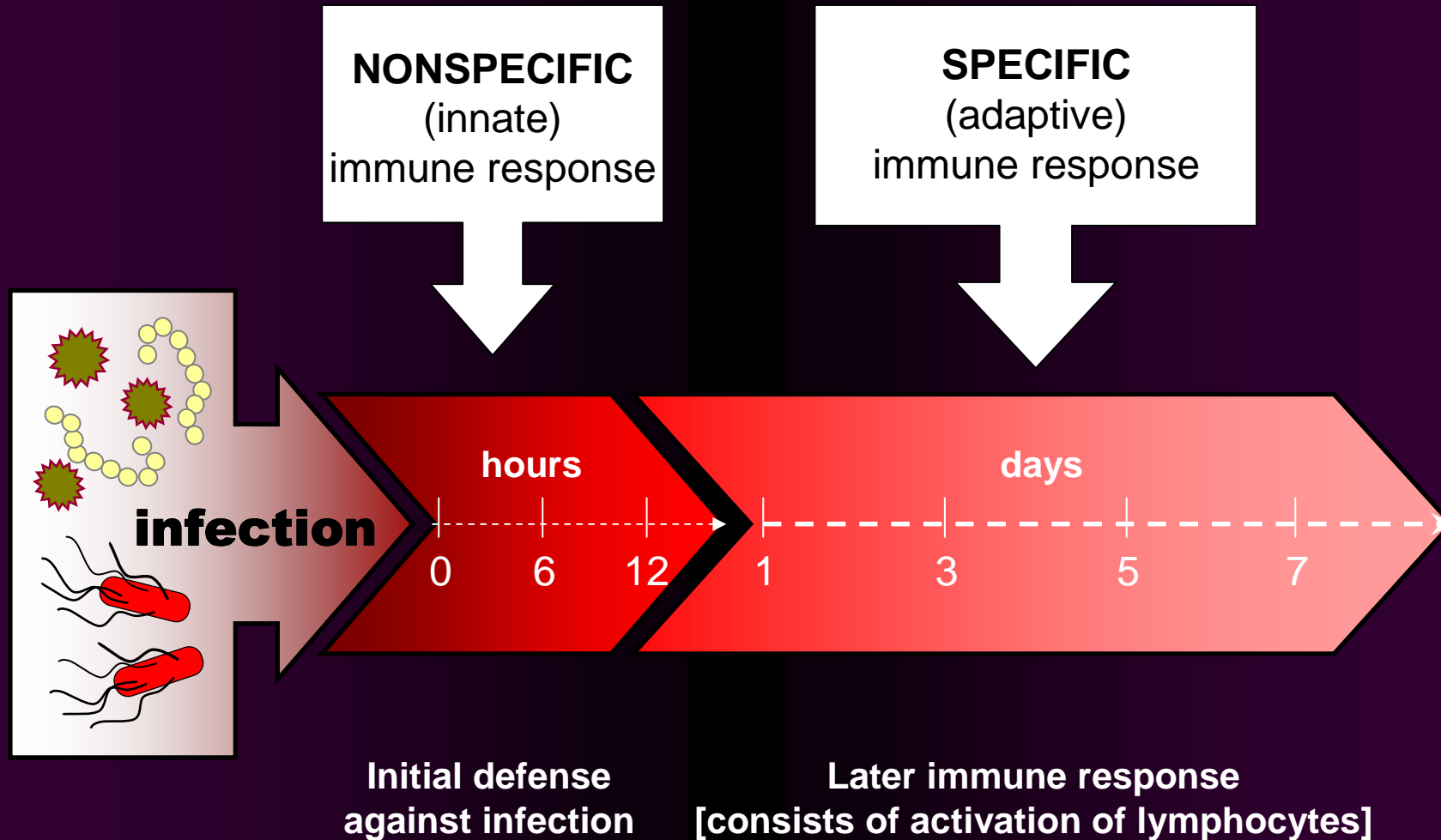
APC

Components of the immune system

C: Molecules of the immune system

- Immunoglobulins (antibodies, gamma globulins)**
- Antigen-binding molecules at the cell membrane of B cell [BCR] and T cell [TCR]**
- MHC glykoproteins (HLA molecules)**
- Cytokines (mediators): i.e. TNF, INF, CSF, interleukins**
- Complement proteins**

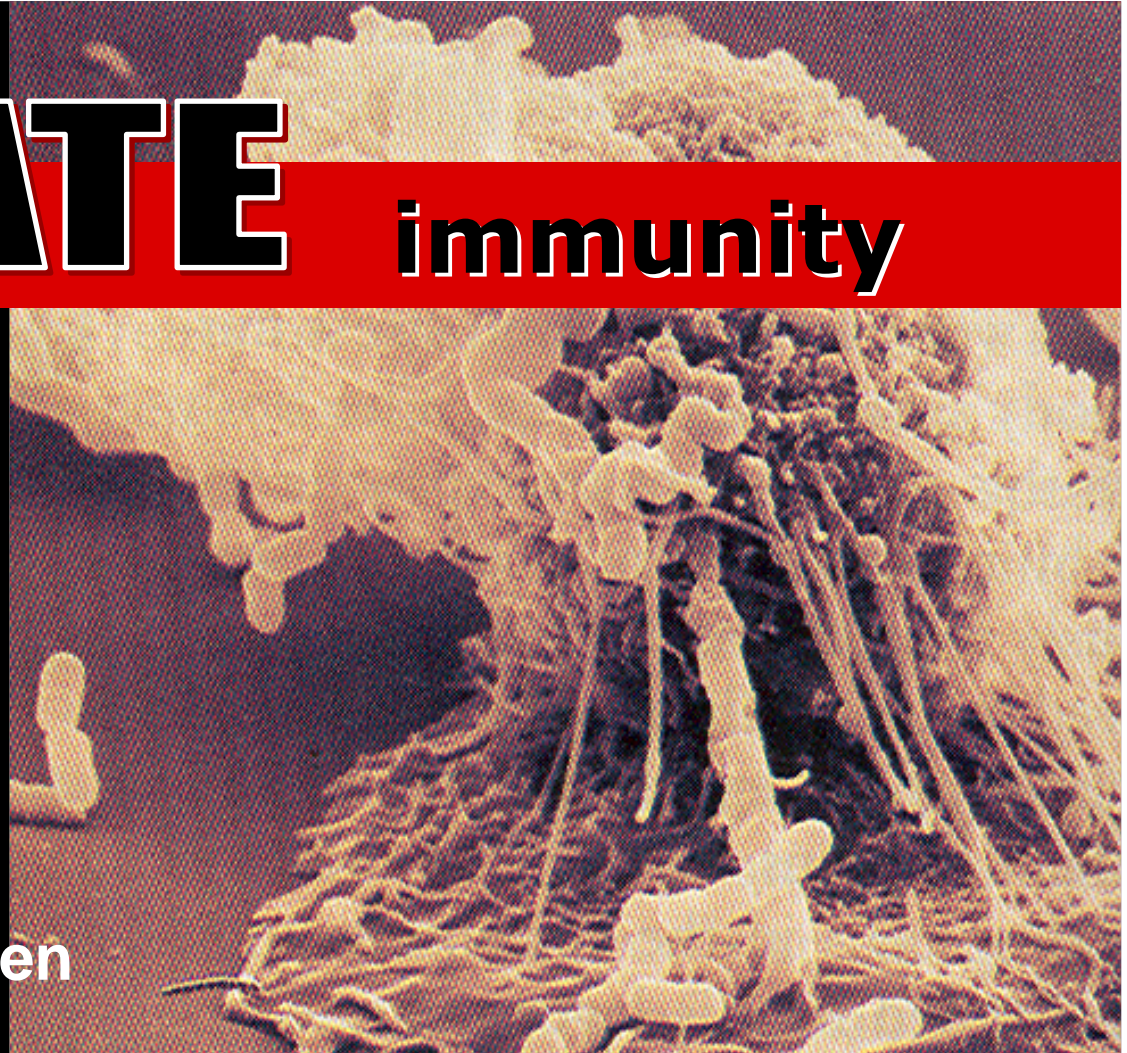
Two categories of immune response



I. INNATE

immunity

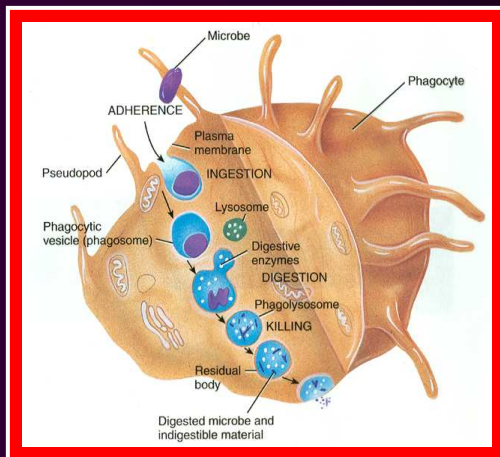
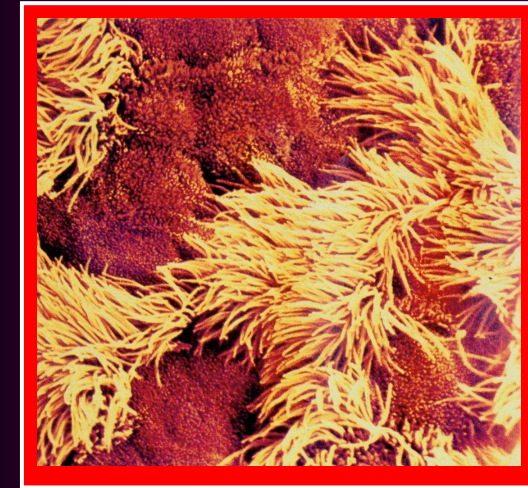
- ❑ First line defense against many common microorganisms
- ❑ Distinguishes between the kind of carbohydrates that are produced by mammalian cells and those produced by bacteria.



The components of innate immunity

Physical and chemical barriers

- **Skin, epithelia** and antimicrobial substances produced at epithelial surface
- **Saliva, tears** (contain lysozyme=enzyme that destroy bacteria)
- **Acidity** of gastric juice, urine, vagina; **Fever**

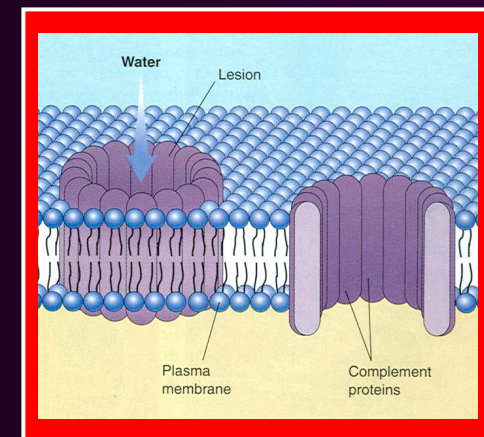


Leukocytes

- Fagocytic cells (neutrophils, macrophages)
- NK cells („natural killers“)
- Bazophils (release histamine)

Chemical mediators

- Complement proteins (group of plasma and membrane proteins)
- Cytokines (released by cells to affect the behavior of other cells)



PHAGOCYTOSIS

Phagocytosis is a cytoskeleton-dependent process of engulfment of large particles (> 0,5µm in diameter)

Process **occurs only** in certain type of **white blood cells** called phagocytes

Neutrophils

Macrophages

Dendritic cells

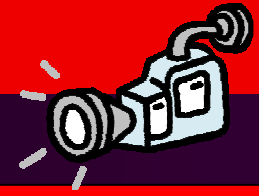
Phagocytes engulfs a foreigner particle into vesicles.

Vesicles fuses with lysosome and digest enzyme destroy the particles.

Phagocytes uses various surfaces receptors to recognize and bind a microbe:

- **TLRs** –Toll like receptors: recognize microbial structure such as endotoxins
- **Mannose receptor (lectine)** – binds mannose at glycoproteins and glycolipids of bacteria (typical for microbial cell wall)
- **Fc receptor** – specific to constant region of immunoglobulins. Fc mediate phagocytosis of antibody-bound antigen

Phagocytosis: video

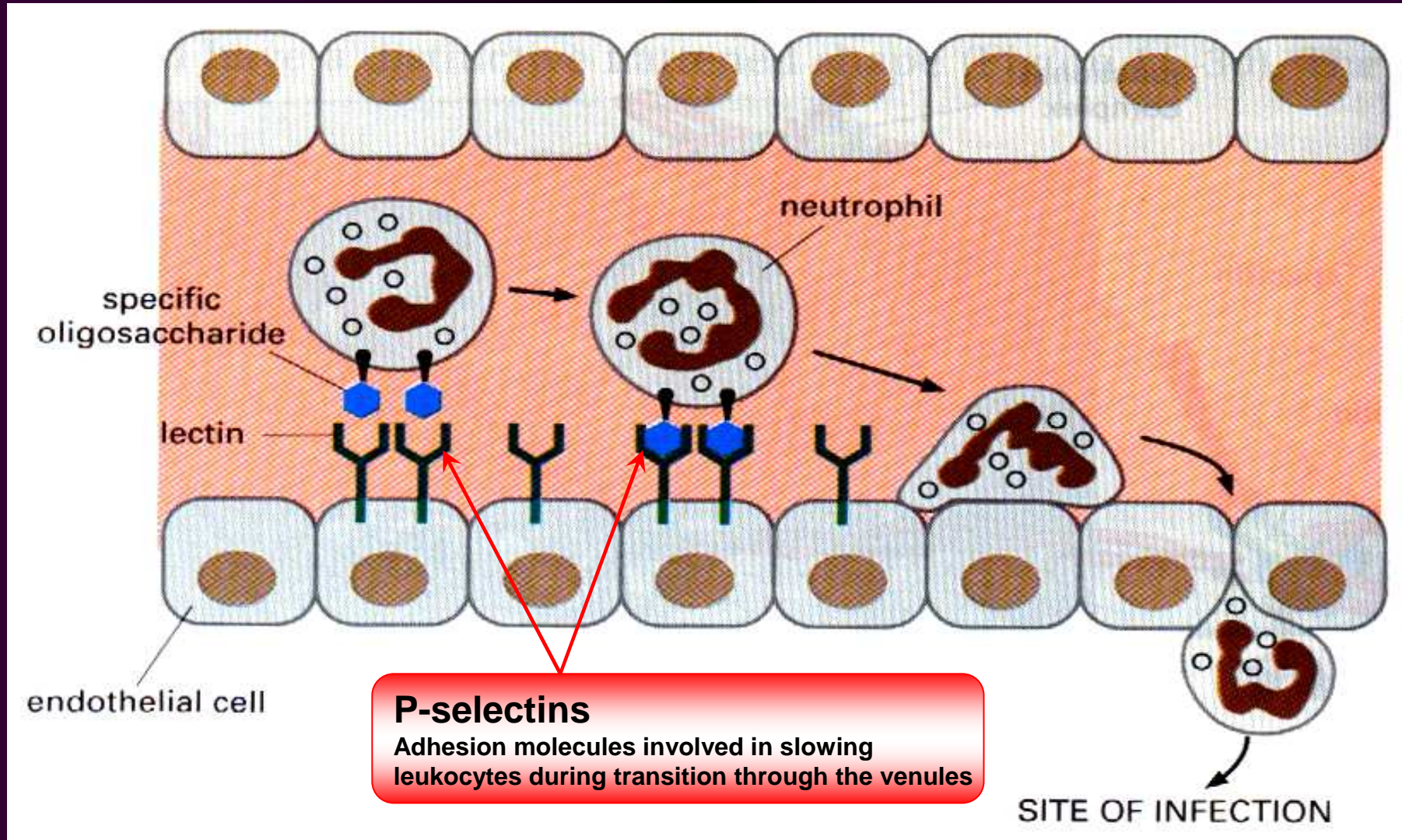


Diapedesis of phagocytes

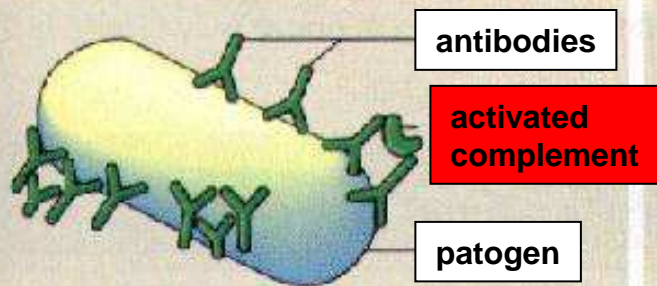
Migration of the leucocytes
from the vessels to the tissue



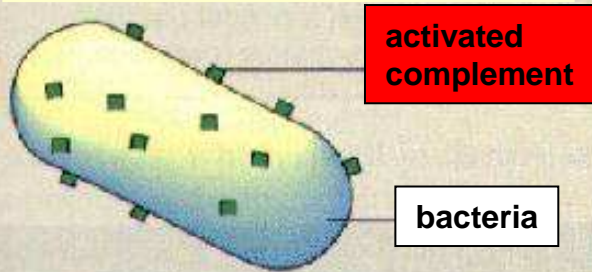
Phagocytes migrate from the vessels to the tissue through endothelial cells



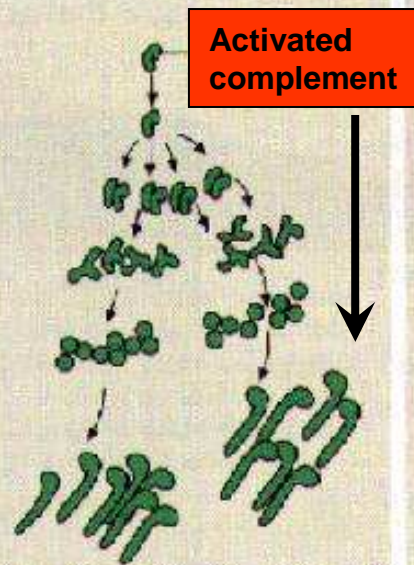
The complement proteins



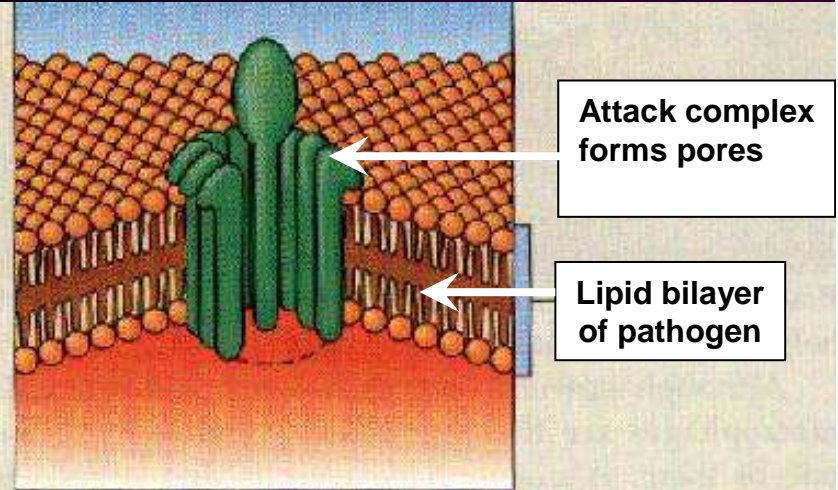
Complement proteins become activated when they bind to antibodies (already bound to a pathogen).



Protein complement also are activated when they bind directly to bacterial surface



Cascading reactions yield a number of different types of proteins. These form many membrane attack complexes



Attack complexes become inserted into the plasma membrane and form large pores



Complement activation

Cascading reaction

Pores forming

Cell lysis

INFLAMMATION

**Inflammation is an innate immune response
to tissue damage
caused by physical agents or by pathogens**

**Series of reactions that bring cells and molecules
of the immune system to the sites of infection or damage:**

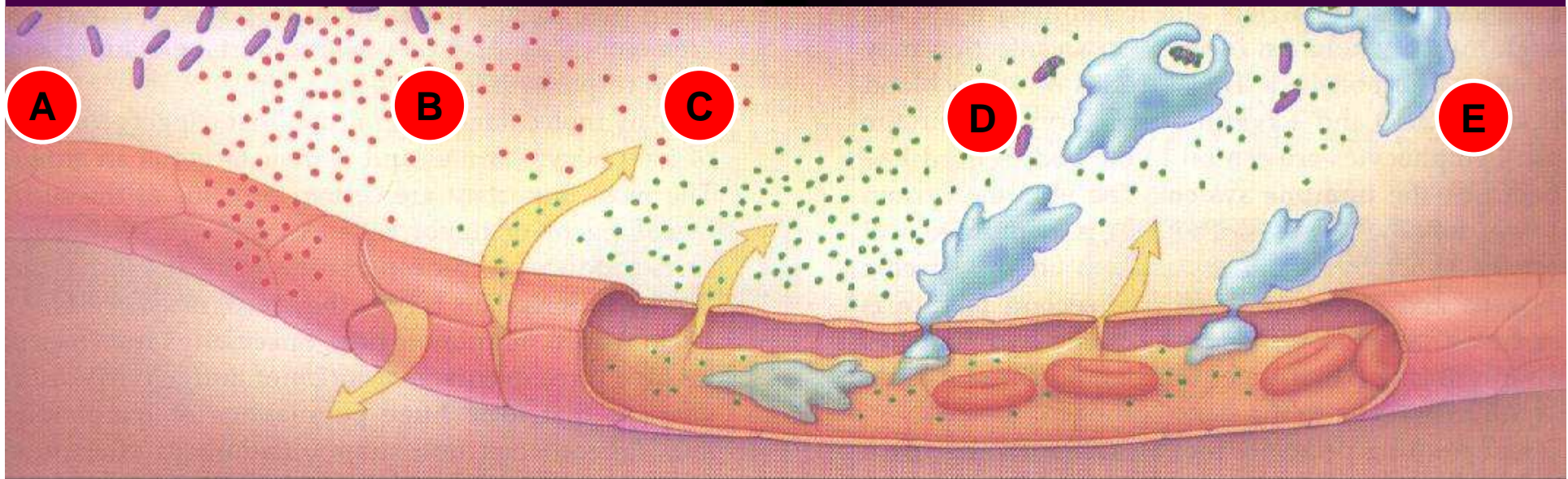
- **Increased blood supply to the infected area**
- **Increased capillary permeability**
- **Increased migration of leukocytes
across the vessel wall**

INFLAMMATORY RESPONSE

A. Tissue injury;
Bacteria invade
the tissue

C. Released substances increase
vessel cell permeability; plasma
proteins escape from vessels

E. Phagocytes engulf
bacteria and
cell debris;
Tissue heals

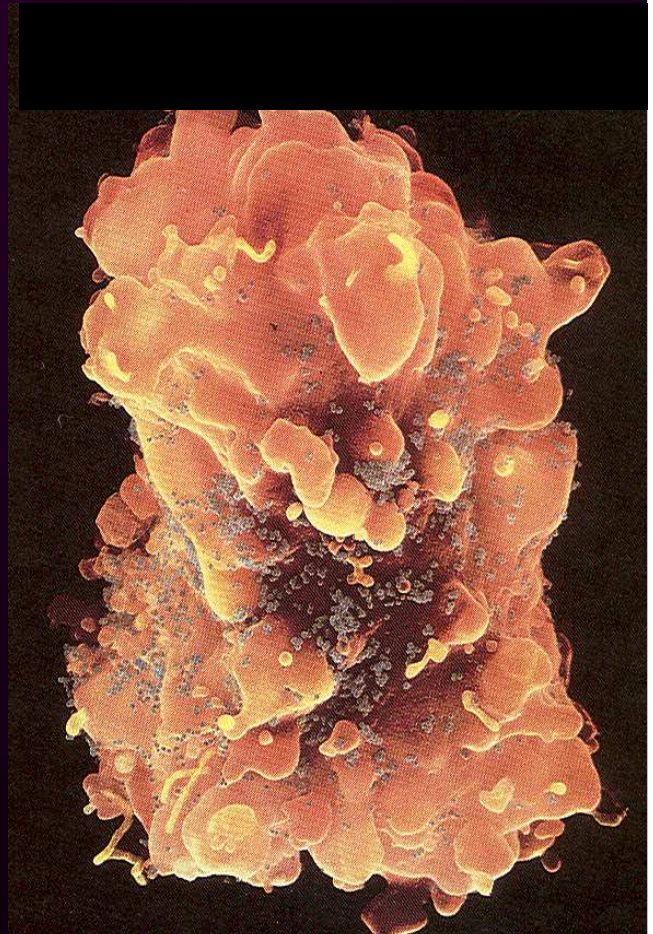


B. Bacterial toxins and chemical
released by damaged cells
[histamine] accumulate in the tissue

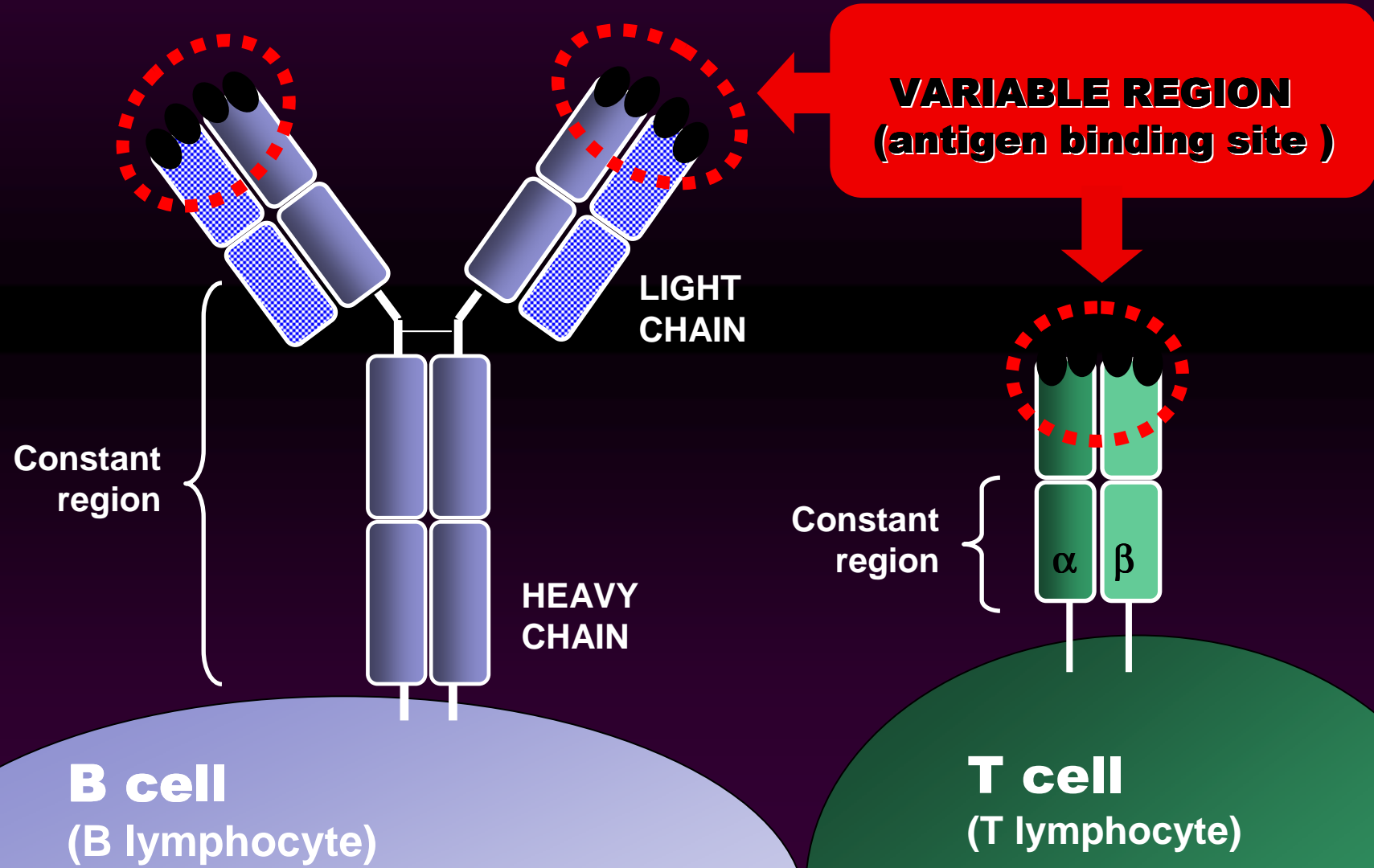
D. Plasma proteins [complement]
attack bacteria;
attracts leucocytes [diapedesis]

II. ADAPTIVE immunity

- ❑ Recognizes a specific foreign substance [peptide] and selectively reacts to it.
- ❑ Is mediated by lymphocytes:
 - B cells** – secrete antibodies
 - T cells** – cell mediates immunity
- ❑ Lymphocytes have specific membrane receptors that allow them to react to only one type of invader



Membrane receptors of lymphocyte



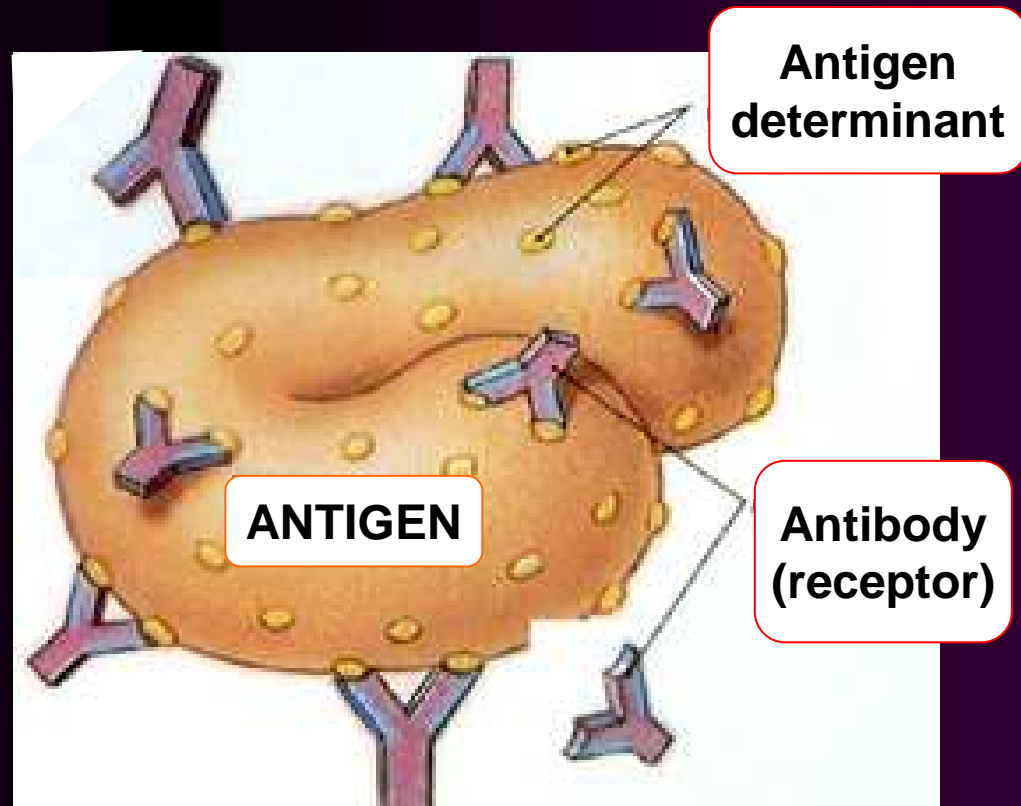
EPITOPE

Specific portion of macromolecular antigen to which an antibody or lymphocyte membrane receptor bind is called:

epitop

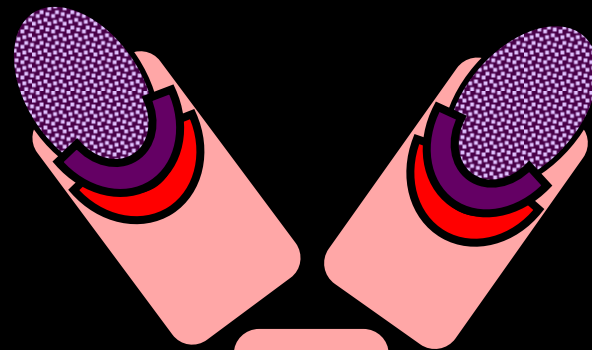
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**antigen
determinant**



COMPLEMENTARITY: variable region - epitope

Sequence at the variable region of a receptor is compatible to....



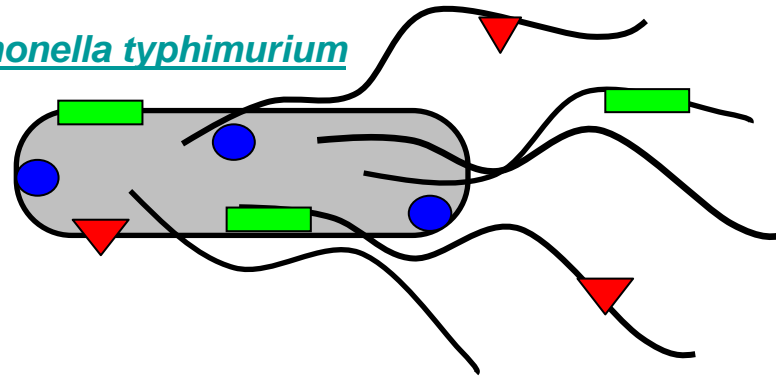
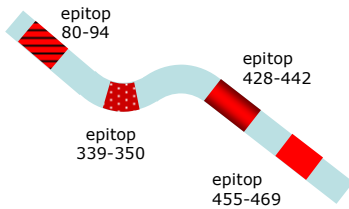
Antigen which specifically binds to a particular receptor

... the sequence at the epitope of a particular antigen

RECEPTOR (antibody) with variable region specific to a particular antigen

PATHOGEN *Salmonella typhimurium*

FljC

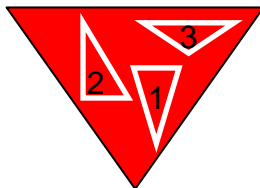


Antigen „A“ ▼

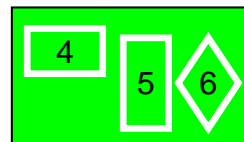
Antigen „B“ ▬

Antigen „C“ ●

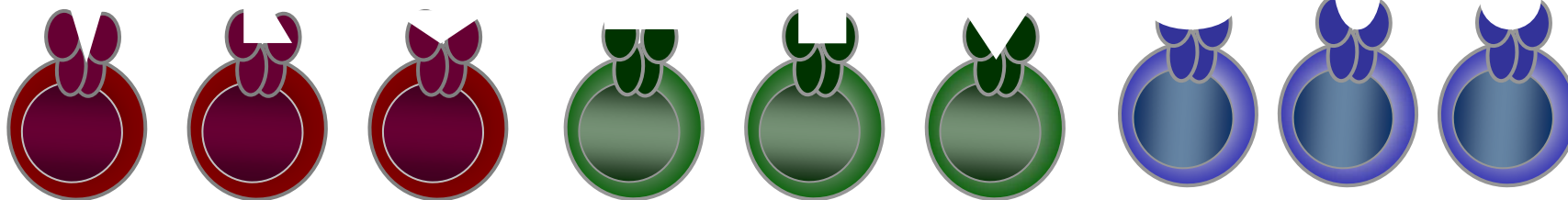
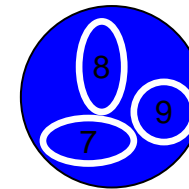
Antigen „A“ contents
epitopes 1, 2, 3



Antigen „B“ contents
epitopes 4, 5, 6



Antigen „C“ contents
epitopes 7, 8, 9



Lymphocytes specific to a particular epitope

B lymphocyte : Humoral immunity

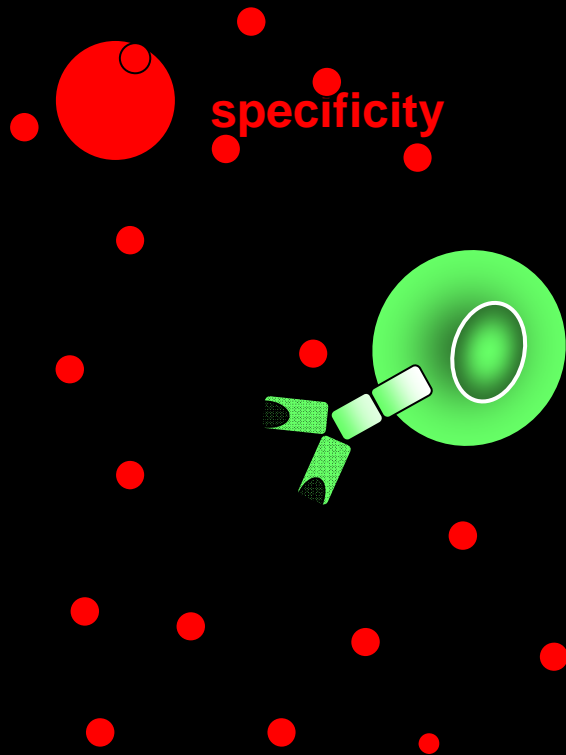
- ❑ Specifically recognizes extracellular antigens
- ❑ Activated B cells - plasma cells - secrete antibodies [immunoglobulins]

B lymphocyte receptor specificity

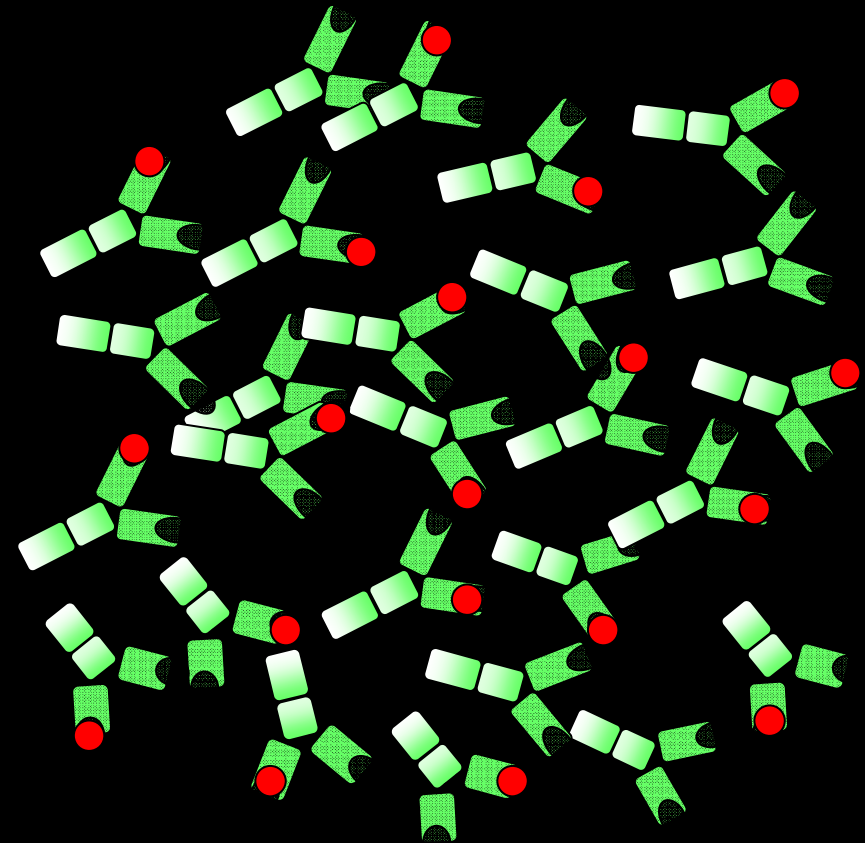


B-lymphocyte activation
[exposure to antigen]

Antibody secretion



Plasma cells



PROLIFERATION

Antigen-antibody binding

B cell membrane

receptor

[BCR]

How do they differ?

How are they similar ?



antibody

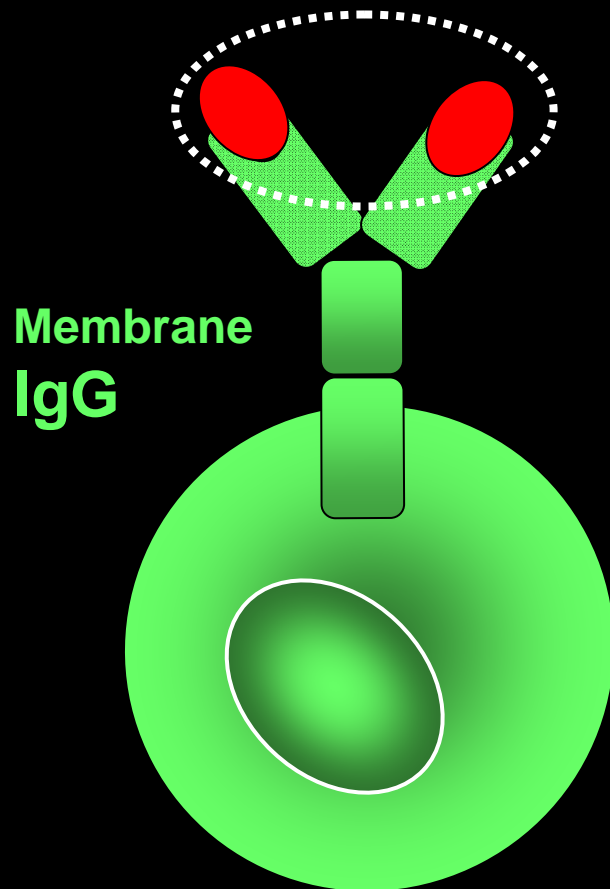
[immunoglobulin]

B cell stimulation by antigen

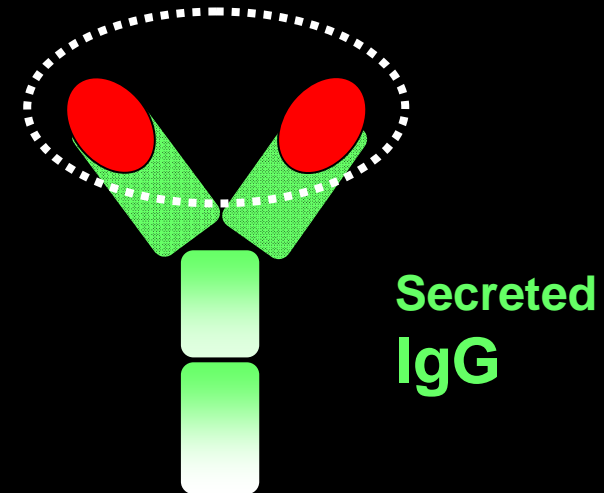


Stimulation

ANTIBODY SECRETION



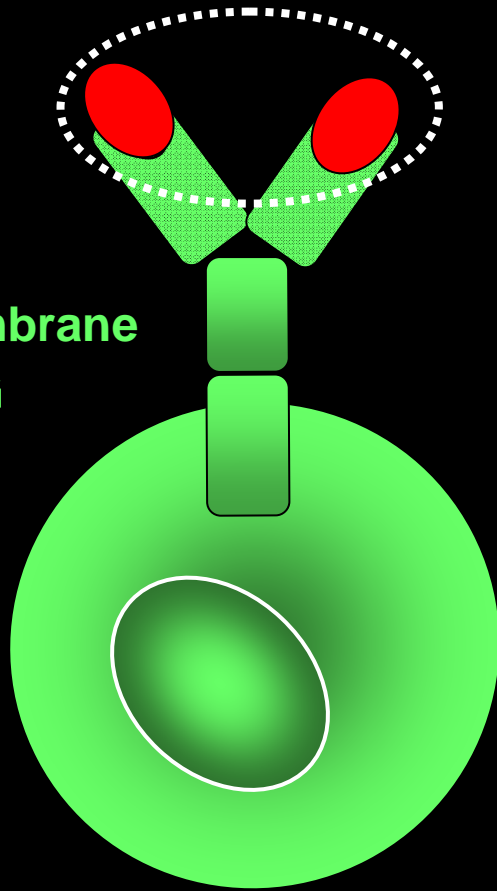
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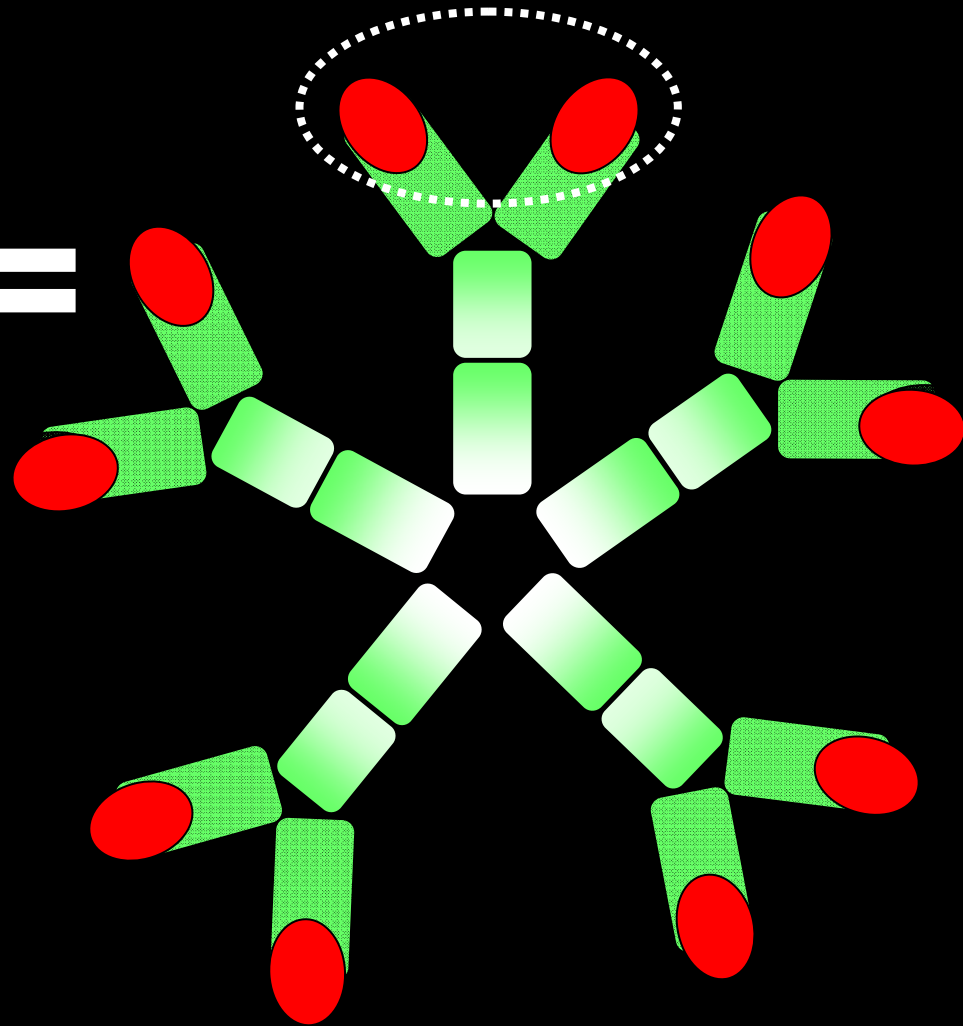
B cell stimulation by antigen



Membrane
IgG

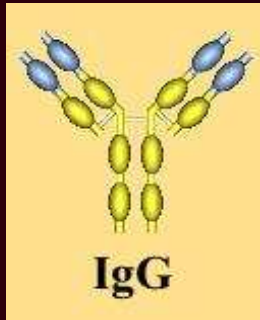


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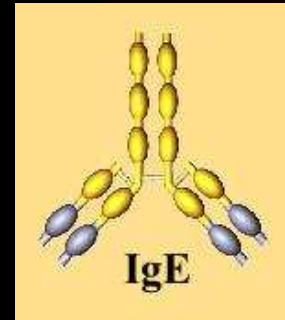
IgM secreted

ISOTYPES of ANTIBODIES



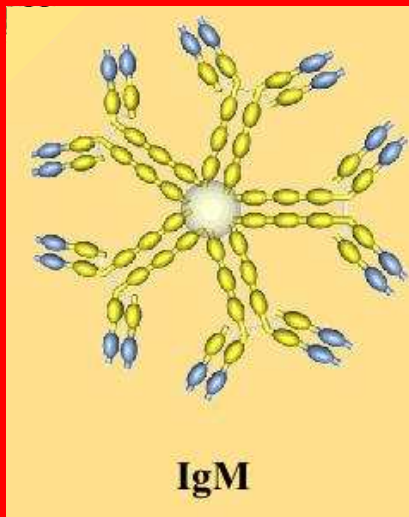
MONOMER

- The most common Ig (70-75% in blood, lymph)
- Complement activation
- Opsonization



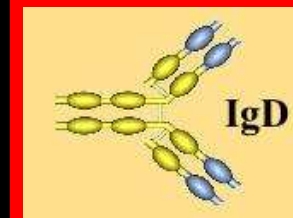
MONOMER

- Immediate hypersensitivity [response for allergic reaction]

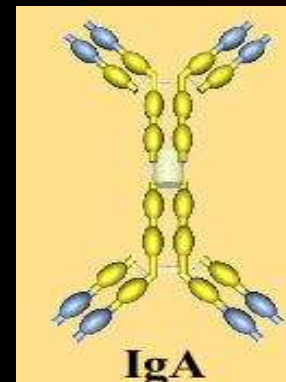


PENTAMER

- Native B cell receptor
- complement activation



- Native B cell antigen receptor

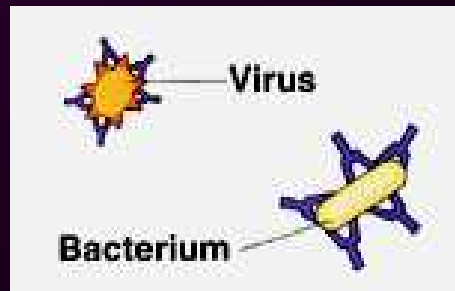


DIMER

- Mucosal immunity
- Found in saliva, milk tears, colostrum

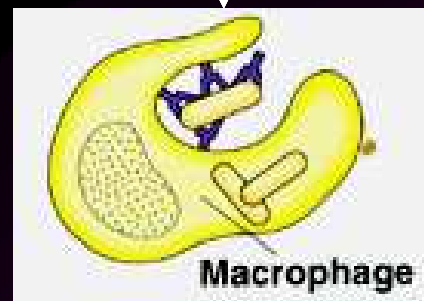
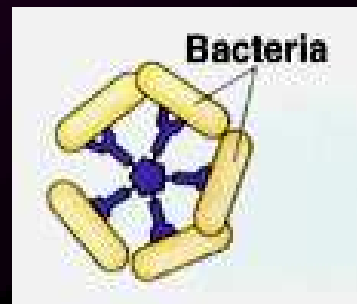
What antibodies do? How they work?

Opsonization:
Attaching to microbial surface

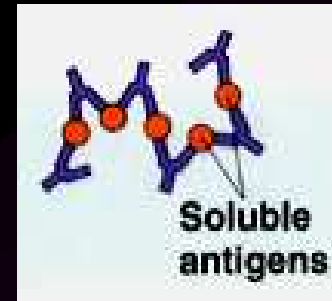


Simulation of phagocytosis

Making clusters of bacteria

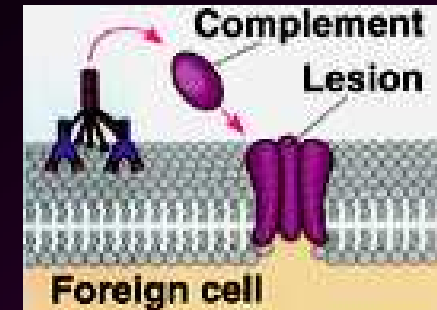


Precipitation:
Inactivation of bacterial toxins



Lysis of bacterial cell

Complement activation



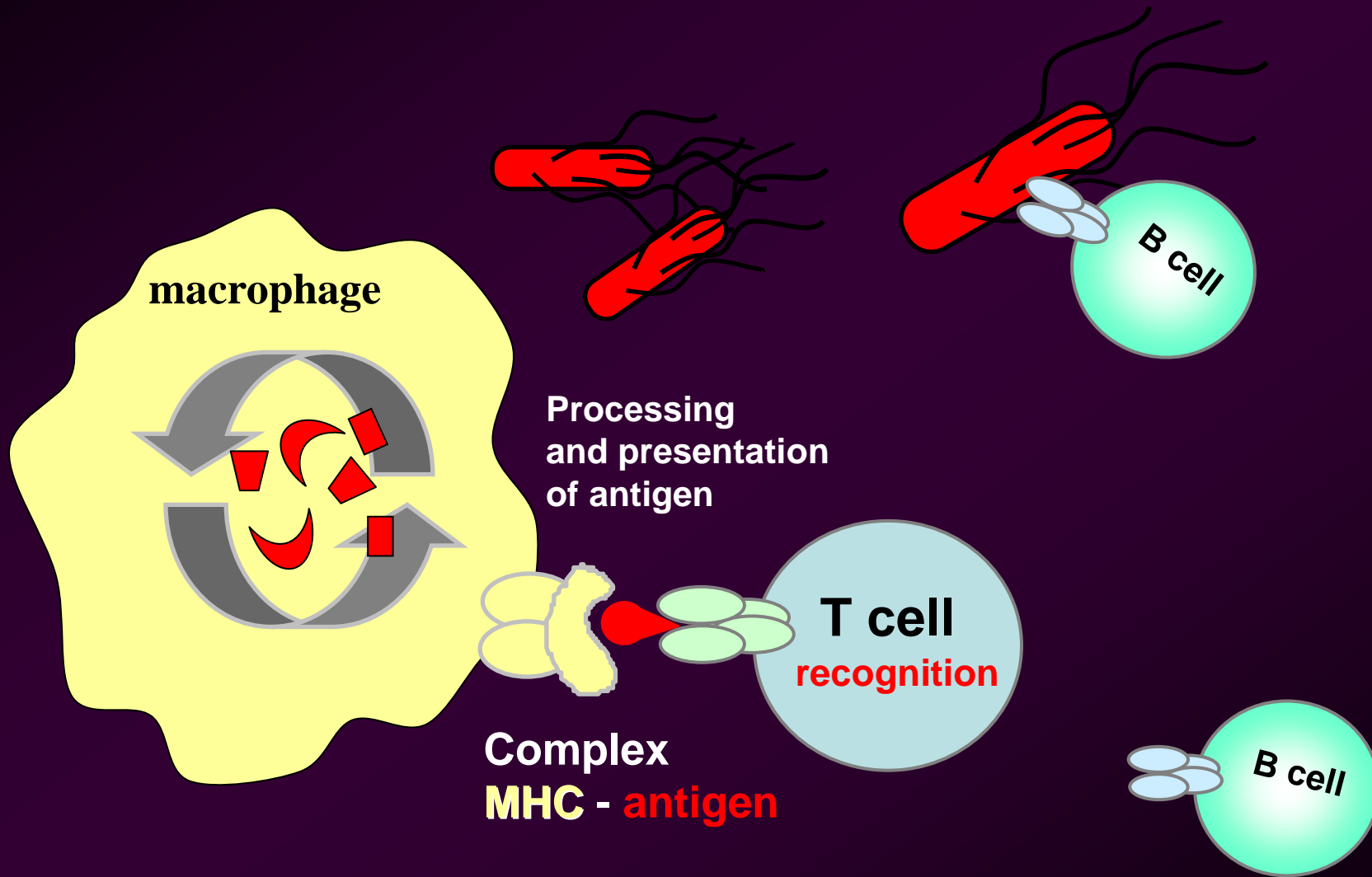
T cell : Cell mediate-immunity

Why B cells [including antibody production] do not protect the body enough?

Why we do need T lymphocytes



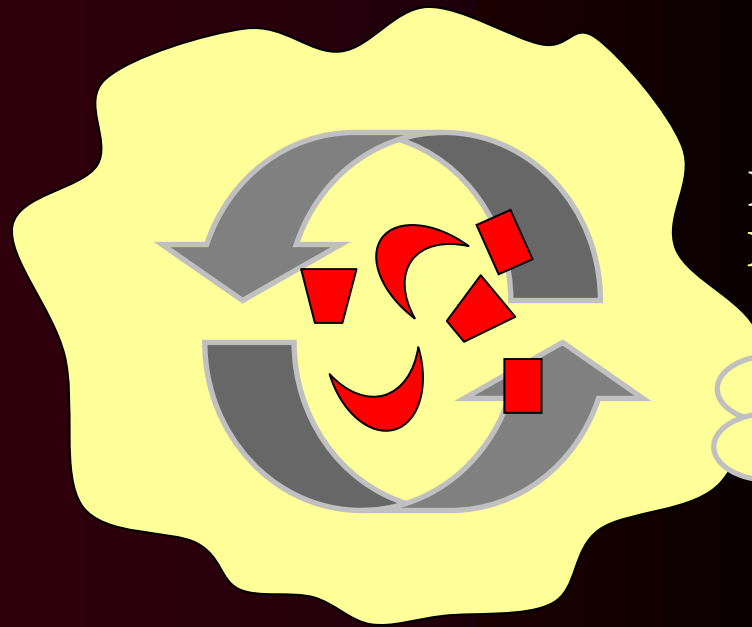
Process of intracellular antigen



T lymfocyty: prezentace antigenu



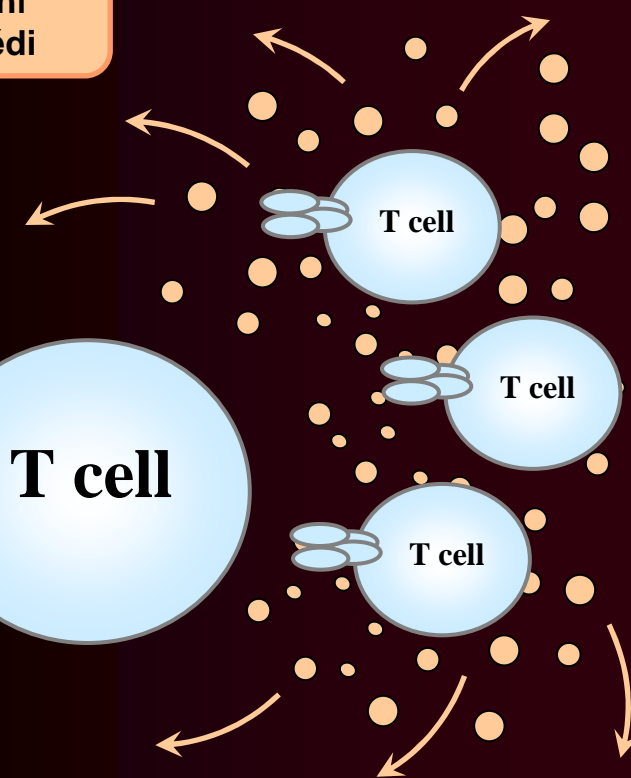
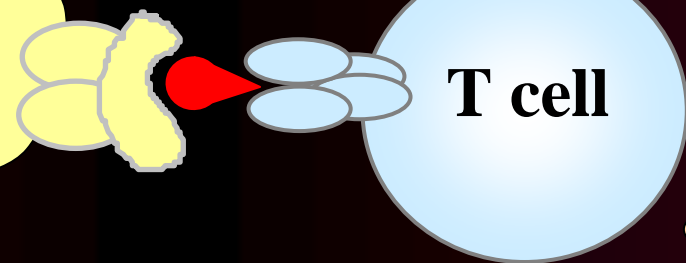
APC (Antigen prezentující buňka)



Komplex
MHC-antigen

Zprostředkování
imunitní
odpovědi

Sekrece cytokinů



T lymphocyte :

- ❑ Recognize **intracellular antigen** (peptide)
- ❑ Recognize peptide fragments of foreign proteins bound to self **MHC molecule** and present on the surface of **antigen presenting cells.**
- ❑ Mature in the thymus

Innate

Adaptive

COMPONENTS

Phagocytes [macrophages, neutrophils]
Natural killer cells



Lymphocytes: T cell, B cell

Complement proteins



Antibodies

Skin, mucosal epithelia
Antimicrobial chemicals



Lymphocytes in the blood, lymph nodes and epithelia

CHARACTERISTICS

Recognize structures shared by groups of related microbes



Recognize specifically microbial or nonmicrobial protein antigen

NO memory



MEMORY

Diversity limited, germ line encoded



Diversity extremely high

Responds immediately



Response develops later