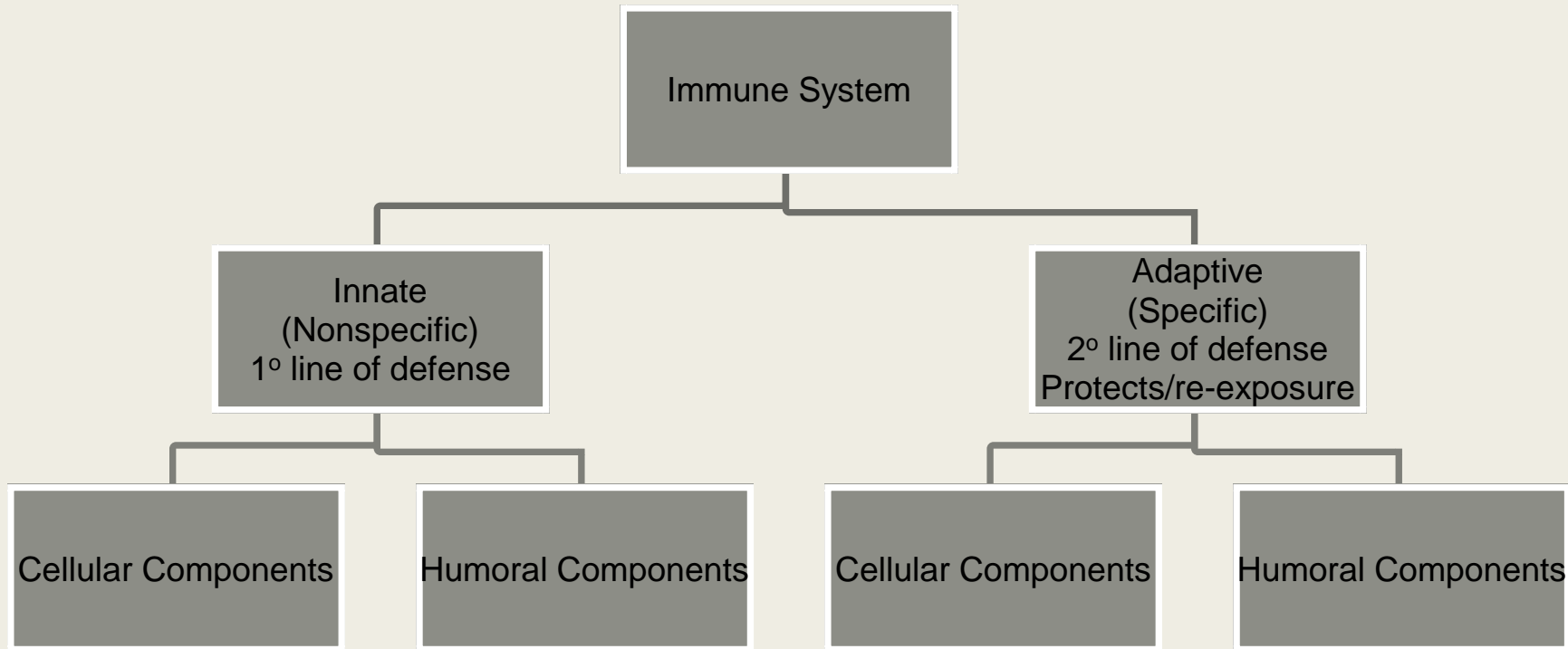


ILMU YANG MEMPELAJARI REAKSI/ PERUBAHAN YANG
TERJADI DI DALAM TUBUH SEBAGAI AKIBAT MASUKNYA
BENDA ASING ATAU YANG DIANGGAP ASING OLEH
TUBUH

Imunologi

Immune System



Interactions between the two systems



Gambar 1. Sistem imun

Key players of Innate and Adaptive Immunity

Innate Immunity

Adaptive Immunity

Physical Barriers

skin, gut villi, lung cilia,
mucous membranes etc

none

Soluble Factors

many protein and
non-protein secretions

Immunoglobulins
(antibody)

Cells

phagocytes, NK cell
eosinophils

T and B lymphocytes

Perbedaan innate dan adaptive immunity

Innate immunity

- Alamiah
- Sejak lahir
- Tanpa didahului kontak dengan antigen spesifik
- Sifat nonspesifik
- Variasi: usia dan aktivitas hormonal atau metabolik

Adaptive immunity

- Paparan antigen pada penjamu yang responsive
- Sifat spesifik
- Dipertarai antibodi atau sel limfoid

Comparison of Innate and Adaptive Immunity

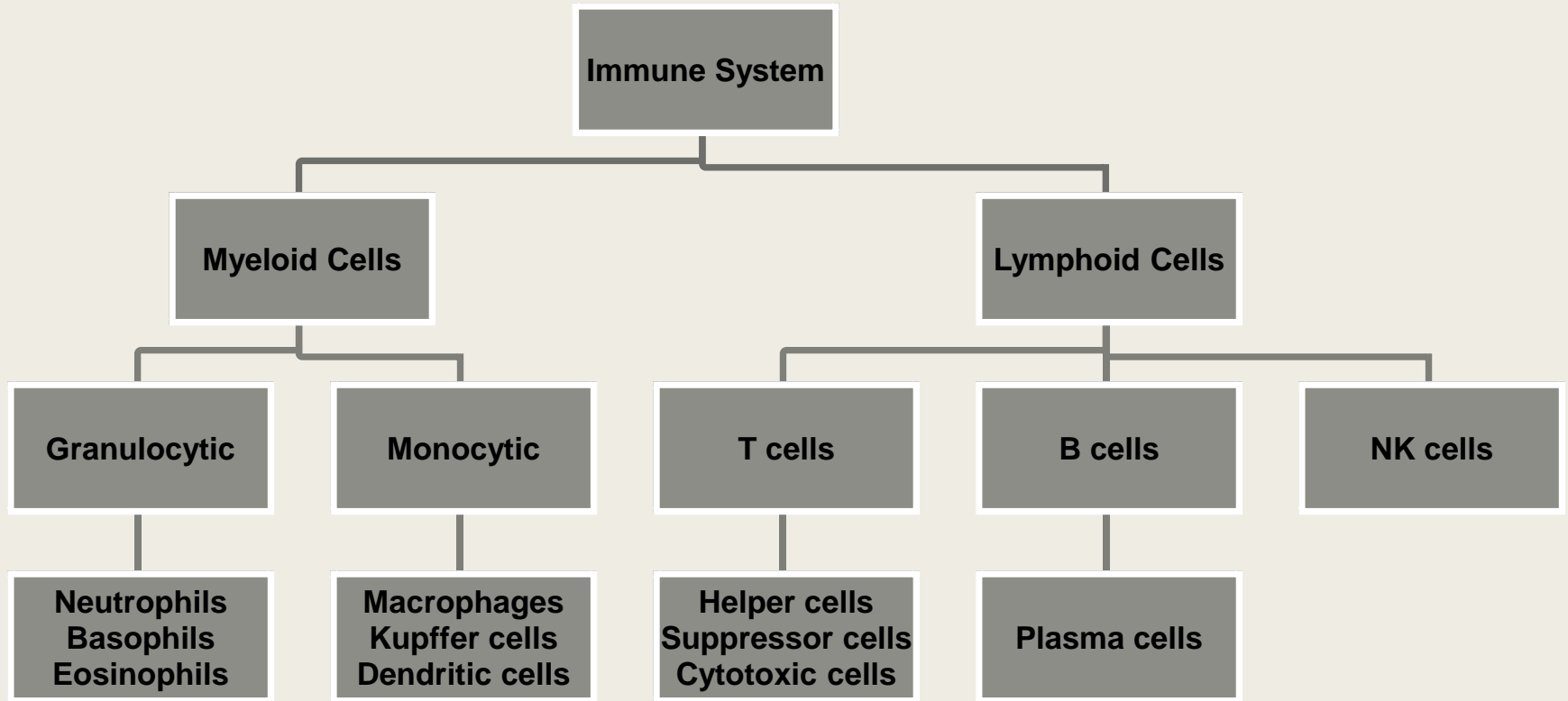
Innate Immunity

- No time lag
- Not antigen specific
- No memory

Adaptive Immunity

- A lag period
- Antigen specific
- Development of memory

Cells of the Immune System



Innate immunity (Cellular component)


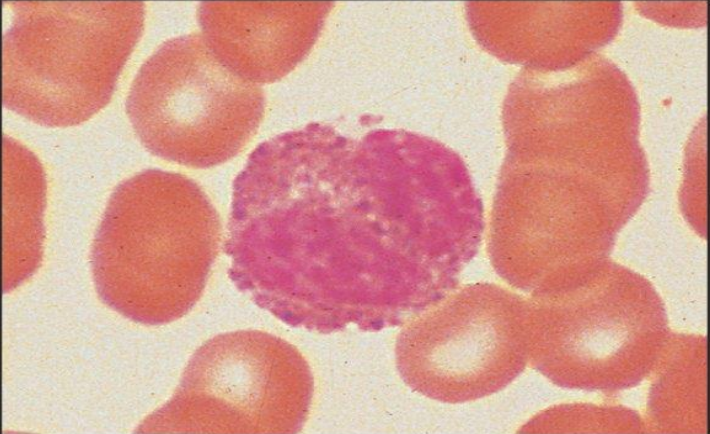
Cell		Activated function
Neutrophil	 A microscopic image of a neutrophil, showing a multi-lobed nucleus and granules. The cell is surrounded by numerous red blood cells for scale.	Phagocytosis and activation of bactericidal mechanisms
Eosinophil	 A microscopic image of an eosinophil, showing a bilobed nucleus and large, reddish-orange granules. The cell is surrounded by numerous red blood cells for scale.	Killing of antibody-coated parasites

Figure 1-4 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Innate immunity (Cellular component)

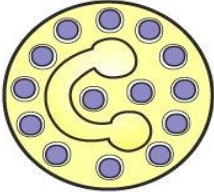
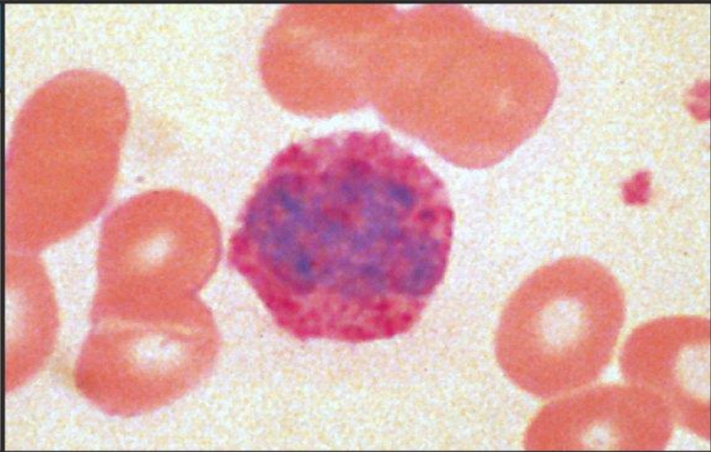
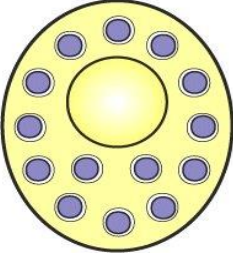

Cell	Activated function	
<p data-bbox="146 354 683 439">Basophil</p>  <p>A diagram of a basophil, showing a circular cell with a yellow cytoplasm and a central nucleus. The cytoplasm is filled with numerous small, dark purple granules. The nucleus is indented and contains a few blue-stained nuclei.</p>	 <p>A light micrograph showing a basophil among several red blood cells. The basophil is a large, spherical cell with a dark purple, granular cytoplasm and a dark, indented nucleus. The red blood cells are smaller, biconcave discs with a reddish-orange color.</p>	<p data-bbox="1398 546 1798 596">Unknown</p>
<p data-bbox="146 825 683 911">Mast cell</p>  <p>A diagram of a mast cell, showing a circular cell with a yellow cytoplasm and a central nucleus. The cytoplasm is filled with numerous small, dark purple granules. The nucleus is large and contains a few blue-stained nuclei.</p>	 <p>A light micrograph showing a mast cell among other cells. The mast cell is a large, oval cell with a dark purple, granular cytoplasm and a large, pale nucleus. Other cells in the background are smaller and less distinct.</p>	<p data-bbox="1398 875 1798 1218">Release of granules containing histamine and other active agents</p>

Figure 1-4 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Innate immunity (Cellular component)



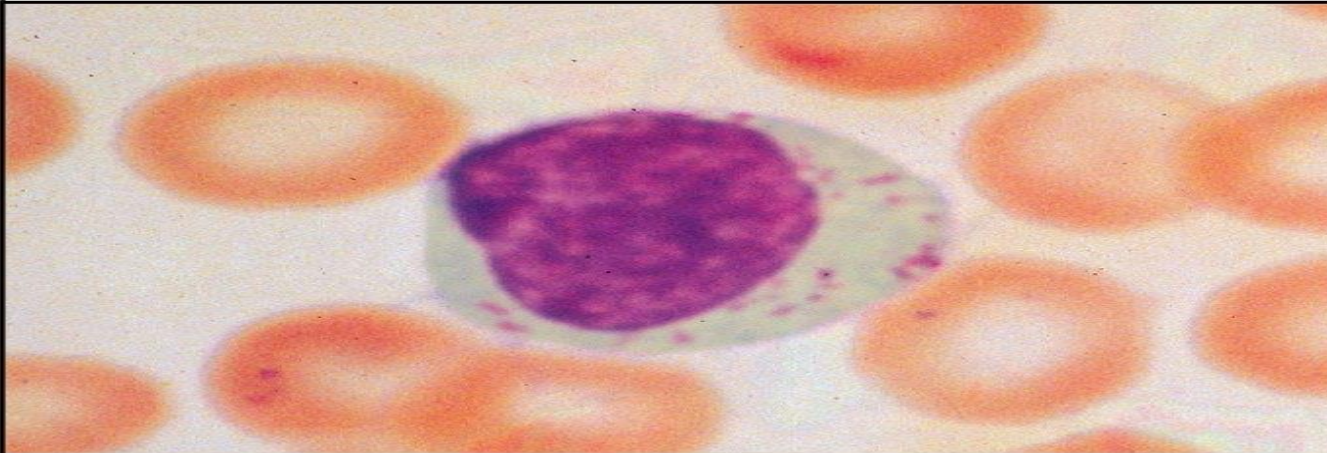
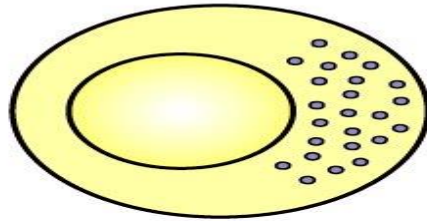
Cell		Activated function
Macrophage		Phagocytosis and activation of bactericidal mechanisms Antigen presentation
Dendritic cell		Antigen uptake in peripheral sites Antigen presentation in lymph nodes

Figure 1-4 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Innate immunity (Cellular component)

Natural killer (NK) cell



Releases lytic granules that kill some virus-infected cells

Figure 1-6 Immunobiology, 6/e. (© Garland Science 2005)

Adaptive immunity

Bone Marrow



Lymphoblasts



Bone marrow maturation

Thymus



B lymphocytes

**Regulator
T cells**

**Effector
T cells**



Memory Cells

Plasma Cells

**Helper
T Cells**

**Supressor
T Cells**

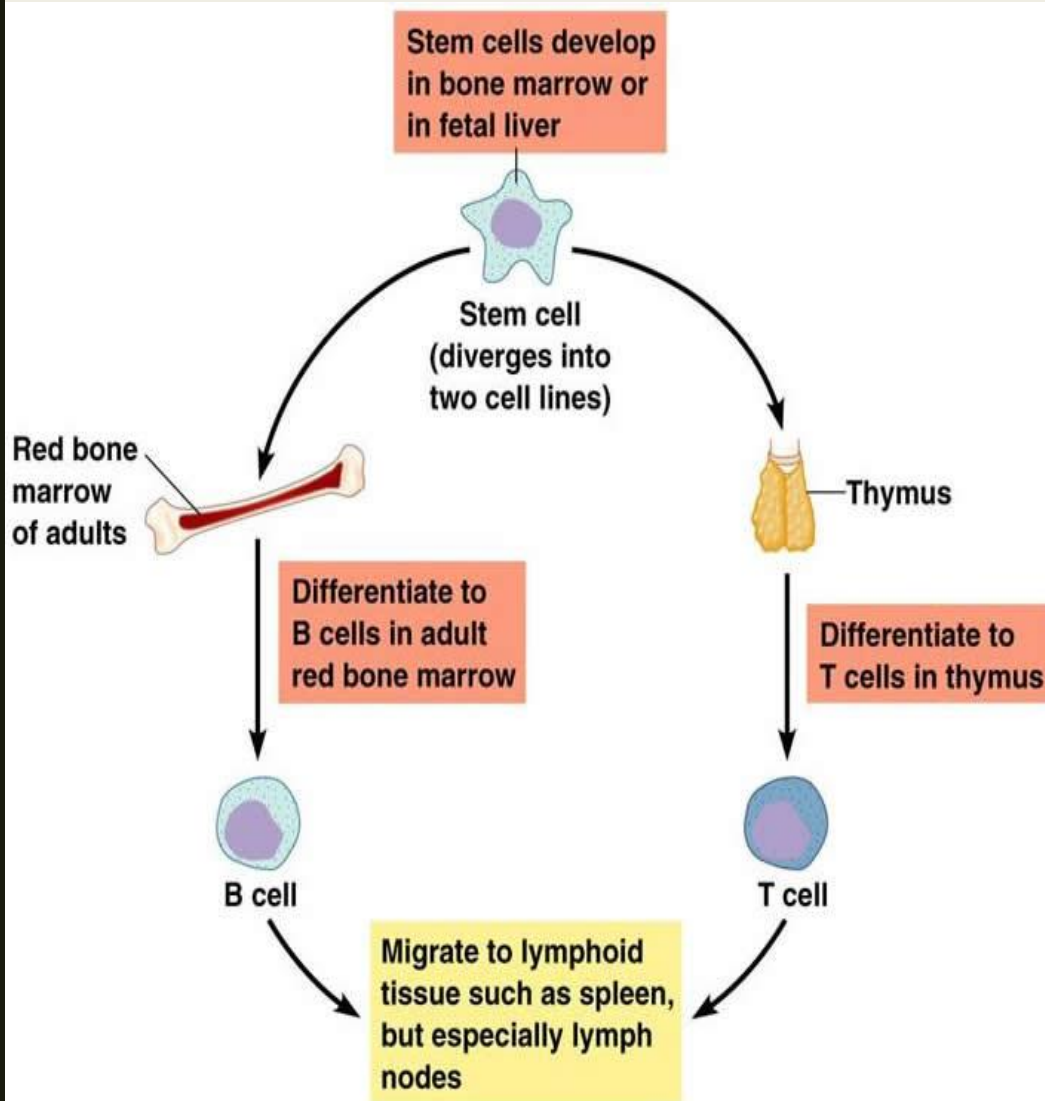
**Cytotoxic
T Cells**

Antobodies

HUMORAL RESPONSES

CELLULAR RESPONSE

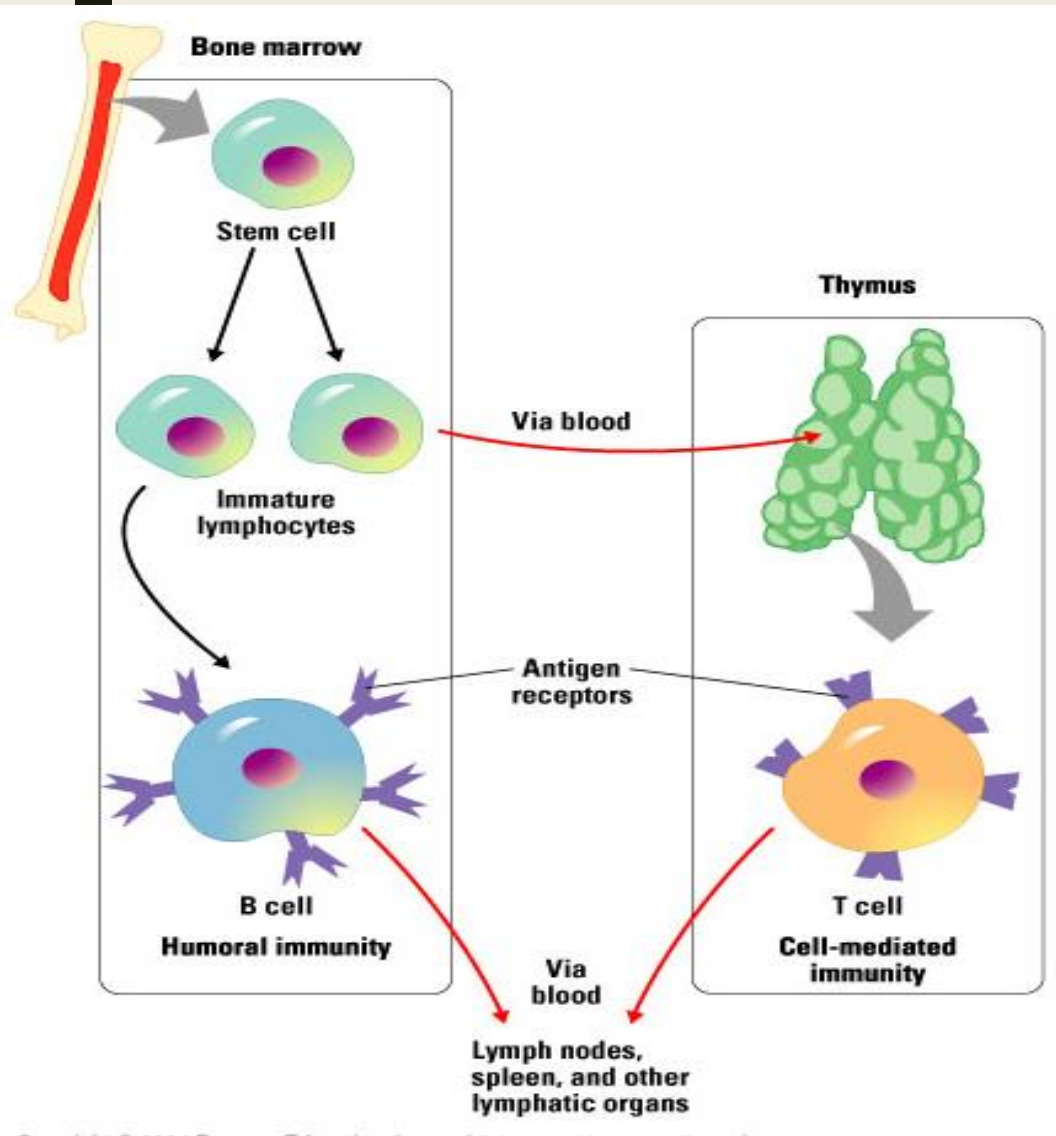
Adaptive immunity



▶ Three important aspects

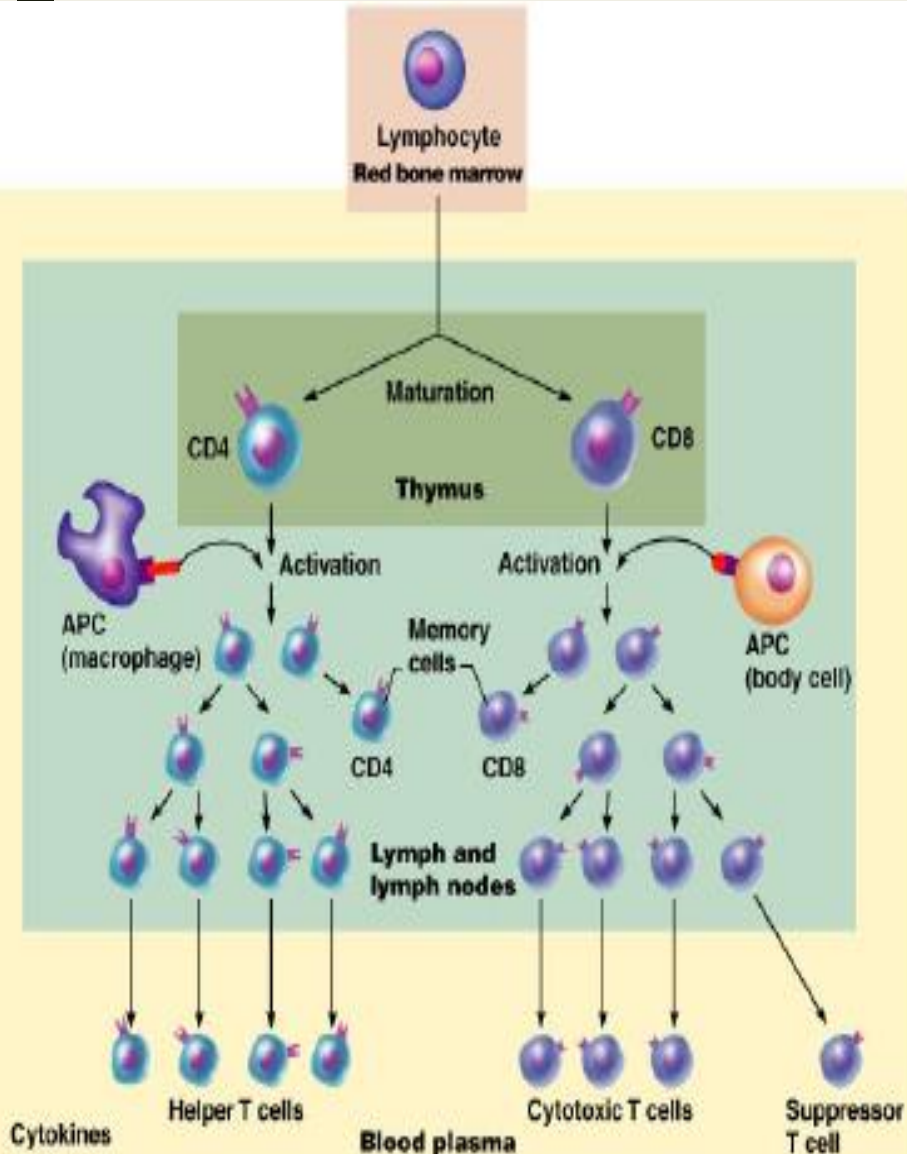
1. Specificity
2. Systemic
3. Prose memory

Adaptive immunity



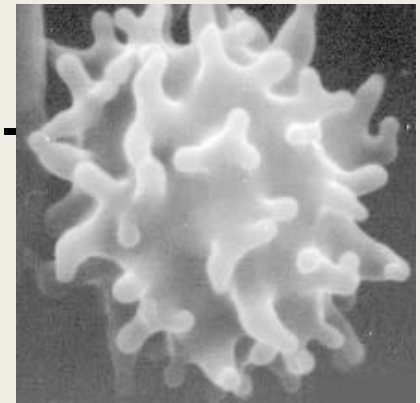
- ▶ **Cell-Mediated Immunity (CMI) – T cells**
 - Fungi, Parasites
 - Viruses, Some cancer cells
 - Foreign tissue transplants
- ▶ **Antibody-Mediated (Humoral) Immunity (AMI) – B cells**
 - Antigens dissolved in body fluids
 - Extracellular pathogens

Adaptive immunity



- **Th lymphocytes (CD4, T4)**
 - *T.helper – immune respon yang awal*
- **Tc lymphocytes (CD8, T8, CTL)**
 - *T.cytotoxic - responsible for cellular immunity*
- **Ts lymphocytes**
 - *T.suppressor - menurunkan immune respon; # Th>Ts*
- **TDH lymphocytes**
 - *delayed hypersensitivity*

CD4 T cells: Th1, Th2 classification:



CD4 T cells

Th1 cell: cytokines secreted: IL-2, IFN- γ , IL-12

“inflammatory” T cells
: involved in activating

Macrophages

NK cells

CD8 T cells

Cell-mediated
immunity
(effector mechanisms
are cellular)

B cells

Th2 cell: cytokines secreted: IL-4, IL-5, IL-6, IL-10, TGF- β

“helper” T cells
: involved in activating

B cells

Antibody-mediated
(humoral) immunity

KONSEP IMUN RESPONS

- 1. ANTIGEN DAN ANTIBODI**
- 2. MHC (MAJOR HISTOCOMPATIBILITY COMPLEX)**
- 3. SITOKIN DAN HANTARAN SIGNAL**
- 4. KOMPLEMEN**

Antigen

- Suatu bahan bila masuk ke dalam tubuh dapat membangkitkan respon imun baik respon imun seluler maupun humoral
- Complete antigen
 - *Immunogenicity*
 - *reactivity*

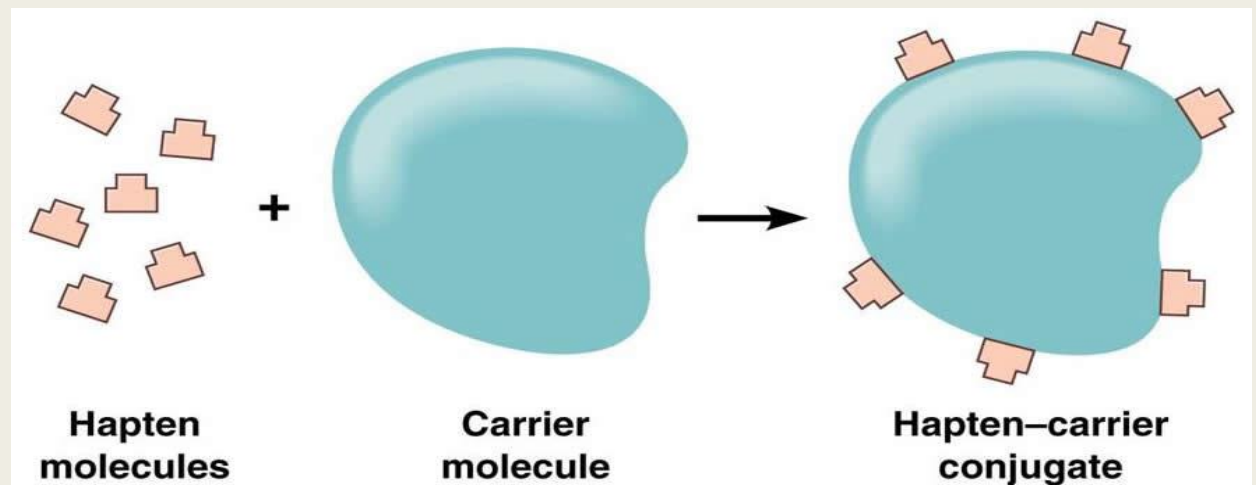
Antigen

Immunogenicity

- Bahan asing (keasingan)
- Ukuran molekul BM > 10,000 (protein, nucleoprotein, lipoprotein, glycoprotein, polysaccharida)
- Kerumitan struktur kimiawi
- Konstitusi genetik
- Metode pemasukan antigen
- Dosis

Antigen

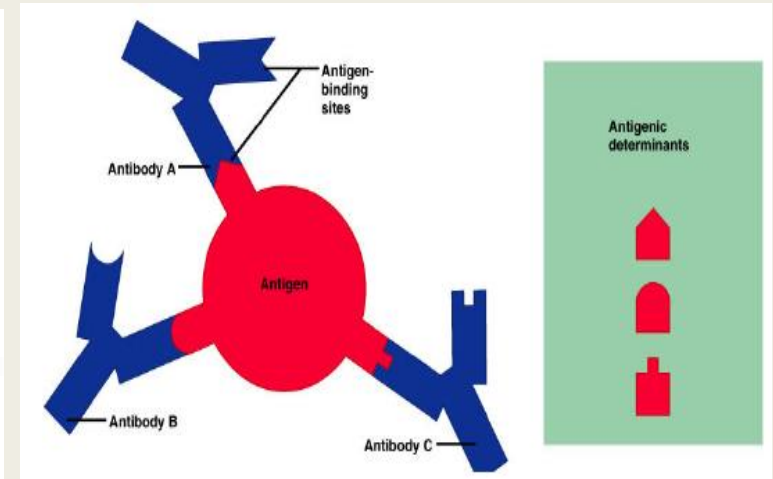
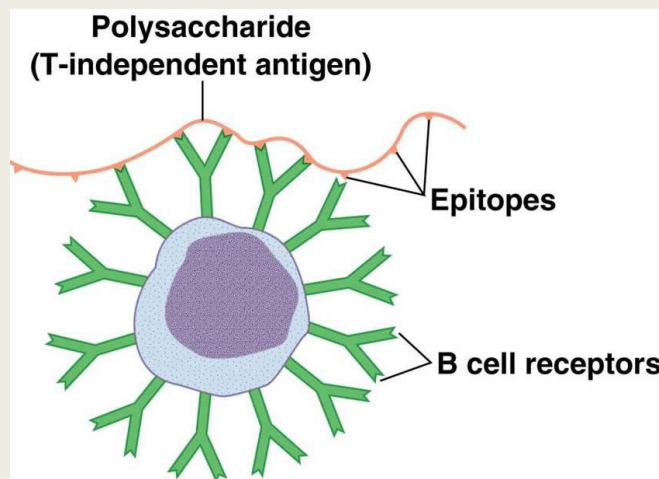
- Incomplete antigen (Hapten)
 - *Not immunogenic*
 - *Antigen yang dapat melakukan reaksi spesifik Ag - Ab, tetapi tidak dapat merangsang pembentukan antibodi*



Antigen

Epitop/antigenic determinants

- Bagian tertentu dari molekul yang terlibat menimbulkan ikatan antibodi (biasanya pada permukaan) ; *antigen binding site*



Antigen

Penggolongan Antigen

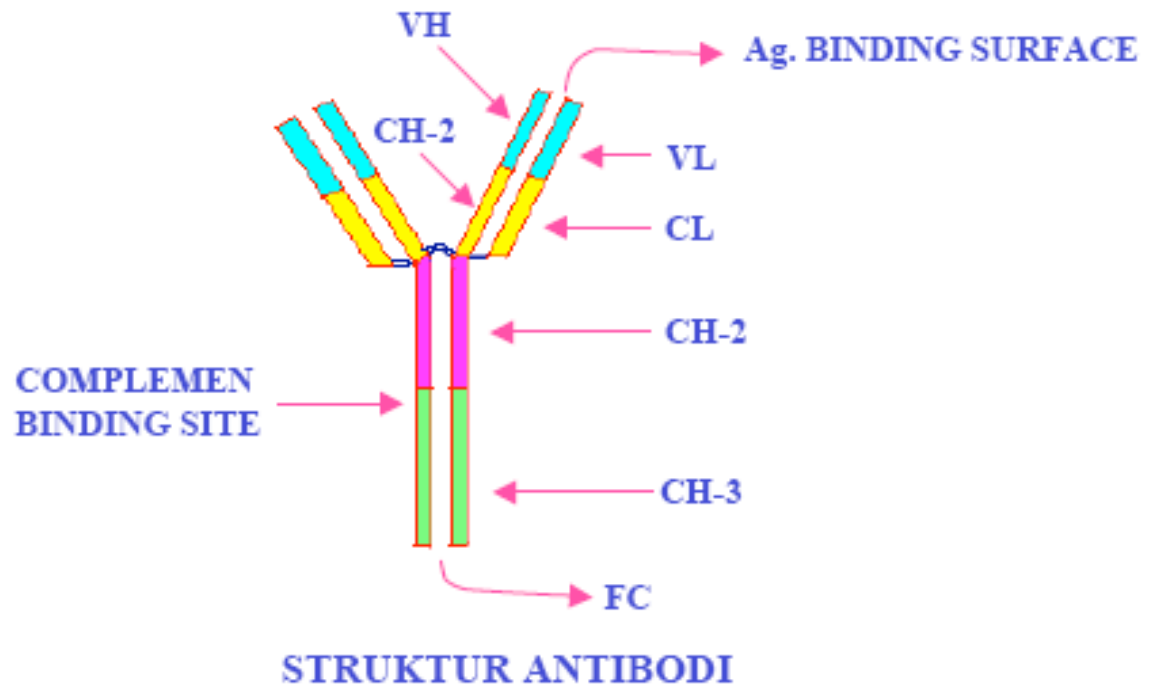
- Jackson 1978, berdasarkan klasifikasi operasional 2 jenis utama :
- **Antigen eksogen** konfigurasi yang disajikan pada tubuh dari luar
 - *mikroorganisme (bakteri, virus, dll), butir sari bunga, obat-obatan atau polutan*
- **Antigen endogen** konfigurasi yang terdapat didalam tubuh
 - *Antigen heterolog/xenogeneic*
 - *Antigen autolog/idiotipik*
 - *Antigen allogeneic/homolog*

Antigen

- Hyde (2000) membagi antigen
 - *T cell dependent antigen* kemampuan menginduksi respons imun dengan bantuan limfosit T
 - *T cell independent antigen* Suatu substansi dapat merangsang respon imun tanpa melibatkan limfosit T dan langsung merangsang limfosit B untuk memproduksi Ab

Antibodi

Gama globulin yang dihasilkan oleh sel plasma



JENIS RANTAI BERAT

RANTAI- μ

RANTAI- α

RANTAI- γ

RANTAI- σ

RANTAI- ϵ

JENIS RANTAI RINGAN

RANTAI- λ

RANTAI- κ

KELAS ANTIBODI

Ig-M

Ig-A

Ig-G

Ig-D

Ig-E

TIPE ANTIBODI

TIPE- λ

TIPE- κ

Antibodi

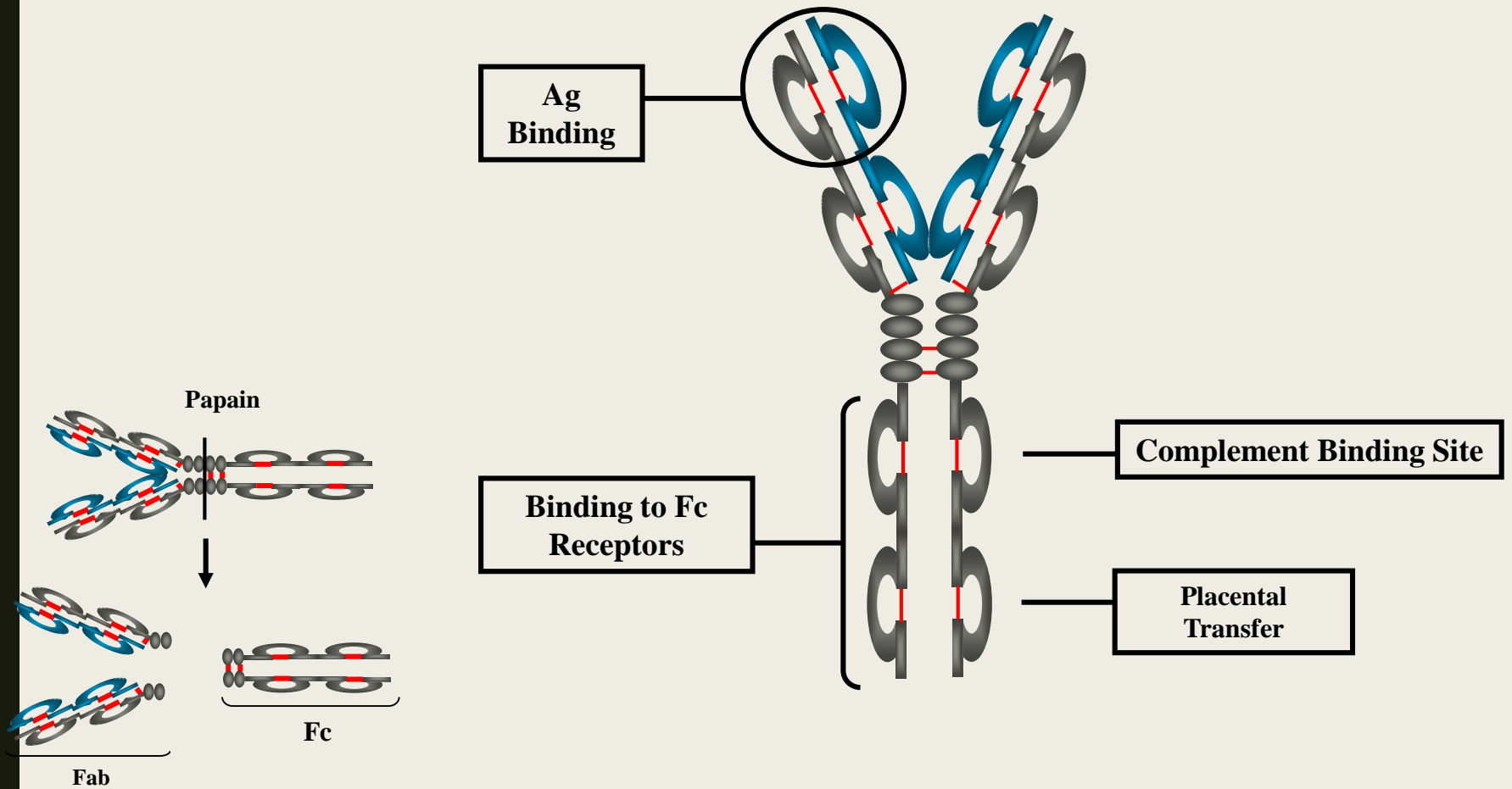

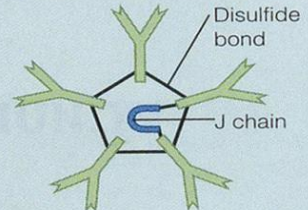
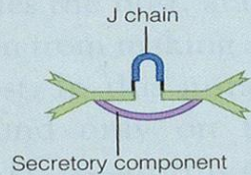




TABLE 17.1

A Summary of Immunoglobulin Classes

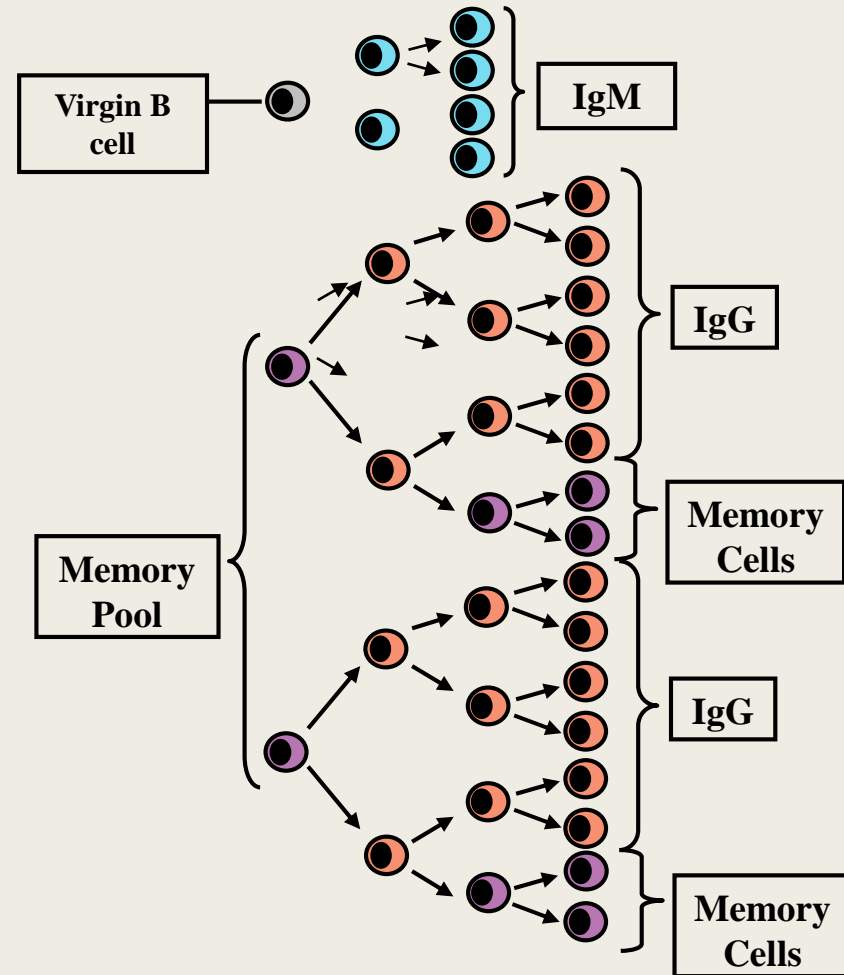
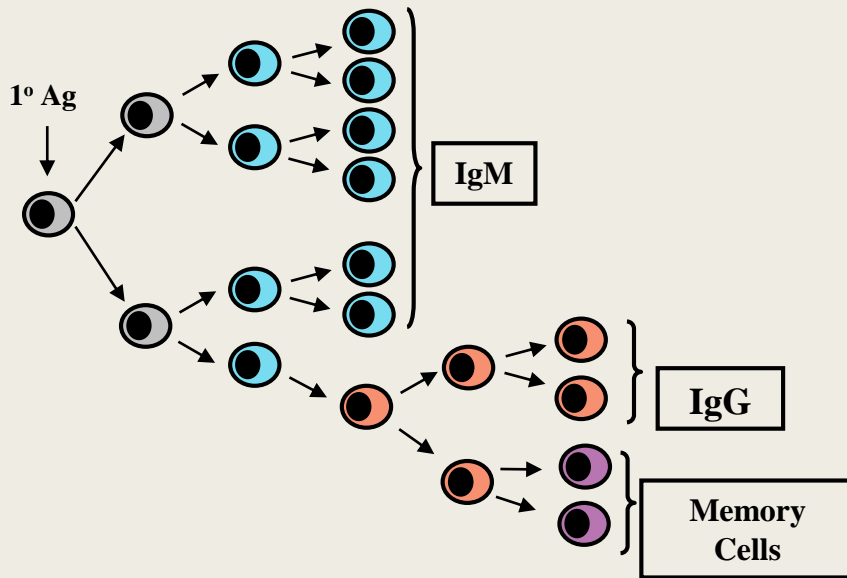
Characteristics	IgG	IgM	IgA	IgD	IgE
					
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
Percentage of total serum antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood, lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Molecular weight	150,000	970,000	405,000	175,000	190,000
Half-life in serum	23 days	5 days	6 days	3 days	2 days
Complement fixation	Yes	Yes	No [†]	No	No
Placental transfer	Yes	No	No	No	No
Known functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

*Percentage in serum only; if mucous membranes and body secretions are included, percentage is much higher.

[†] May be yes via alternate pathway.

Antibodi

Celluler 1° dan 2° Response to T-dependent Ags



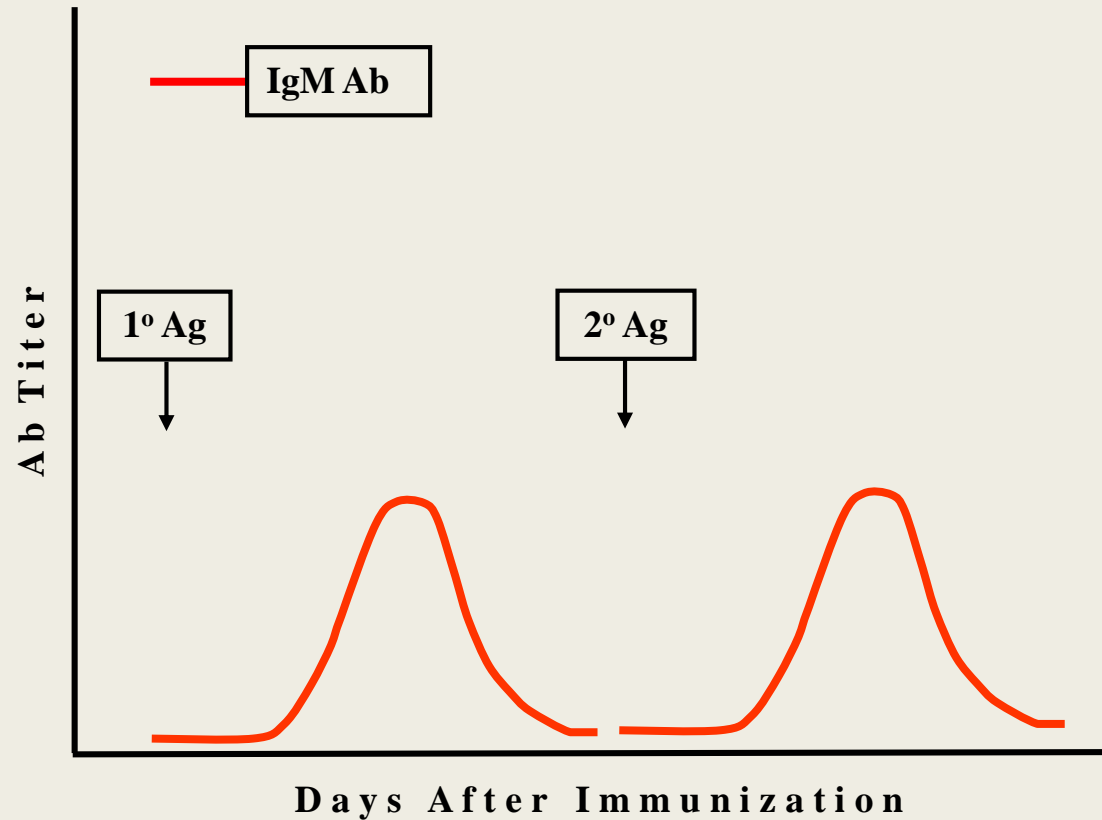
Antibodi

Ab Response T-independent Ags

4 Phases

IgM antibody

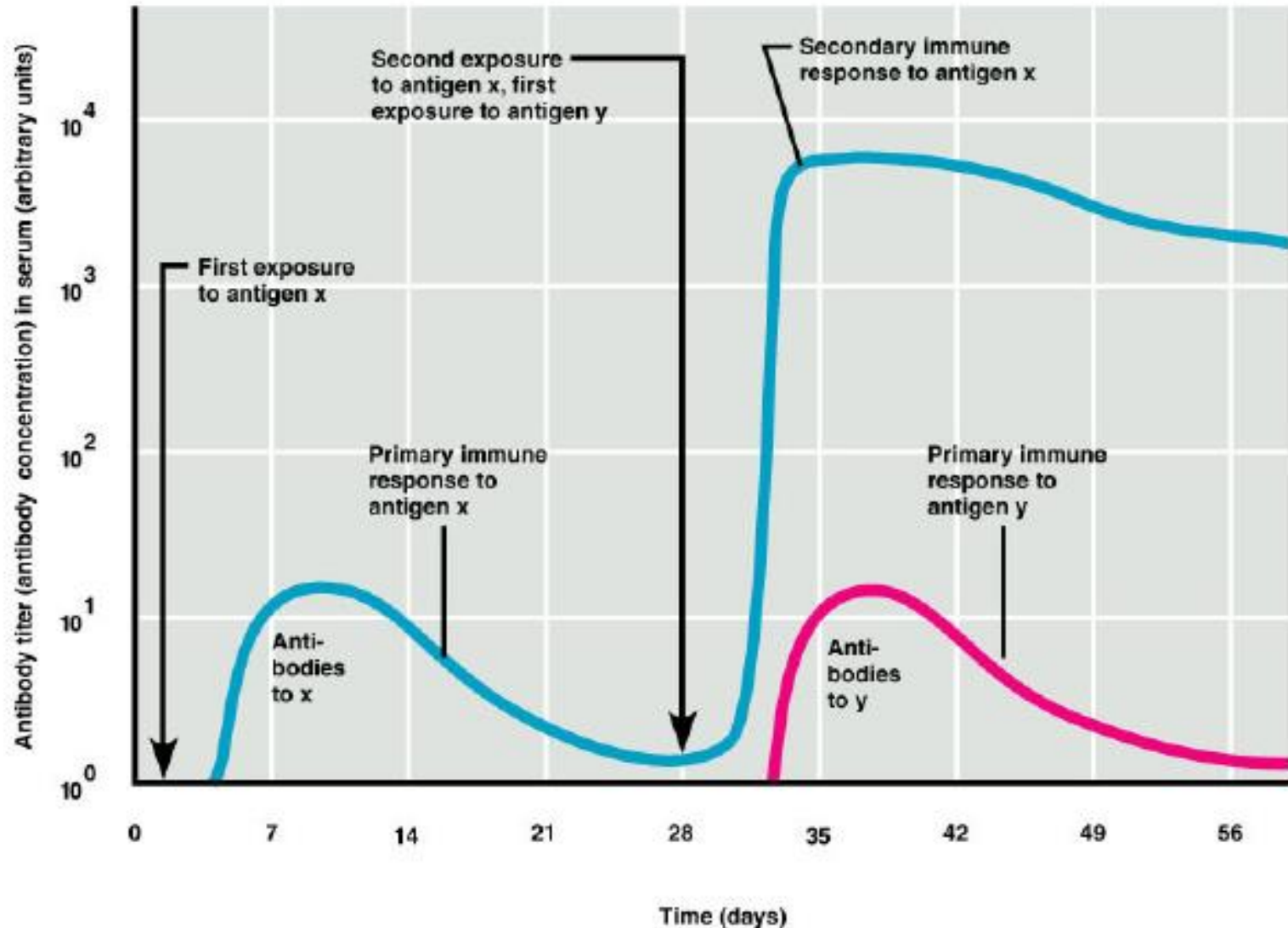
No secondary
response



Antibodi

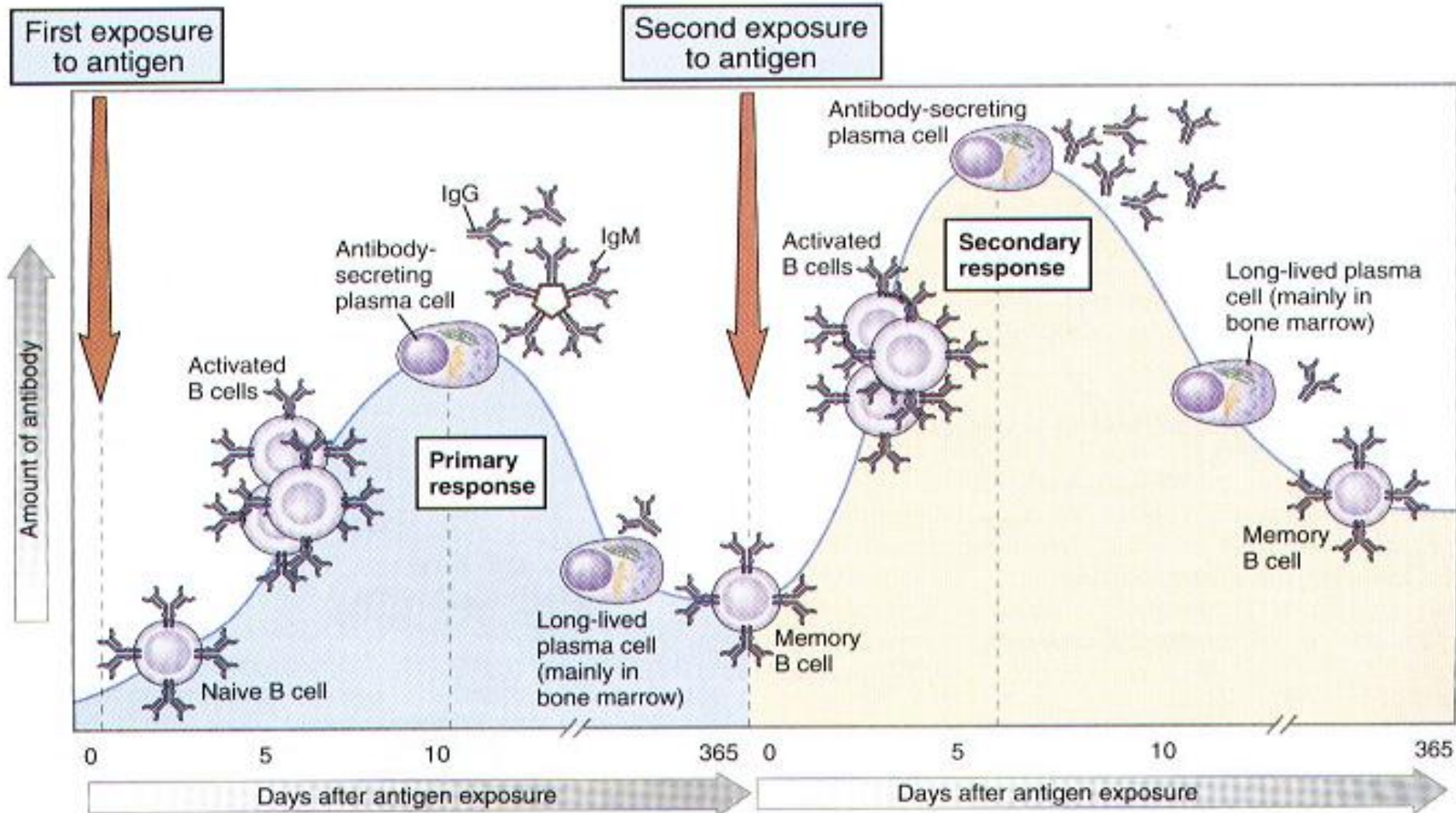
Perubahan Ab

1° and 2° Responses

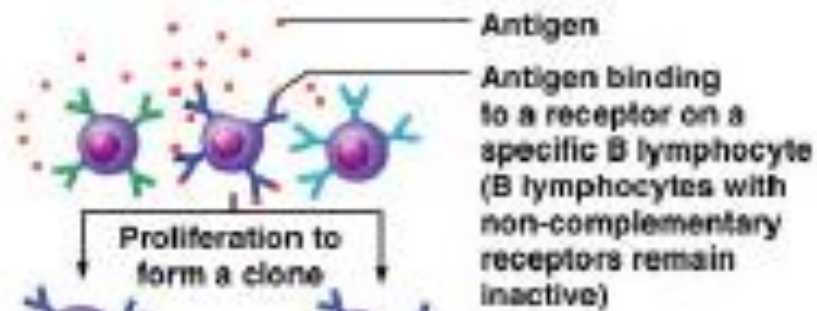


Antibodi

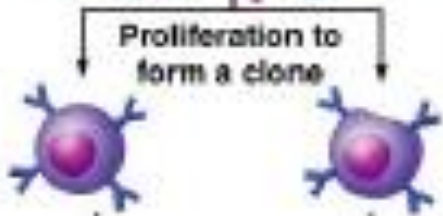
Primary and secondary antibody responses to protein antigens differ qualitatively and quantitatively



Primary Response
(initial encounter with antigen)



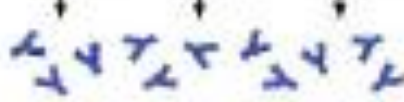
B lymphoblasts



Plasma cells



Secreted antibody molecules



Secondary Response
(can be years later)

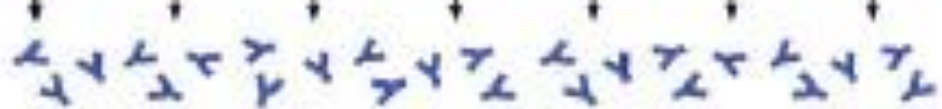
Clone of cells identical to ancestral cells

Subsequent challenge by same antigen

Plasma cells



Secreted antibody molecules



Memory B cells

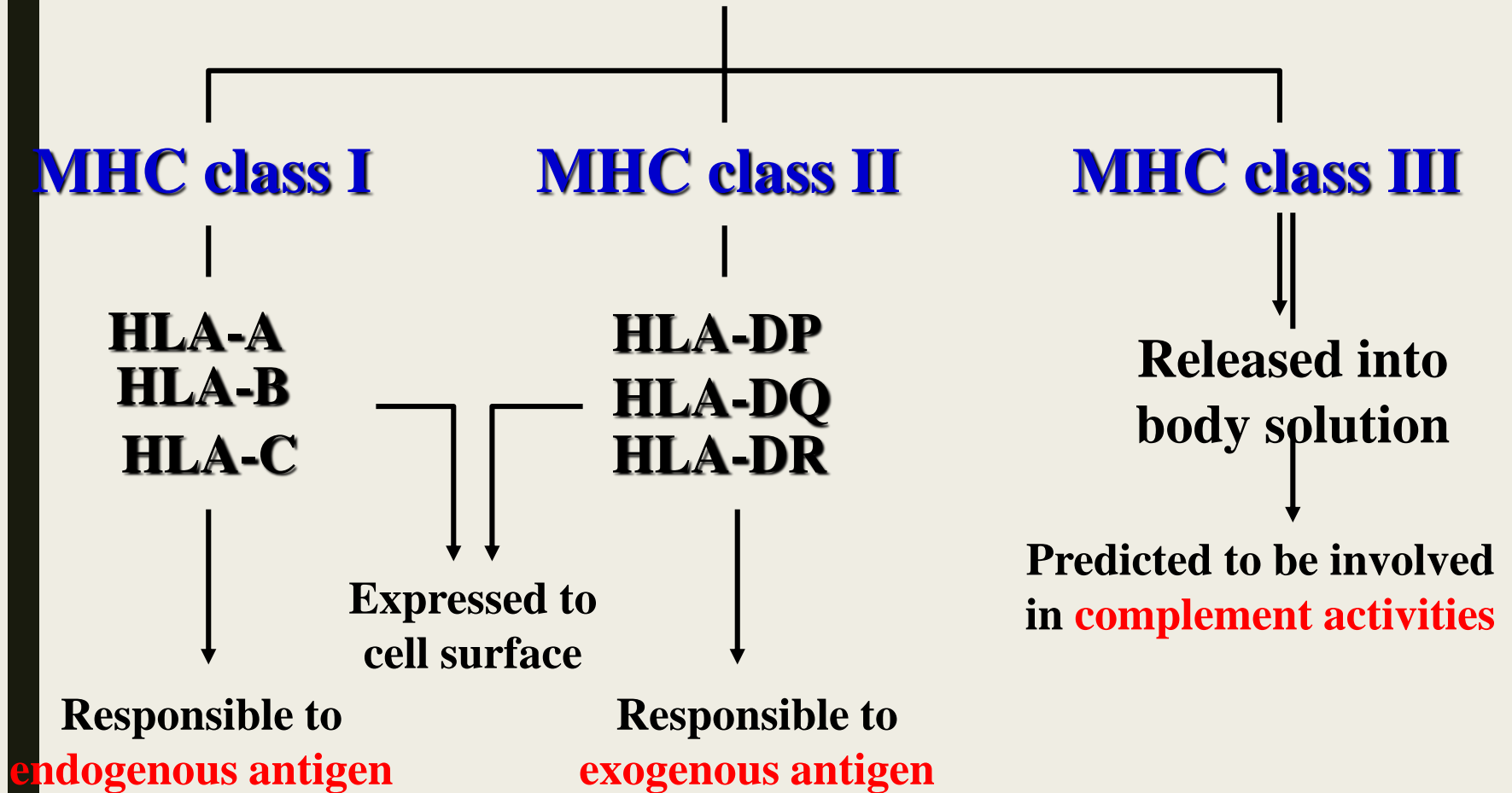
MHC

Self-antigens : MHC Proteins

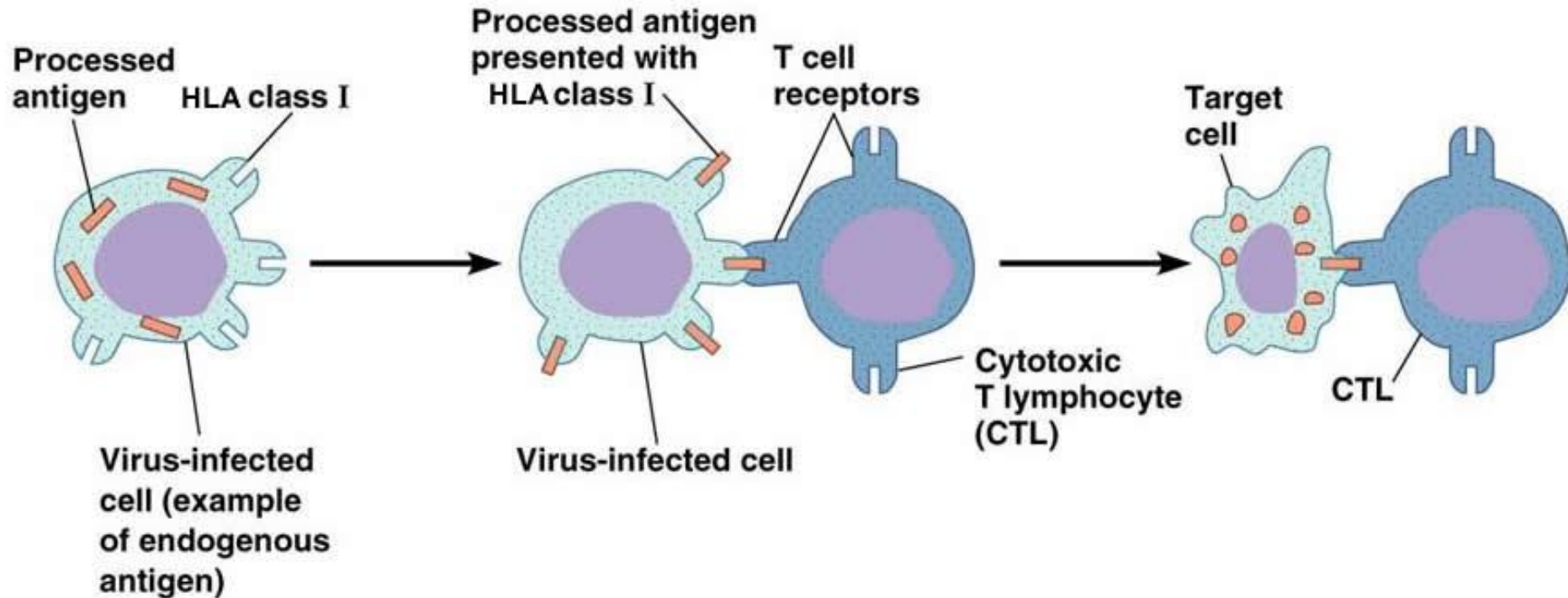
- Major Histocompatibility Complex (MHC) Ag = human *leucocyte-associated antigen* (HLA)
- Kompleks aloantigen pada permukaan sel manusia = **Kode yg terikat pd permukaan membran sel**; khas pd setiap individu

MHC

MHC (Major Histocompatibility Complex)



MHC

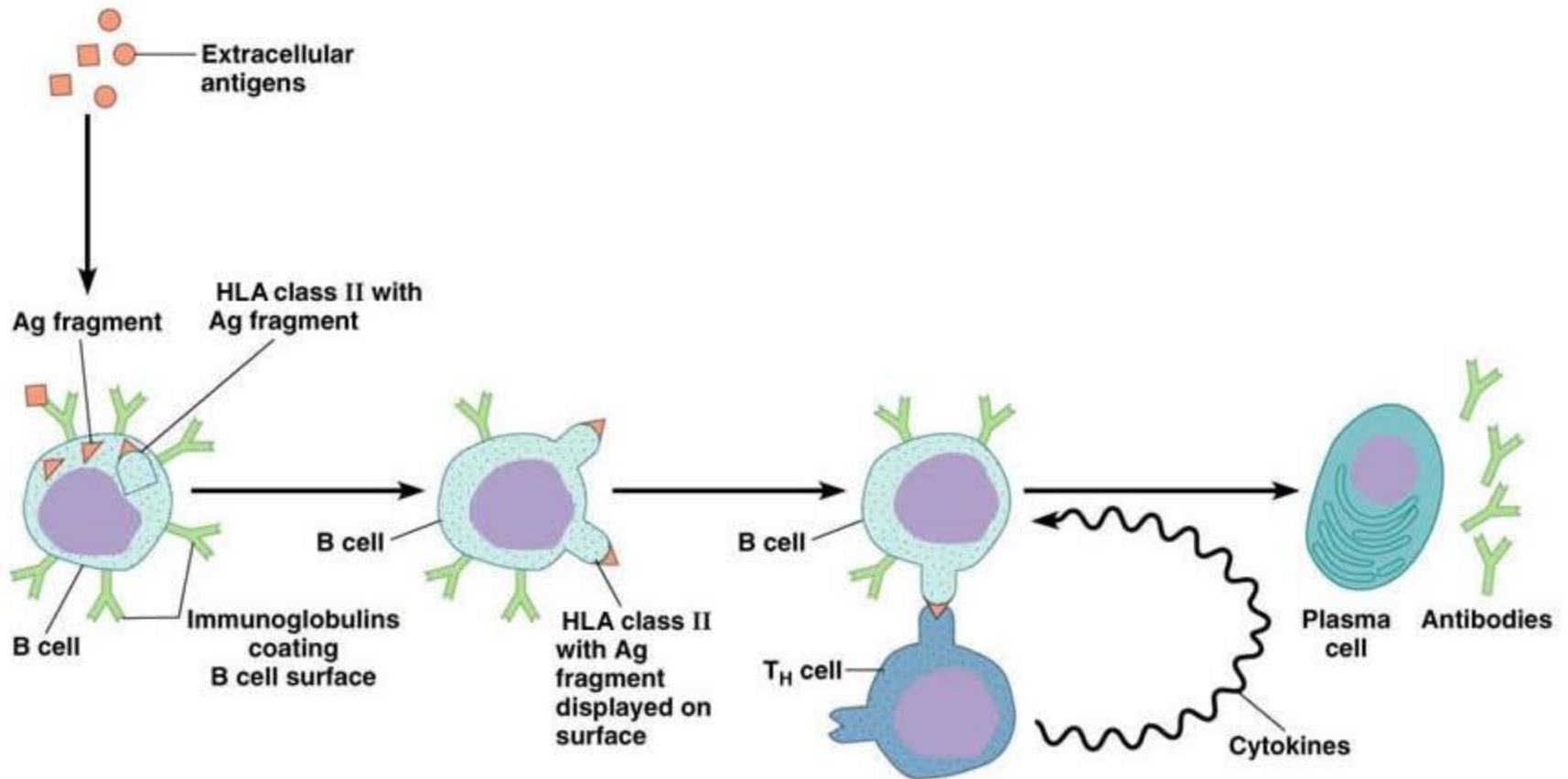


1 A normal cell will produce endogenous antigens that will not trigger a response by a cytotoxic T lymphocyte (CTL), but a virus-infected cell or a cancer cell produces abnormal endogenous antigens.

2 The abnormal antigen is presented on the cell surface in association with HLA class I molecules. CD8 cells with receptors for the antigen are transformed into CTLs.

3 The CTL induces destruction of the virus-infected cell by apoptosis.

MHC



1 Immunoglobulins on B cell surface recognize and attach to antigen, which is then internalized and processed. Within the B cell a fragment of the antigen combines with HLA class II.

2 HLA class II-antigen-fragment complex is displayed on B cell surface.

3 Receptor on the helper T cell (T_H) recognizes complex of HLA class II and antigen fragment and is activated—producing cytokines, which activate the B cell.

4 B cell is activated by cytokines and begins clonal expansion. Some of the progeny become antibody-producing plasma cells.

Cytokines

- ▶ Mediator yang dihasilkan oleh sel dalam reaksi radang atau imunologik

TABLE 17.3		A Summary of Some Important Cytokines
Cytokine	Representative Activity	
Interleukin-1 (IL-1)	Stimulates T _H cells in presence of antigens; chemically attracts phagocytes in inflammatory response	
Interleukin-2 (IL-2)	Involved in proliferation of antigen-stimulated T _H cells, proliferation and differentiation of B cells, and activation of T _C cells and NK cells	
Interleukin-8 (IL-8)	Chemoattractant for immune system cells and phagocytes to site of inflammation	
Interleukin-10 (IL-10)	Secreted by T _H 2 cells and T _R cells; interferes with activation of T _H 1 cells	
Interleukin-12 (IL-12)	Mainly involved in differentiation of CD4 T cells	
Interferons (IFNs)		
α-IFN and β-IFN	Induces antiviral activity in nucleated cells (interferes with protein synthesis)	
γ-IFN	Activates macrophages; improves antigen presentation	
Alpha-tumor necrosis factor (α-TNF)	Cytotoxic to tumor cells; enhances activity of phagocytic cells	

Cytokines

- ▶ Mediator yang dihasilkan oleh sel dalam reaksi radang atau imunologik

Sitokin	Sumber sel utama	Daya kerja imunologik utama
IL-1 (α , β)	Makrofag Sel-sel endotel Sel-sel dendrit Sel-sel langerhans	Merangsang reseptor IL-2 muncul dalam sel-sel T Meningkatkan pengaktifan sel-B Menginduksi timbulnya demam . Reaktan akut dan IL-6 Meningkatkan resistensi non spesifik Dihambat oleh antagonis reseptor IL-1 endogen
IL-2	Sel-sel T _h 1	Faktor pertumbuhan sel-T Mengaktifkan sel-sel NK dan B

Cytokines

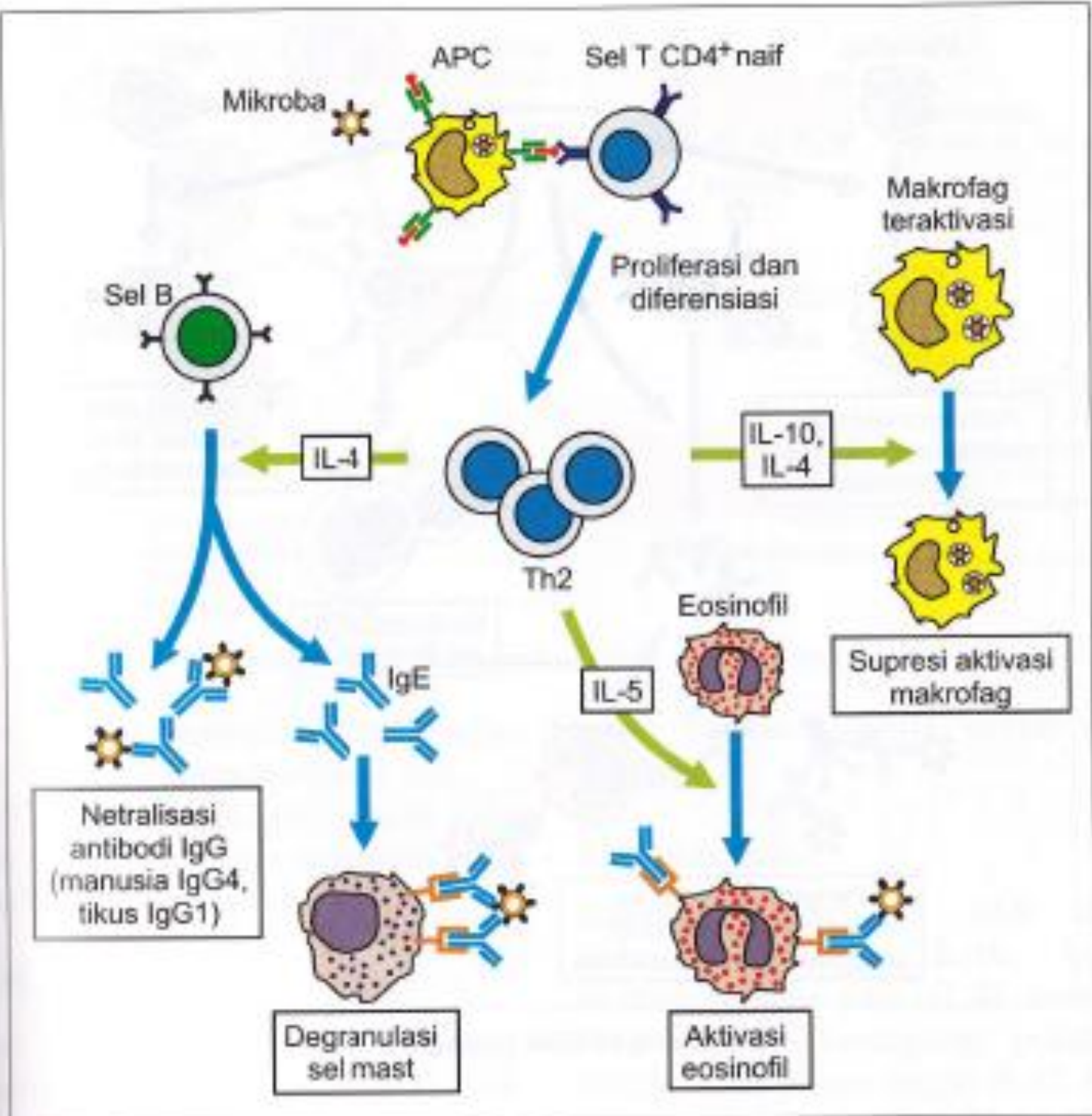
Sitokin	Sumber sel utama	Daya kerja imunologik utama
IL-4	Sel-sel T	Merangsang sintesis IgE oleh sel-B Menurunkan produksi IFN- γ
IL-5	Sel-sel T	Merangsang pertumbuhan dan diferensiasi eosinofil Faktor pertumbuhan sel-B Meningkatkan sintesis IgA
IL-6	Monosit Sel-sel T Sel-sel endotel	Menginduksi reaktan fase akut, demam , dan diferensiasi sel-B lanjut

Cytokines

Sitokin	Sumber sel utama	Daya kerja imunologik utama
IL-7	Sumsum tulang	Merangsang sel pra-B dan pra-T
IL-8	Monosit Sel-sel endotel Limfosit Fibroblas	Faktor kemotaktik untuk neutropil dan sel-sel T
IL-9	Sel-sel T _H	Mitogen sel-T
IL-10	Sel-sel T _H 2	Menghambat sintesis IFN- γ oleh sel-sel T _H 1 Menekan sintesis sitokin lain

Cytokines

Sitokin	Sumber sel utama	Daya kerja imunologik utama
IL-11	Sumsum tulang	Merangsang hemopoisis Meningkatkan sintesis protein fase akut
IL-12	Makrofag Sel-sel B	Meningkatkan diferensiasi T _H 1 dan sintesis IFN- γ Merangsang sel-sel NK dan sel T CD8 pada sitolisis Bekerja sinergistik dengan IL-2
IL-13	Sel-sel T _H 2	Menghambat sitokin peradangan (IL-1, IL-6, IL-8, IL10, MCP)
IL-15	Sel-sel T	Mitogen sel-sel T Memacu pertumbuhan epitel usus

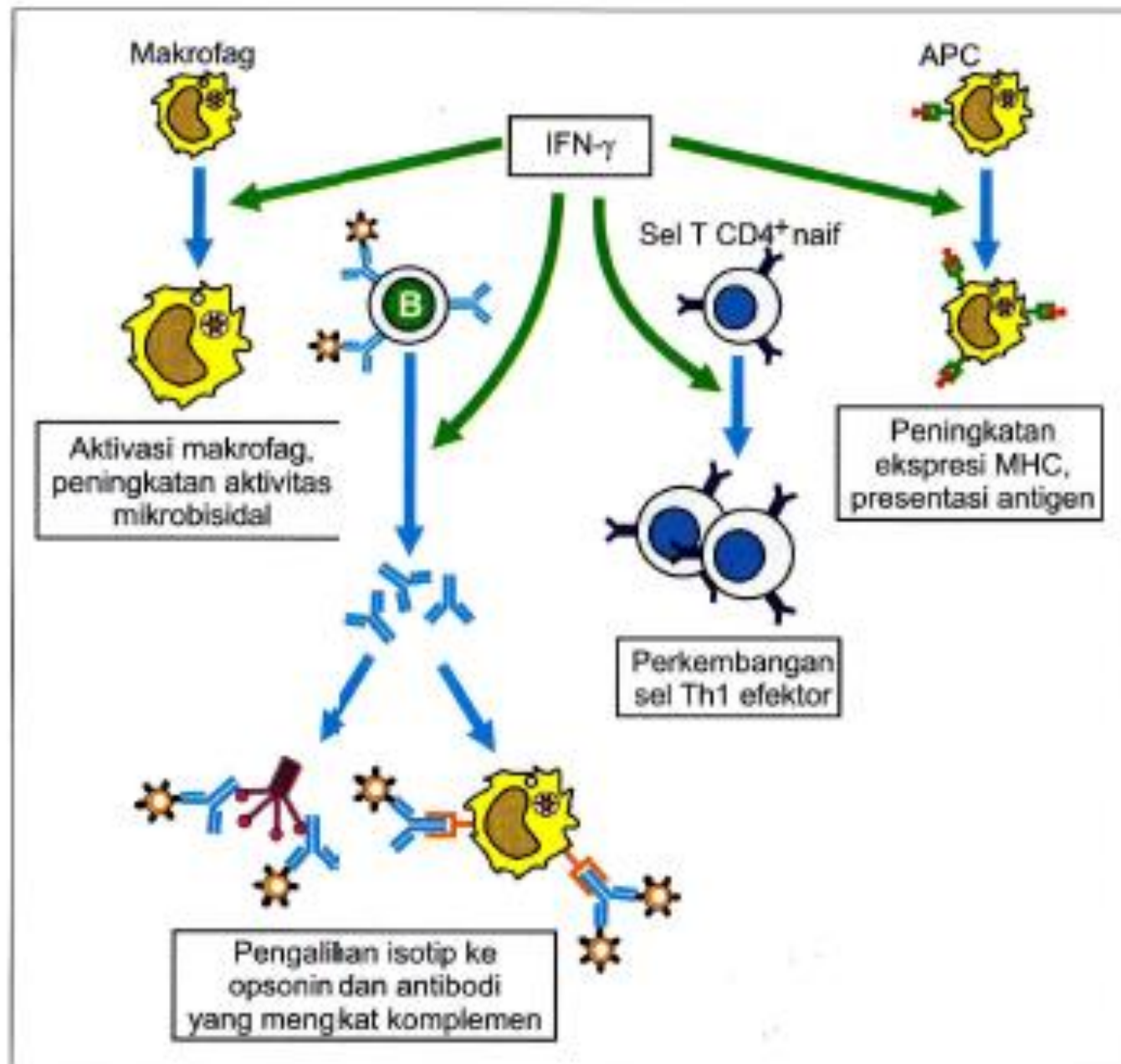


TNF

- Sitokin utama pada respon inflamasi akut
- Sumber utama : sel fagosit MN dan sel T, sel NK, mast sel.
- Efek biologis :
 - *Mengerahkan neutrofil dan monosit ke tempat infeksi dan mengaktifkan sel dalam menyingkirkan mikroba*
 - *Memacu molekul adhesi sel endotel vascular leukosit*
 - *Merangsang makrofag mensekresi kemokin, kemotaksis dan pengerahan leukosit*
 - *Merangsang sel fagosit MN untuk mensekresi IL-1*
 - *Menginduksi apoptosis sel inflamasi*
 - *Menginduksi panas*

Interferon (IFN)

- Ditemukan th 1957 oleh Isaacs dan Lindenmann
- Protein yang pembentukannya diinduksi oleh sel yang terinfeksi virus dan berperan mengganggu replikasi virus (antivirus)
- Berdasarkan sumber
 - *Interferon fibroblas dan interferon imun*
- Kelompok ; α -IFN, β -IFN, δ -IFN

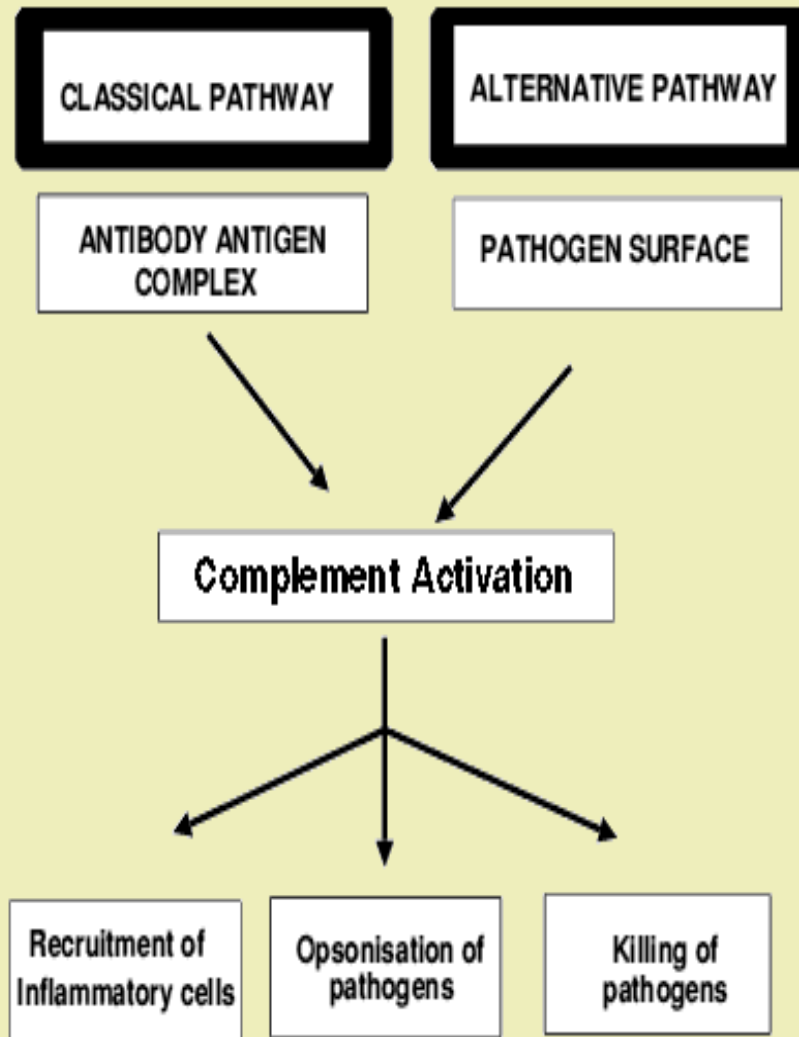


Zambar 9.19 Efek biologis IFN- γ

Sitokin dan Daya Kerjanya

Sitokin	Sumber sel utama	Daya kerja imunologik utama
TNF- α	Makrofag Sel-sel T Sel-sel B Limfosit granular besar	Sitotoksik untuk tumor Menyebabkan kakeksia Memediasi renjatan (syok) bakteri
TNF- β	Sel-sel T	Sitotoksik untuk tumor
Mengubah pertumbuhan faktor- β	Hampir semua tipe sel-sel normal	Menghambat proliferasi sel-sel T maupun sel-sel B Mengurangi respon sitokin Zat kemotaktik kuat untuk leukosit Memediasi peradangan dan perbaikan jaringan

Complement



COMPLEMENT

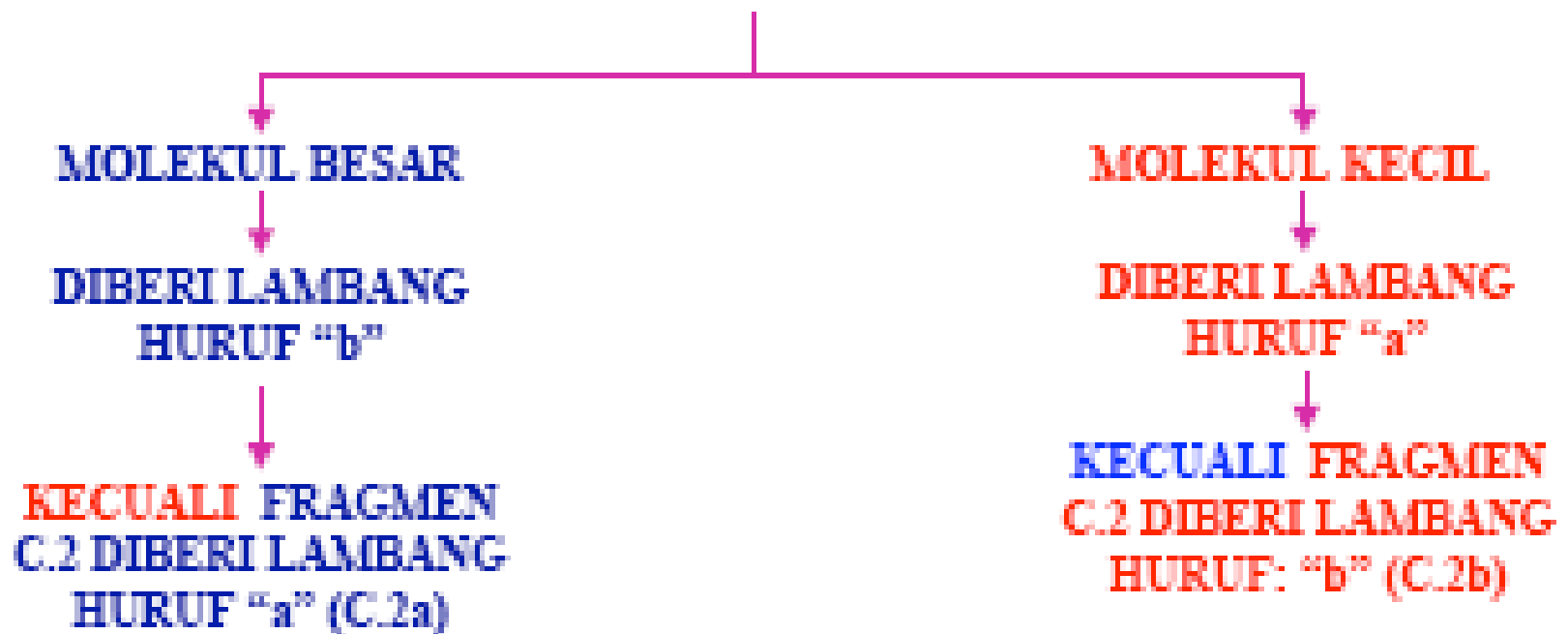
Protein yang meningkatkan fungsi respon terhadap infeksi/inflamasi

Classical pathway – requires an antibody and antigen to form a complex

Alternate pathway – requires certain polysacharrides on the surface

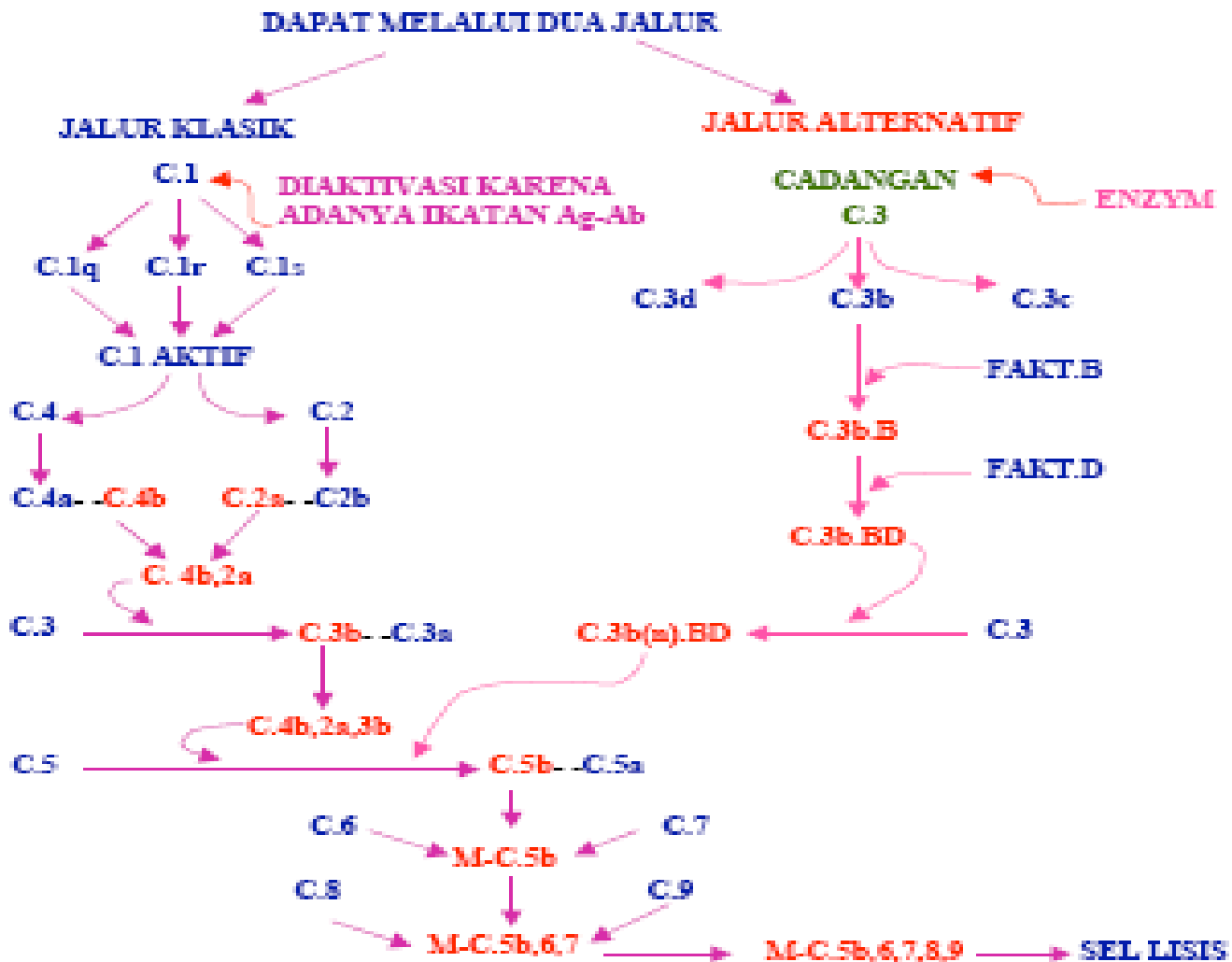
Complement

**DALAM MELAKUKAN AKTIVITASNYA
SETIAP KOMPLEMEN AKAN TERURAI
MENJADI 2(DUA) MOLEKUL**

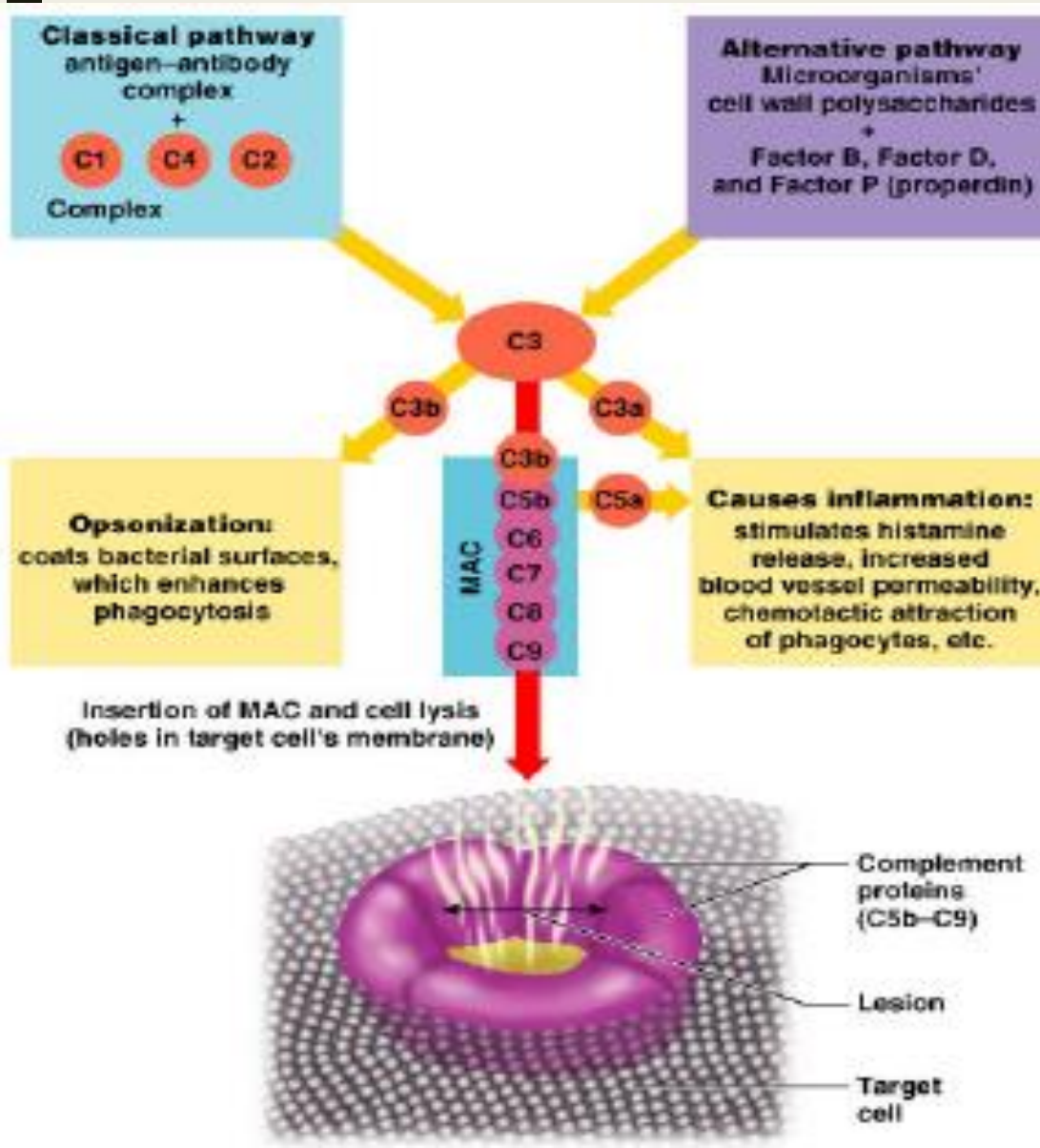


Complement

2.3 AKTIVITAS KOMPLEMEN



Complement



- Lysis of bacteria and some viruses**
- Opsonin**
- Increase in vascular permeability**
- Recruitment and activation of phagocytic cells**

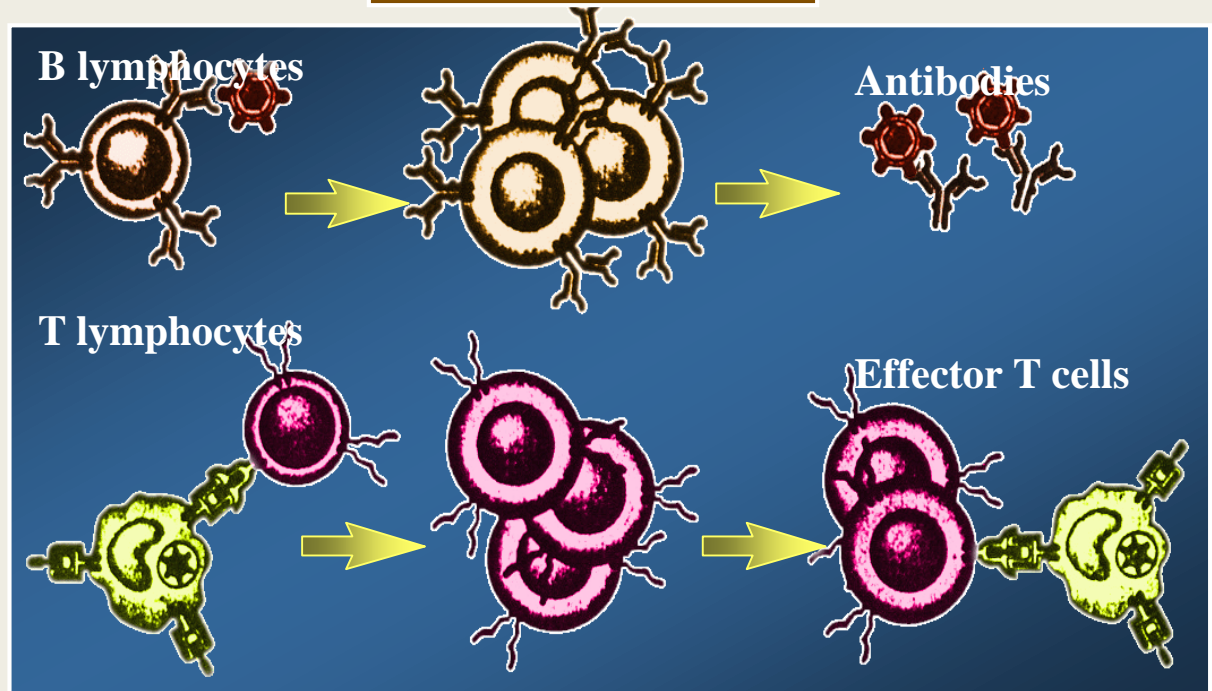
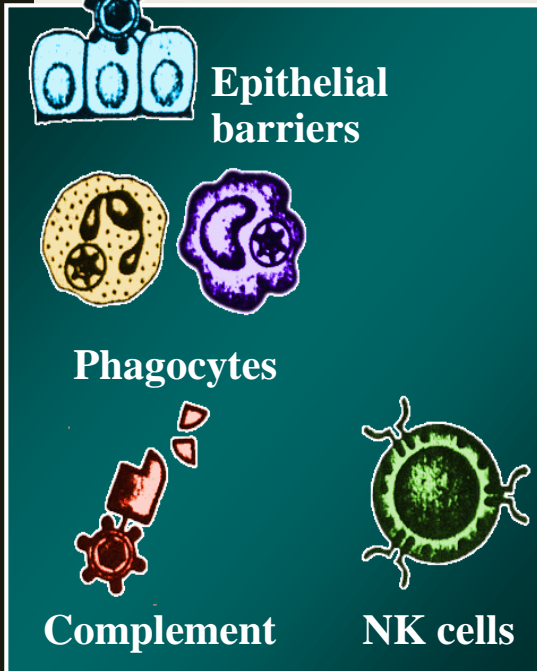
IMMUNE RESPONSE

Innate and adaptive immunity

Microbe

Innate immunity

Adaptive immunity



Hours

Days

0

6

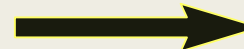
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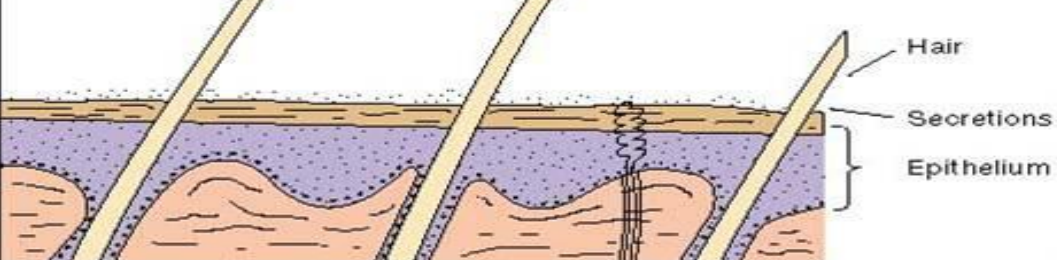

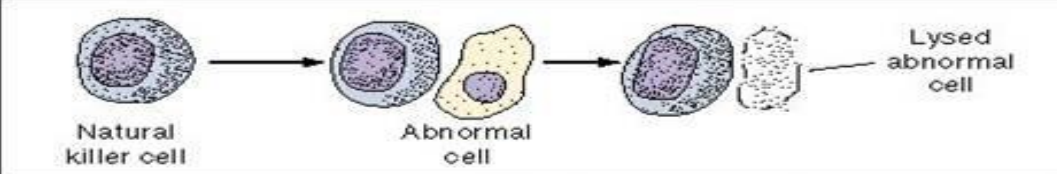


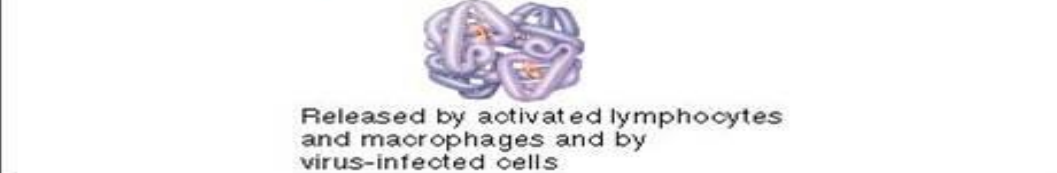
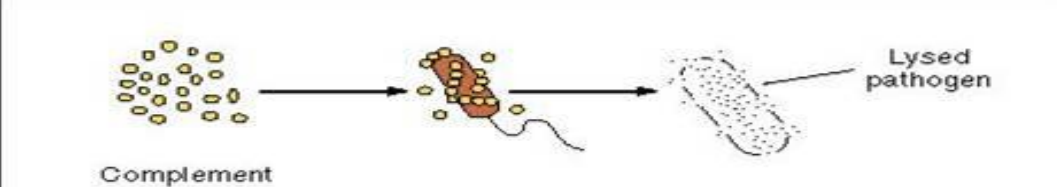
3

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Time after infection

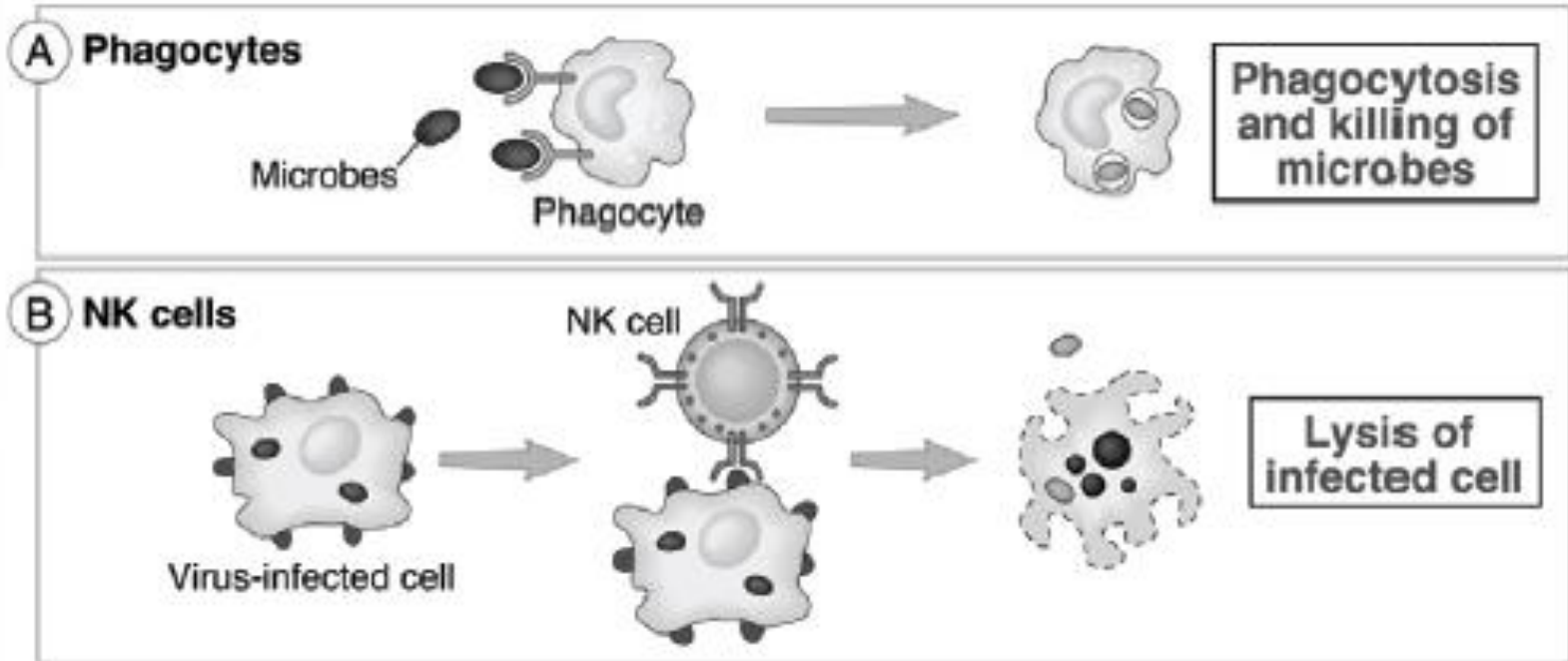


Innate immunity

<p>PHYSICAL BARRIERS</p> <p>Prevent approach and deny access to pathogens</p>	 <p>Hair</p> <p>Secretions</p> <p>Epithelium</p>
<p>PHAGOCYTES</p> <p>Remove debris and pathogens</p>	 <p>Fixed macrophage</p> <p>Neutrophil</p> <p>Free macrophage</p> <p>Eosinophil</p> <p>Monocyte</p>
<p>EXTRACELLULAR KILLING</p> <p>Destroys abnormal cells</p>	 <p>Natural killer cell</p> <p>Abnormal cell</p> <p>Lysed abnormal cell</p>
<p>INFLAMMATORY RESPONSE</p> <p>Multiple effects</p>	 <ol style="list-style-type: none"> 1. Blood flow increased 2. Phagocytes activated 3. Capillary permeability increased 4. Complement activated 5. Clotting reaction walls off region 6. Regional temperature increased 7. Specific defenses activated
<p>FEVER</p> <p>Mobilizes defenses, accelerates repairs, inhibits pathogens</p>	 <p>Body temperature rises above 37°C in response to pyrogens</p>
<p>INTERFERONS</p> <p>Increase resistance of cells to infection, slow the spread of disease</p>	 <p>Released by activated lymphocytes and macrophages and by virus-infected cells</p>
<p>COMPLEMENT SYSTEM</p> <p>Attacks and breaks down cell walls, attracts phagocytes, stimulates inflammation</p>	 <p>Complement</p> <p>Lysed pathogen</p>

Innate immunity/phagocyt & extracellular killing

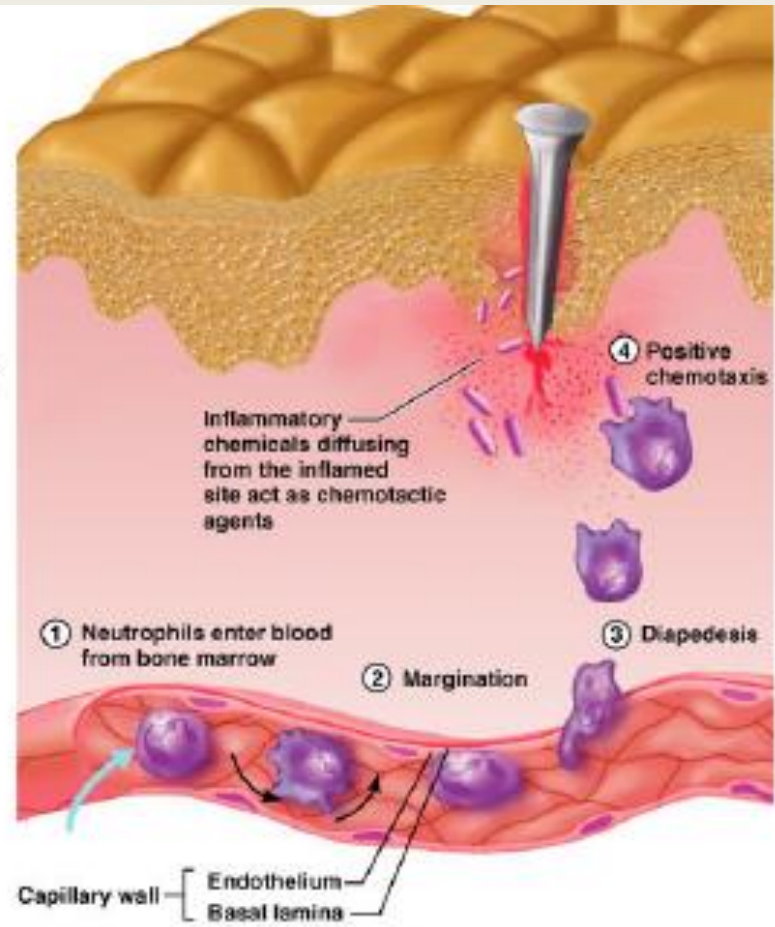
Components of innate immunity (a)



Innate immunity/Inflamasi

- Stages of the Inflammatory Response

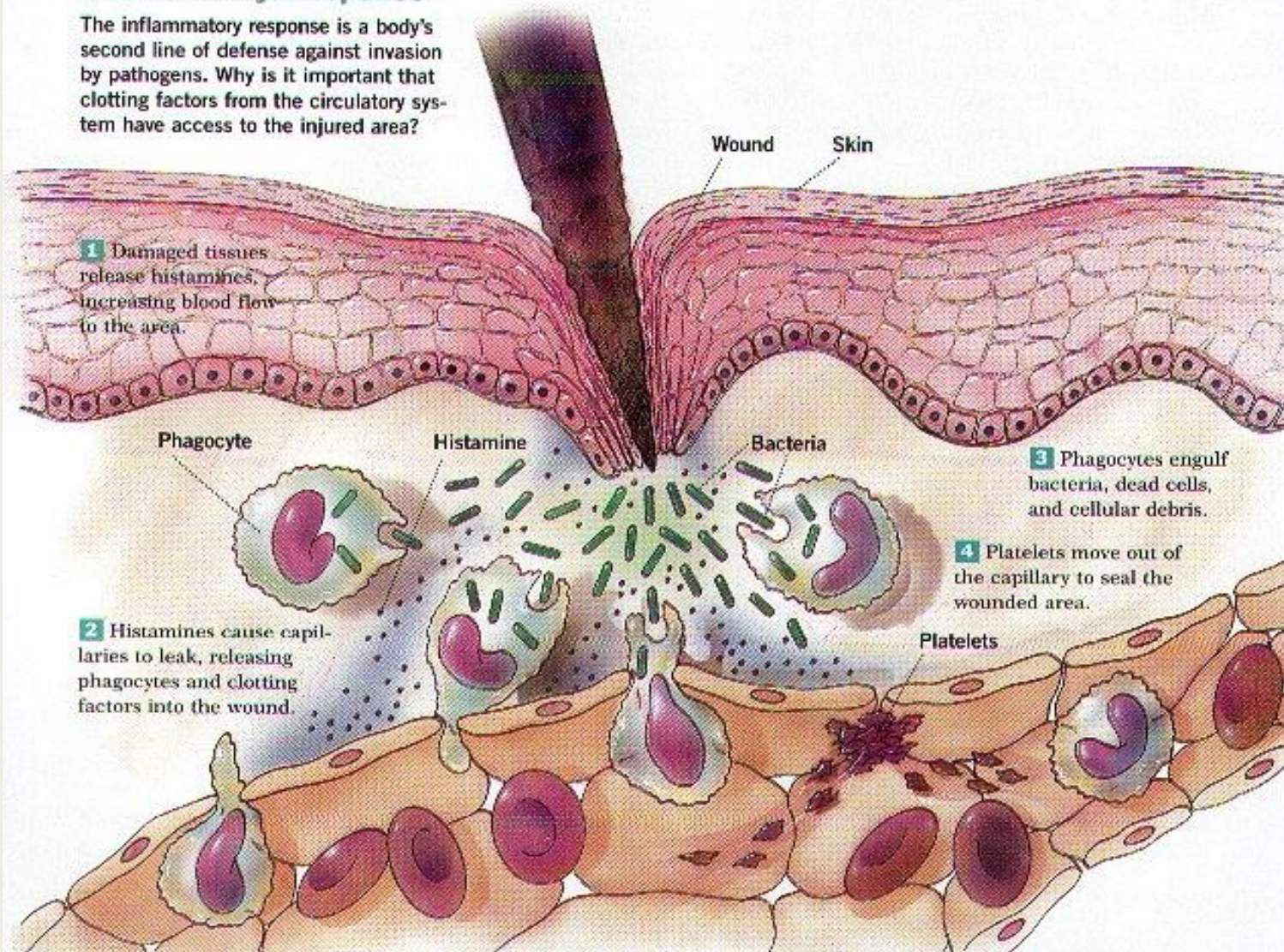
- Vasodilation and increased permeability of blood vessels
- Phagocytic migration
- Repair



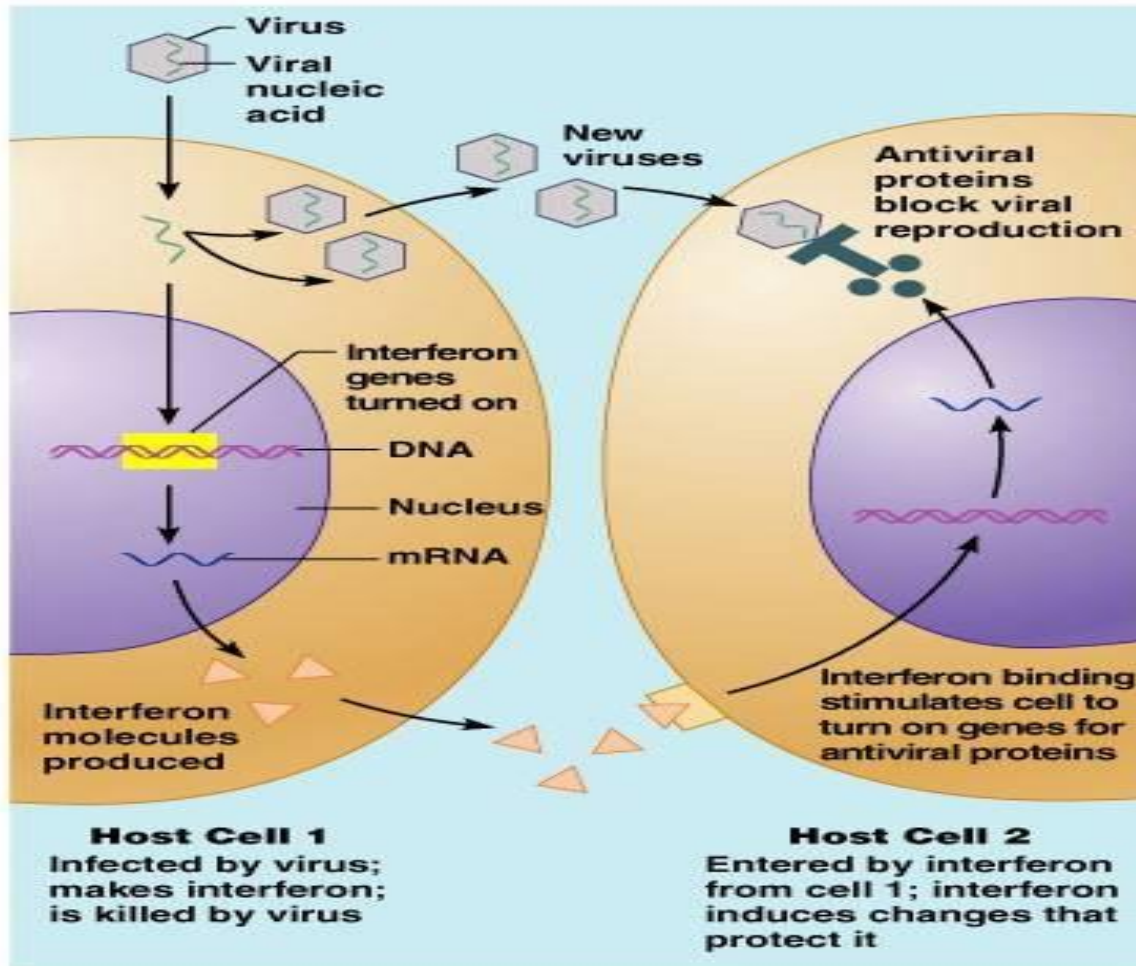
Innate immunity/Inflamasi

Steps of the Inflammatory Response

The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



Innate immunity/Interferon

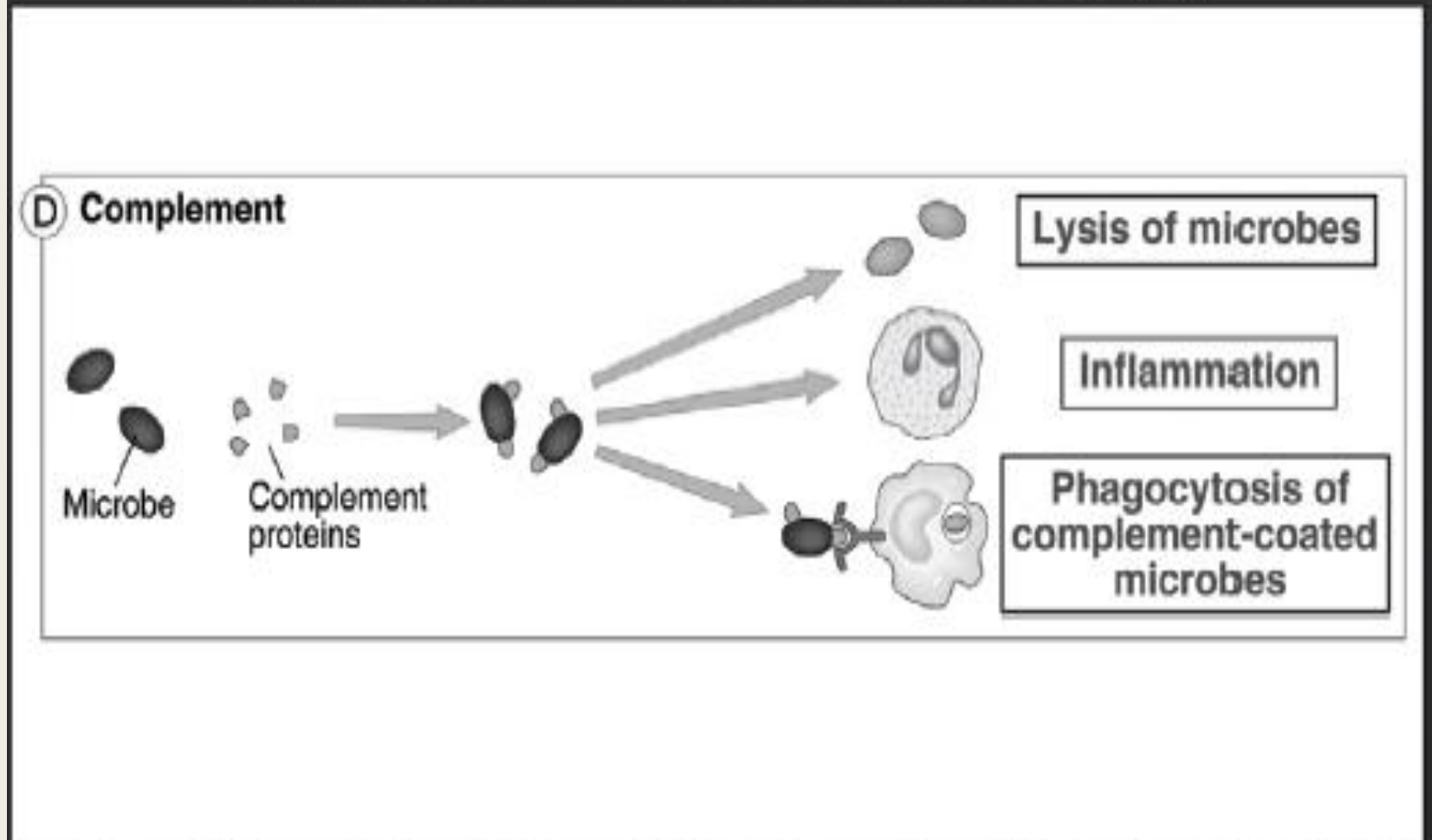


Interferon

Produce by virus infected cells,
Enhance the activity of phagocytes and NK cells
Inhibit cell growth
Supress tumor formation

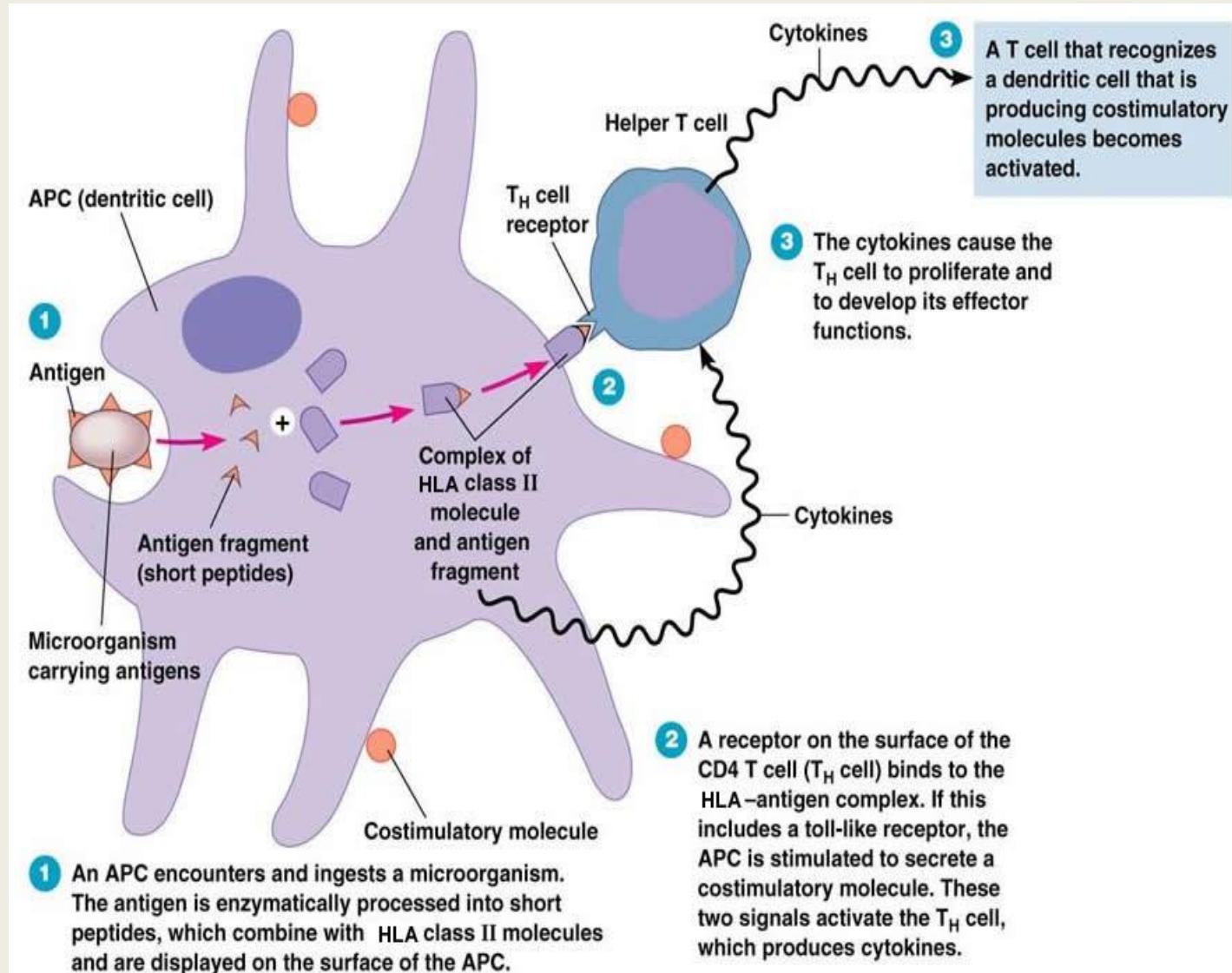
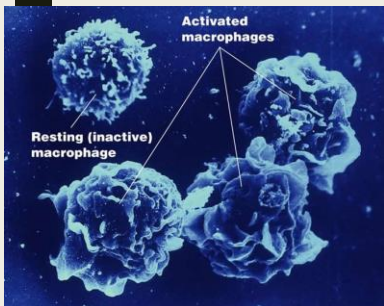
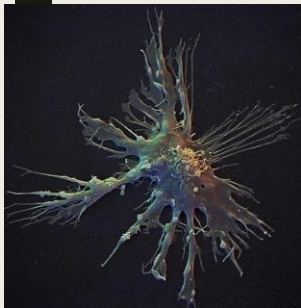
Innate immunity / complemen

Components of innate immunity (c)



Antigen presenting cells (APCs)

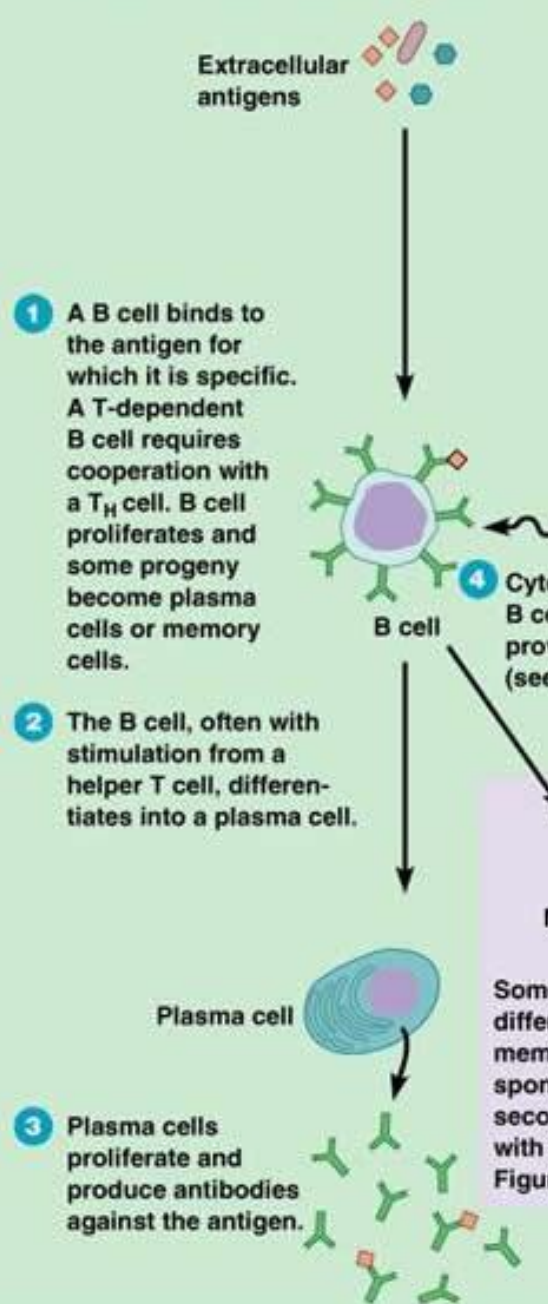
- Dendritic cells
- Langerhan's cells
- Macrophages
- B cells



adaptive immunity

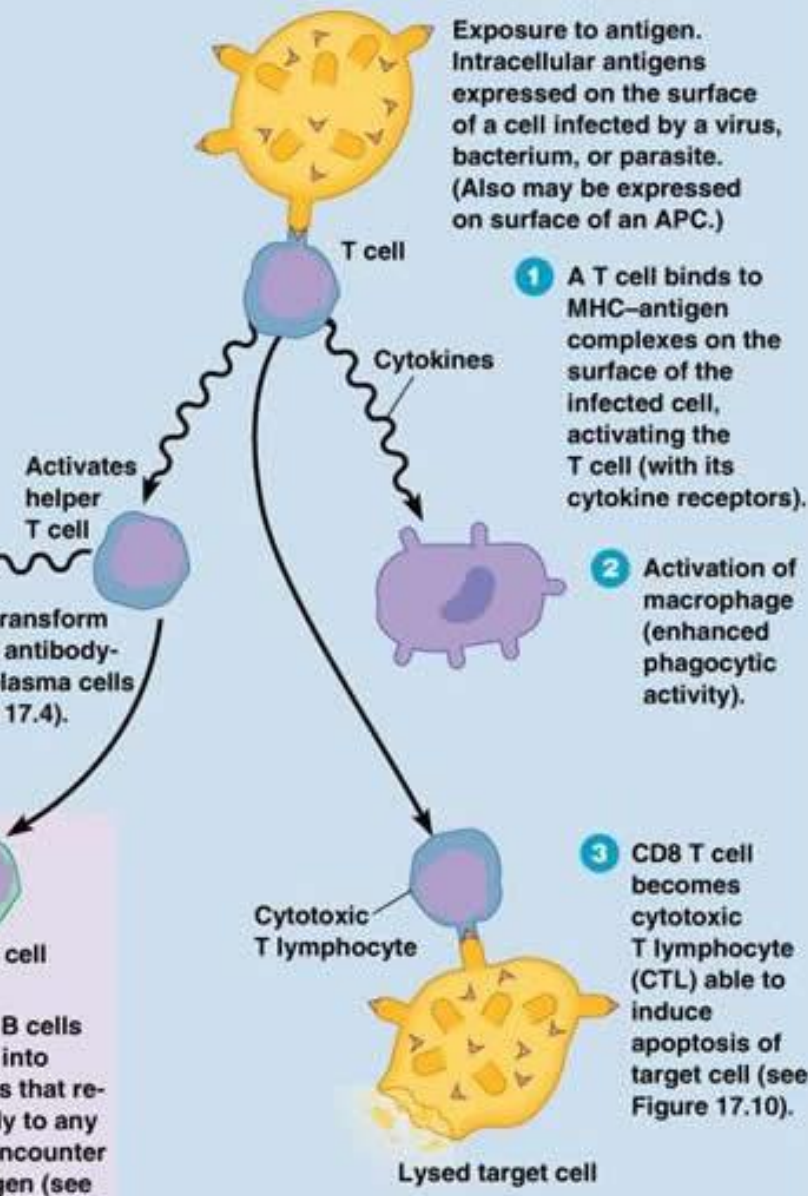
HUMORAL (ANTIBODY-MEDIATED) IMMUNE SYSTEM

Control of freely circulating pathogens

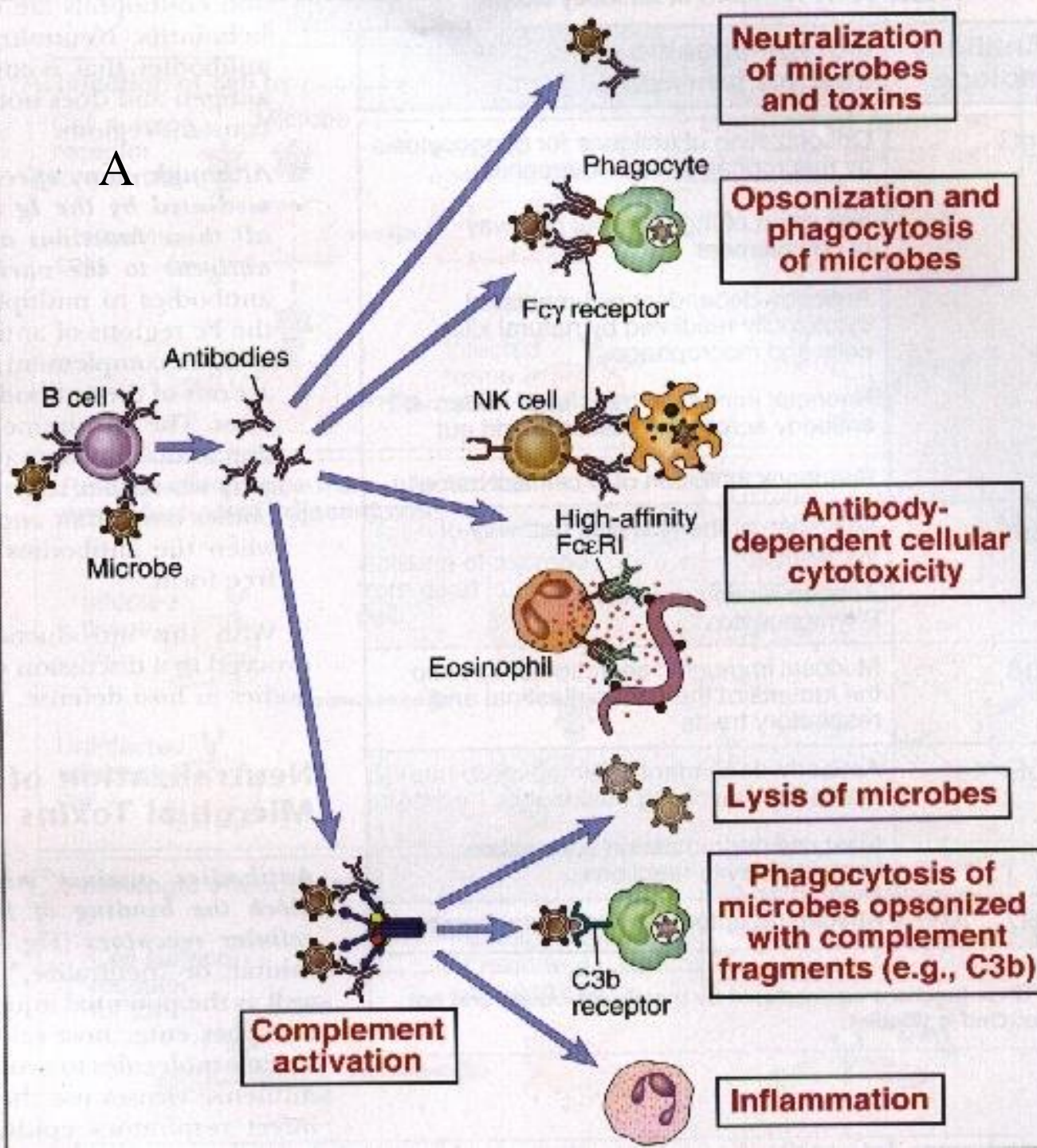


CELLULAR (CELL-MEDIATED) IMMUNE SYSTEM

Control of intracellular pathogens

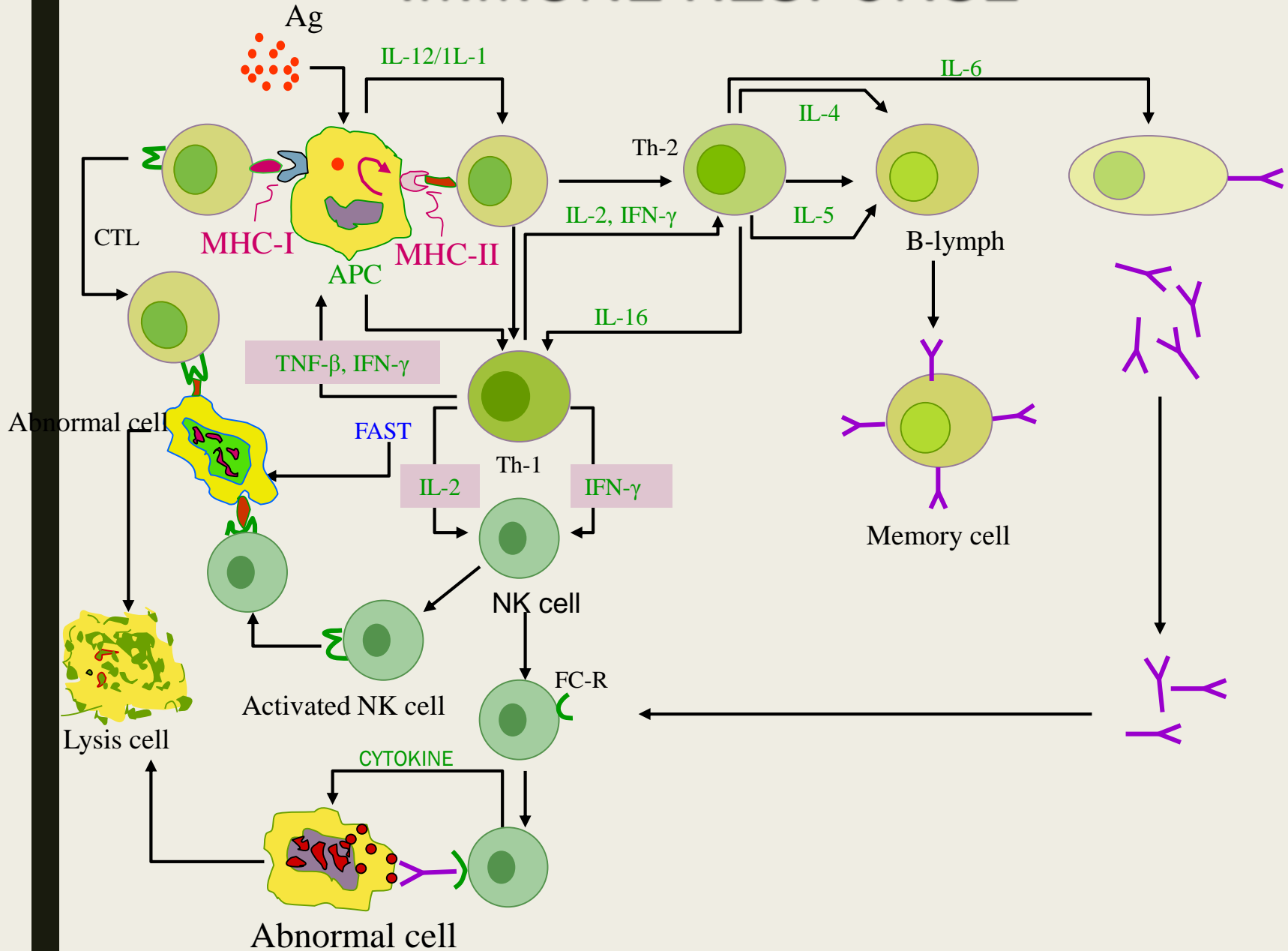


IMMUNE RESPONSE



Fungsi Efektor Antibodi

IMMUNE RESPONSE



WASSALAM