

Anatomi hematologi dan imunologi

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Anatomi hematologi

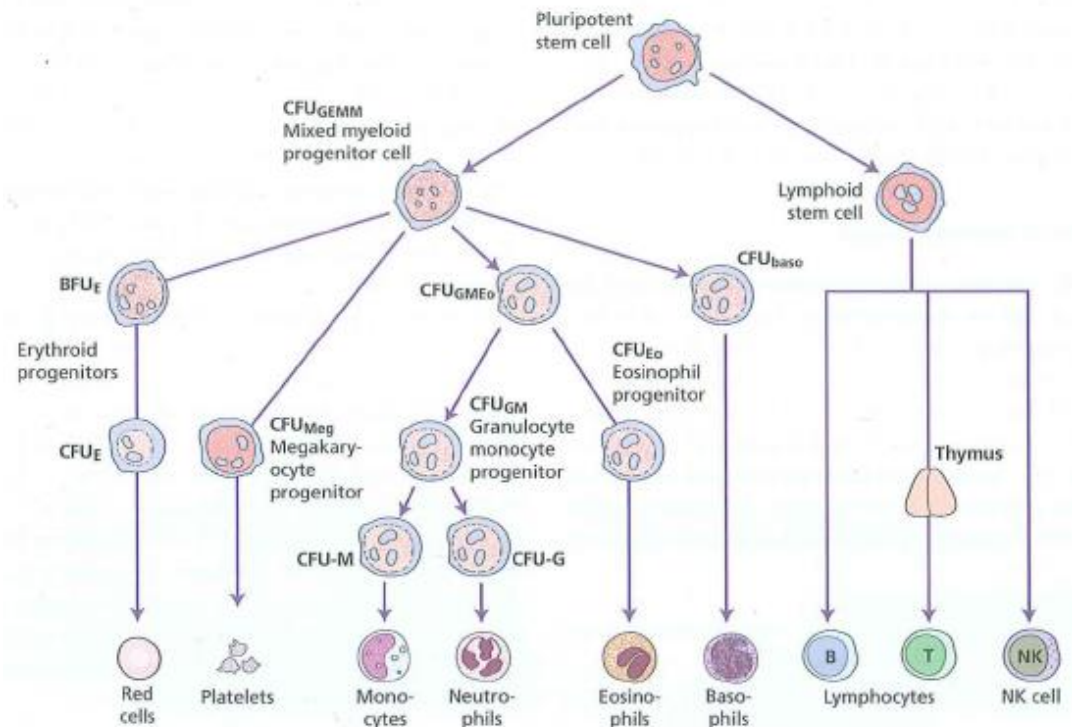
- Hematologi : cabang ilmu yang mempelajari darah dan organ pembentuk darah
- Yang akan dipelajari :
 - Komponen darah
 - Organ hematopoietik

haemopoiesis

- Haemopoiesis : general aspects of blood formation
- Site of haemopoiesis :
 - Fetus :
 - 0-2 m : yolk sac
 - 2-7 m : liver spleen
 - 5-9 m : bone marrow
 - Infants : bone marrow (all bones)
 - during childhood → progressive fatty replacement of marrow
 - Adults : (bone marrow) vertebra, ribs, sternum, sacrum, pelvis, proximal ends of femur

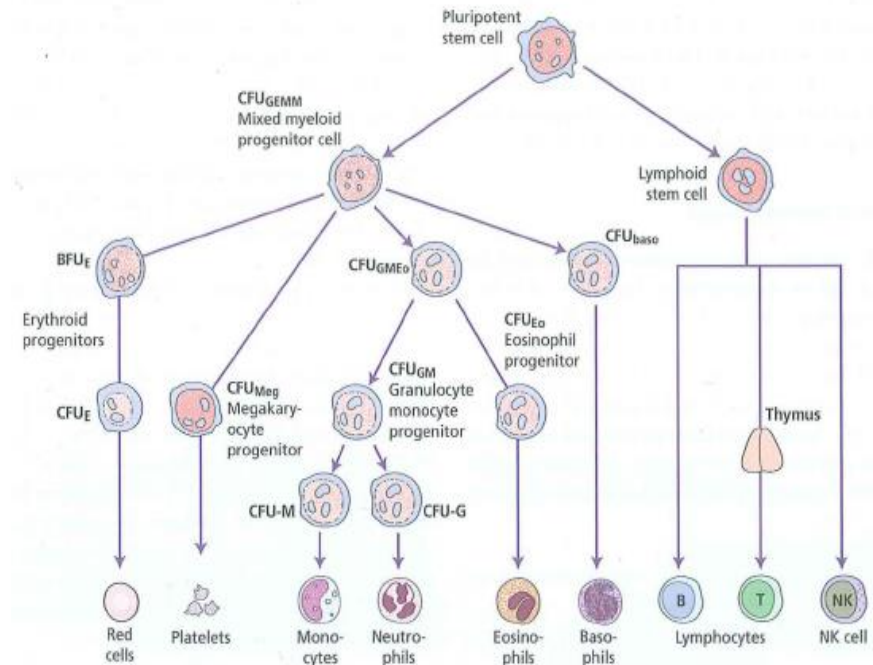
Haemopoietic and progenitor cells

- Haemopoiesis bermula dari stem cell yang dapat berkembang menjadi berbagai jenis sel
- *Stem cells haemopoietic* sangat jarang ditemukan di BM , mungkin 1 dalam 20 juta sel berinti di BM



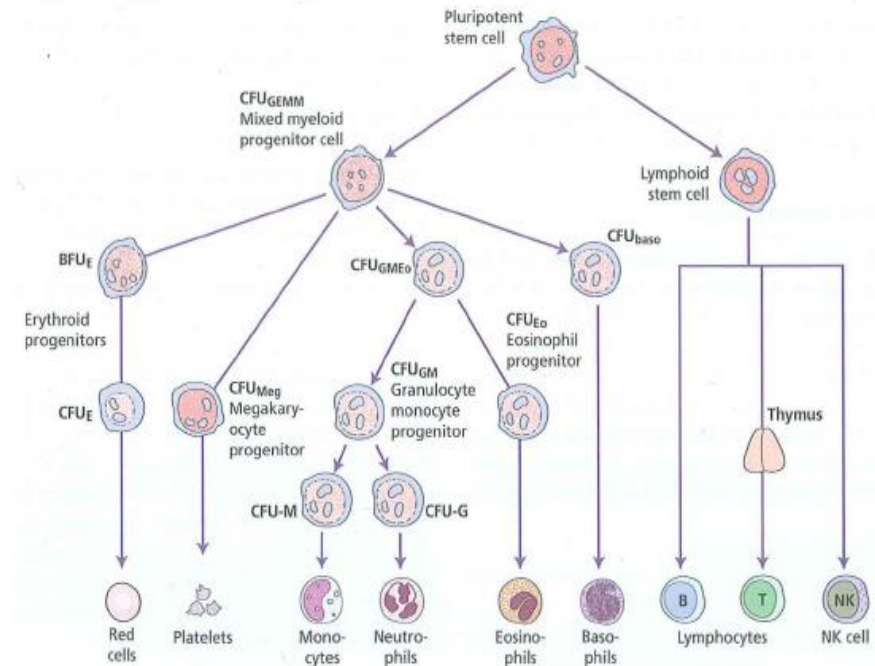
Haemopoietic and progenitor cells

- Stem cells → differensiasi menjadi progenitor hemapoietik yg berbeda-beda
 - Lymfoid stem cells
 - CFU_{GEMM} mixed myeloid progenitor cells
- diferensiasi menjadi prekursor myeloid/eritroid/limfoid
- Limfoid di maturasi sebagian di timus sebagian di sumsum tulang → dibentuk di spleen dan limfonodi
- Sel lainnya dimaturasi di sumsum tulang



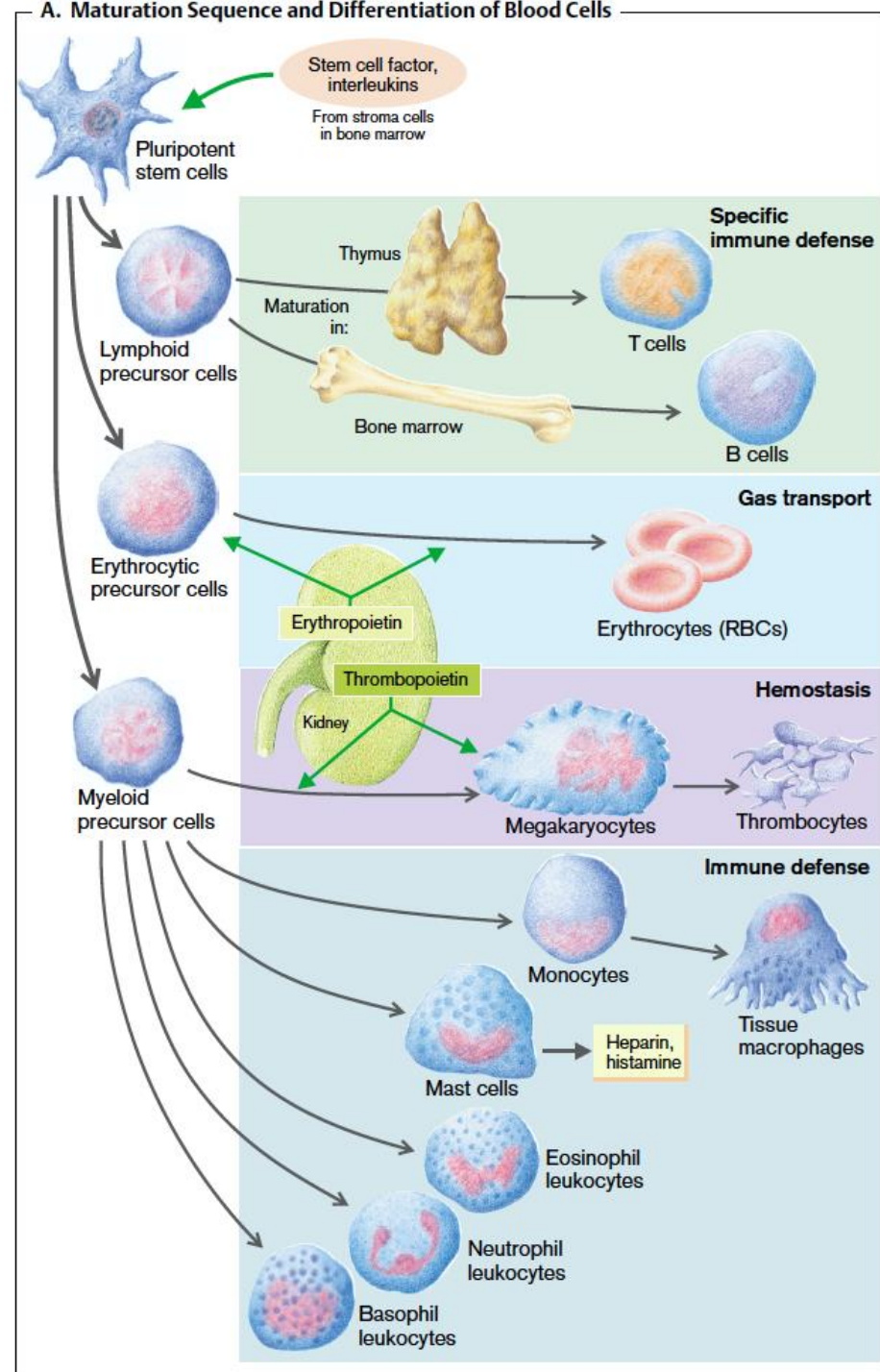
Haemopoietic and progenitor cells

- Stem cells memiliki kemampuan self-renewal → populasi sel di BM konstan pada orang sehat
- 1 stem cells dapat memproduksi 10^6 sel matur
- Sel prekursor respon terhadap growth factor dan bisa meningkatkan produksinya jika diperlukan



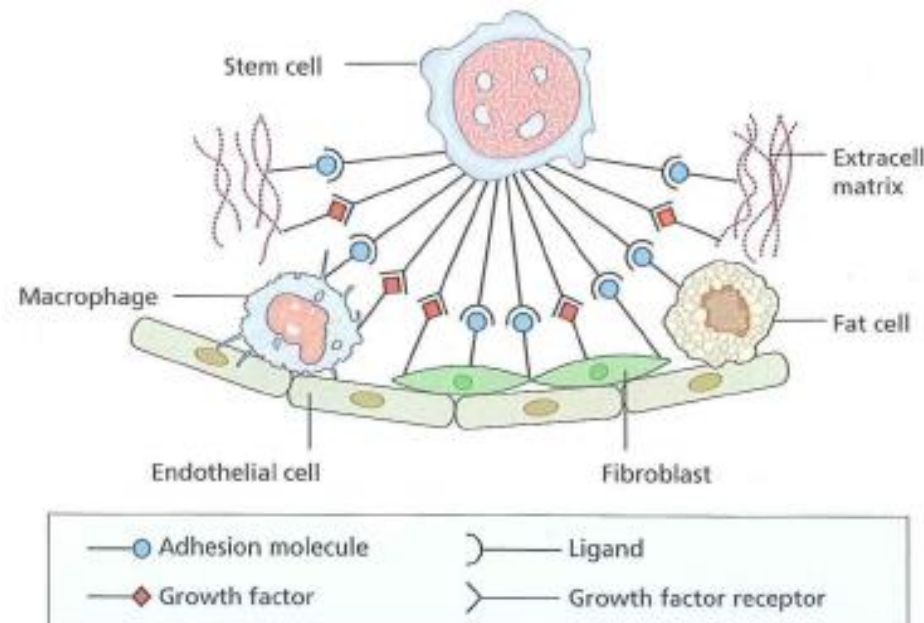
Pembentukan darah

- Selama proses hematopoietik →
 - Hormon eritropoietin
 - Hormon trombopoietin



Stroma bone marrow

- BM merupakan lingkungan yang sesuai untuk survival, pertumbuhan dan perkembangan stem cells
- BM tersusun :
 - Stromal cells
 - Microvascular network
- Stromal cells tersusun atas :
 - Adipocytes
 - Fibroblasts
 - Endothelial cells
 - Macrophage
 - Extracellular secreted molecules : collagen, glycoprotein, glycosaminoglycan



Struktur Darah



- Darah → dewasa : 4-6 L
- Homeostasis → mengatur 2 kondisi darah
 - Viskositas / kekentalan
 - Osmolalitas : kejenuhan larutan darah → diatur protein plasma

Table 18.2 General Properties of Blood *

<i>Mean Fraction of Body Weight</i>	8%
<i>Volume in Adult Body</i>	Female: 4–5 L; male: 5–6 L
<i>Volume/Body Weight</i>	80–85 mL/kg
<i>Mean Temperature</i>	38°C (100.4°F)
<i>pH</i>	7.35–7.45
<i>Viscosity (relative to water)</i>	Whole blood: 4.5–5.5; plasma: 2.0
<i>Osmolarity</i>	280–296 mOsm/L
<i>Mean Salinity (mainly NaCl)</i>	0.9%
<i>Hematocrit (packed cell volume)</i>	Female: 37%–48% male: 45%–52%
<i>Hemoglobin</i>	Female: 12–16 g/dL male: 13–18 g/dL
<i>Mean RBC Count</i>	Female: 4.2–5.4 million/ μ L male: 4.6–6.2 million/ μ L
<i>Platelet Count</i>	130,000–360,000/ μ L
<i>Total WBC Count</i>	5,000–10,000/ μ L

Table 18.1 Functions of the Blood

Transport

- Carries O₂ and CO₂ between the lungs and other organs
- Carries nutrients from the digestive system and storage depots to other organs
- Carries wastes to the liver and kidneys for detoxification or removal
- Carries hormones from endocrine glands to target cells
- Carries heat to the skin for removal; helps regulate body temperature

Protection

- Plays several roles in inflammation
- Leukocytes destroy microorganisms and cancer cells
- Antibodies and other proteins neutralize or destroy pathogens
- Platelet factors initiate clotting and minimize blood loss

Regulation

- Transfers water to and from the tissues; helps stabilize water balance
- Buffers acids and bases; helps stabilize pH

Struktur Darah

- Darah → komponen sel dan plasma
 - Komponen sel
 - 45%
 - eritrosit, leukosit dan trombosit
 - Komponen plasma
 - 55%
 - Berisi molekul organik dan anorganik
- Fungsi :
 - Transport
 - Pertahanan
 - Regulasi



Komponen darah

- Komponen darah :

- Sel

- Eritrosit (transport O₂ dan Co₂, bagian dari keseimbangan asam basa)
- Leukosit (pertahanan tubuh adaptif dan bawaan)
- Trombosit (hemostasis)

- Plasma

- Mengandung
 - Elektrolit
 - Nutrien
 - Produk metabolik
 - Protein plasma
 - gas

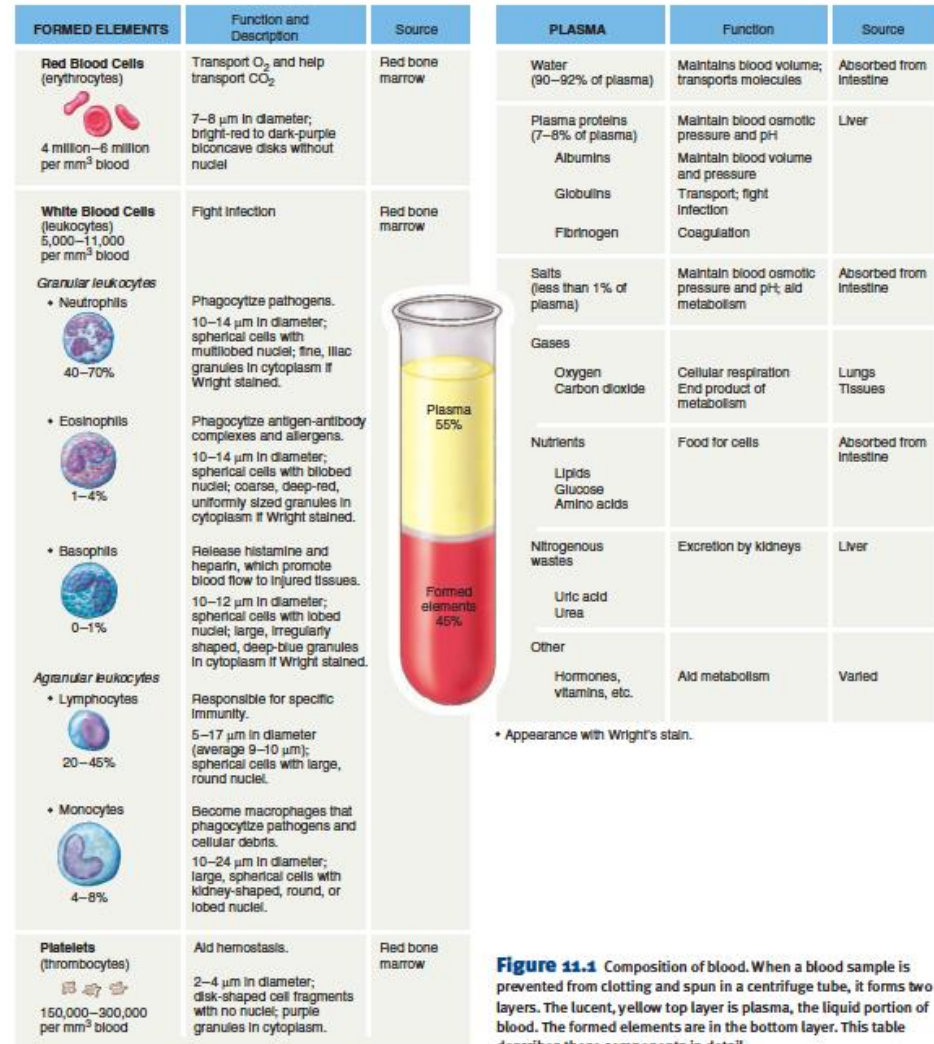
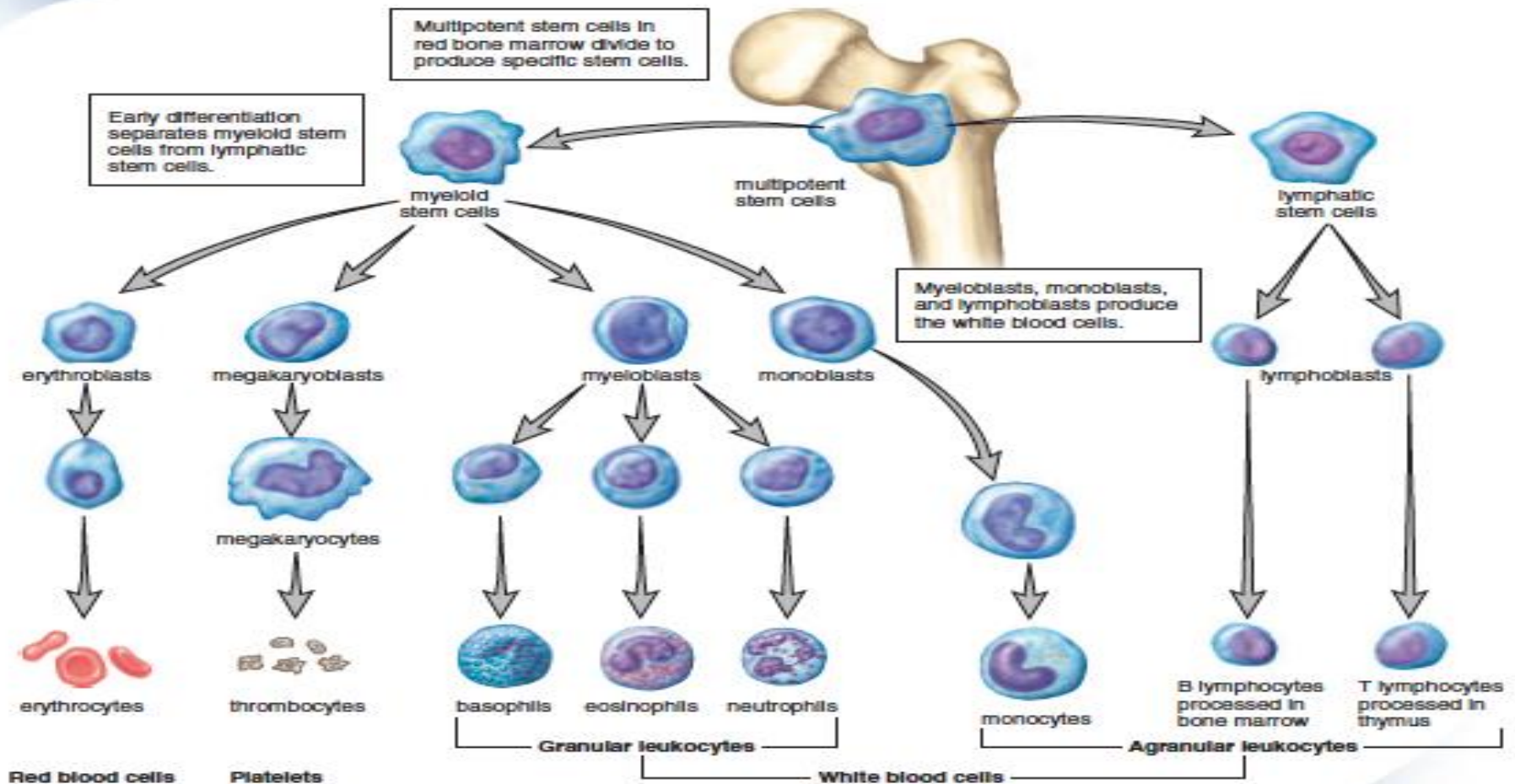


Figure 11.1 Composition of blood. When a blood sample is prevented from clotting and spun in a centrifuge tube, it forms two layers. The lucent, yellow top layer is plasma, the liquid portion of blood. The formed elements are in the bottom layer. This table describes these components in detail.

1. Komponen sel darah

- Proses produksi → hematopoiesis → di sumsum tulang (tengkorak, costae, vertebrae, iliaka, tulang panjang lainnya)
- Stem cell → memproduksi sel darah khusus
 - Myeloid → eritrosit, trombosit, granulosit, monosit
 - Lymphatic → limfosit

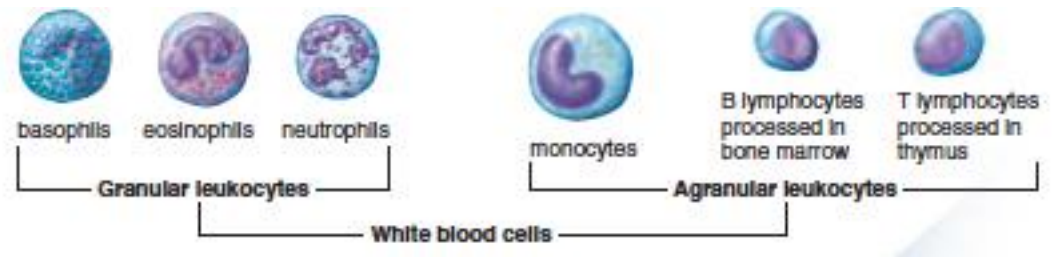


1.1 eritrosit

- * Bikonkaf , saat matur tidak ada nucleus
- * 4-6 juta/mm³
- * Mengandung hemoglobin
 - * Molekul polipeptida yang tersusun dari globin, heme yang mengandung besi
 - * Mengambil O₂ di alveolus → jaringan
- * Produksi : di stem cell sumsum tulang
 - * Myeloid stem cell → eritroblast → maturasi → eritrosit
- * Umur : 120 hari
- * Penghancuran : di hati dan limpa (dihancurkan oleh makrofag) → hemoglobin →
 - * Globin → asam amino
 - * Besi → re-use di bone marrow → Bilirubin
 - * Heme → degradasi



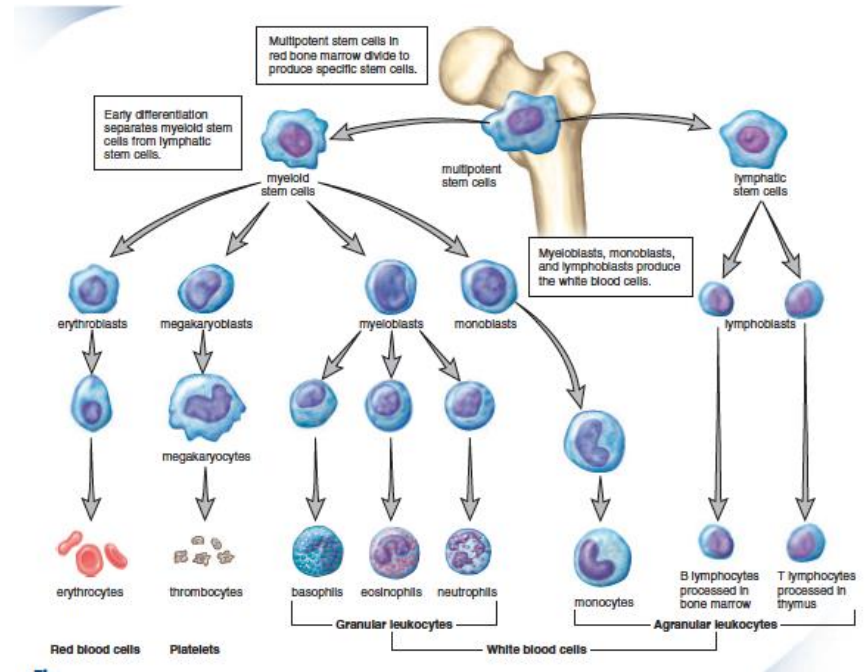
1.2 Leukosit



- Lebih besar dari eritrosit, Memiliki inti sel , 5.000-11.000/mm³
- Dapat melewati pori-pori pada dinding pembuluh darah → jaringan
- Jenis :
 - Granulosit
 - Netrofil/PMN : inti berlobus-lobus, menfagositosis patogen
 - Eosinofil : inti bilobus granul sitoplasma (menyerap eosin → warna merah) → meningkat pada reaksi alergi, (menfagositosis kompleks Ag-Ab saat reaksi alergi
 - Basofil : granula sitoplasma → hitam kebiruan, dapat memproduksi histamin(dilatasi pembuluh darah dan kontraksi otot halus) dan heparin (cegah pembekuan darah)
 - Agranulosit
 - Limfosit : imunitas spesifik
 - Sel T → langsung menyerang dan menghancurkan sel patogen atau antigen
 - Sel B-- > memproduksi antibodi
 - Monosit : leukosit paling besar, di jaringan → makrofag → fagositosis patogen , sebagai APC

1.3 trombosit

- Penting untuk hemostasis
- Fragmentasi megakariosit
- 150.000-300.000/mm³
- Usia 10 hari



2. Komponen plasma

- Cairan , 92% air, 8% molekul lain yaitu ion dan molekul organik lain(glukosa, asam amino, urea , hormon, plasma protein)
- Plasma protein
 - terutama : albumin, globulin, fibrinogen
 - Diproduksi mayoritas di hati
 - Berfungsi menjaga homeostasi
 - Menjaga pH normal 7.4
 - Mempengaruhi tekanan osmotik (α)
 - Melawan infeksi (gamma globulin)
 - Pembekuan darah (fibrinogen)

Table 11.1 Blood Plasma Solutes

Plasma proteins	Albumin, globulins, fibrinogen
Inorganic ions (salts)	Na^+ , Ca^{2+} , K^+ , Mg^{2+} , Cl^- , HCO_3^- , HPO_4^{2-} , SO_4^{2-}
Gases	O_2 , CO_2
Organic nutrients	Glucose, fats, phospholipids, amino acids, etc.
Nitrogenous waste products	Urea, ammonia, uric acid
Regulatory substances	Hormones, enzymes

SISTEM IMUN

Sistem Imun

- Fungsi:
 1. Melindungi tubuh dari invasi penyebab penyakit; menghancurkan & menghilangkan mikroorganisme atau substansi asing (bakteri, parasit, jamur, dan virus, serta tumor) yang masuk ke dalam tubuh
 2. Menghilangkan jaringan atau sel yg mati atau rusak (debris sel) untuk perbaikan jaringan.
 3. Mengenali dan menghilangkan sel yang abnormal
- Sasaran utama: patogen (virus, bakteri, parasit), antigen
- Leukosit mrpkn sel imun utama

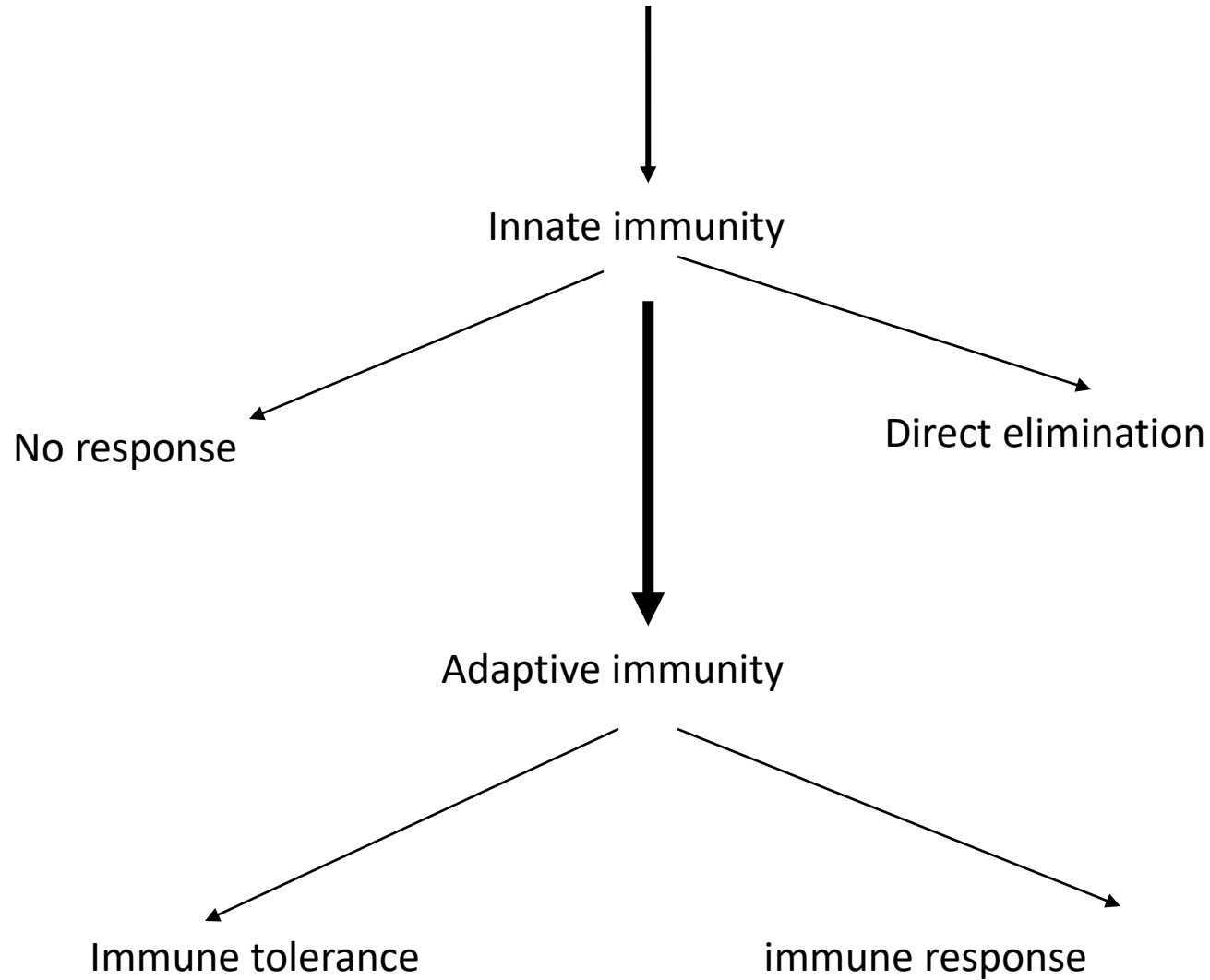
Sistem imun

Fungsi Sistem imun → mencegah atau membatasi infeksi / adanya benda asing/ kerusakan/injury sel

SISTEM PERTAHANAN TUBUH :



Immune defense to non-pathogenic and pathogenic materials



Imun innate vs adaptive

innate

- Ada sel/molekul yang dapat mengenali patogen/ antigen secara langsung
- Sel Efektor : makrofag, granulosit, sel NK
- Non spesifik
- Non memori

adaptive

- Diinduksi interaksi antigen presenting cell dengan limfosit
- Sel efektor : sel T dan sel B memproduksi antibodi
- Spesifik
- Memori

Pertahanan Lapis Pertama

- Kulit & membran mukosa yang utuh
- Kelenjar keringat, sebum, & airmata → mensekresi zat kimia & bersifat bakterisid
- Mukus, silia, *tight junction*, desmosom, sel keratin & lysozim di lapisan epitel
- Flora normal

Imunitas bawaan / innate

- Respon imun pertama jika ada exposure antigen/mikroba
- Sifatnya non spesifik
- Pengenalan awal deteksi patogen
- Respon cepat
- Tidak ada memori
- barier terhadap agen infeksius → respon inflamasi dan fagositosis
 - Fisik : kulit, membran mukosa, lisozyme
 - Sel : NK cell, makrofag, netrofil, sel dendritik
 - protein tertentu : komplemen
- Jika ada exposure, maka sistem imun bawaan akan :
 - Membunuh/merusak antigen/mikroba yang masuk
 - Mengaktifkan sistem imun adaptive/didapat

Imunitas bawaan / innate

- Imunitas bawaan → mengenali mikroba / antigen
 - Beberapa komponen imunitas bawaan → mengenali molekul karbohidrat/ lemak tertentu pada permukaan mikroorganisme
 - Komponen imunitas bawaan memiliki reseptor “***pattern-recognition receptors***” (***PRR***) yang mengenali tipe molekul yang disebut *pathogen-associated molecular pattern (PAMP)* yang ada di permukaan mikroba yang tidak dipresentasikan oleh sel manusia
 - Ada 2 jenis reseptor
 - Mengenali mikroba di luar sel
 - Toll-like receptors
 - Manna binding lectin receptors
 - Mengenali mikroba di dalam sitoplasma sel
 - NOD receptors
 - RIG-I helicase receptors

Mekanisme imunitas bawaan terhadap mikroba

- *pathogen-associated molecular pattern (PAMP) diantaranya*
 - Endotoksin (LPS) pada permukaan bakteri gram negatif → dipresentasikan CD14 di makrofag → Toll like receptor 4 (TLR4) → stimulasi sintesis sitokin
 - Mannan Polysacarida di jamur dan bakteri lain → Mannan—binding lectin (MBL)
 - Peptidoglycan pada permukaan bakteri → NOD receptors
 - Asam nukleat virus → RIG-I helicase reseptors

Macrophages express receptors for many microbial constituents

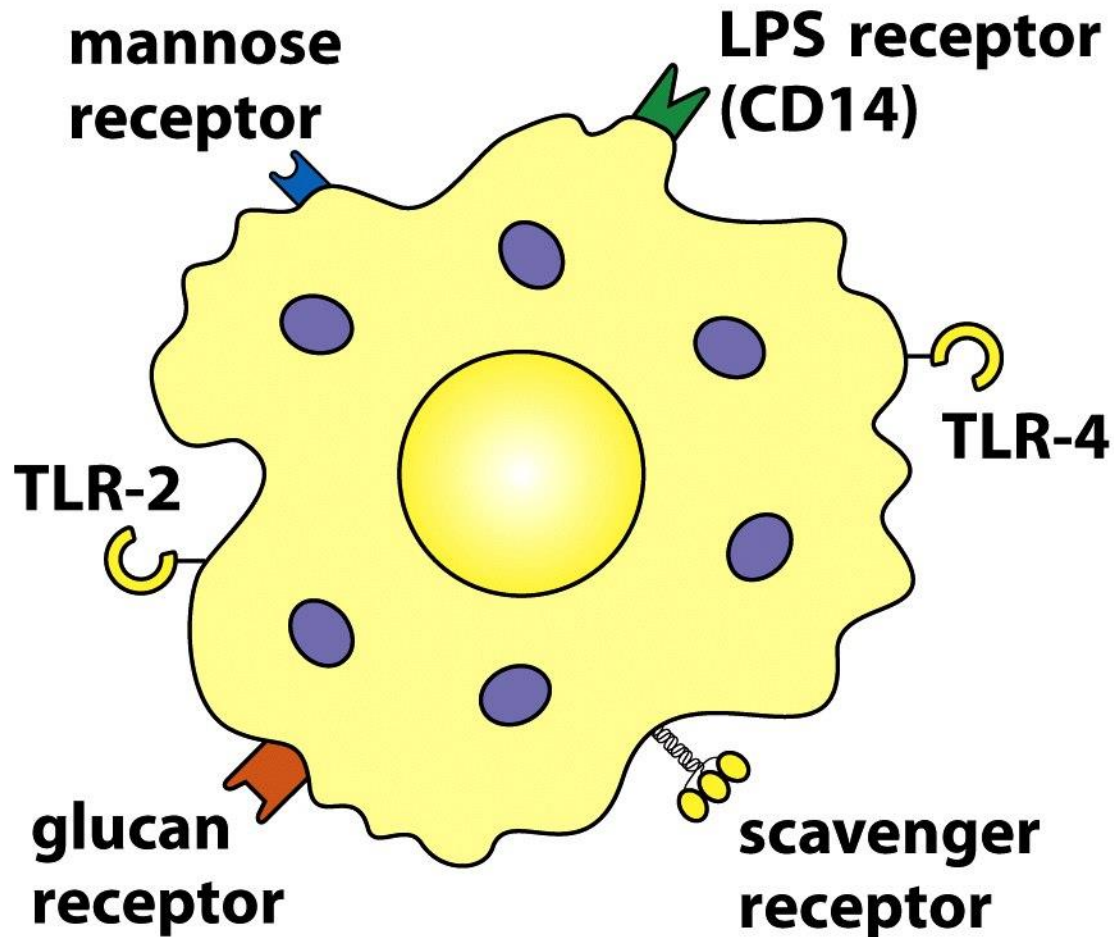
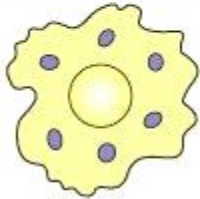
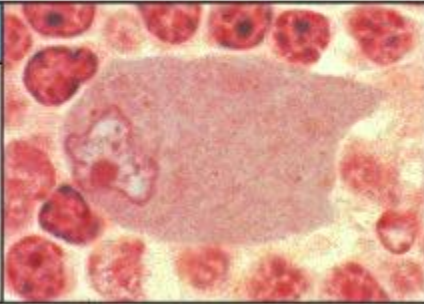

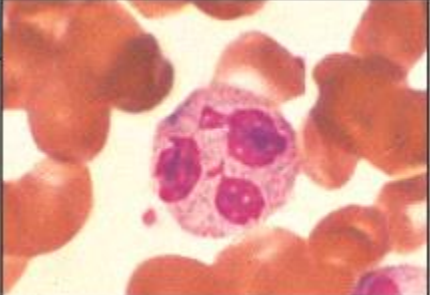


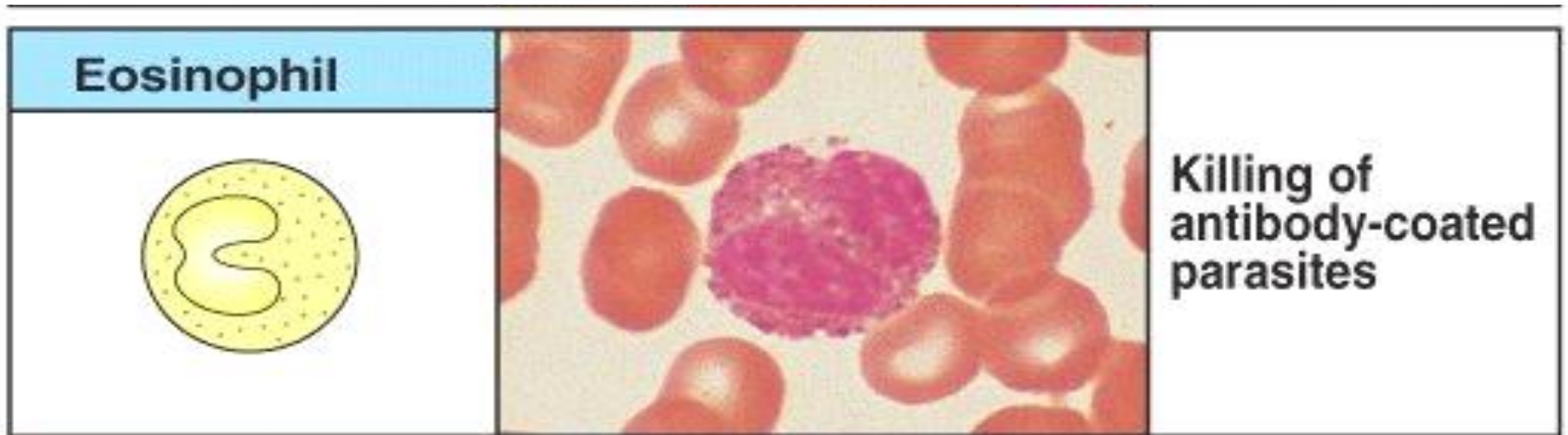
Figure 1-10 Immunobiology, 7ed. (© Garland Science 2008)

Sistem Imun alamiah

- *Phagocytes*

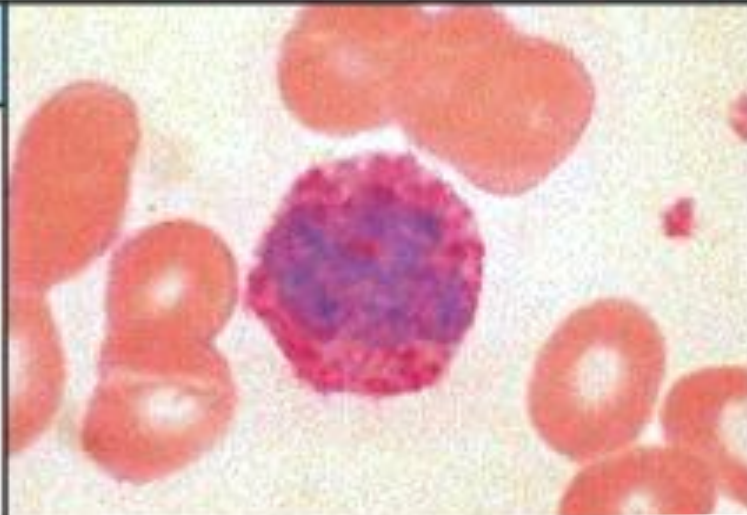
Cell		Activated function
Macrophage 		Phagocytosis and activation of bactericidal mechanisms Antigen presentation
Neutrophil 		Phagocytosis and activation of bactericidal mechanisms

- Eosinophil
 - degranulasi bila terstimulasi
 - melepaskan histaminase dan aryl sulphatase



- Basophil

Basophil

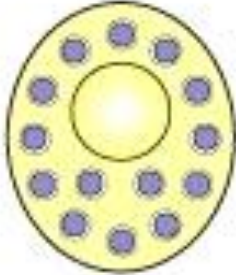
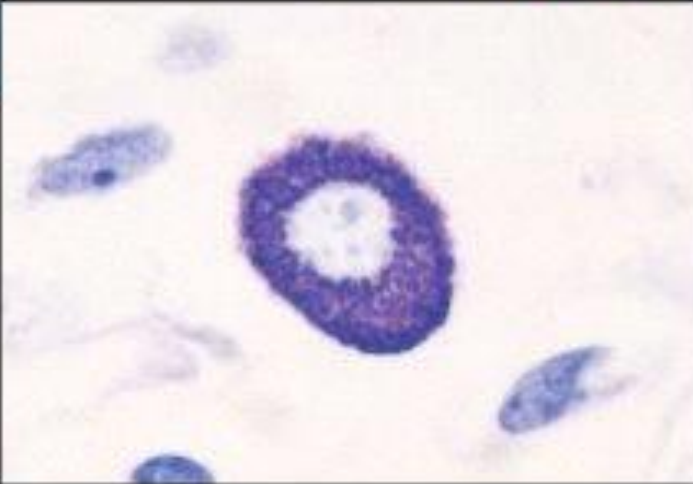


Unknown

- Sel Mast

- mucosal mast cell (MMC)

- connective tissue mast cell (CTMC)

Mast cell		
		Release of granules containing histamine and other active agents

- Sel Natural Killer (NK)
 - ☉ mengekspresikan CD16 (FcγRIII), CD56
 - ☉ berperan pada antibody-dependent cellular cytotoxicity (ADCC)
 - ☉ melepaskan IFN- γ, IL-1, GM-CSF

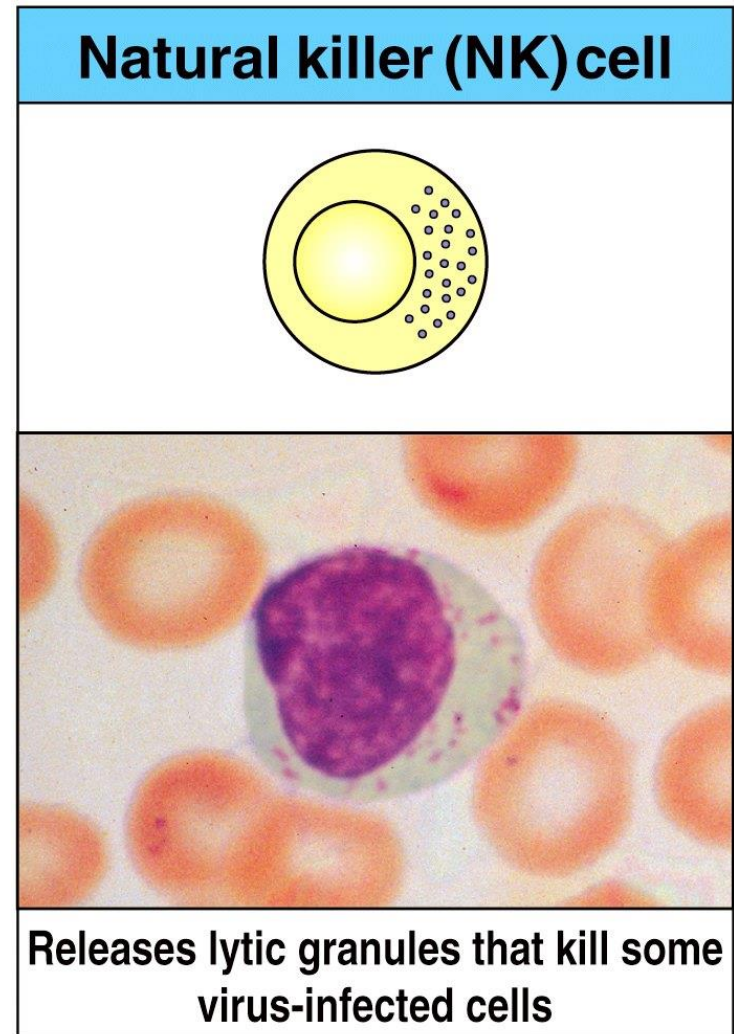
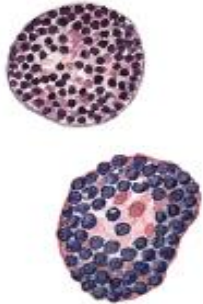


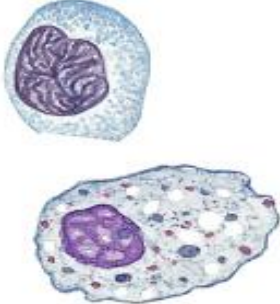




Figure 1-6 Immunobiology, 6/e. (© Garland Science 2005)

Imunitas adaptive

- Respon lebih lama bisa hingga mingguan setelah patogen masuk
- Lebih spesifik
- Sel memori
- Terjadi setelah exposure dengan agent patogen/non patogen
- Dimediasi sel B limfosit dan sel T limfosit (T cytotoxic dan T helper)

Sel dalam sistem imun

	Basophils and Mast Cells	Neutrophils	Eosinophils	Monocytes and Macrophages	Lymphocytes and Plasma Cells	Dendritic Cells
						
% of WBCs in blood	Rare	50-70%	1-3%	1-6%	20-35%	NA
Subtypes and nicknames		Called "polys" or "segs" Immature forms called "bands" or "stabs"		Called the mononuclear phagocyte system	B lymphocytes, Memory cells Plasma cells T lymphocytes Cytotoxic T cells Helper T cells Natural killer cells	Also called Langerhans cells, veiled cells
Primary function(s)	Release chemicals that mediate inflammation and allergic responses	Ingest and destroy invaders	Destroy invaders, particularly parasites	Ingest and destroy invaders Antigen presentation	Specific responses to invaders, including antibody production	Recognize pathogens and activate other immune cells by antigen presentation
		Phagocytes				
		Granulocytes				
Classifications			Cytotoxic cells		Cytotoxic cells (some types)	
					Antigen-presenting cells	

All white blood cells originate from the bone marrow

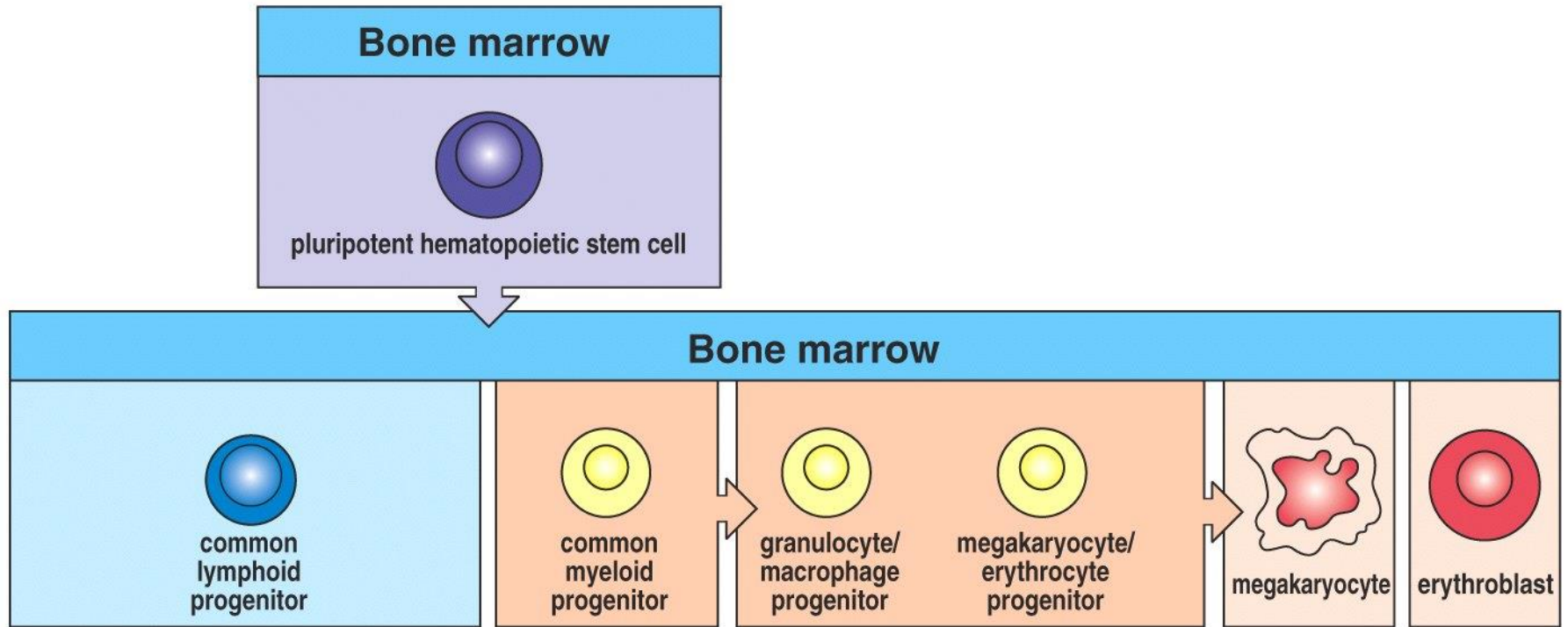


Figure 1-3 part 1 of 4 Immunobiology, 6/e. (© Garland Science 2005)

Growth and differentiation factors (cytokines) produced by and present on bone marrow stromal cells determine the type of white blood cell that will emerge, as well as their relative numbers.

Blood cells derived from bone marrow cells

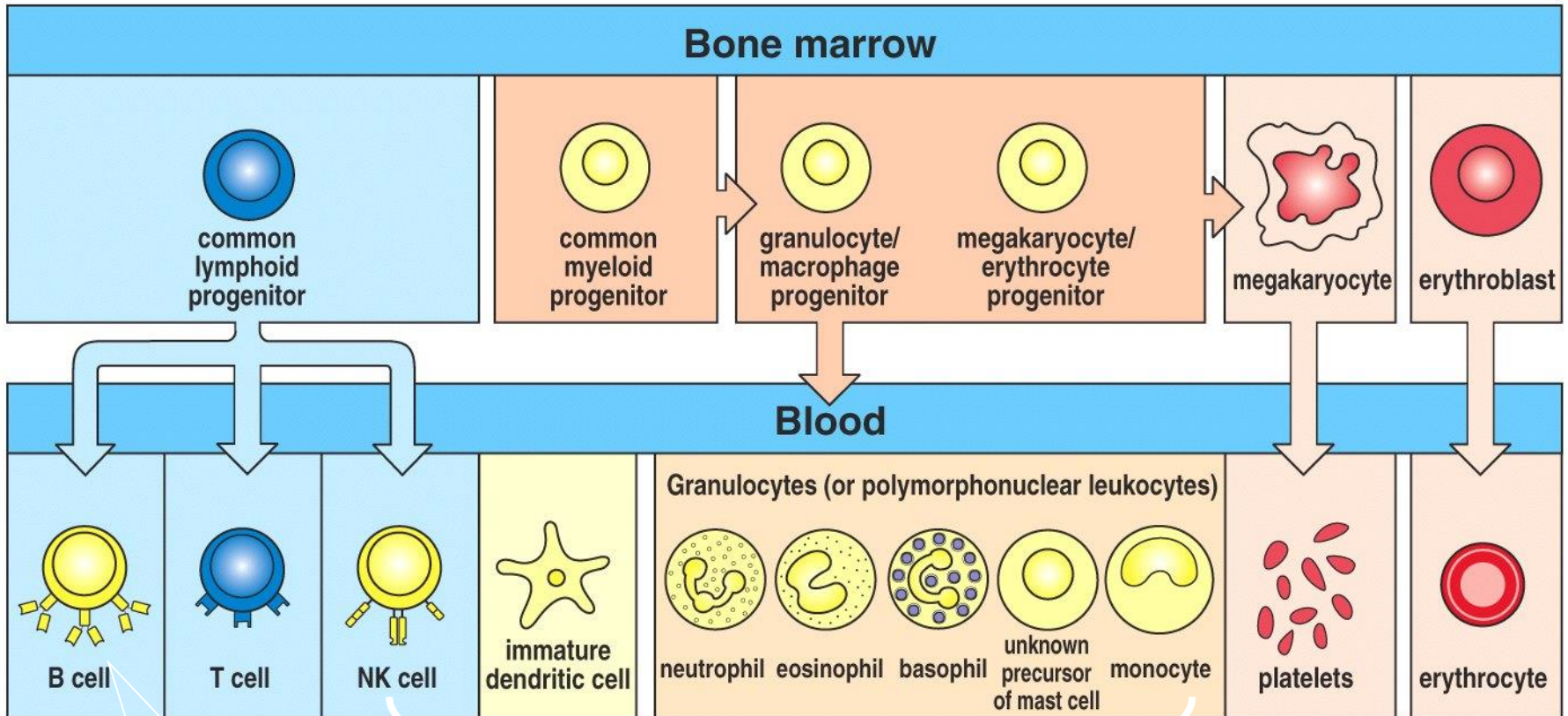


Figure 1-3 part 2 of 4 Immunobiology, 6/e. (© Garland Science 2005)

Adaptive imm

Innate imm

Blood cells migrate through blood and lymph nodes or home to tissues

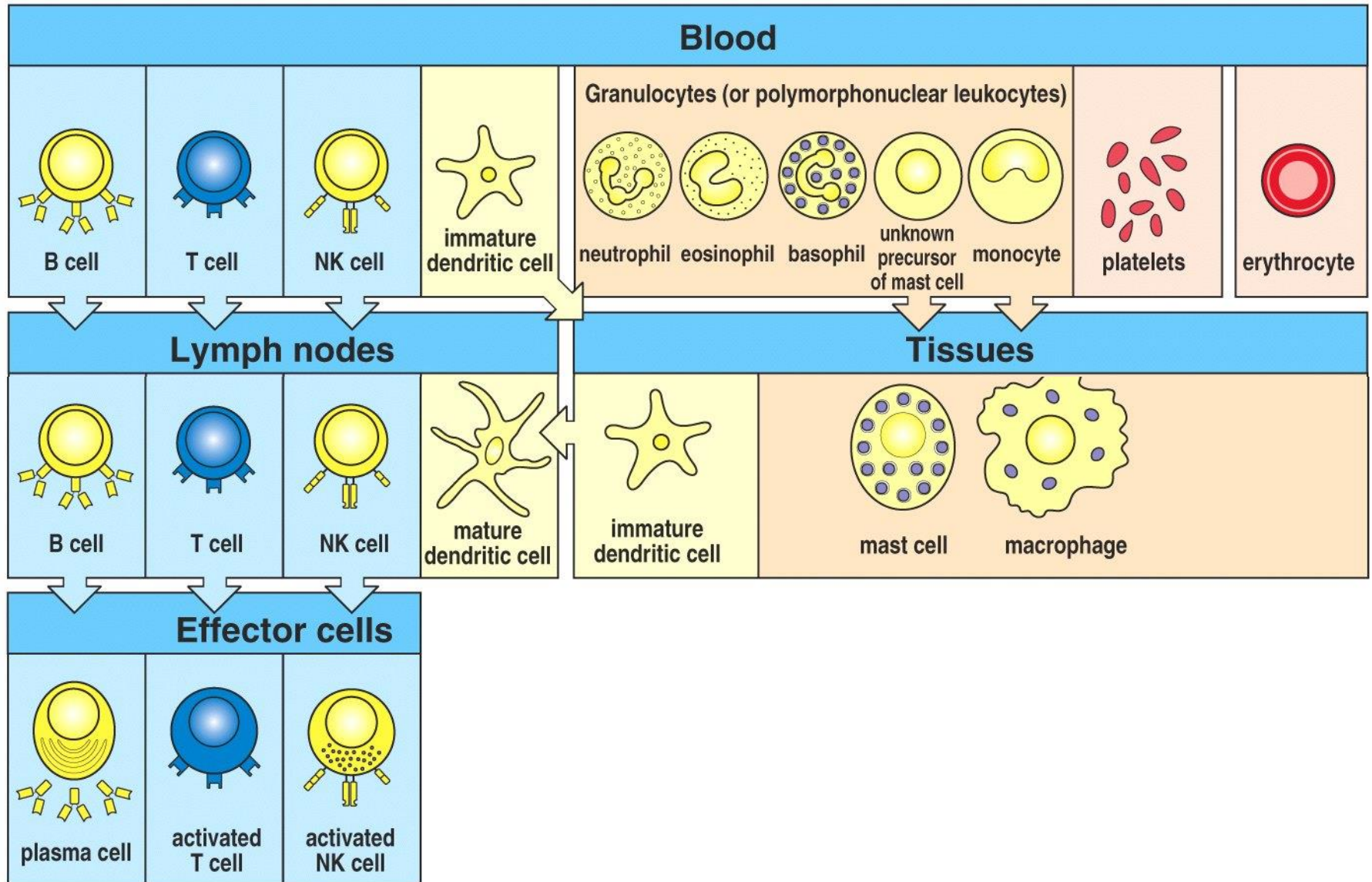
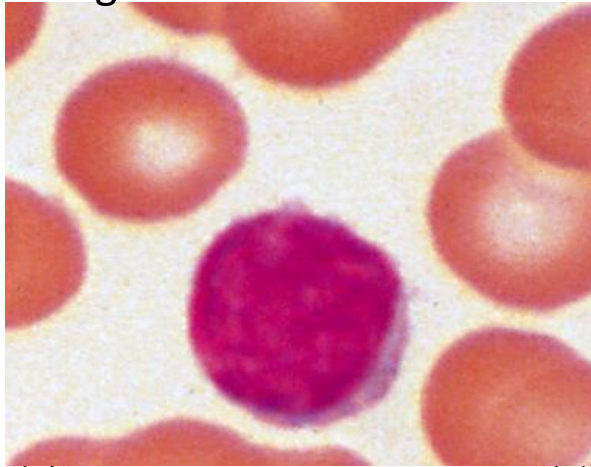


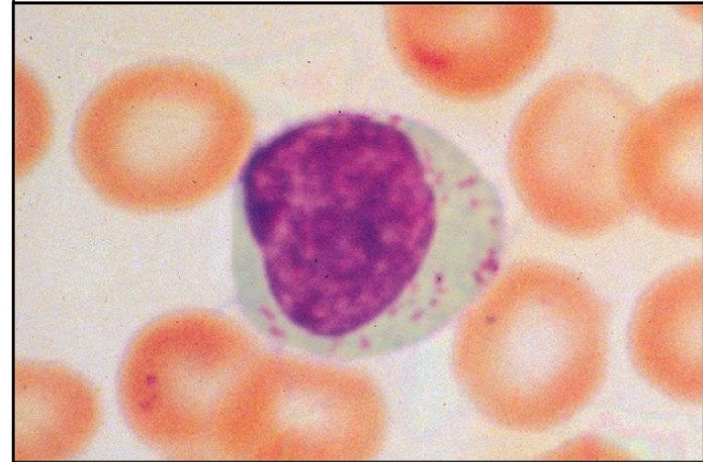
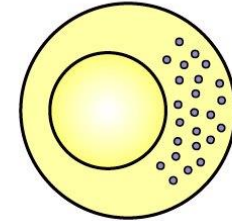
Figure 1-3 part 4 of 4 Immunobiology, 6/e. (© Garland Science 2005)

Lymphoid cells

Resting lymphocytes are round cells with a large nucleus



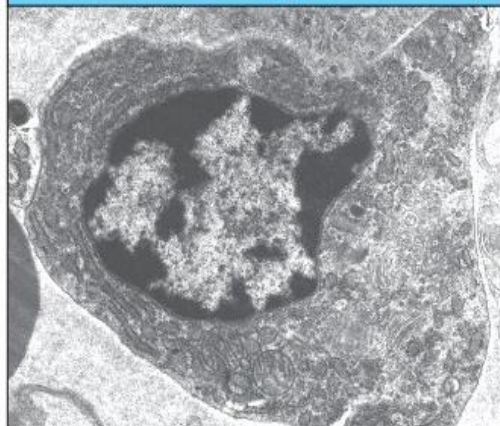
Natural killer (NK) cell



Releases lytic granules that kill some virus-infected cells

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

Effector B cell (plasma cell)



Effector T cell

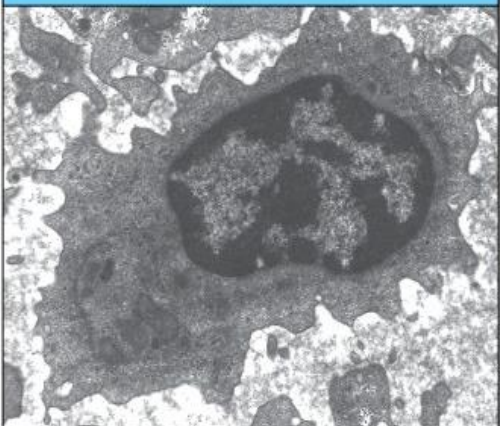
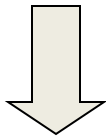


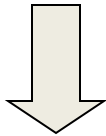
Figure 1-19 Immunobiology, 6/e. (© Garland Science 2005)

Lymphocyte proliferate and differentiate into effector and memory cells

Lymphocyte stimulation



Lymphocytes change function and morphology on antigen stimulation



Effector cells attack invading pathogens

Memory cells protect against a new infection

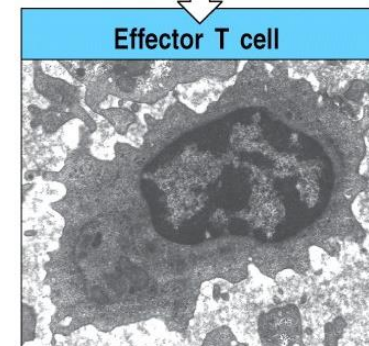
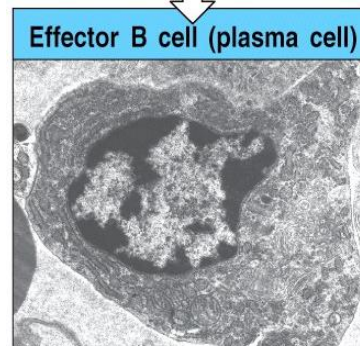
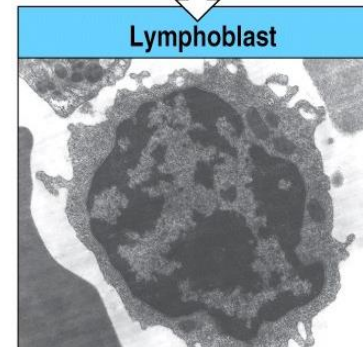
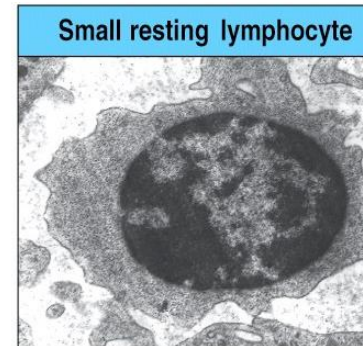


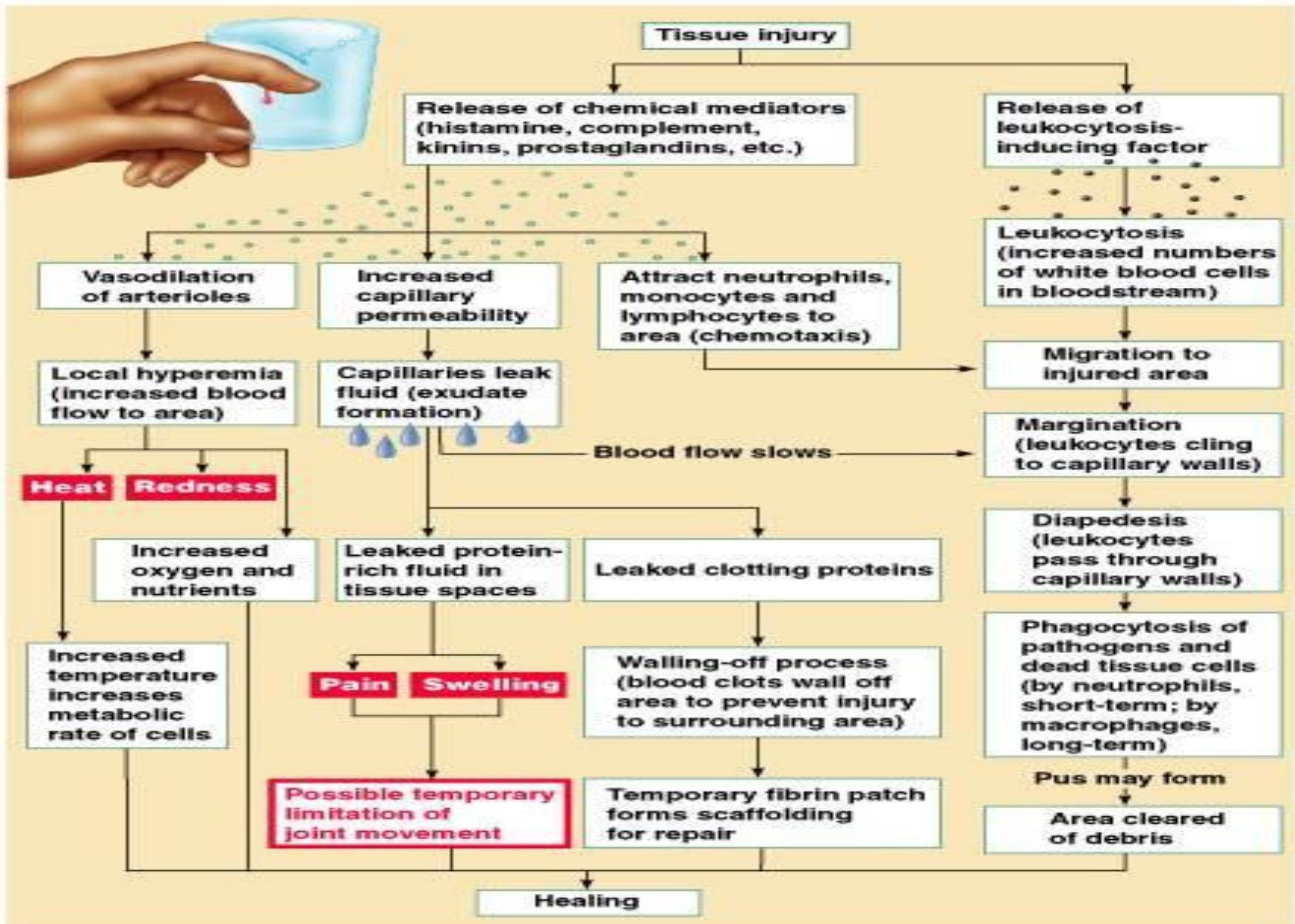
Figure 1-19 Immunobiology, 6/e. (© Garland Science 2005)

Inflamasi/ Peradangan

- Merupakan respons lokal tubuh thd infeksi atau perlukaan
- Tidak spesifik hanya untuk infeksi mikroba, tetapi respons yg sama juga terjadi pada perlukaan akibat suhu dingin, panas, atau trauma
- Pemeran utama: fagosit, a.l: neutrofil, monosit, & makrofag

Tahap inflamasi

1. Masuknya bakteri ke dalam jaringan
2. Vasodilatasi sistem mikrosirkulasi area yg terinfeksi → meningkatkan aliran darah (RUBOR/kemerahan & CALOR/panas)
3. Permeabilitas kapiler & venul yang terinfeksi terhadap protein meningkat → difusi protein & filtrasi air ke interstisial (TUMOR/bengkak & DOLOR/nyeri)
4. Keluarnya neutrofil lalu monosit dari kapiler & venula ke interstisial
5. Penghancuran bakteri di jaringan → fagositosis (respons sistemik: demam)
6. Perbaikan jaringan



Step of immune response

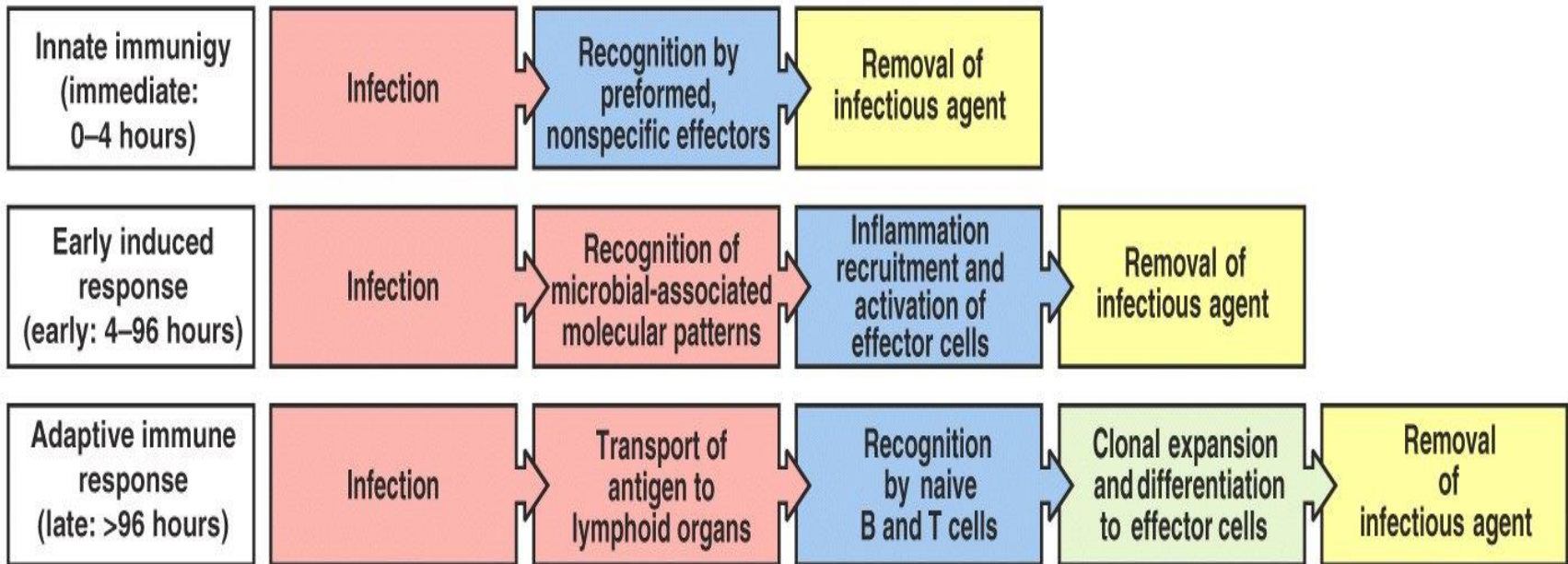


Figure 2-1 Immunobiology, 6/e. (© Garland Science 2005)

The response to an initial infection occurs in three phases

Inflammation

Infection triggers **inflammatory response** by activating innate immunity

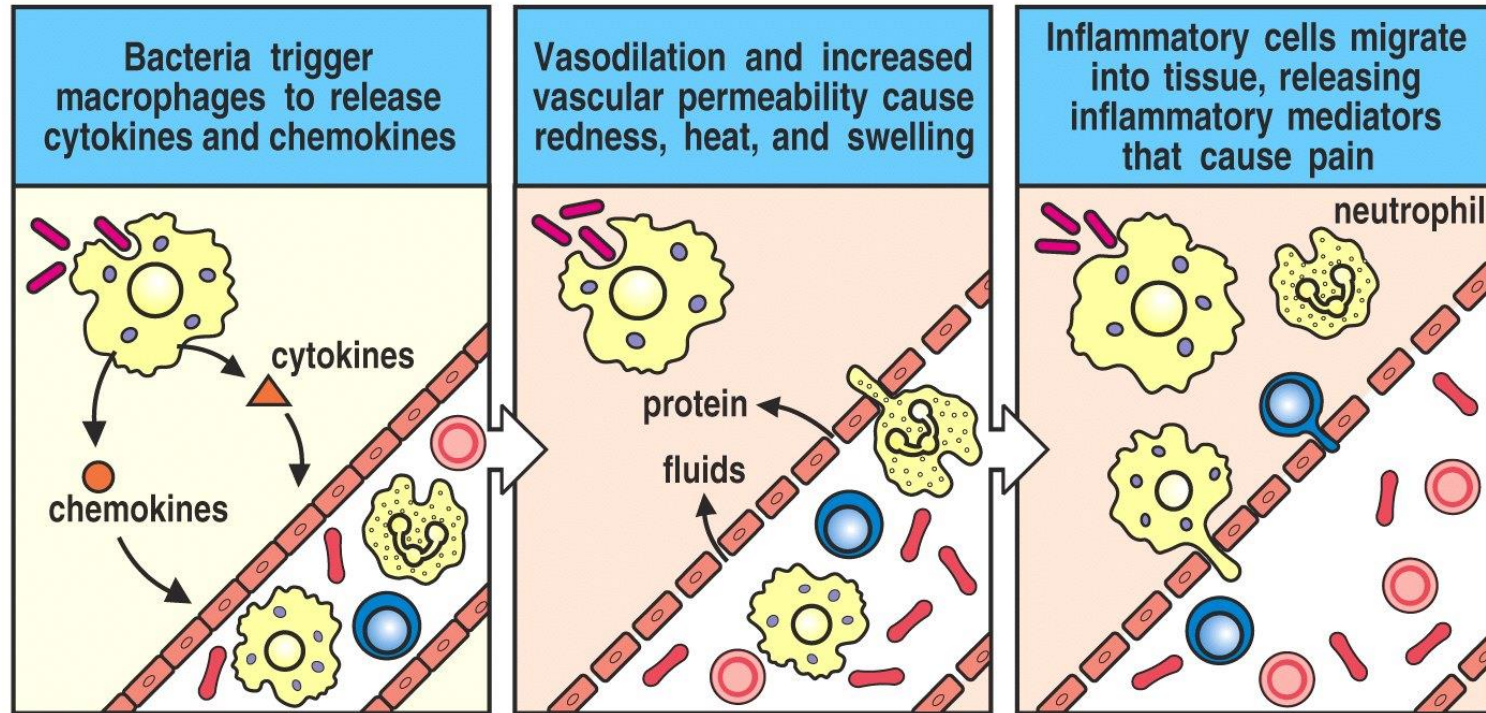


Figure 1-12 Immunobiology, 6/e. (© Garland Science 2005)

Inflammatory cells: macrophages, granulocytes

Inflammatory mediators: chemokines, cytokines, complement etc.

Inflammation increase flow of lymph containing Ag-bearing cells to LN

Antibodies

Immunity mediated by Ab:
humoral immunity

B cells produce antibodies
which can recognize **soluble**
antigen → **ch.9**

An immunoglobulin molecule
has two identical H-chains
and two identical L-chains

The variable regions of Abs
are encoded by multiple gene
fragments (**chapter 4**)

Variable region determine Ag
binding specificity

Structure of an antibody molecule

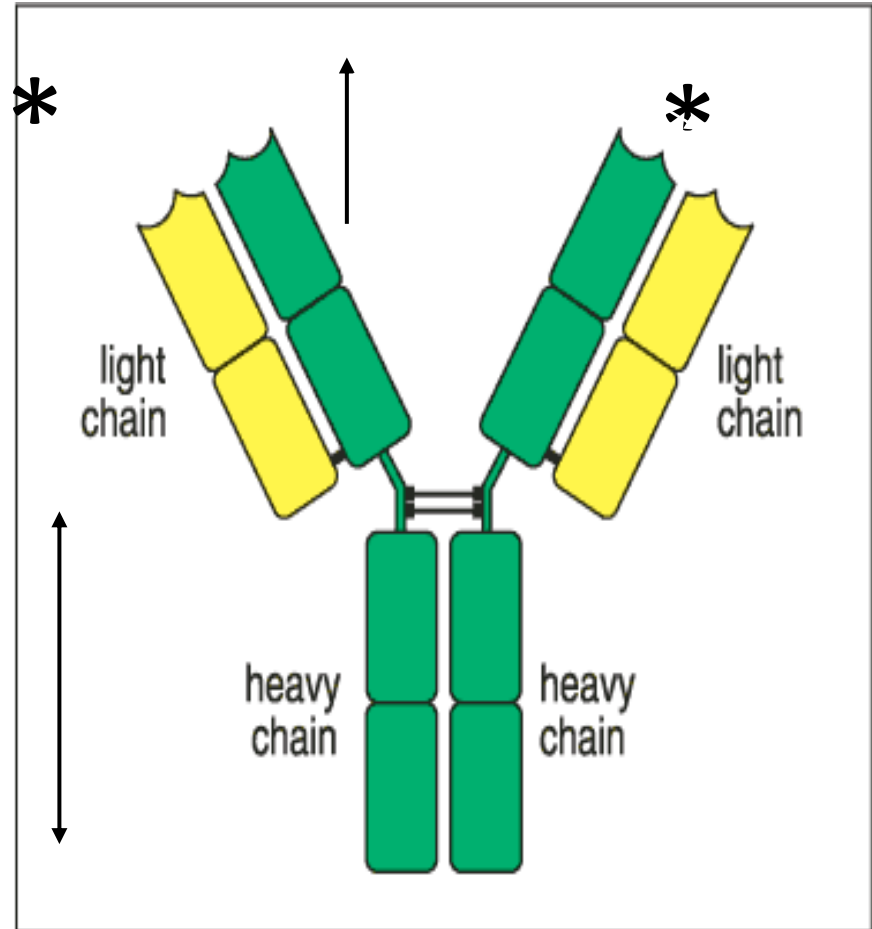
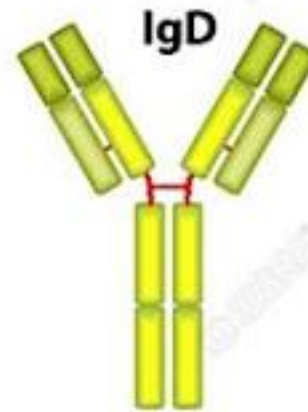
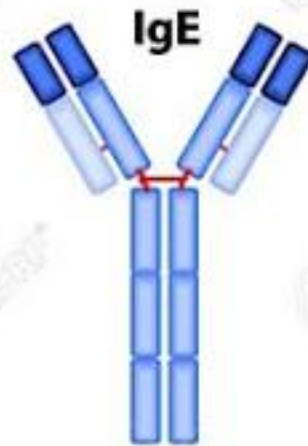
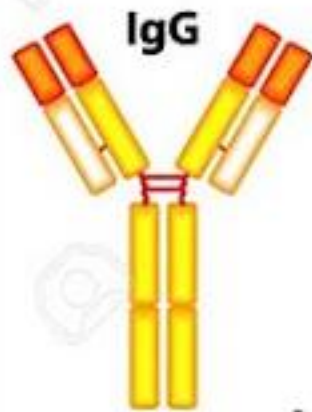


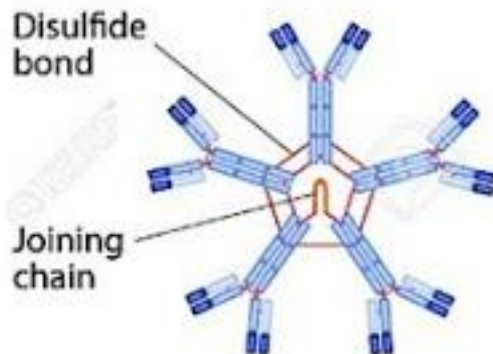
Fig 1.17 © 2001 Garland Science

Immunoglobulin is a general term for antibody

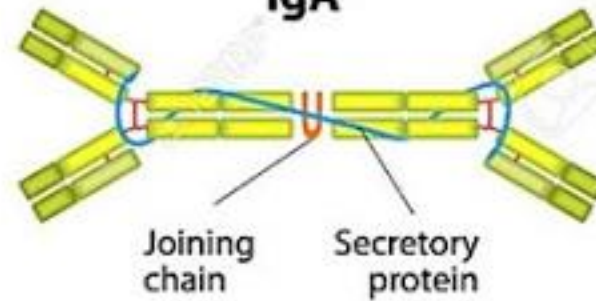
ANTIBODY CLASSIFICATION



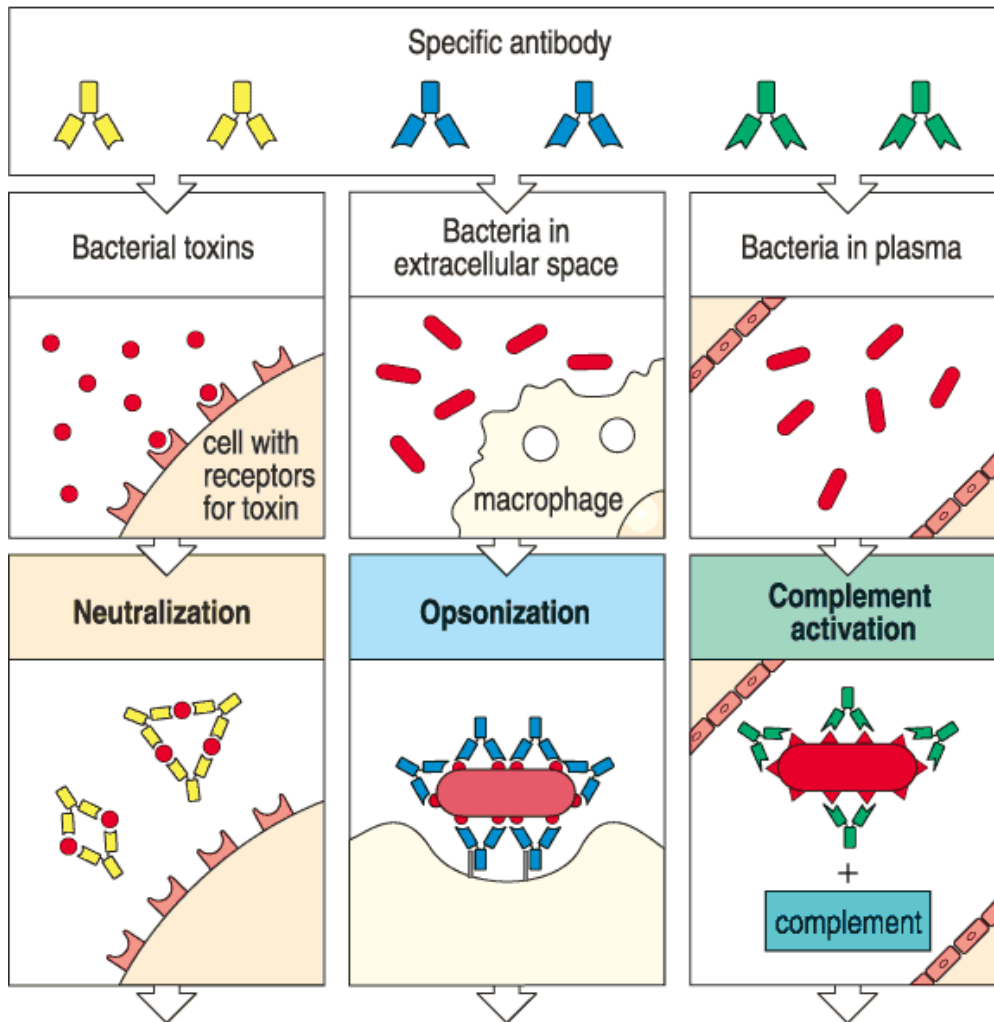
IgM



IgA



Protective function of antibodies



- a. Blockage of adhesion to cell surface
- b. Attachment of antibodies to enhance uptake and degradation in phagocytes
- c. Attachment of antibodies to enhance lysis by complement (chapter 2)

Fig 1.24 part 1 of 2 © 2001 Garland Science

a b c

Macrophages and antibodies play a prominent role in the removal of antigens and cell debris

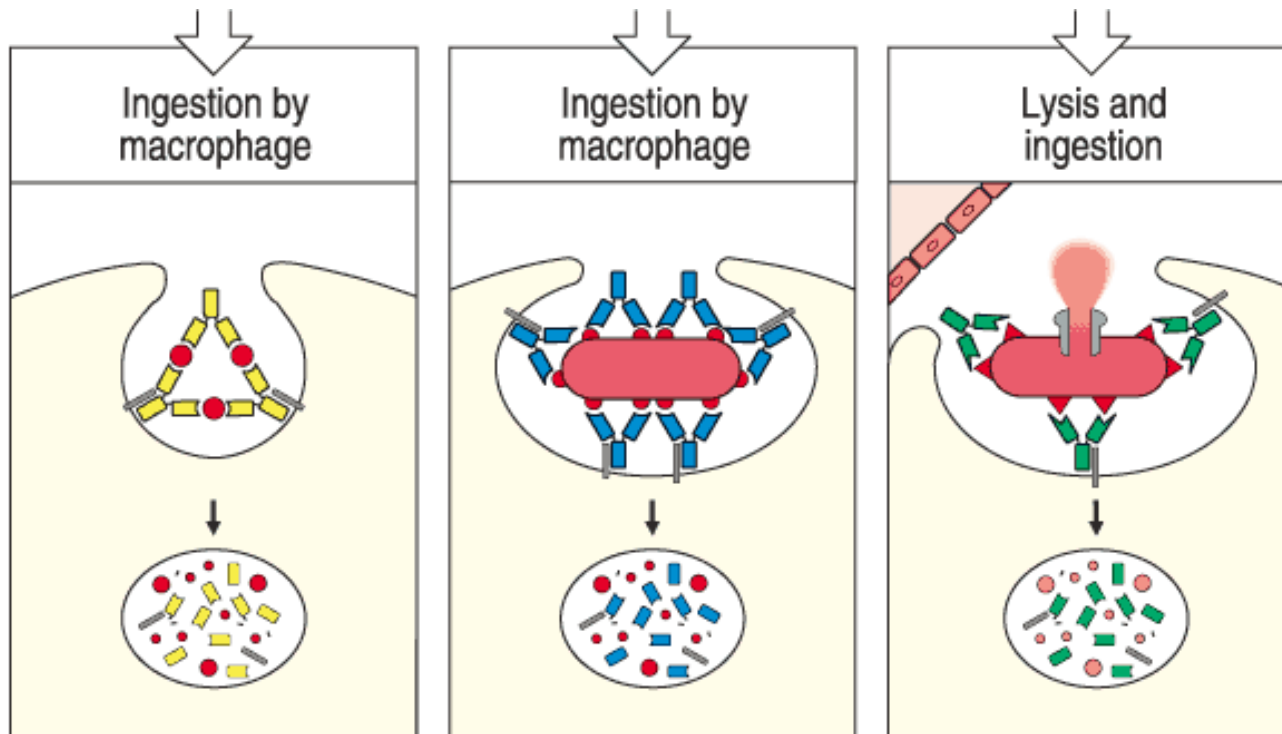


Fig 1.24 part 2 of 2 © 2001 Garland Science

Opsonisation by antibodies / complement enhances uptake and degradation

The course of typical antibody response

Vaccination induces the production of protective antibodies by plasma cells B cells

Ch.14

B cells response to antigenic stimulation:

1. Proliferation and maturation: formation of plasma cells + memory cells
2. Secretion of antibodies

Repeated stimulation with the **same** antigen increases the antibody concentration to that antigen

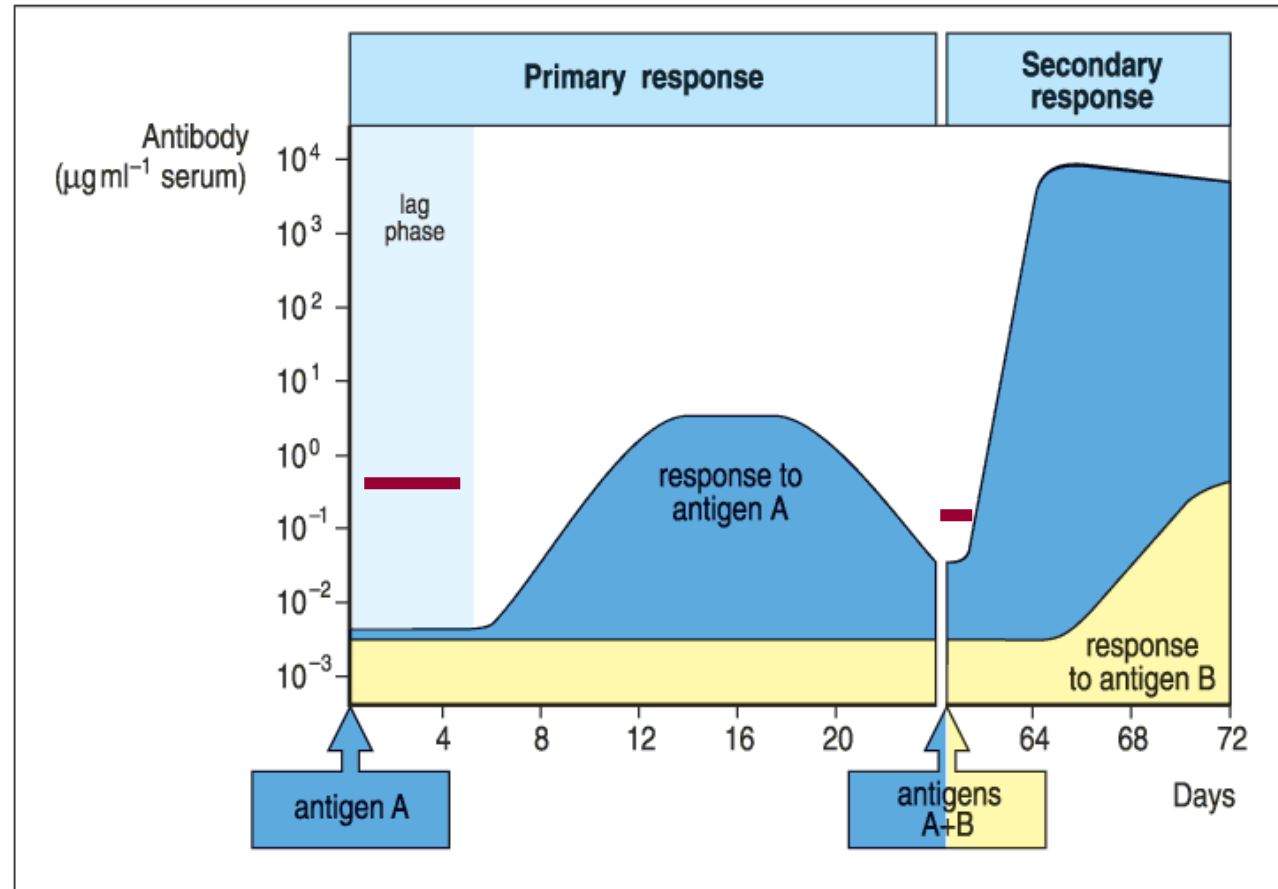


Fig 1.20 © 2001 Garland Science

Immunological memory

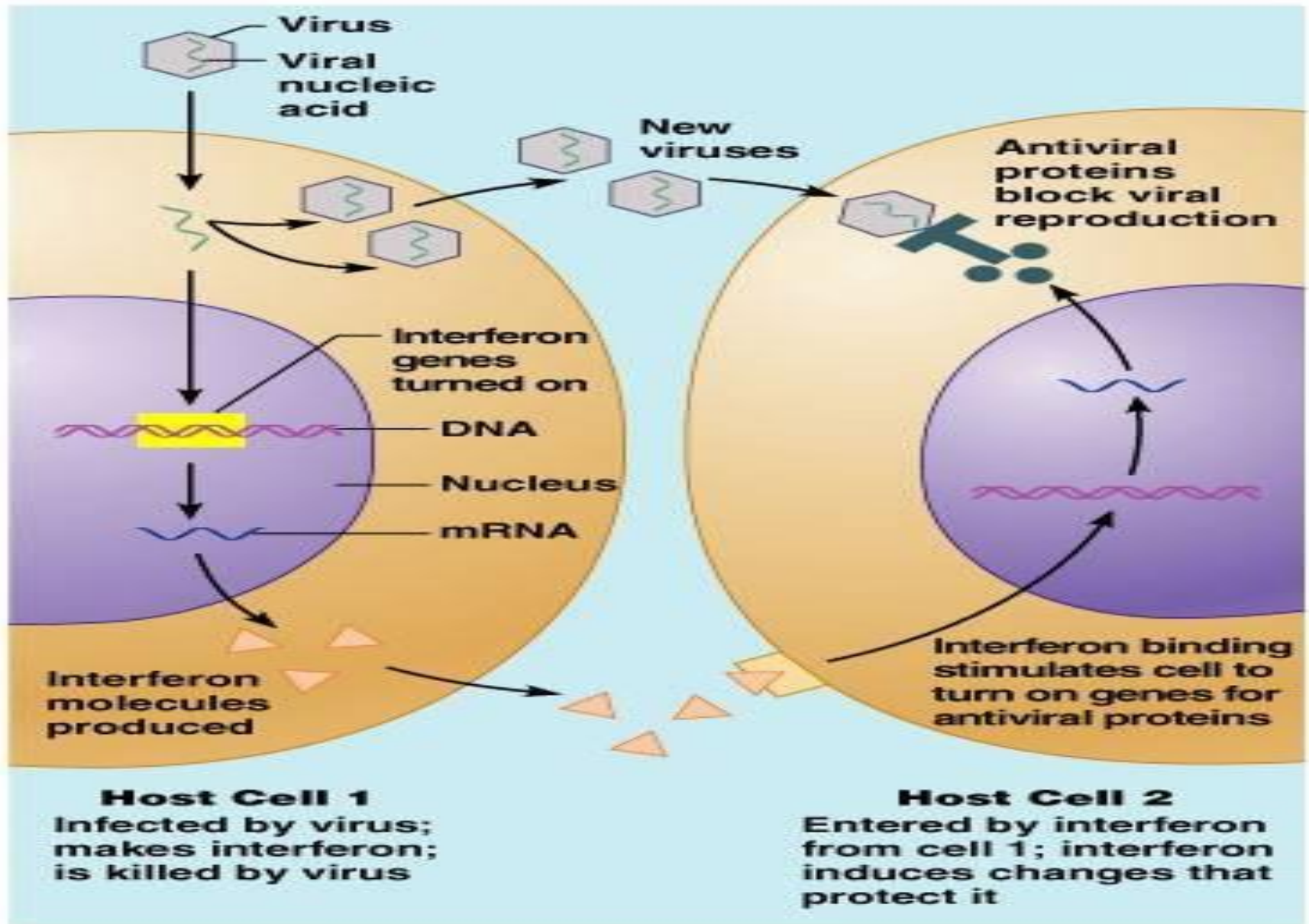
Ability of immune system to make second response to same ag more effective & efficiently

Find me → nafida@gmail.com

TERIMAKASIH

Interferon

- Sel yang terinfeksi virus akan mengeluarkan interferon
- Interferon mengganggu replikasi virus (antivirus); 'interfere'
- Interferon juga memperlambat pembelahan & pertumbuhan sel tumor dgn meningkatkan potensi sel NK & sel T sitotoksik (antikanker)
- Peran interferon yg lain: meningkatkan aktivitas fagositosis makrofag & merangsang produksi antibodi



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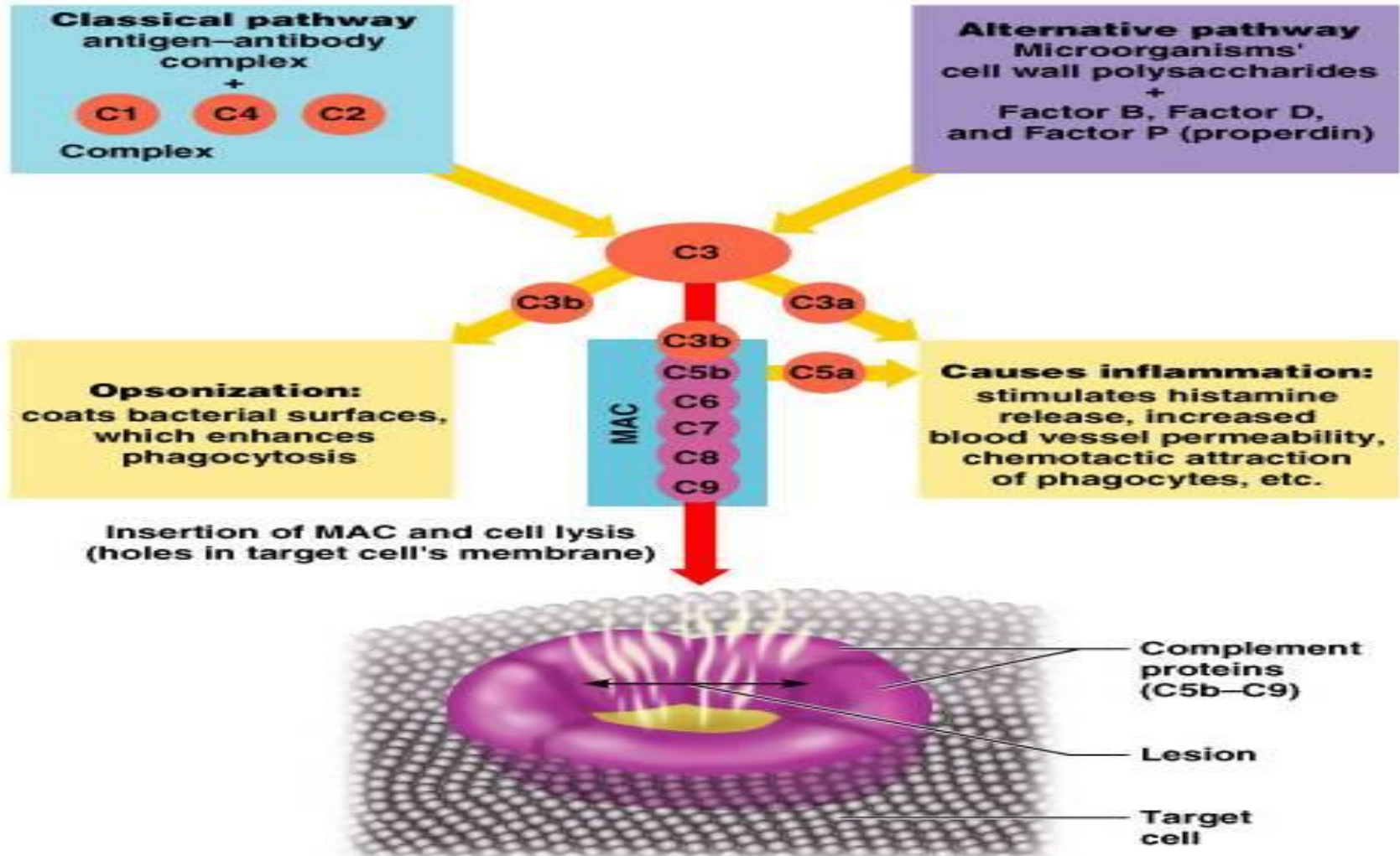
Sel *Natural Killer* (NK)

- Merusak sel yg terinfeksi virus & sel kanker dengan melisiskan membran sel pd paparan I
- Kerjanya = sel T sitotoksik, ttp lebih cepat, non-spesifik, & bekerja sebelum sel T sitotoksik mnjd lebih banyak & berfungsi

Sistem Komplemen

- Sistem ini diaktifkan oleh:
 - (1) paparan rantai karbohidrat yg ada pd permukaan mikroorganisme yg tdk ada pd sel manusia
 - (2) paparan antibodi yang diproduksi spesifik untuk zat asing tertentu oleh sistem imun adaptif
- Bekerja sbg ‘komplemen’ dari kerja antibodi

Aktivasi Sistem Komplemen

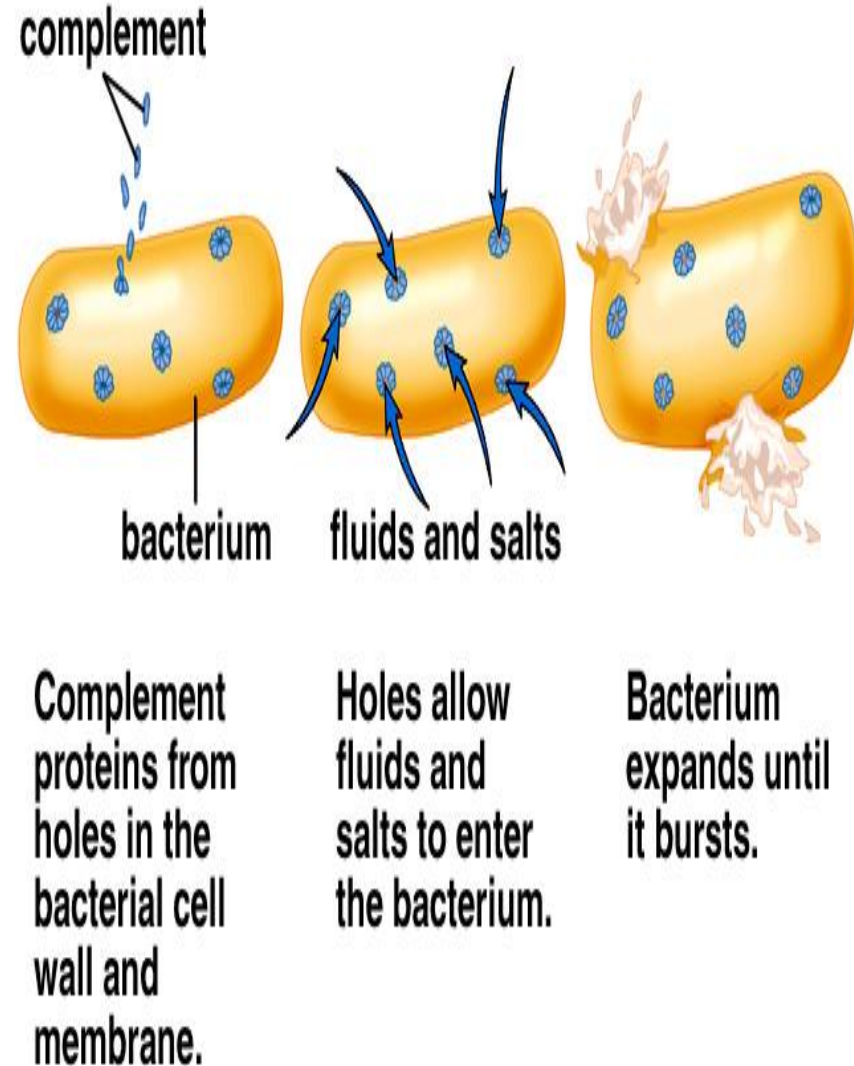


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Komplemen yg teraktivasi akan:

1. Berikatan dg basofil & sel mast & menginduksi pelepasan histamin → reaksi inflamasi
2. Berperan sbg faktor kemotaksis yang meningkatkan fagositosis
3. Berikatan dg permukaan bakteri & bekerja sbg opsonin (opsonisasi) → fagositosis
4. Menempel pd membran & membentuk struktur berbentuk tabung yg melubangi membran sel & menyebabkan lisis sel.

Action of the complement system against a bacterium



Sistem Kekebalan Spesifik

- Atau sistem kekebalan adaptif dapat menghancurkan patogen yang lolos dari sistem kekebalan non-spesifik.
- Mencakup:
 - (1) kekebalan humoral → produksi antibodi oleh limfosit B (sel plasma)
 - (2) kekebalan selular → produksi limfosit T yg teraktivasi
- Harud dapat membedakan sel asing yg harus dirusak dari sel-diri → antigen (molekul besar, kompleks, & unik yg memicu respons imun spesifik jika masuk ke dalam tubuh)

Sistem Kekebalan Humoral

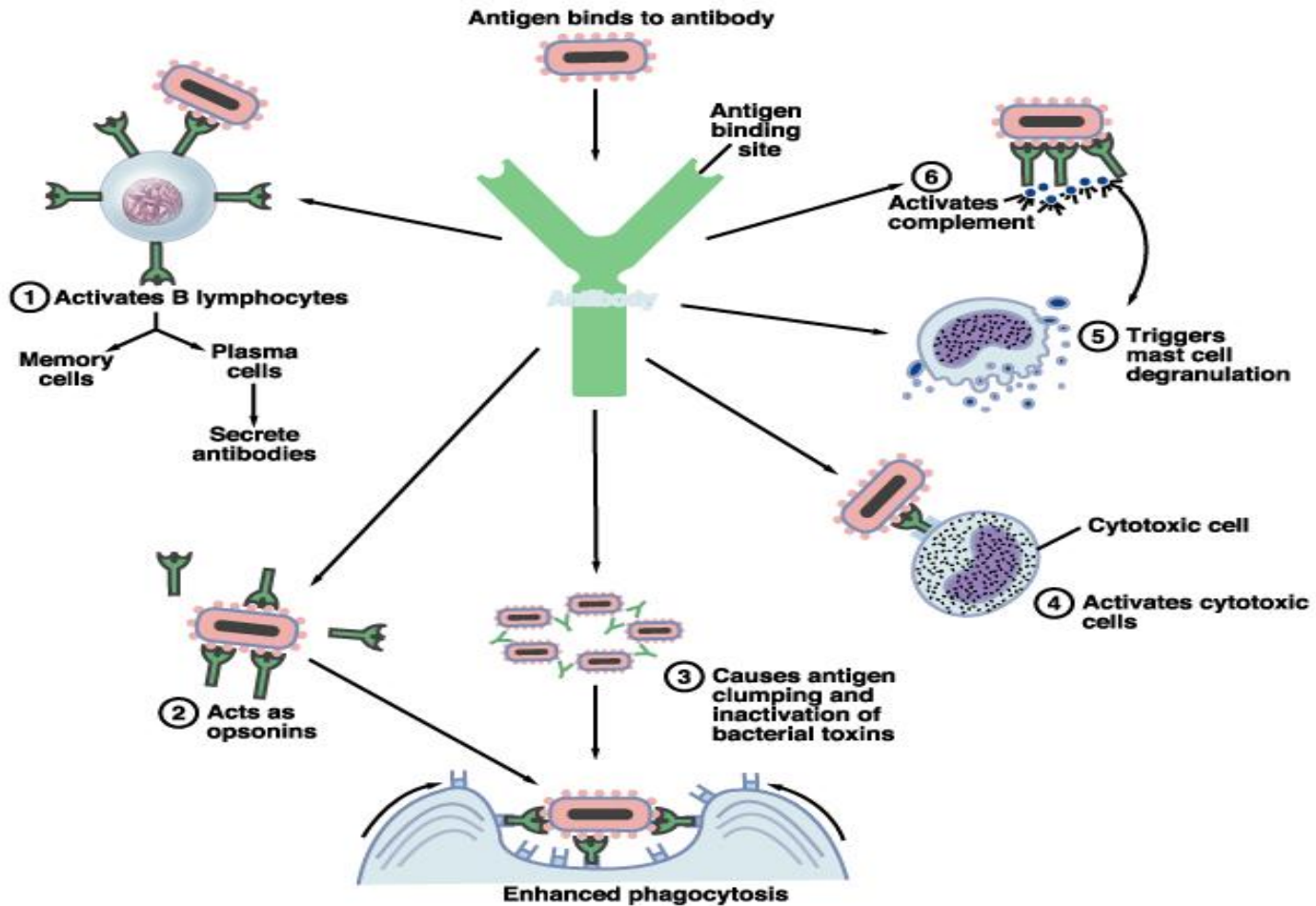
- Antigen (Ag) merangsang sel B berubah menjadi sel plasma yg memproduksi antibodi (Ab).
- Ab disekresi ke darah atau limf ~ lokasi sel plasma yg teraktivasi; semua Ab akan mencapai darah \Rightarrow gamma globulin = imunoglobulin (Ig)

Imunoglobulin (Ig)

Ada 5 kelas:

1. Ig M → berperan sbg reseptor permukaan sel B & disekresi pd tahap awal respons sel plasma
2. Ig G → Ig terbanyak di darah, diproduksi jika tubuh berespons thd antigen yg sama
Ig M & IgG berperan jika tjd invasi bakteri & virus serta aktivasi komplemen
3. Ig E → melindungi tubuh dr infeksi parasit & mrp mediator pd reaksi alergi; melepaskan histamin dari basofil & sel mast
4. Ig A → ditemukan pd sekresi sistem pencernaan, pernapasan, & perkemihan (cth: pd airmata & ASI)
5. Ig D → terdapat pada banyak permukaan sel B; mengenali antigen pd sel B

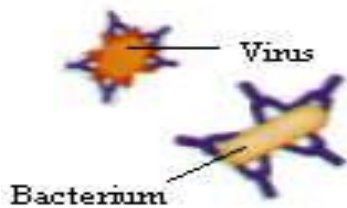
Fungsi Antibodi



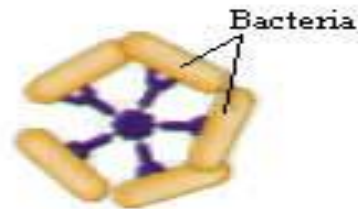
Reaksi Ag-Ab

Binding of antibodies to antigens
inactivates antigens by

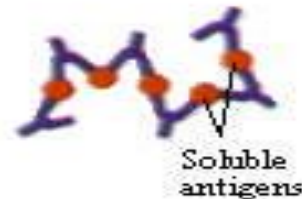
Blocking of viral binding
sites or bacterial antigens



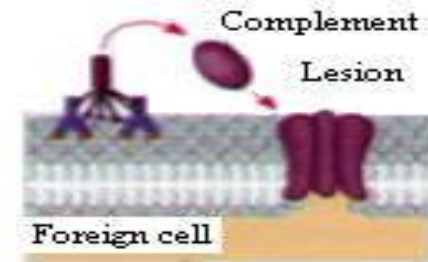
Agglutination of
particulate antigens



Precipitation of
soluble antigens

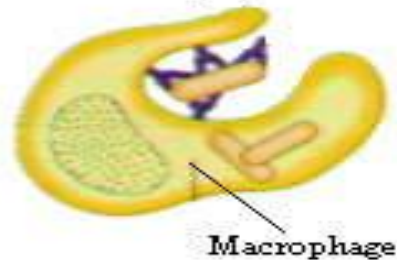


Activation of complement



Enhances

Phagocytosis

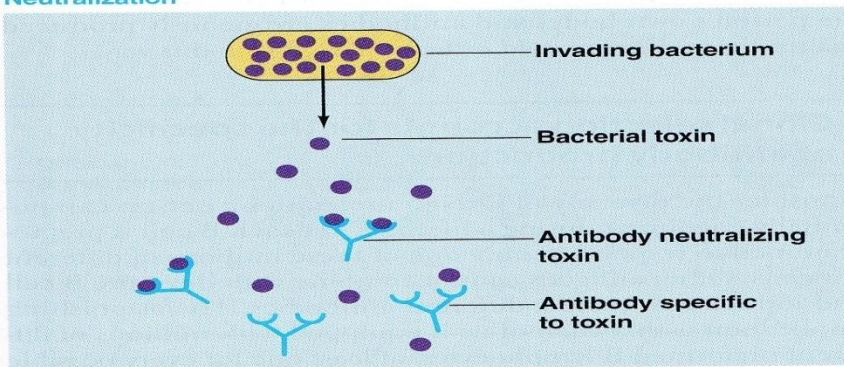


Leads to

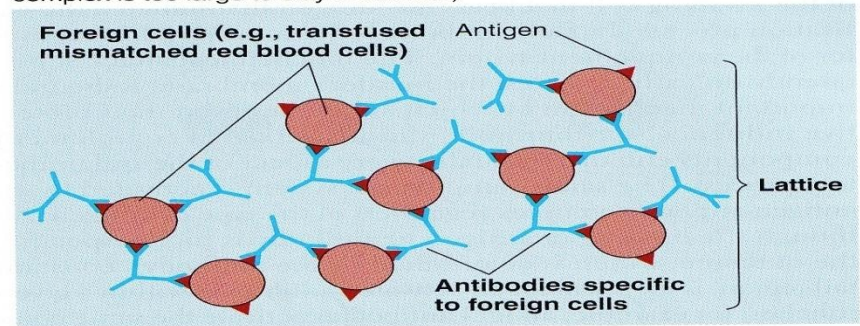
Cell lysis



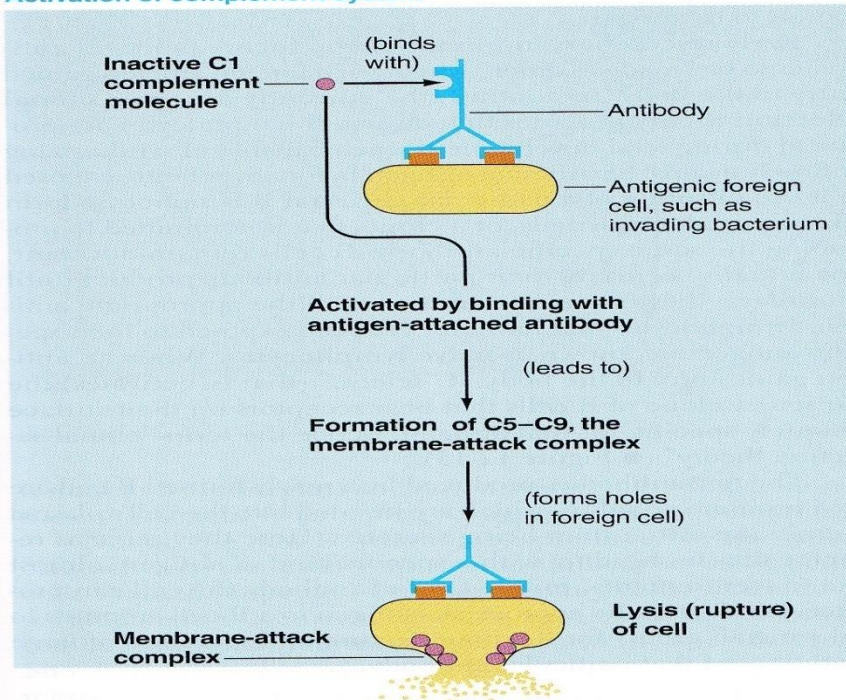
Neutralization



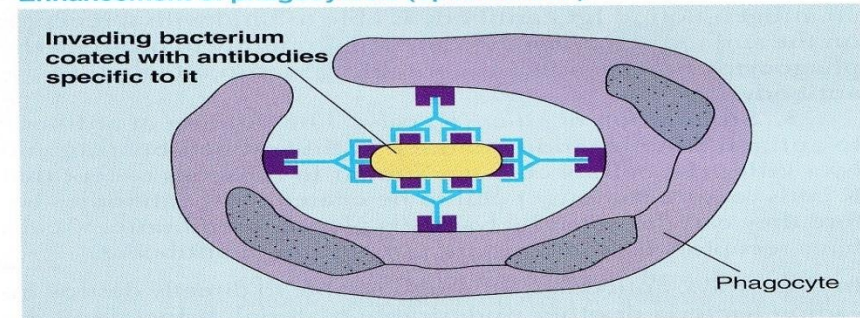
Agglutination (clumping of antigenic cells) and **precipitation** (if soluble antigen-antibody complex is too large to stay in solution)



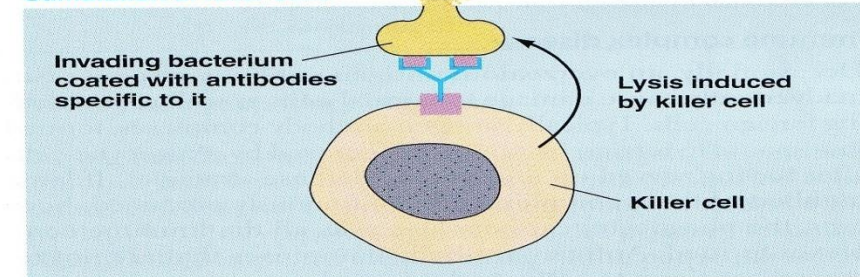
Activation of complement system



Enhancement of phagocytosis (opsonization)



Stimulation of killer cells



Structures are not drawn to scale.

● FIGURE 12-12

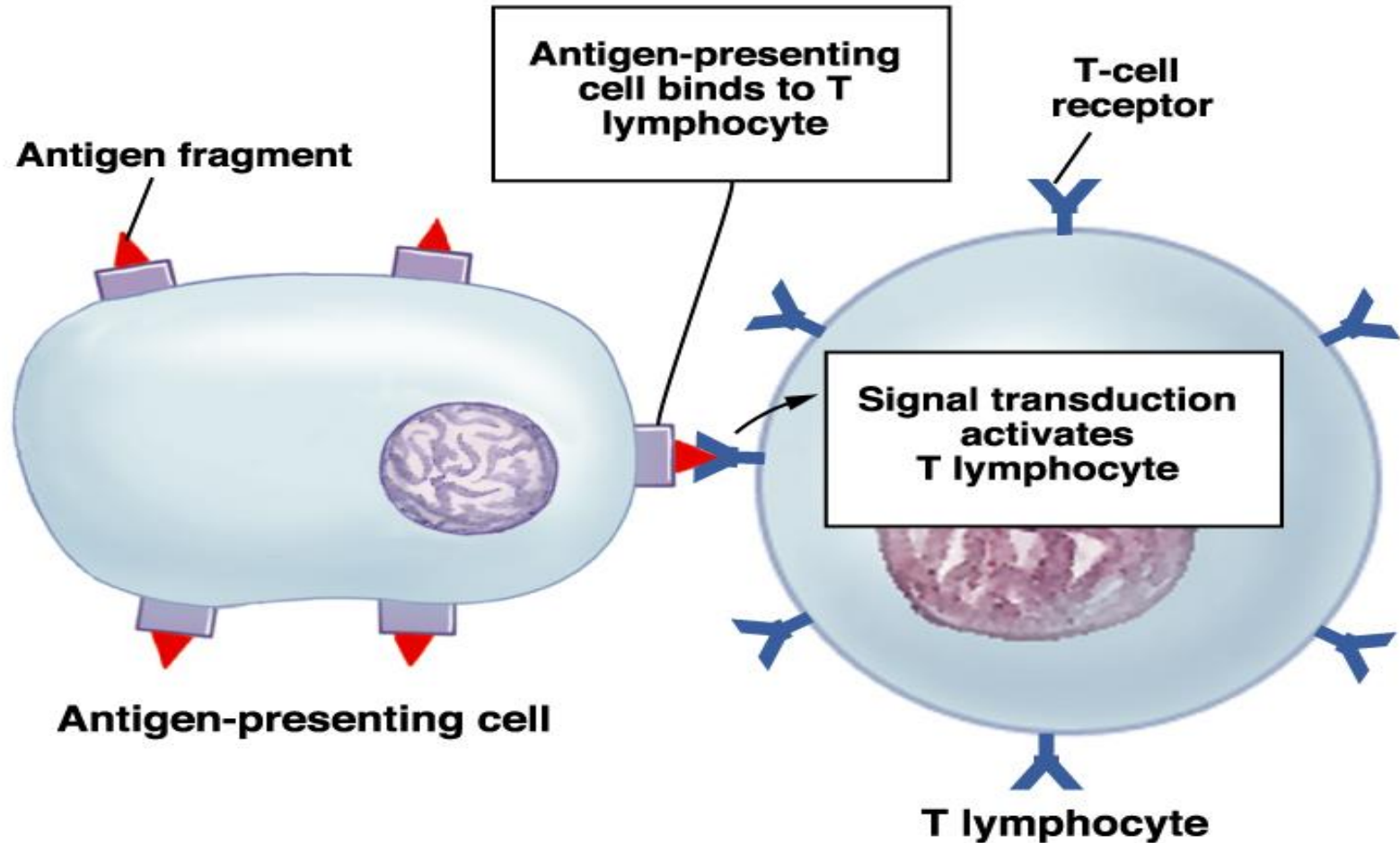
How antibodies help eliminate invading microbes

Antibodies physically hinder antigens through (1) neutralization or (2) agglutination and precipitation. Antibodies amplify innate immune responses by (1) activating the complement system, (2) enhancing phagocytosis by acting as opsonins, and (3) stimulating killer cells.

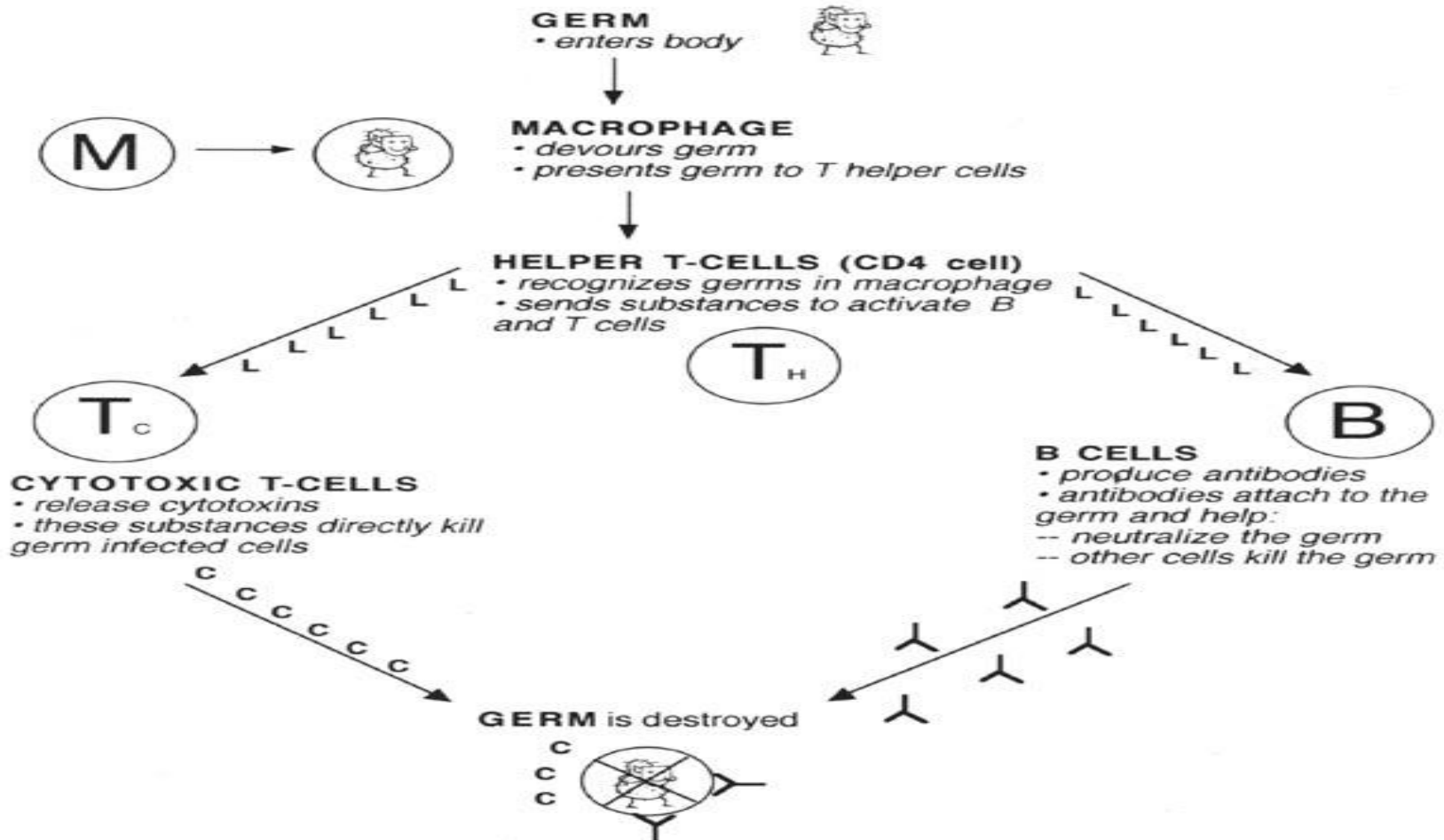
Sistem Kekebalan Seluler

- Limfosit T spesifik untuk kekebalan terhadap infeksi virus & pengaturan pd mekanisme kekebalan.
- Sel-sel T harus kontak langsung dg sasaran
- Ada 3 subpopulasi sel T: sel T sitotoksik, sel T penolong, & sel T penekan
- *Major histocompatibility complex* (MHC): kode human *leucocyte-associated antigen* (HLA) yg terikat pd permukaan membran sel; khas pd setiap individu
- Surveilans imun: kerjasama sel T sitotoksik, sel NK, makrofag, & interferon

Aktivasi Sel T



How the Immune System Works



If **GERM** enters the body again, **B-CELLS** and **T-CELLS** have a **MEMORY** and they will recognize the **GERM** and make **ANTIBODIES** and **CYTOTOXIC T-CELLS** to destroy it.

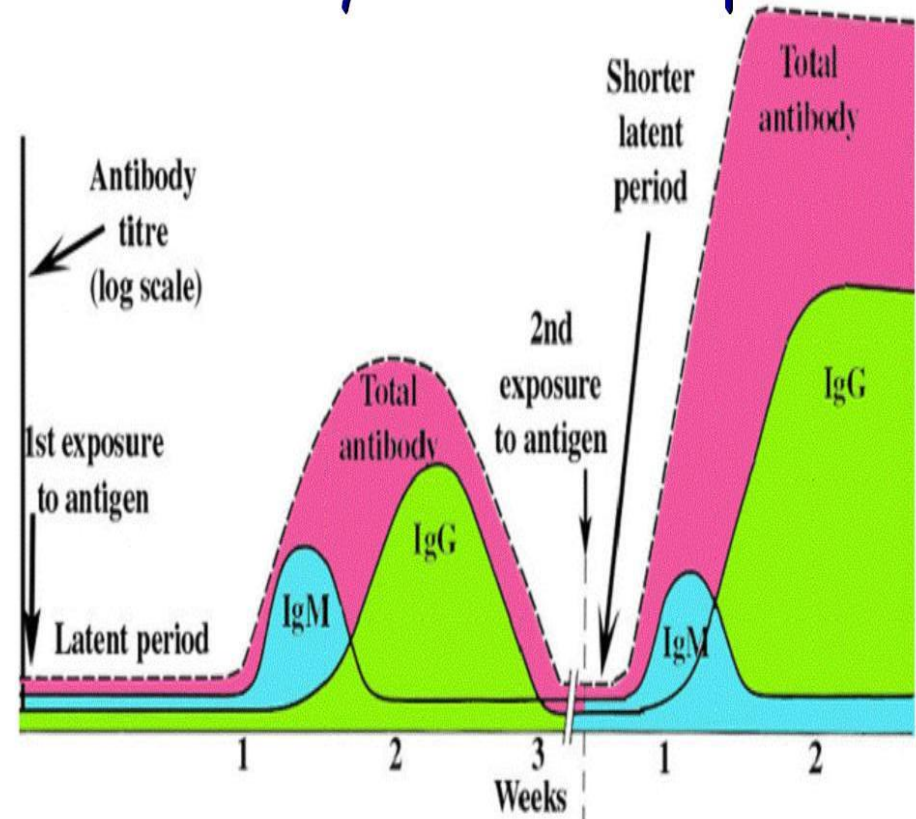
* Adapted from NYC Comprehensive Health Curriculum

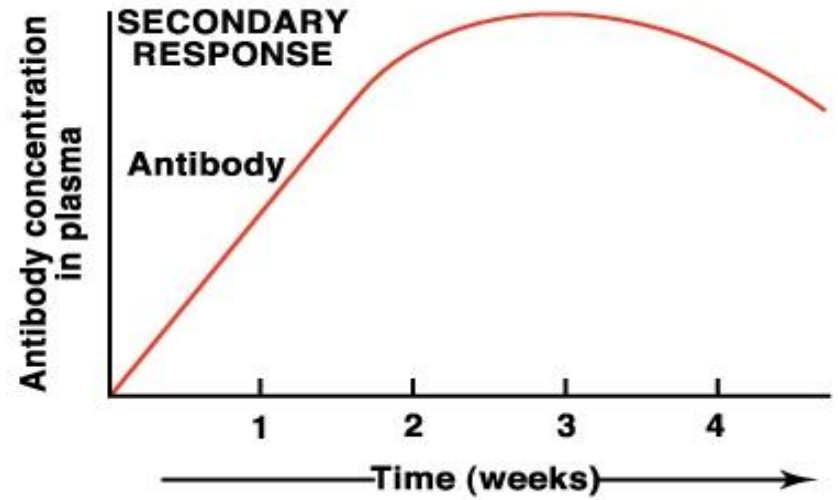
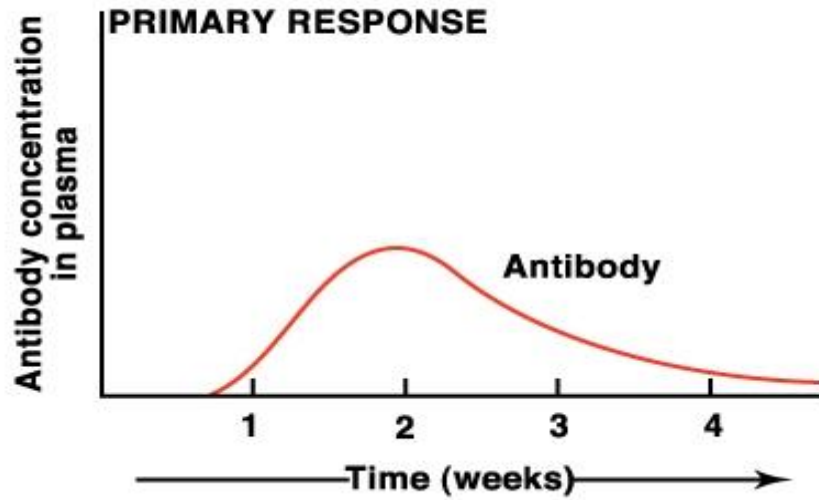
Pembentukan Kekebalan Jangka Panjang

(*long-term*)

- Pada kontak pertama dg antigen mikroba, respons antibodi terjadi lambat dlm bbrp hari sampai terbentuk sel plasma & akan mencapai puncak dlm bbrp minggu (Respons primer); & akan membentuk sel memori
- Jika terjadi kontak dg antigen yg sama, krn adanya sel memori, respons yg terjadi mjdn lebih cepat (Respons sekunder)

The Memory Immune Response





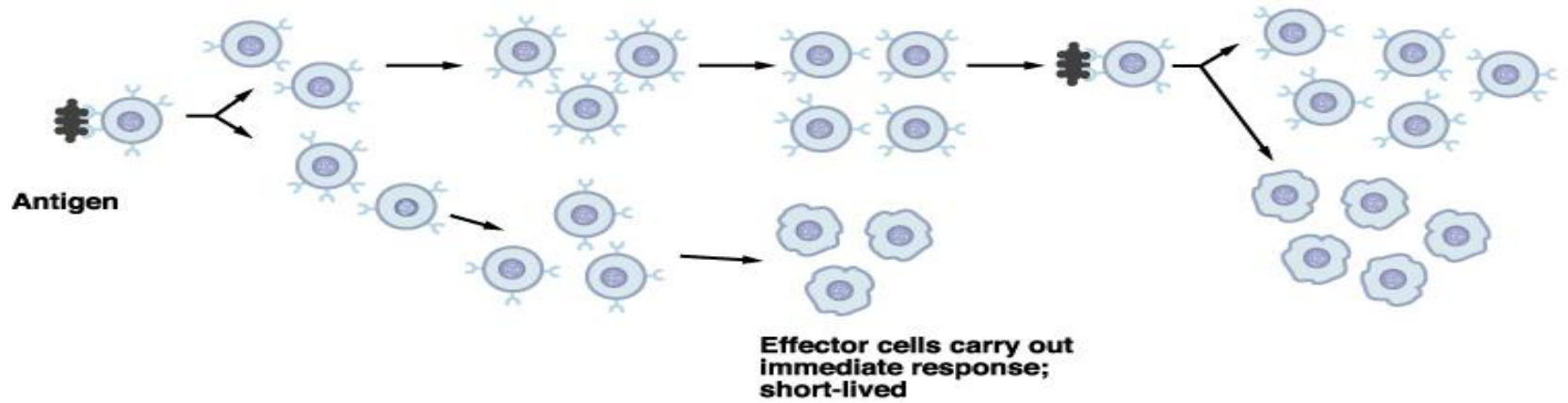
First exposure to antigen

Clonal expansion

Memory cells are long-lived, continue to reproduce

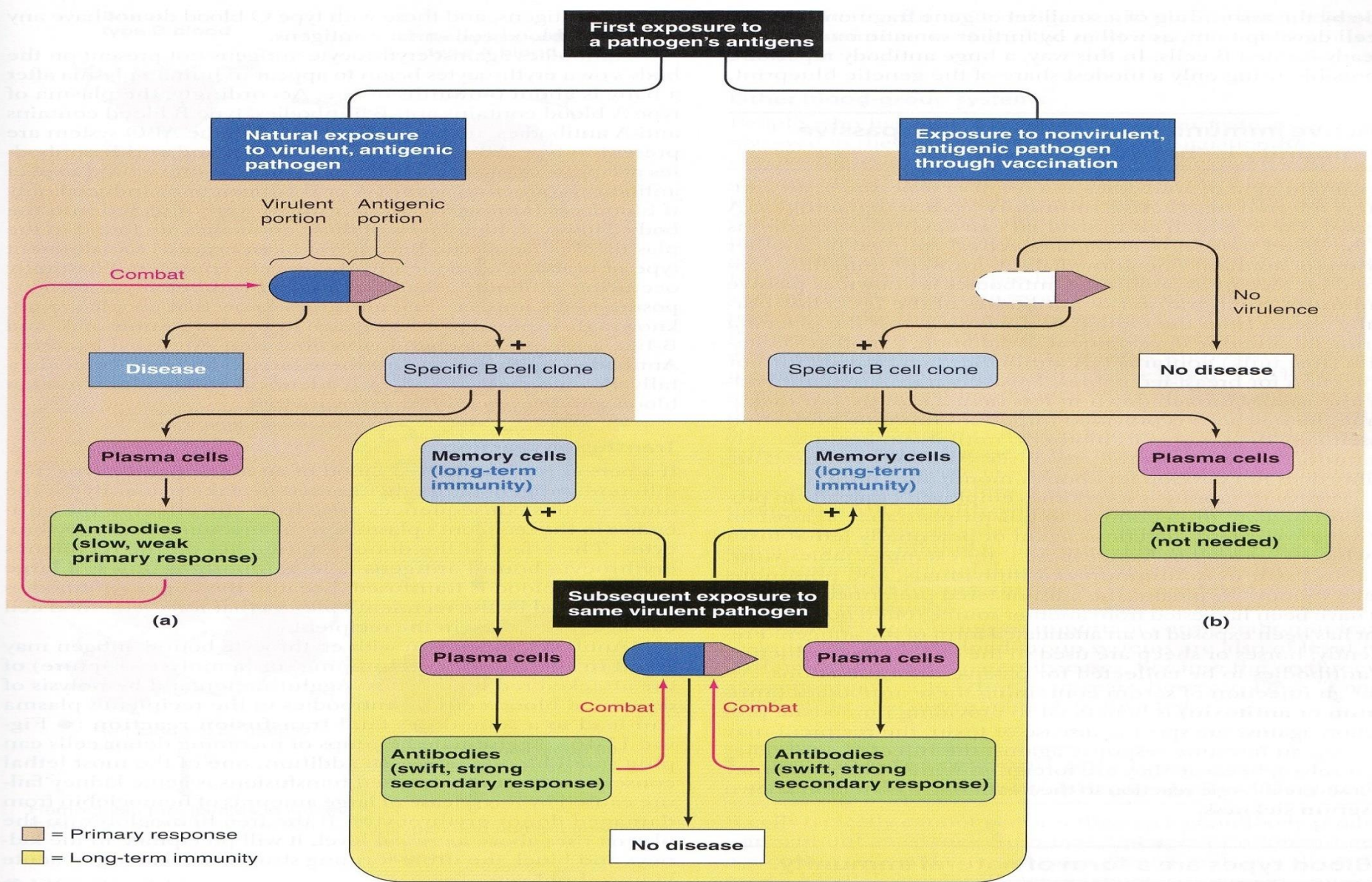
Second exposure to antigen

Stronger and more rapid response



Primary response

Secondary response

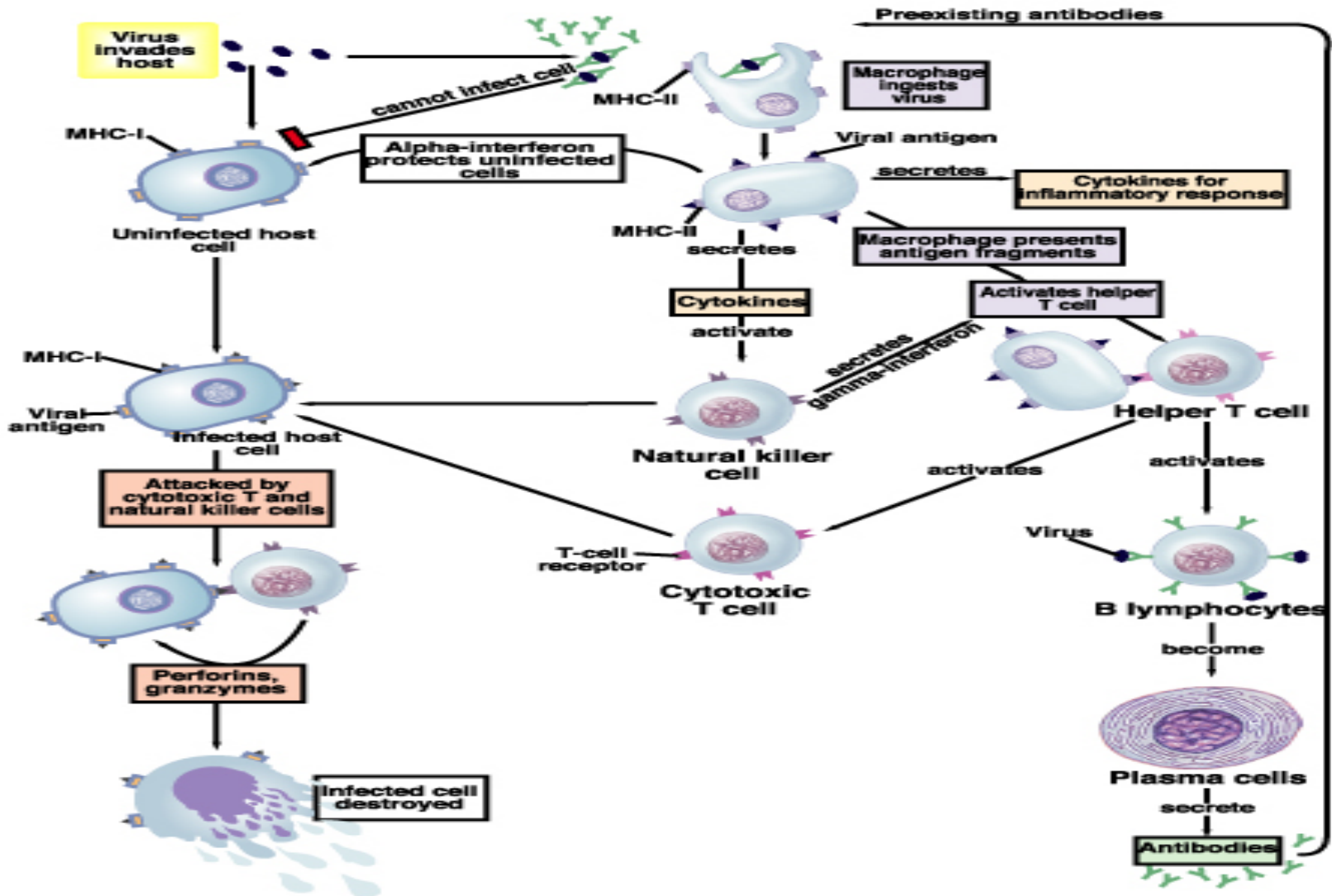


● FIGURE 12-15

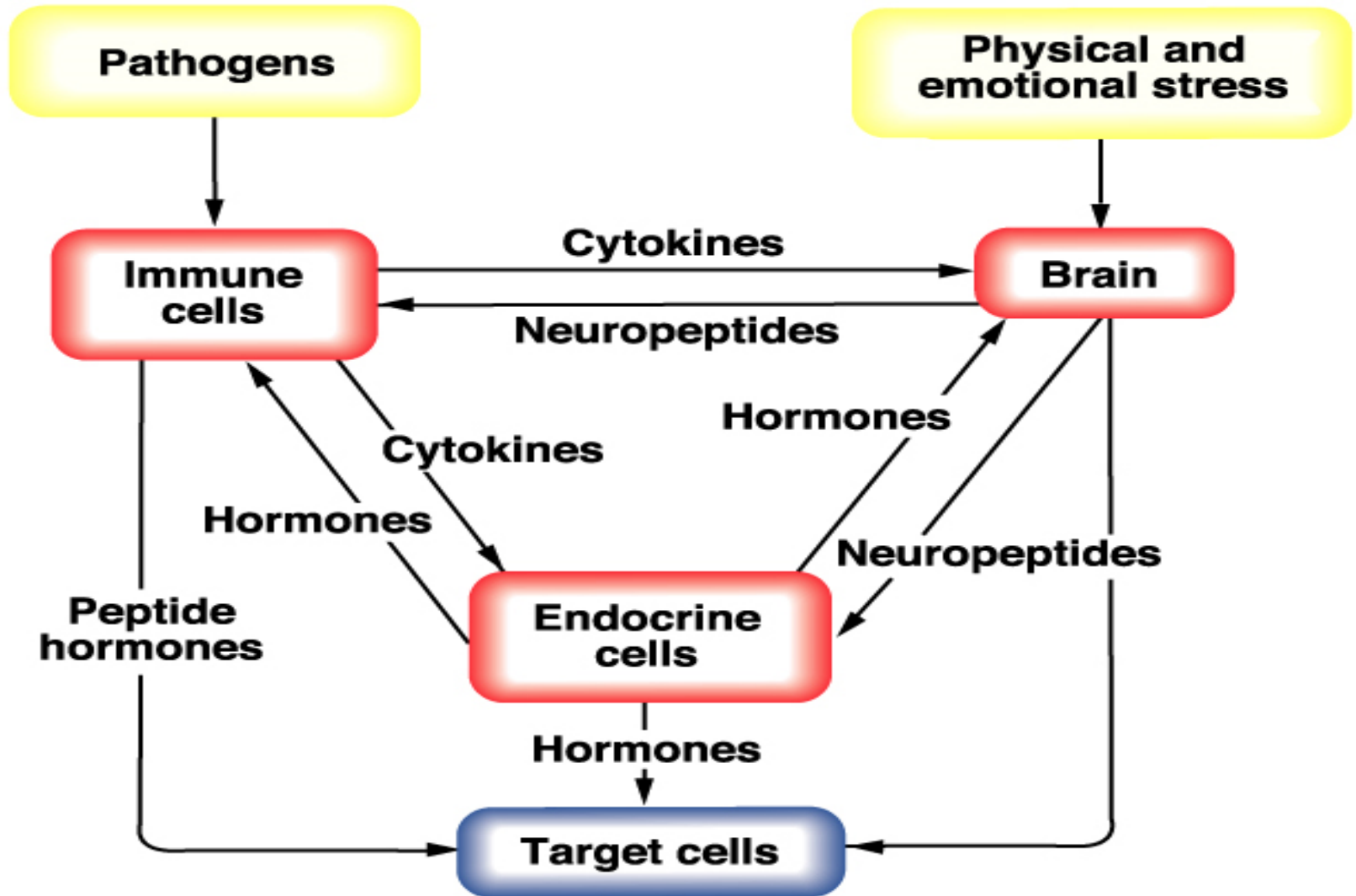
Means of acquiring long-term immunity

Long-term immunity against a pathogen can be acquired through having the disease or being vaccinated against it. (a) Exposure to a virulent (disease-producing) pathogen. (b) Vaccination with a modified pathogen that is no longer virulent (that is, can no longer produce disease) but is still antigenic. In both cases, long-term memory cells are produced that mount a swift, secondary response that prevents or minimizes symptoms on a subsequent natural exposure to the same virulent pathogen.

Respons Immun thd Invasi Virus



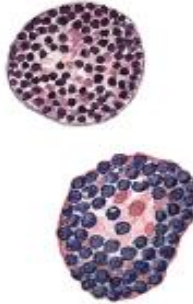


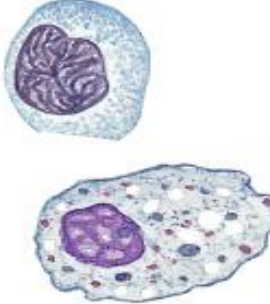


Interaksi Sistem Imun-Saraf- Endokrin



Gangguan sistem imun

1. *Lack of response* (imunodefisiensi)
contoh: AIDS, leukemia
2. *Incorrect response* (peny. autoimun)
contoh: DM tipe I, miastenia gravis,
multiple sclerosis; penyakit Graves.
3. *Overactive response* (alergi/
hipersensitivitas)
contoh: asma, *rhinitis allergic*, rx
transfusi

Sel dlm Sistem Imun

	Basophils and Mast Cells	Neutrophils	Eosinophils	Monocytes and Macrophages	Lymphocytes and Plasma Cells	Dendritic Cells
						
% of WBCs in blood	Rare	50-70%	1-3%	1-6%	20-35%	NA
Subtypes and nicknames		Called "polys" or "segs" Immature forms called "bands" or "stabs"		Called the mononuclear phagocyte system	B lymphocytes, Memory cells Plasma cells T lymphocytes Cytotoxic T cells Helper T cells Natural killer cells	Also called Langerhans cells, veiled cells
Primary function(s)	Release chemicals that mediate inflammation and allergic responses	Ingest and destroy invaders	Destroy invaders, particularly parasites	Ingest and destroy invaders Antigen presentation	Specific responses to invaders, including antibody production	Recognize pathogens and activate other immune cells by antigen presentation
		Phagocytes				
		Granulocytes				
Classifications			Cytotoxic cells		Cytotoxic cells (some types)	
					Antigen-presenting cells	

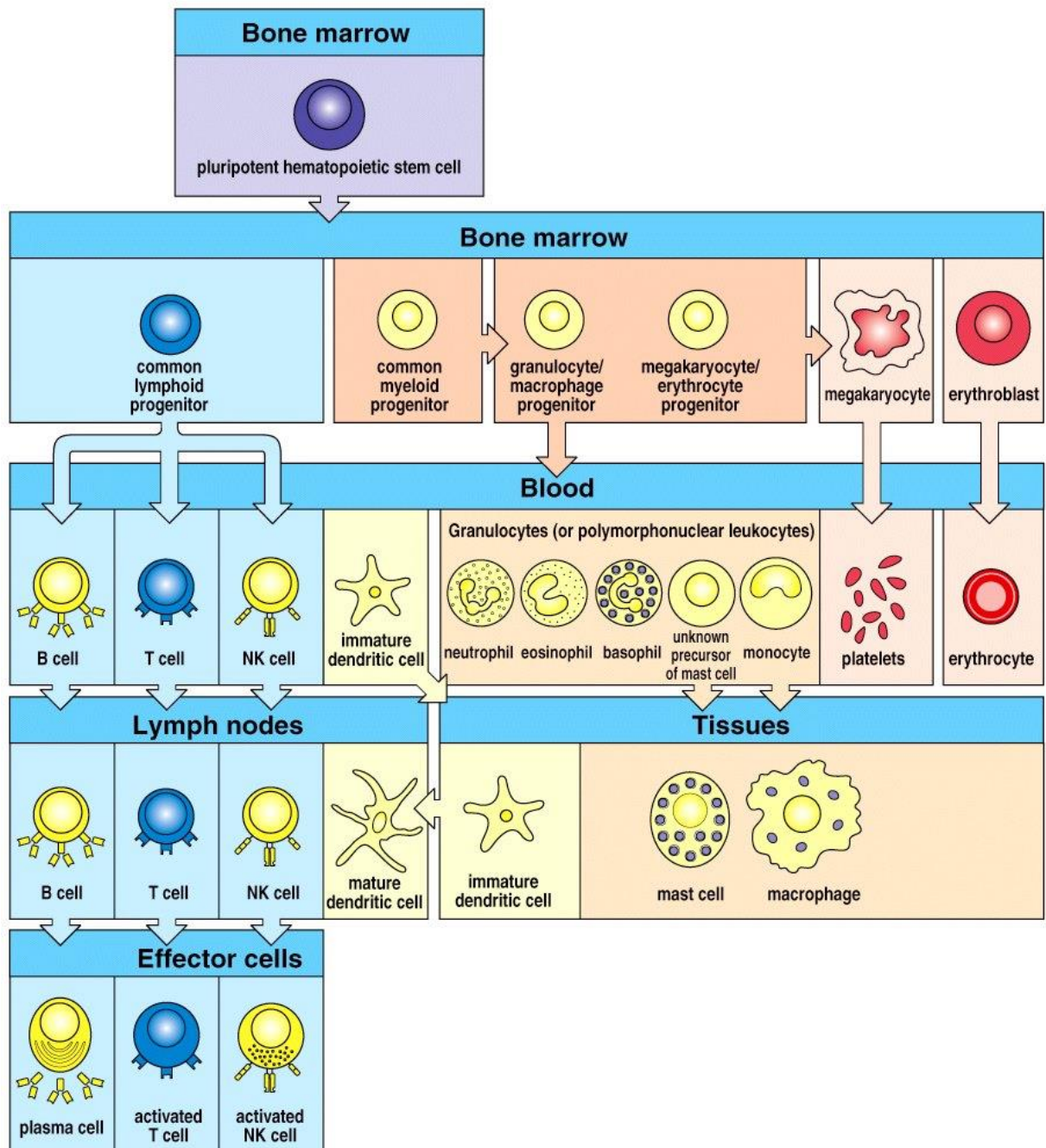
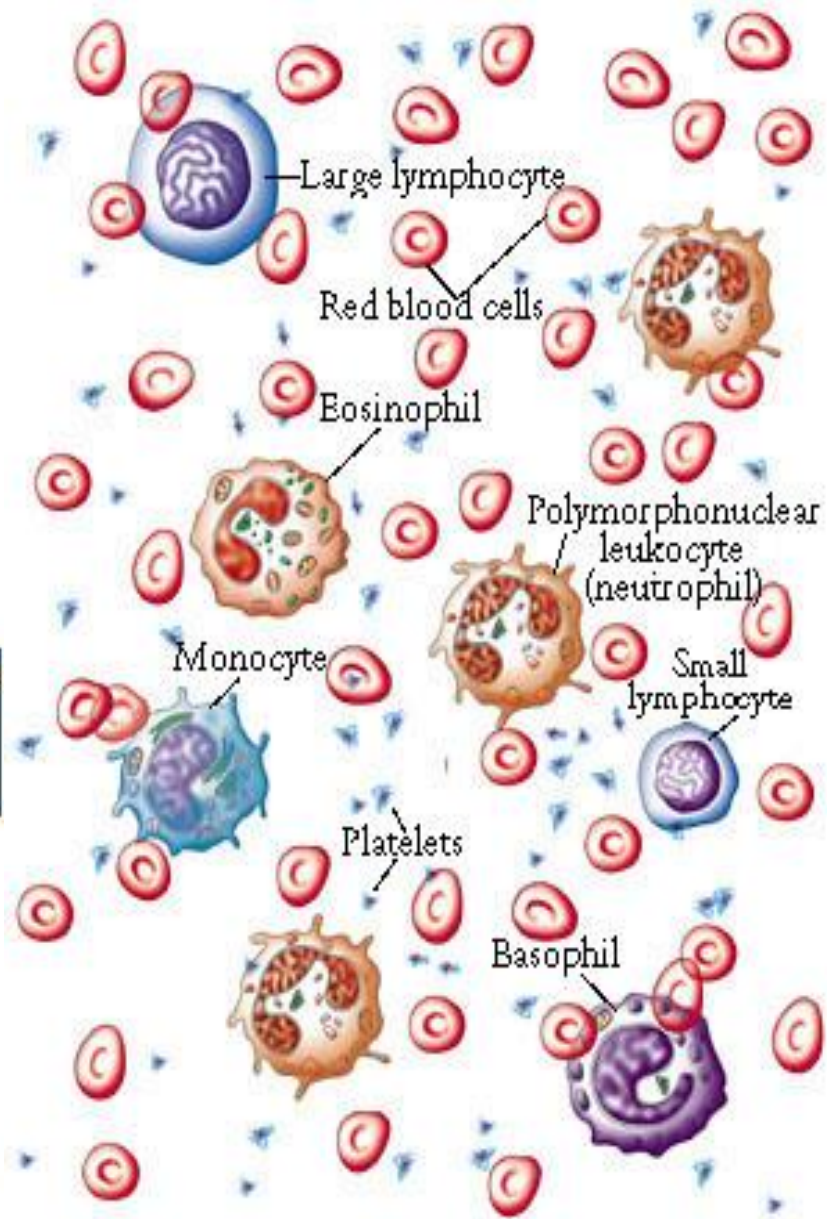
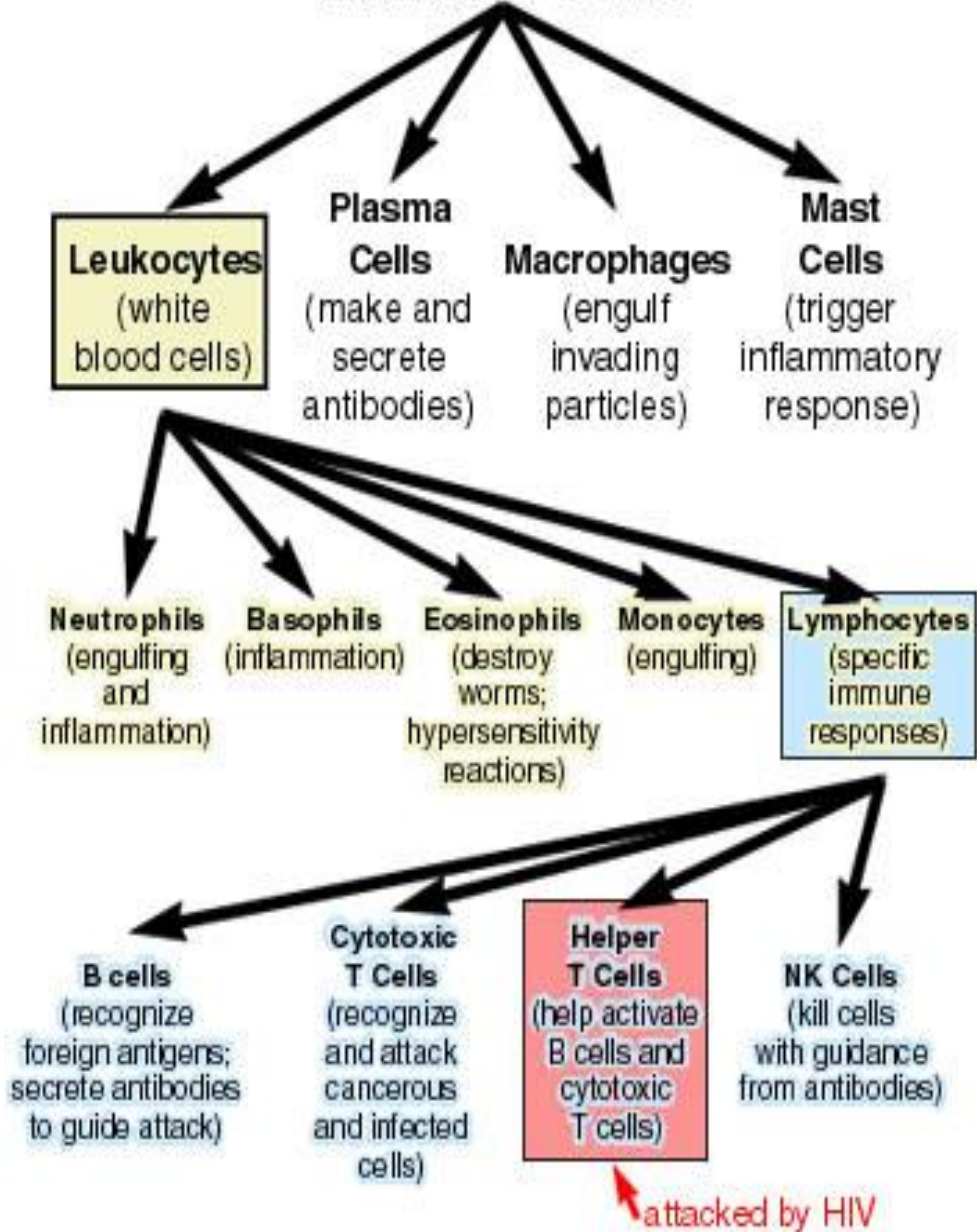


Figure 1-3 Immunobiology, 6/e. (© Garland Science 2005)

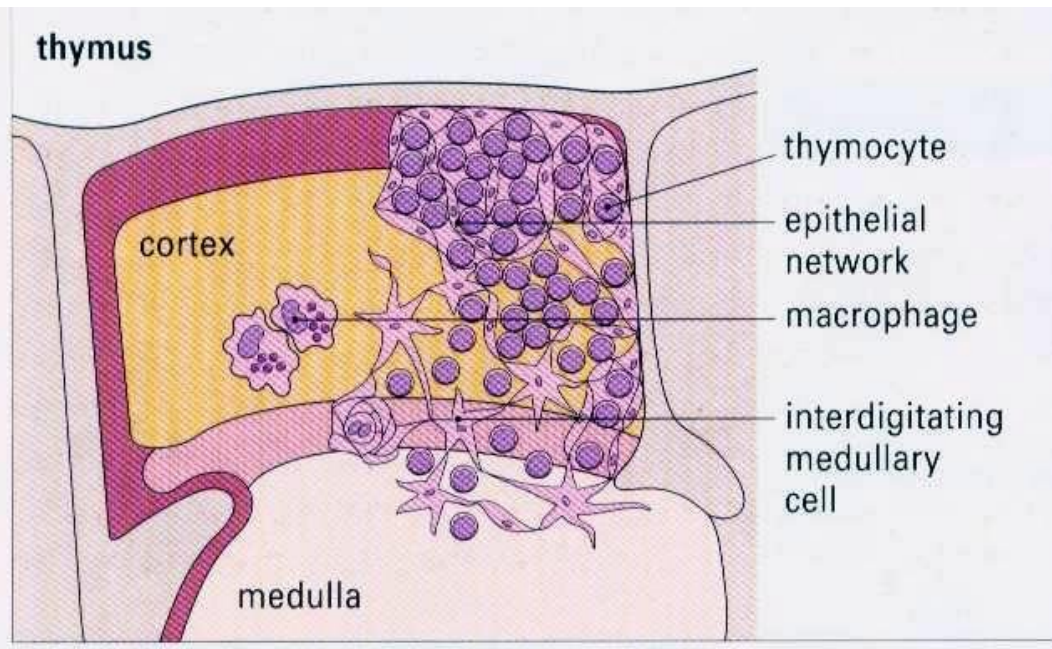
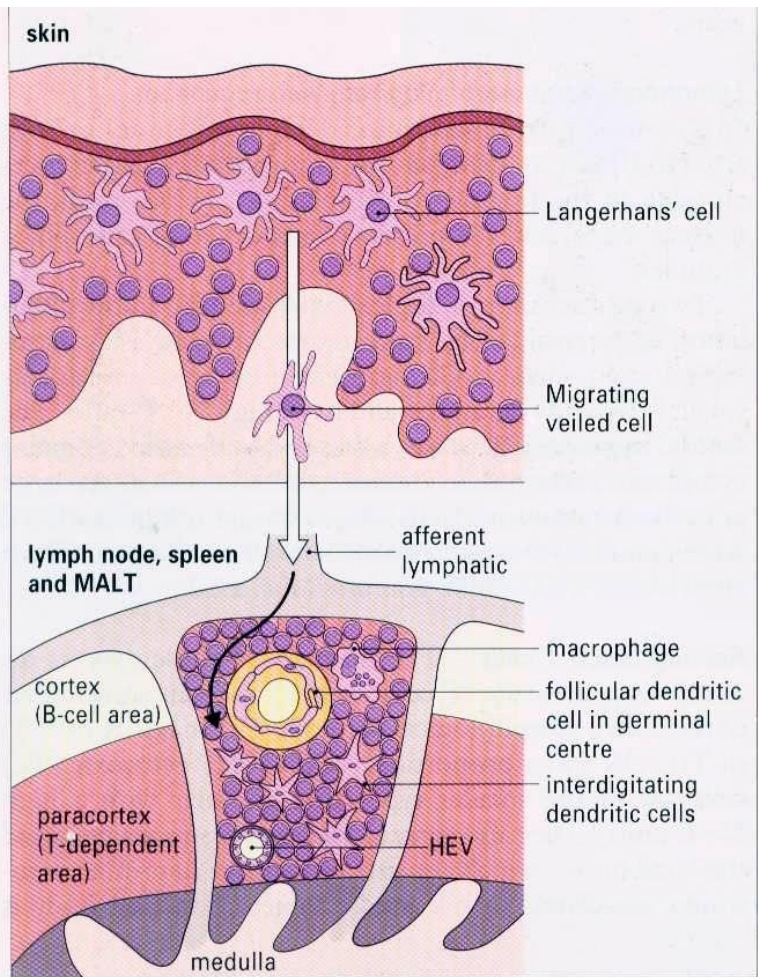
Immune Cells



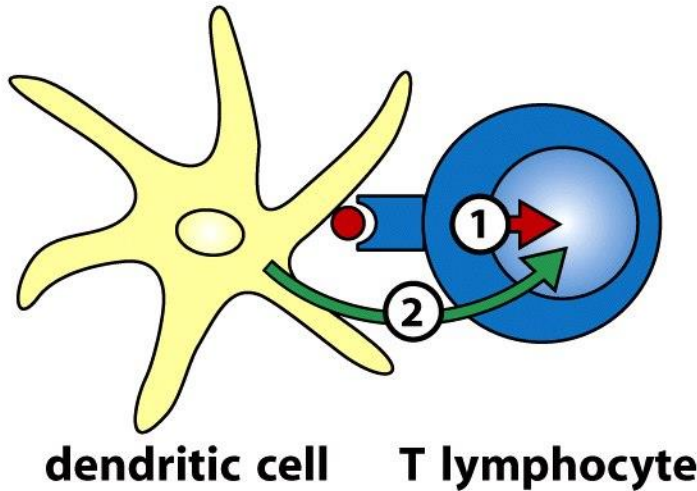
Sistem Imun Adaptif

■ Sel Dendritik

- *Sel Langerhans*
- *Veiled cells*
- *Interdigitating dendritic cells (IDC)*
- *Follicular dendritic cells (FDC)*
- *Germinal center dendritic cells (GCDC)*

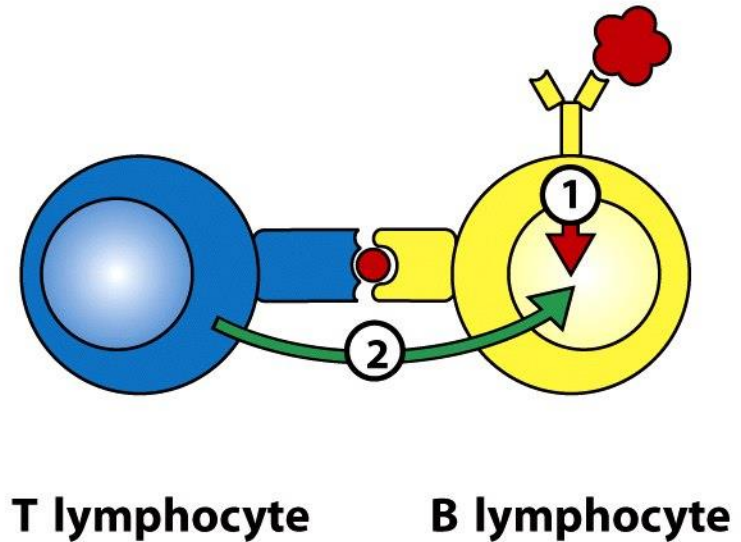


Antigen-receptor binding and co-stimulation of T cell by dendritic cell



Proliferation and differentiation of T cell to acquire effector function

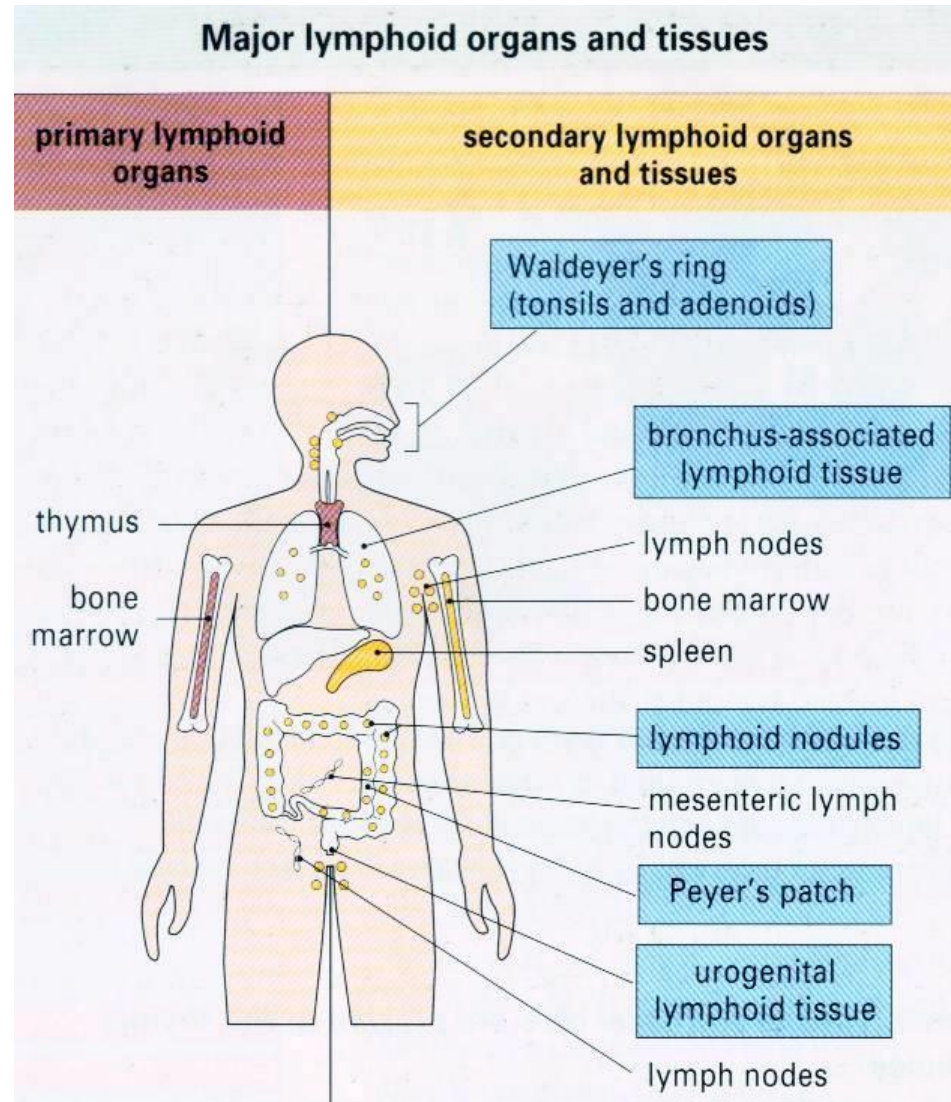
Antigen-receptor binding and activation of B cell by T cell



Proliferation and differentiation of B cell to acquire effector function

Figure 1-21 Immunobiology, 7ed. (© Garland Science 2008)

Organ Limfoid



A lymph node

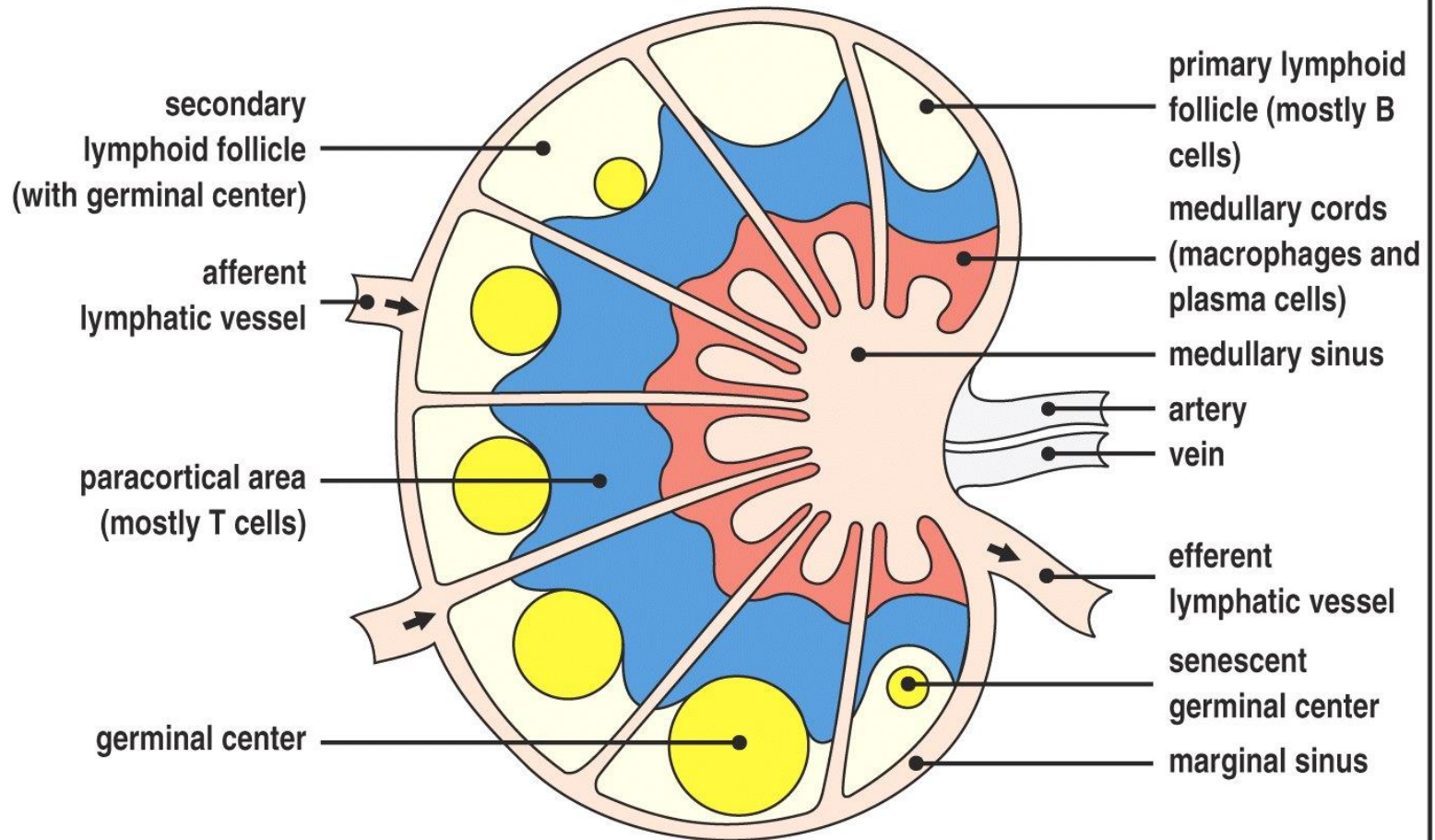


Figure 1-8 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

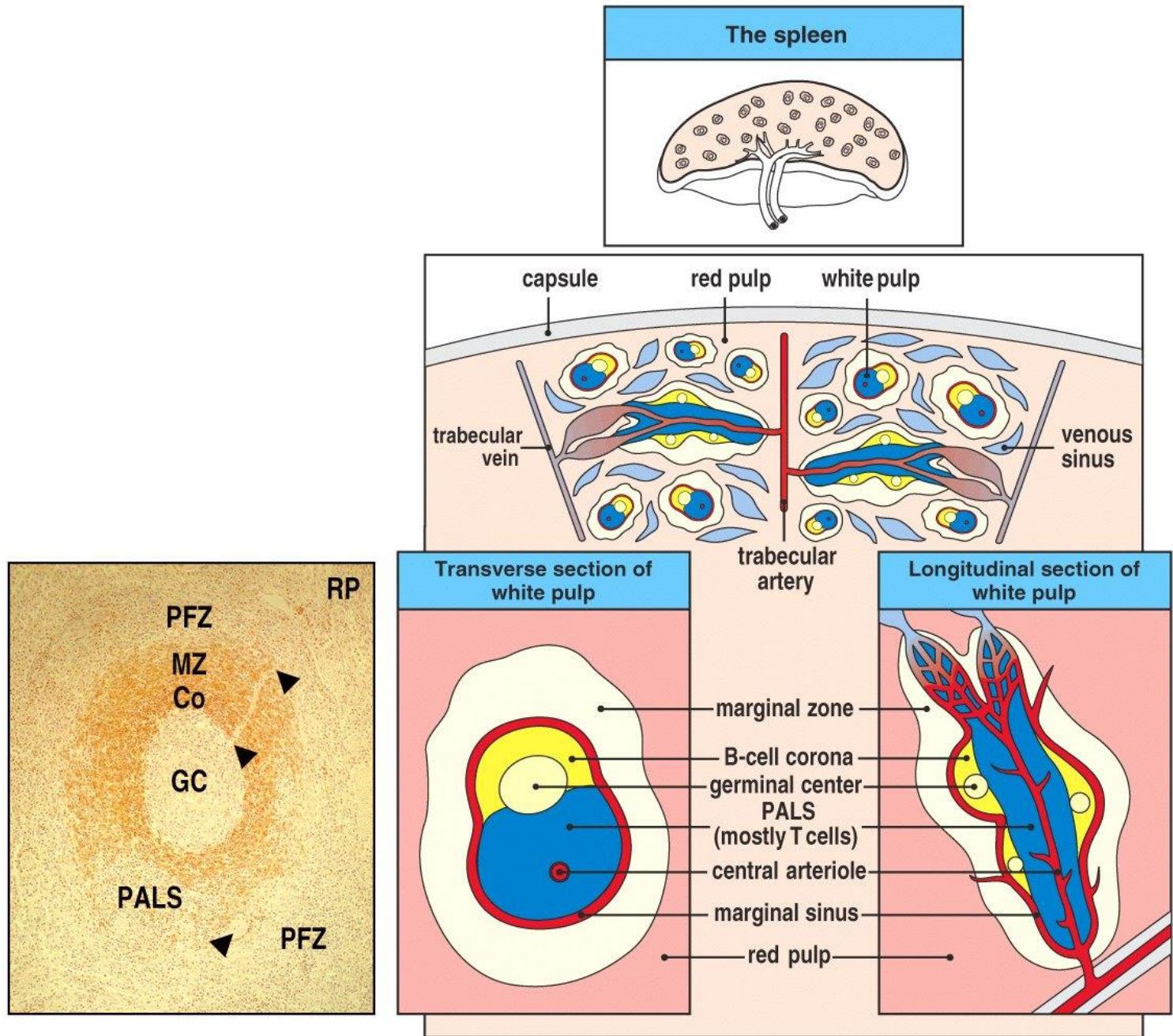


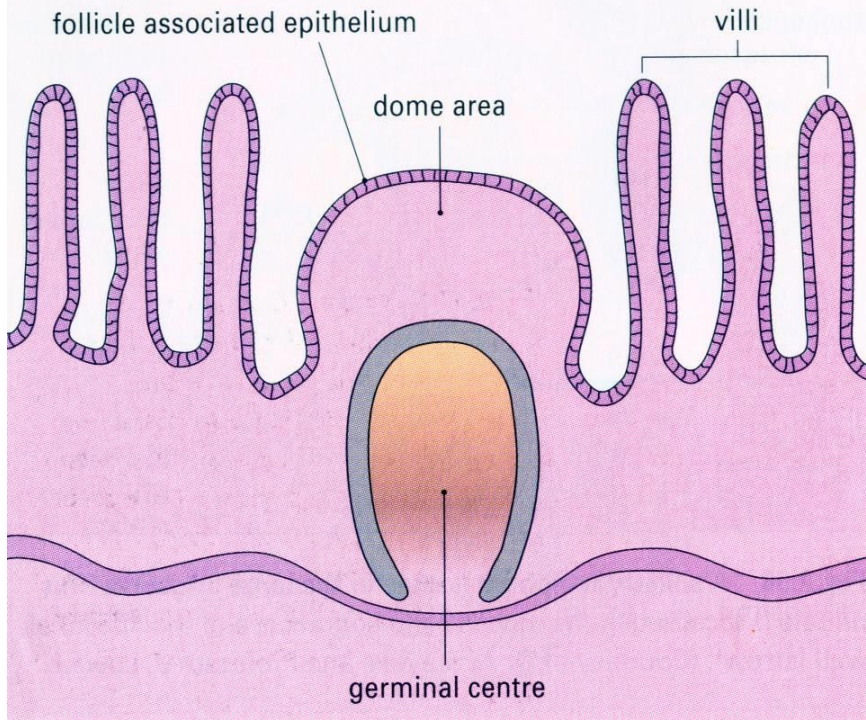
Figure 1-9 Immunobiology, 6/e. (© Garland Science 2005)

Mucosa-associated lymphoid tissue (MALT)

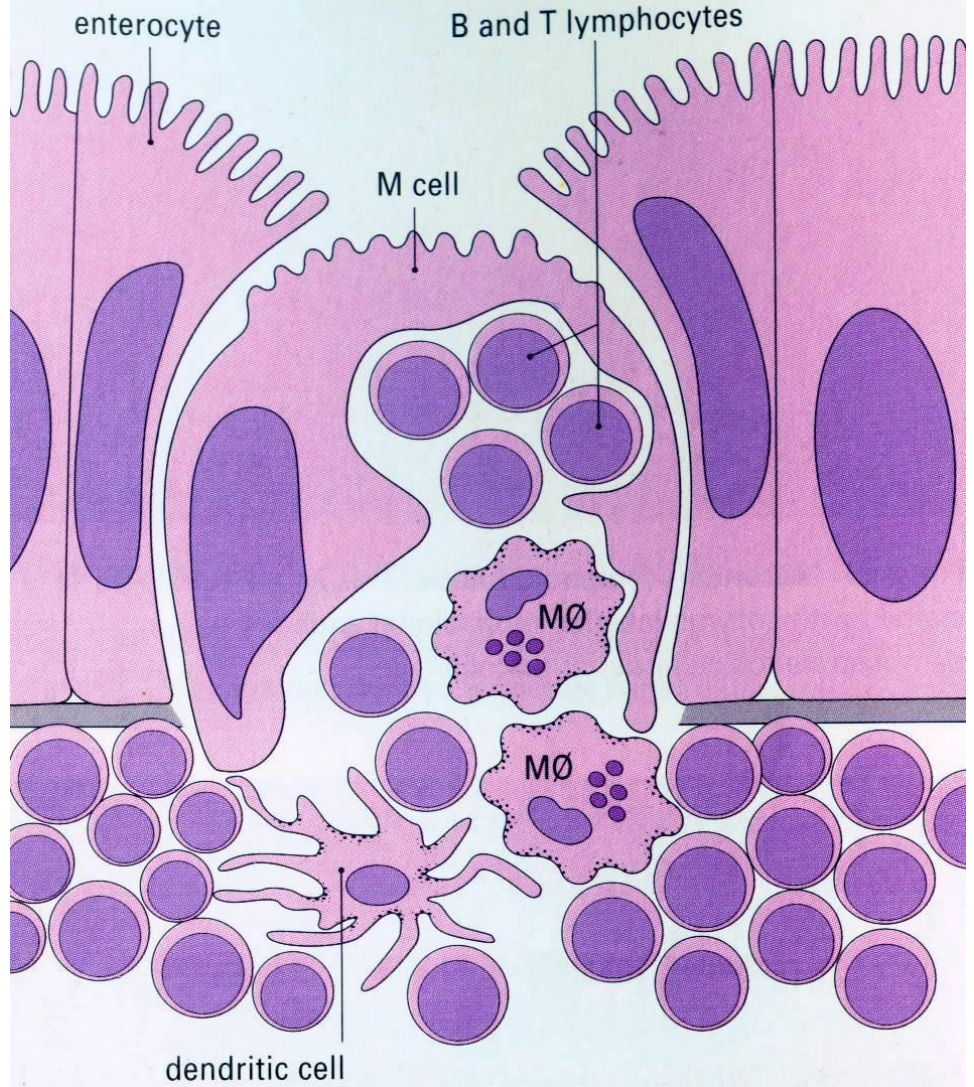


Palatine Tonsil

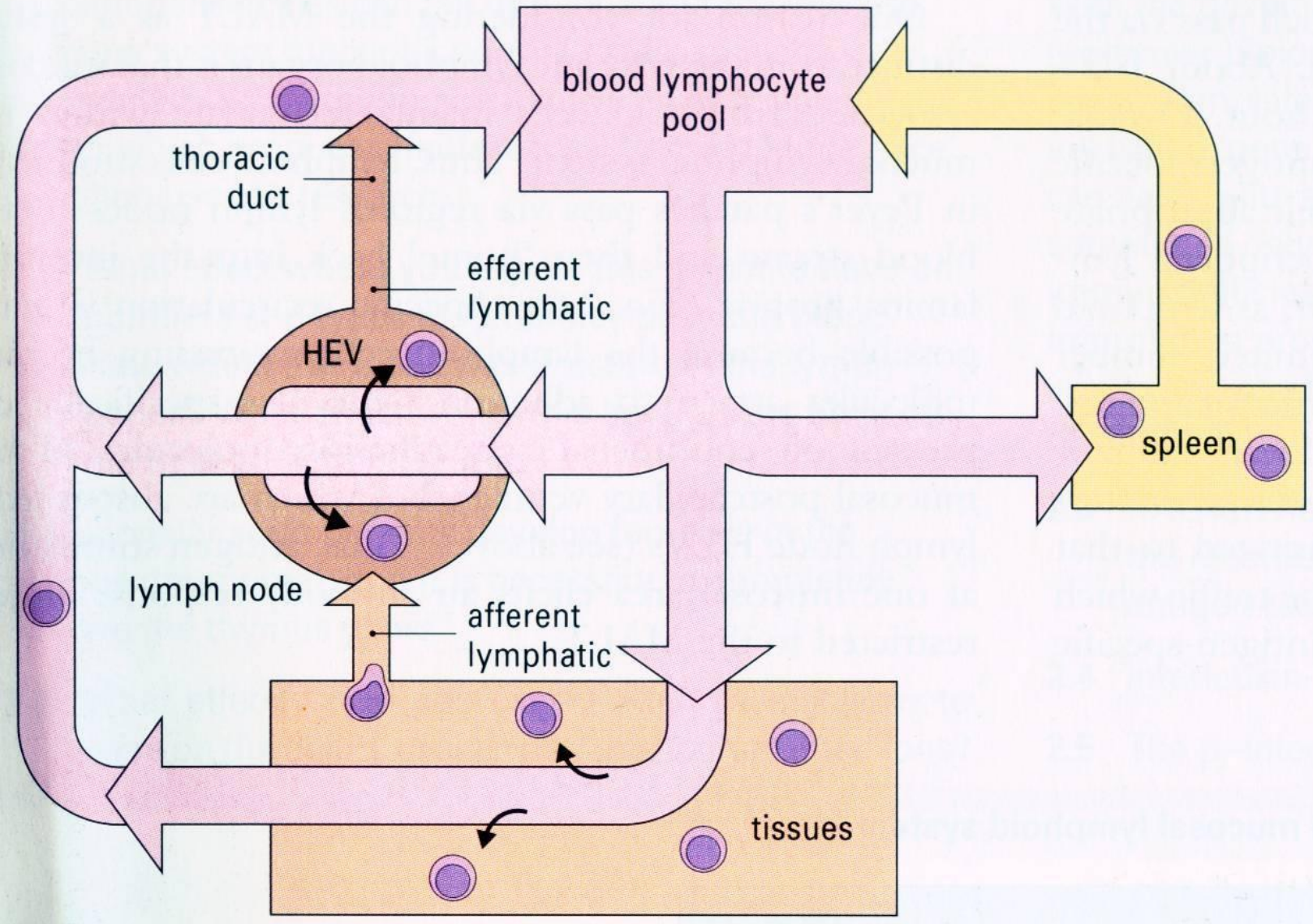
Structural organization of a Peyer's patch



Location of M cells



Patterns of lymphocyte traffic

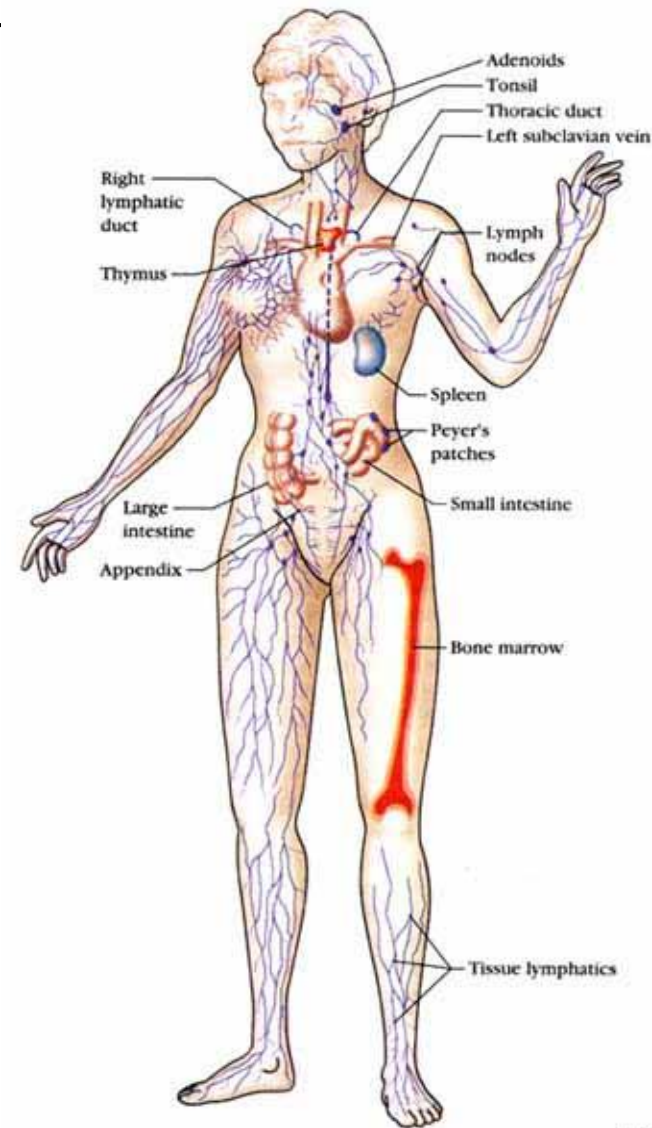


Struktur Sistem Imun

- Organ sistem imun berada di seluruh bagian tubuh → organ limfoid
- Organ limfoid: ‘rumah’ bg limfosit
- Jaringan limfoid primer:
 - (1) kelenjar thymus
 - (2) sumsum tulang
- Jaringan limfoid sekunder:
 - (1) berkapsul: limpa & kelenjar limf
 - (2) tdk berkapsul: tonsil, GALT (*gut-associated lymphoid tissue*), jar.limfoid di kulit, sal.napas, kemih, & reproduksi

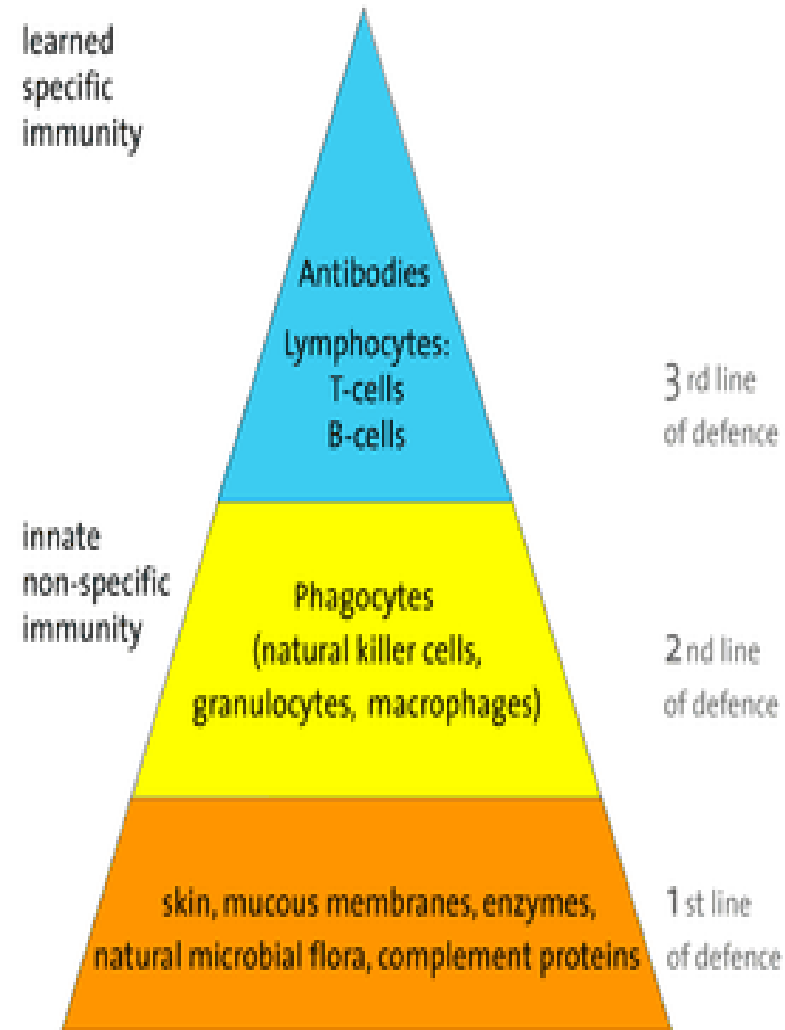
Jaringan Limfoid

- Merupakan jaringan yang memproduksi, menyimpan, & memproses limfosit
- Mencakup: sumsum tulang, kel.limfe, limpa, thymus, tonsil, adenoid, appendiks, & agregat jar.limf di sal.cerna (GALT= *gut-associated lymphoid tissue/* Plak Peyer)



Sistem Imun

- Pertahanan lapis pertama:
Pertahanan fisik (*physical barrier*)
- Ada 2 sistem kekebalan tubuh:
 1. Sistem kekebalan nonspesifik (didapat) (*innate immune system*)
 2. Sistem kekebalan spesifik (dipelajari/adaptif) (*learned/adaptive immune system*)



Respons Imun

Tahap:

- Deteksi & mengenali benda asing
- Komunikasi dg sel lain untuk berespons
- Rekrutmen bantuan & koordinasi respons
- Destruksi atau supresi penginvasi

⇒ antibodi & sitokin

Respons Imun

1. Respons imun alami nonspesifik
 - ada sejak lahir
 - tdk memiliki target ttt
 - terjadi dlm bbrp menit – jam
 - Reaksi inflamasi
2. Respons imun didapat spesifik
 - spesifik untuk jenis ttt
 - respons thd paparan I tjd dlm bbrp hari, paparan berikutnya lebih cepat

Pertahanan Lapis Pertama

- Kulit & membran mukosa yang utuh
- Kelenjar keringat, sebum, & airmata → mensekresi zat kimia & bersifat bakterisid
- Mukus, silia, *tight junction*, desmosom, sel keratin & lysozim di lapisan epitel
- Rambut pd lubang hidung
- Flora normal

Sistem Kekebalan Non-spesifik

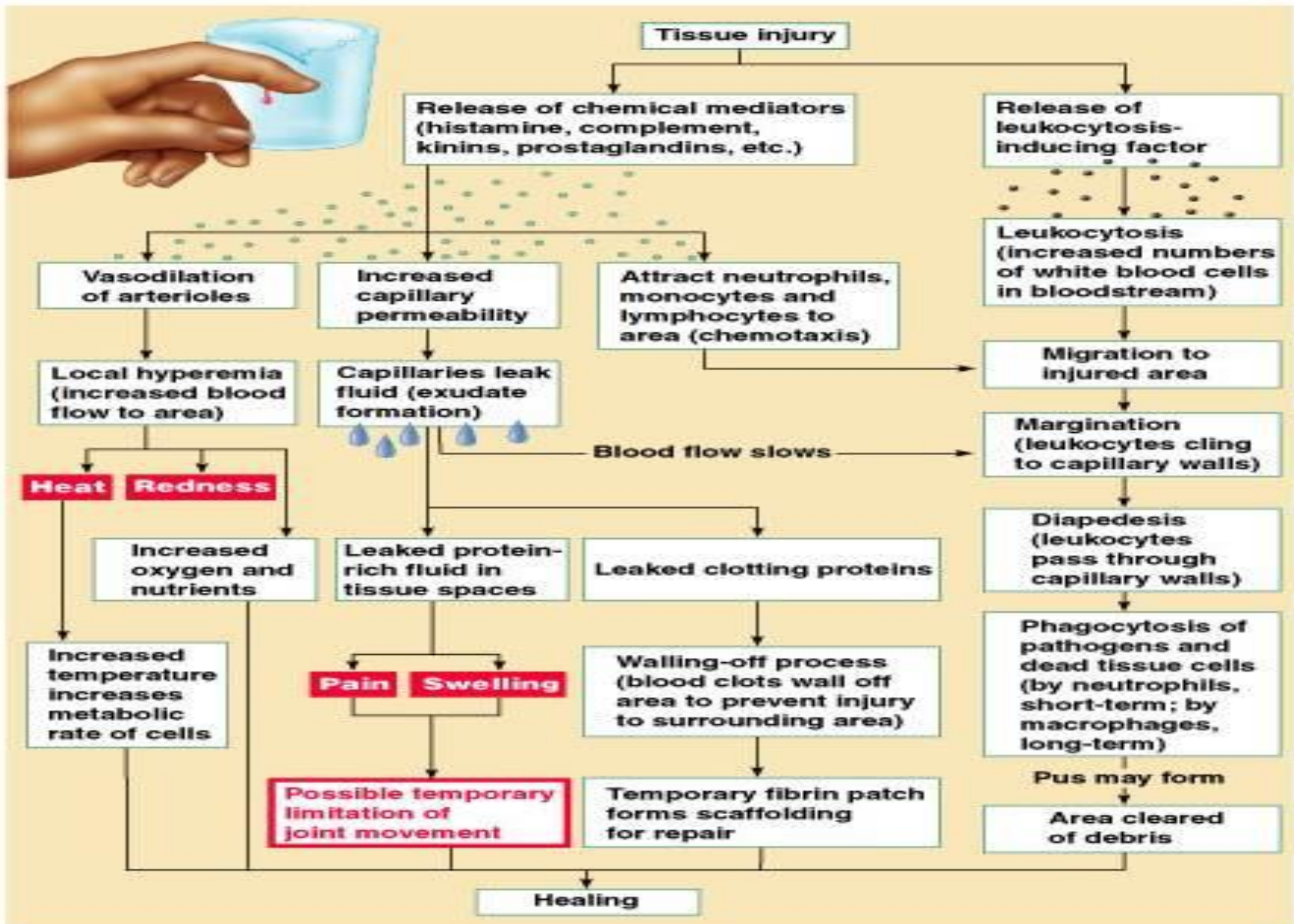
- Dapat mendeteksi adanya benda asing & melindungi tubuh dari kerusakan yang diakibatkannya, namun tdk dpt mengenali benda asing yang masuk ke dalam tubuh.
- Yang termasuk dlm sistem ini:
 1. Reaksi inflamasi/peradangan
 2. Protein antivirus (interferon)
 3. Sel *natural killer* (NK)
 4. Sistem komplemen

Inflamasi/ Peradangan

- Merupakan respons lokal tubuh thd infeksi atau perlukaan
- Tidak spesifik hanya untuk infeksi mikroba, tetapi respons yg sama juga terjadi pada perlukaan akibat suhu dingin, panas, atau trauma
- Pemeran utama: fagosit, a.l: neutrofil, monosit, & makrofag

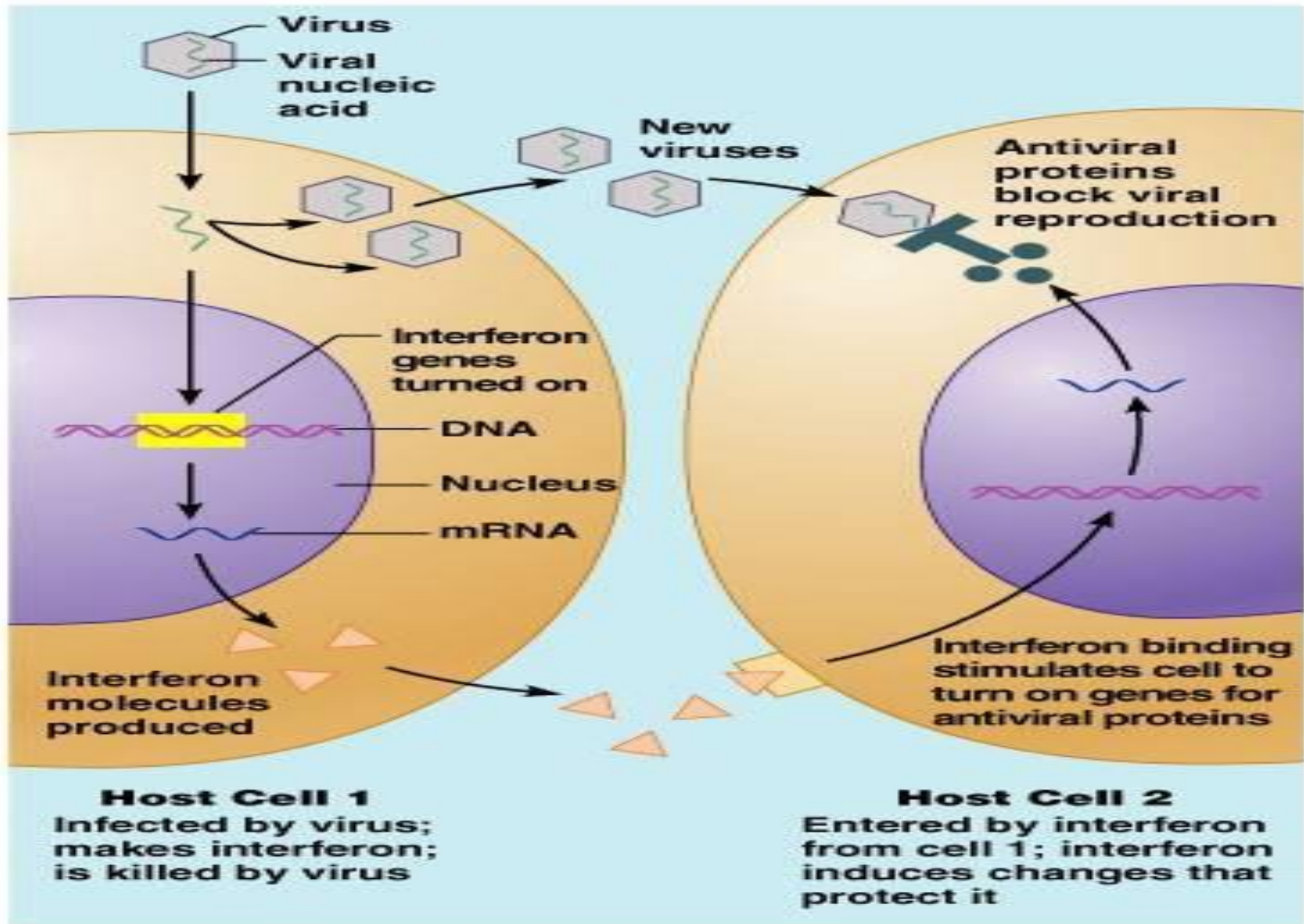
Tahap inflamasi

1. Masuknya bakteri ke dalam jaringan
2. Vasodilatasi sistem mikrosirkulasi area yg terinfeksi → meningkatkan aliran darah (RUBOR/kemerahan & CALOR/panas)
3. Permeabilitas kapiler & venul yang terinfeksi terhadap protein meningkat → difusi protein & filtrasi air ke interstisial (TUMOR/bengkak & DOLOR/nyeri)
4. Keluarnya neutrofil lalu monosit dari kapiler & venula ke interstisial
5. Penghancuran bakteri di jaringan → fagositosis (respons sistemik: demam)
6. Perbaikan jaringan



Interferon

- Sel yang terinfeksi virus akan mengeluarkan interferon
- Interferon mengganggu replikasi virus (antivirus); 'interfere'
- Interferon juga memperlambat pembelahan & pertumbuhan sel tumor dgn meningkatkan potensi sel NK & sel T sitotoksik (antikanker)
- Peran interferon yg lain: meningkatkan aktivitas fagositosis makrofag & merangsang produksi antibodi



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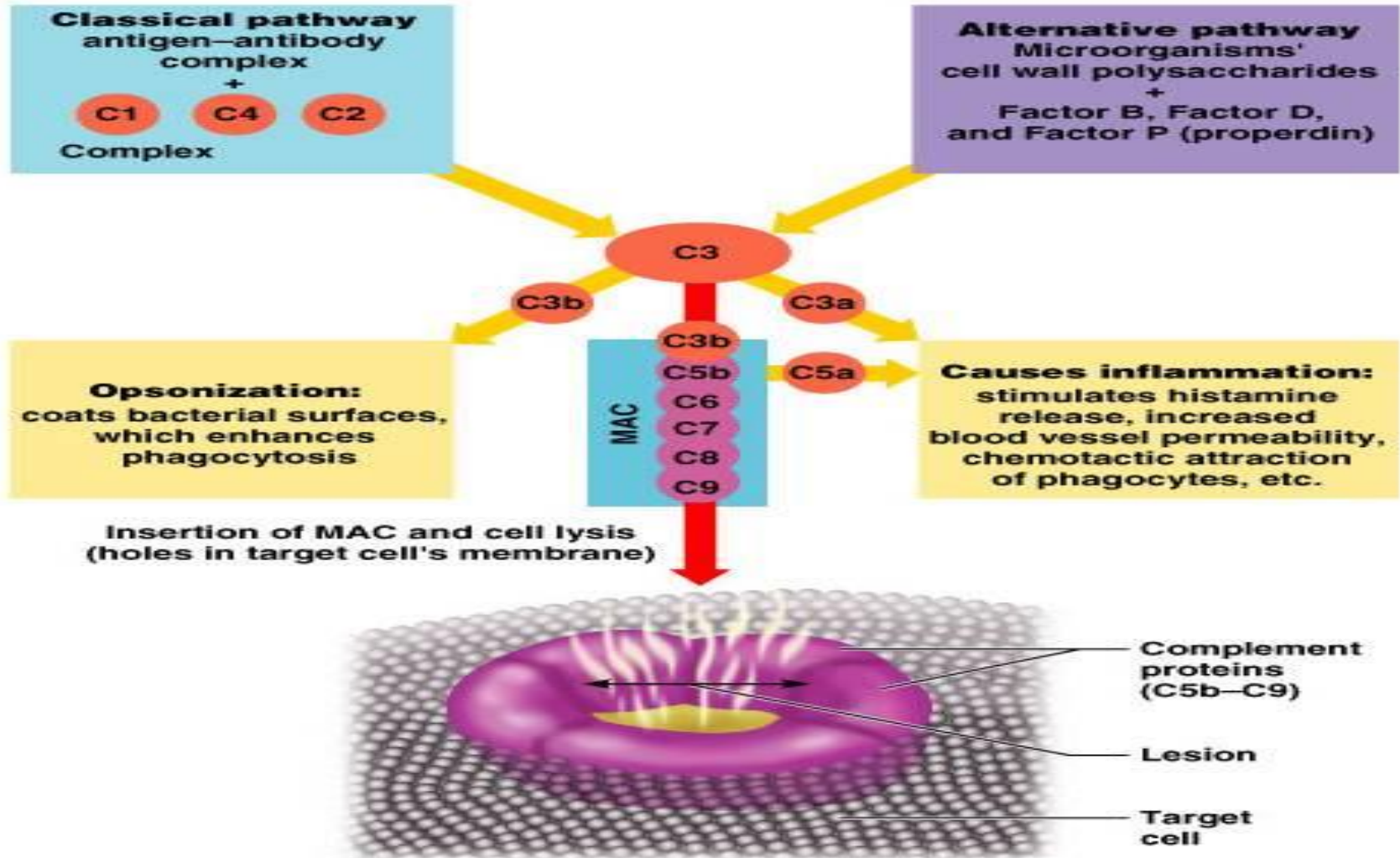
Sel *Natural Killer* (NK)

- Merusak sel yg terinfeksi virus & sel kanker dengan melisiskan membran sel pd paparan I
- Kerjanya = sel T sitotoksik, ttp lebih cepat, non-spesifik, & bekerja sebelum sel T sitotoksik mnjd lebih banyak & berfungsi

Sistem Komplemen

- Sistem ini diaktifkan oleh:
 - (1) paparan rantai karbohidrat yg ada pd permukaan mikroorganisme yg tdk ada pd sel manusia
 - (2) paparan antibodi yang diproduksi spesifik untuk zat asing tertentu oleh sistem imun adaptif
- Bekerja sbg ‘komplemen’ dari kerja antibodi

Aktivasi Sistem Komplemen

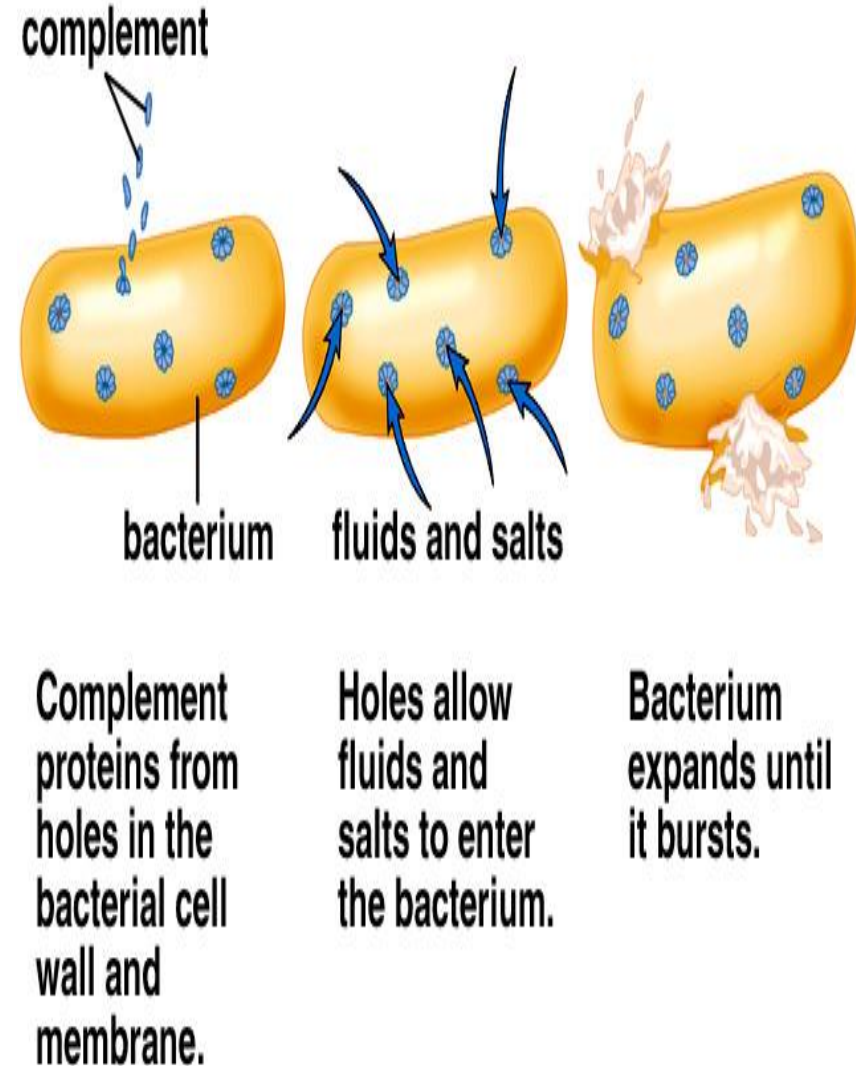


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Komplemen yg teraktivasi akan:

1. Berikatan dg basofil & sel mast & menginduksi pelepasan histamin → reaksi inflamasi
2. Berperan sbg faktor kemotaksis yang meningkatkan fagositosis
3. Berikatan dg permukaan bakteri & bekerja sbg opsonin (opsonisasi) → fagositosis
4. Menempel pd membran & membentuk struktur berbentuk tabung yg melubangi membran sel & menyebabkan lisis sel.

Action of the complement system against a bacterium



Sistem Kekebalan Spesifik

- Atau sistem kekebalan adaptif dapat menghancurkan patogen yang lolos dari sistem kekebalan non-spesifik.
- Mencakup:
 - (1) kekebalan humoral → produksi antibodi oleh limfosit B (sel plasma)
 - (2) kekebalan selular → produksi limfosit T yg teraktivasi
- Harud dapat membedakan sel asing yg harus dirusak dari sel-diri → antigen (molekul besar, kompleks, & unik yg memicu respons imun spesifik jika masuk ke dalam tubuh)

Sistem Kekebalan Humoral

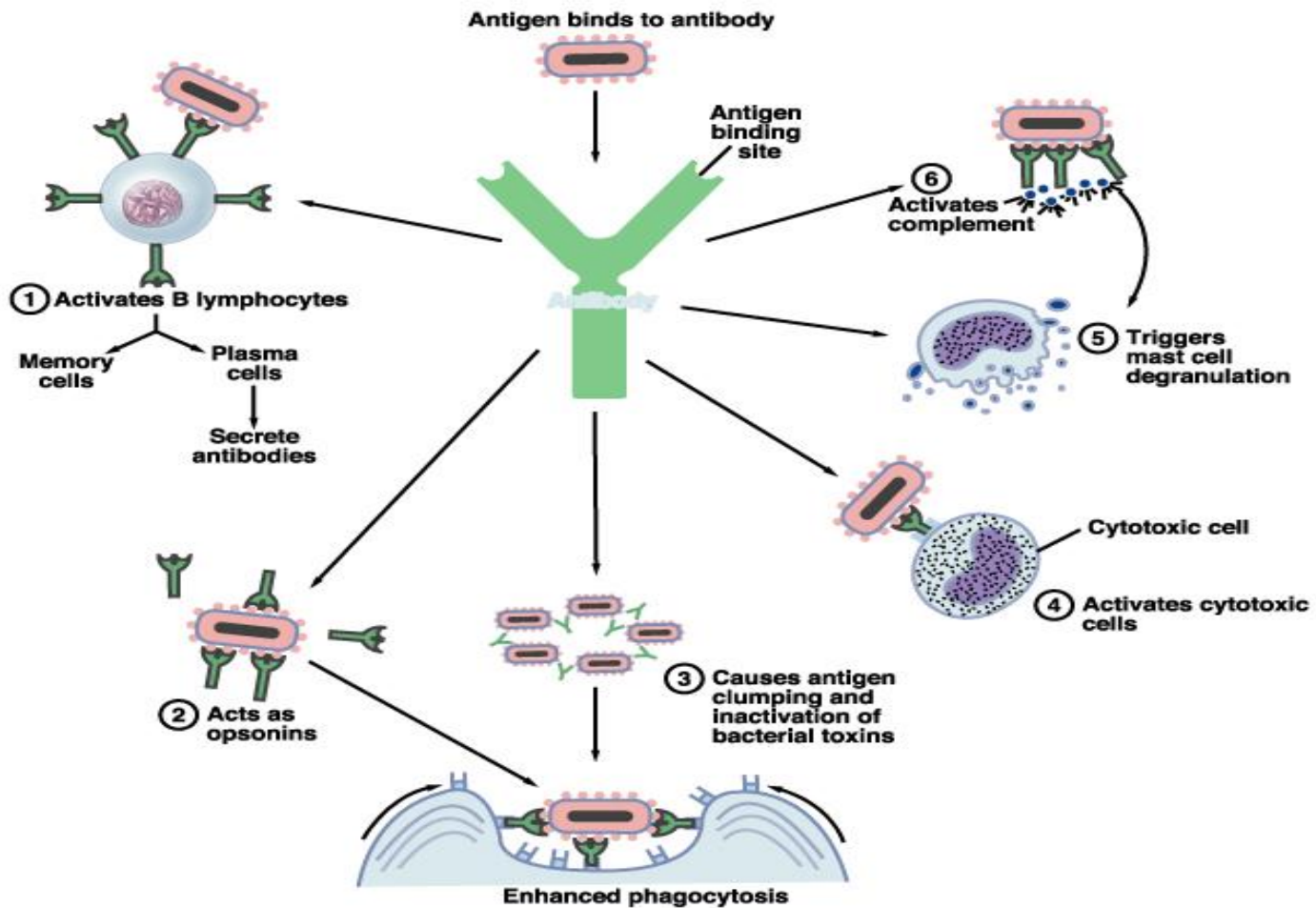
- Antigen (Ag) merangsang sel B berubah menjadi sel plasma yg memproduksi antibodi (Ab).
- Ab disekresi ke darah atau limf ~ lokasi sel plasma yg teraktivasi; semua Ab akan mencapai darah \Rightarrow gamma globulin = imunoglobulin (Ig)

Imunoglobulin (Ig)

Ada 5 kelas:

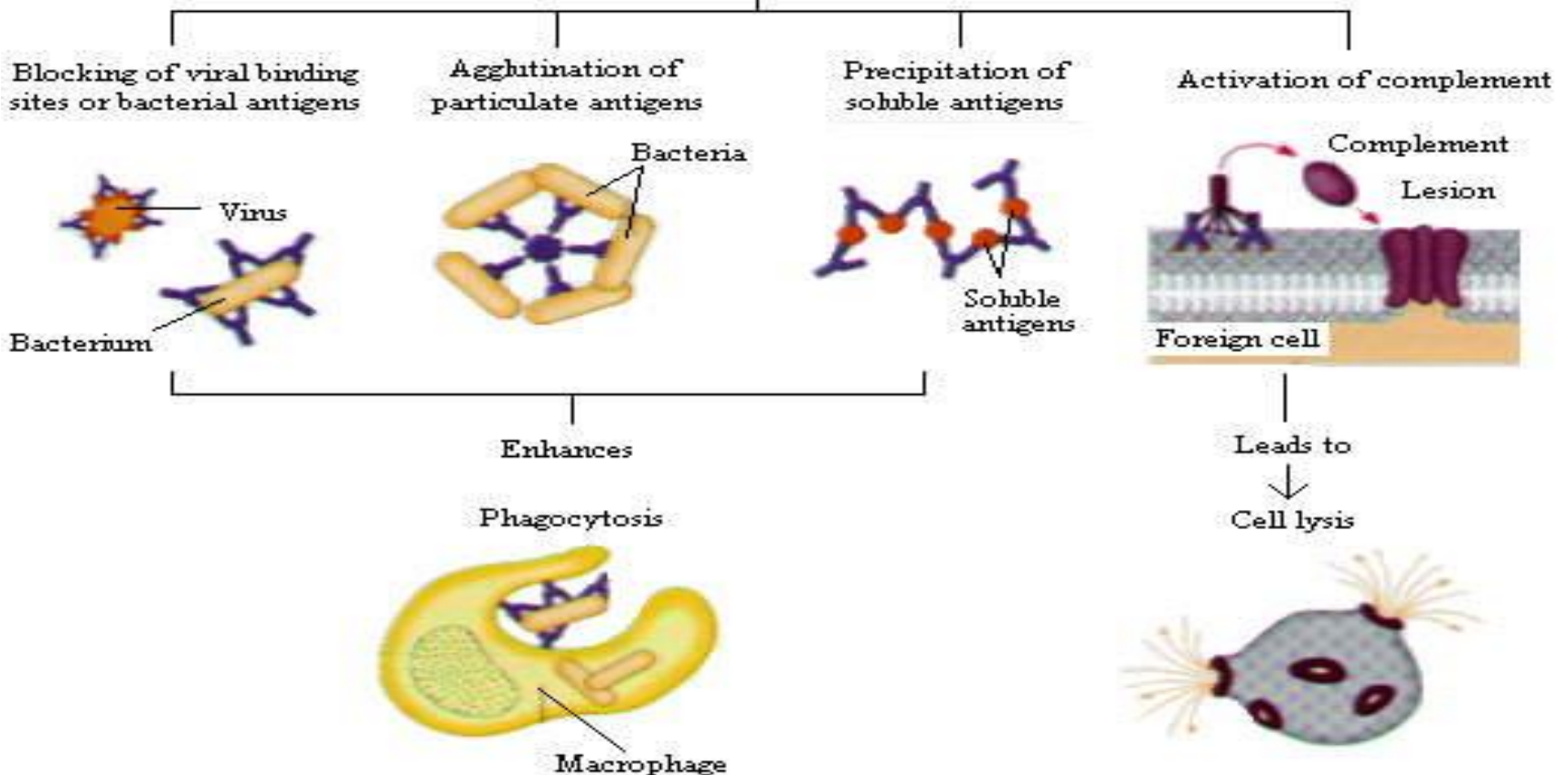
1. Ig M → berperan sbg reseptor permukaan sel B & disekresi pd tahap awal respons sel plasma
2. Ig G → Ig terbanyak di darah, diproduksi jika tubuh berespons thd antigen yg sama
Ig M & IgG berperan jika tjd invasi bakteri & virus serta aktivasi komplemen
3. Ig E → melindungi tubuh dr infeksi parasit & mrp mediator pd reaksi alergi; melepaskan histamin dari basofil & sel mast
4. Ig A → ditemukan pd sekresi sistem pencernaan, pernapasan, & perkemihan (cth: pd airmata & ASI)
5. Ig D → terdapat pada banyak permukaan sel B; mengenali antigen pd sel B

Fungsi Antibodi

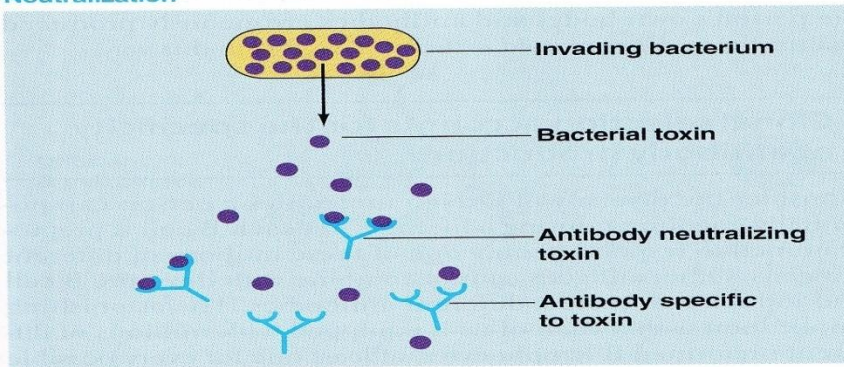


Reaksi Ag-Ab

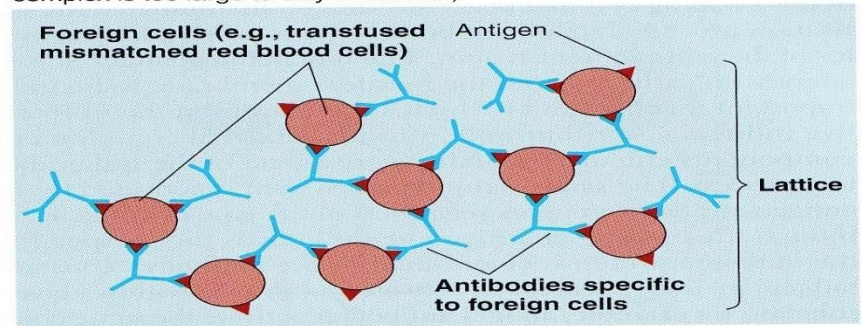
Binding of antibodies to antigens
inactivates antigens by



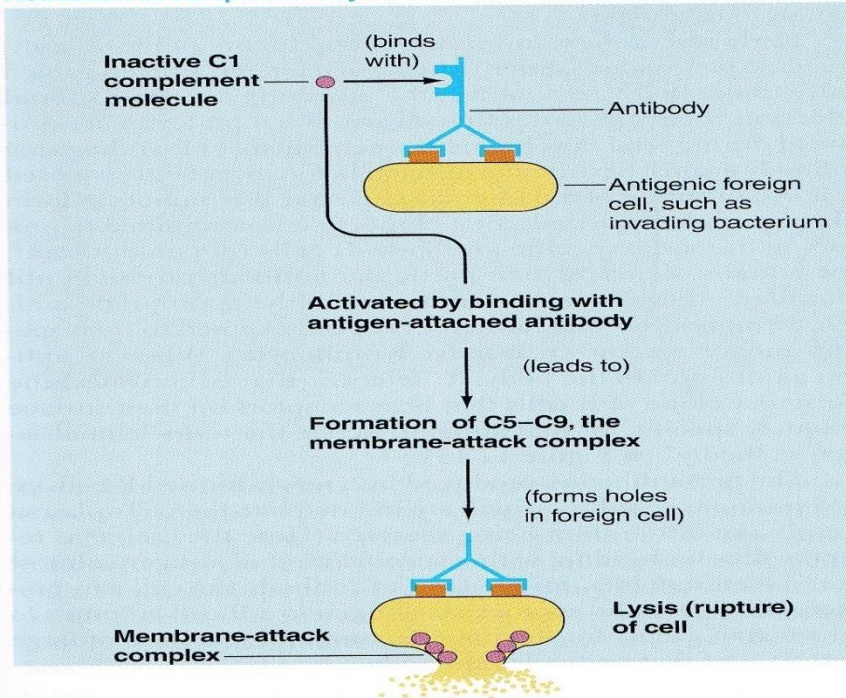
Neutralization



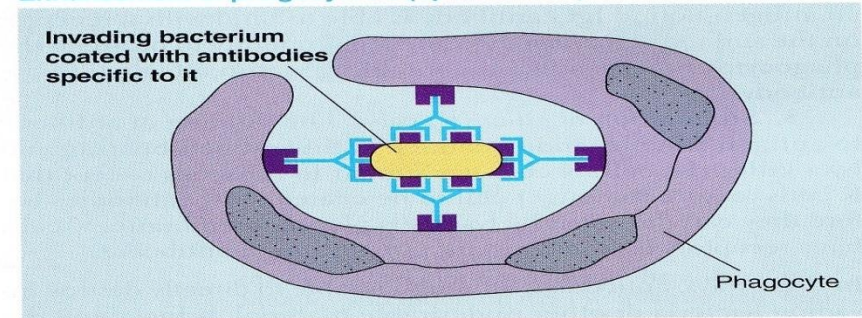
Agglutination (clumping of antigenic cells) and **precipitation** (if soluble antigen-antibody complex is too large to stay in solution)



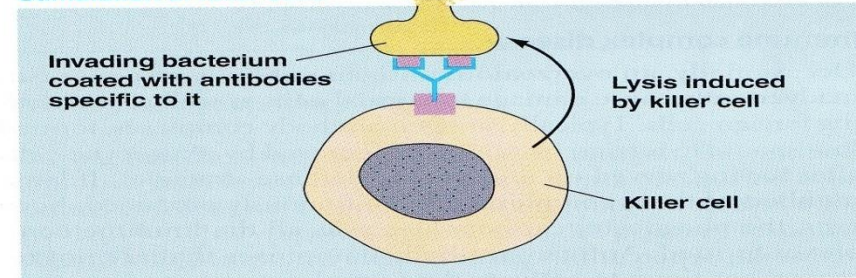
Activation of complement system



Enhancement of phagocytosis (opsonization)



Stimulation of killer cells



Structures are not drawn to scale.

● FIGURE 12-12

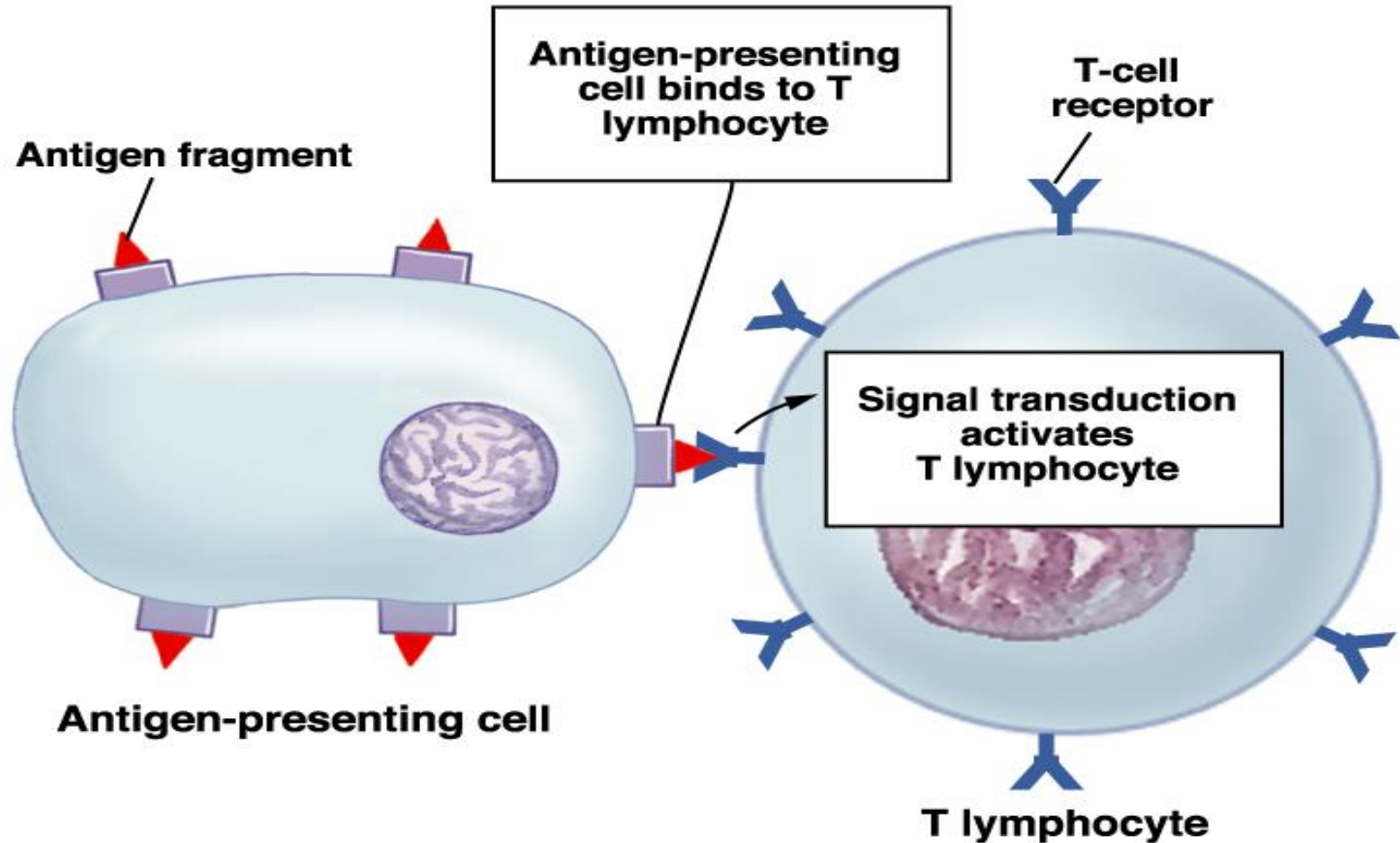
How antibodies help eliminate invading microbes

Antibodies physically hinder antigens through (1) neutralization or (2) agglutination and precipitation. Antibodies amplify innate immune responses by (1) activating the complement system, (2) enhancing phagocytosis by acting as opsonins, and (3) stimulating killer cells.

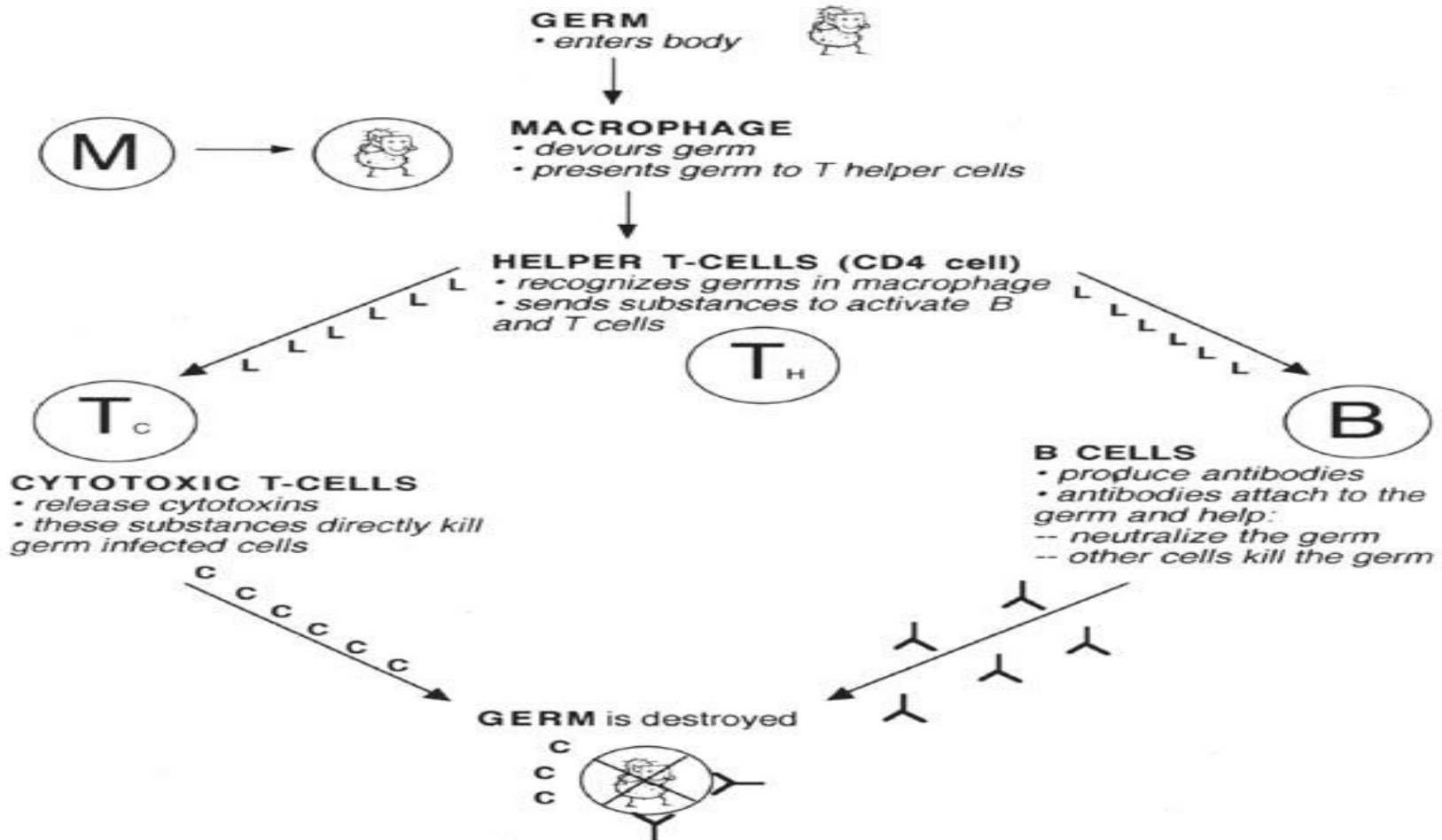
Sistem Kekebalan Seluler

- Limfosit T spesifik untuk kekebalan terhadap infeksi virus & pengaturan pd mekanisme kekebalan.
- Sel-sel T harus kontak langsung dg sasaran
- Ada 3 subpopulasi sel T: sel T sitotoksik, sel T penolong, & sel T penekan
- *Major histocompatibility complex* (MHC): kode human *leucocyte-associated antigen* (HLA) yg terikat pd permukaan membran sel; khas pd setiap individu
- Surveilans imun: kerjasama sel T sitotoksik, sel NK, makrofag, & interferon

Aktivasi Sel T



How the Immune System Works



If **GERM** enters the body again, **B-CELLS** and **T-CELLS** have a **MEMORY** and they will recognize the **GERM** and make **ANTIBODIES** and **CYTOTOXIC T-CELLS** to destroy it.

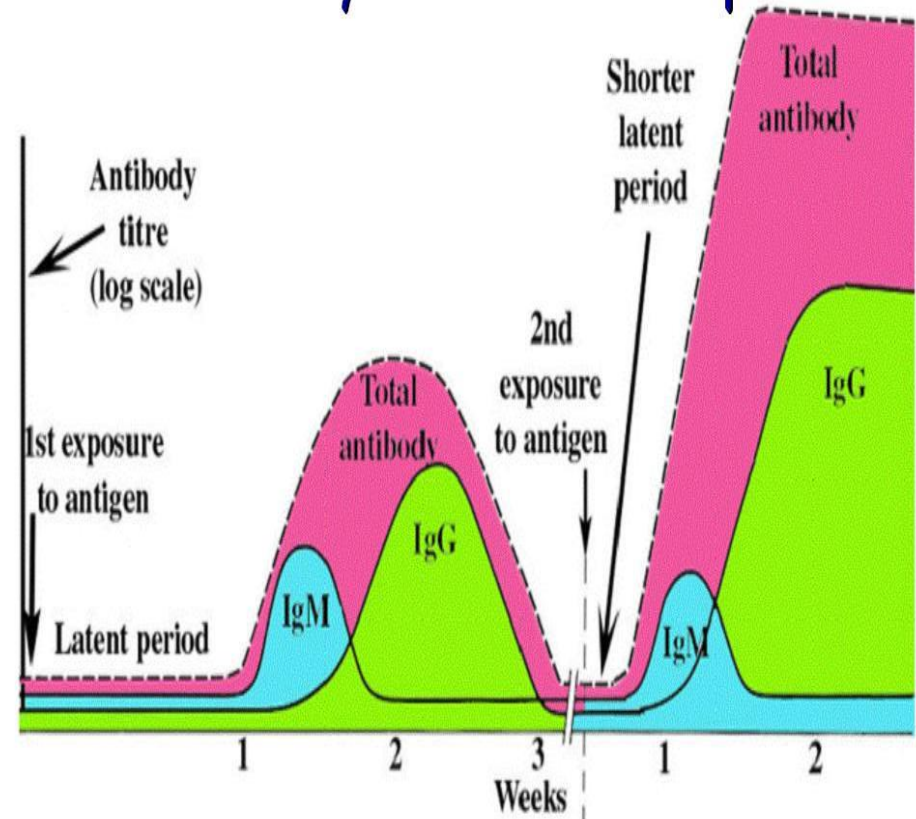
* Adapted from NYC Comprehensive Health Curriculum

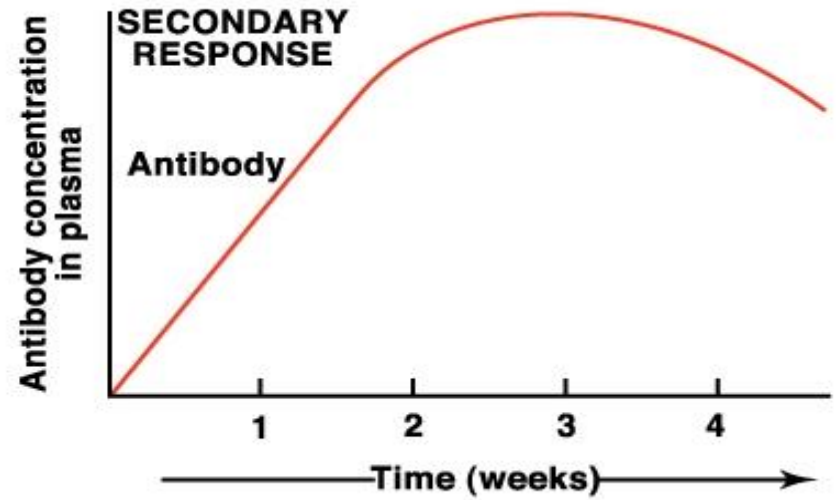
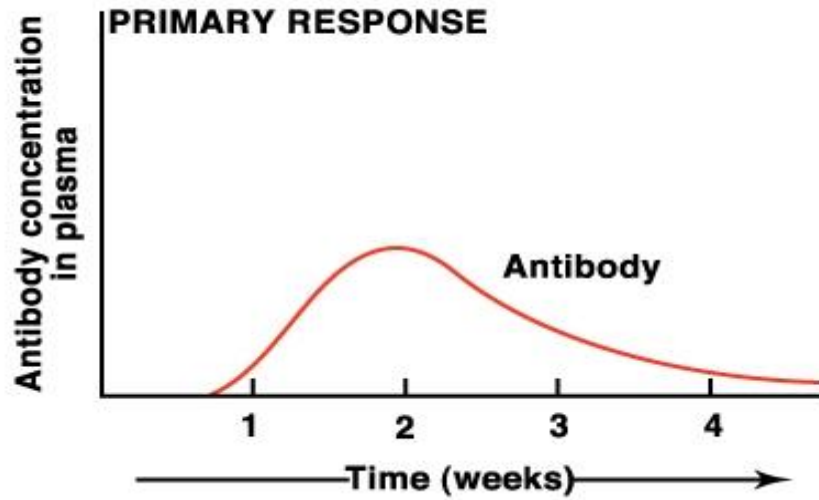
Pembentukan Kekebalan Jangka Panjang

(*long-term*)

- Pada kontak pertama dg antigen mikroba, respons antibodi terjadi lambat dlm bbrp hari sampai terbentuk sel plasma & akan mencapai puncak dlm bbrp minggu (Respons primer); & akan membentuk sel memori
- Jika terjadi kontak dg antigen yg sama, krn adanya sel memori, respons yg terjadi mjdn lebih cepat (Respons sekunder)

The Memory Immune Response





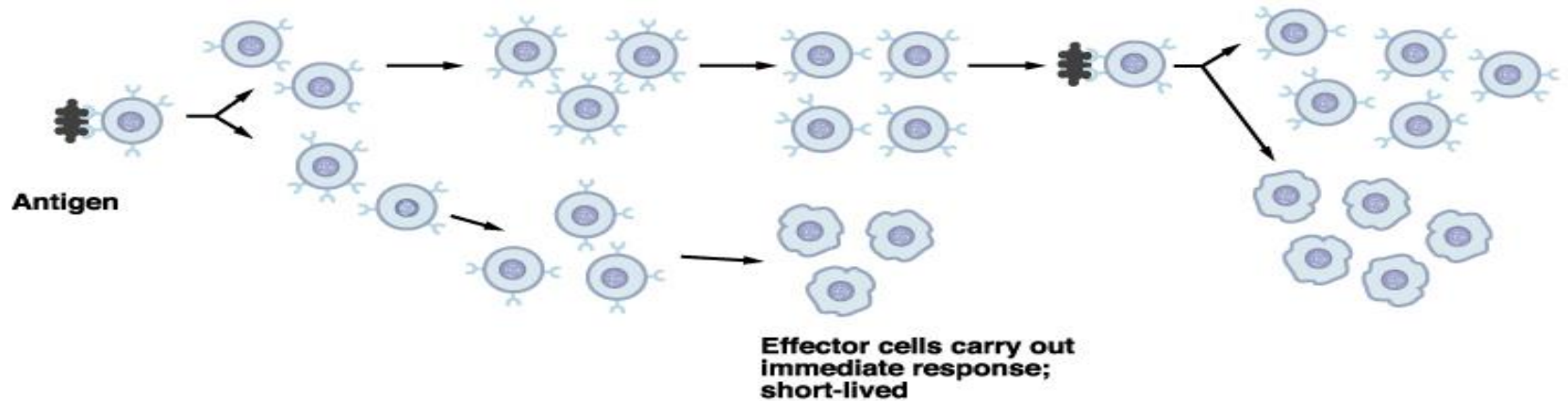
First exposure to antigen

Clonal expansion

Memory cells are long-lived, continue to reproduce

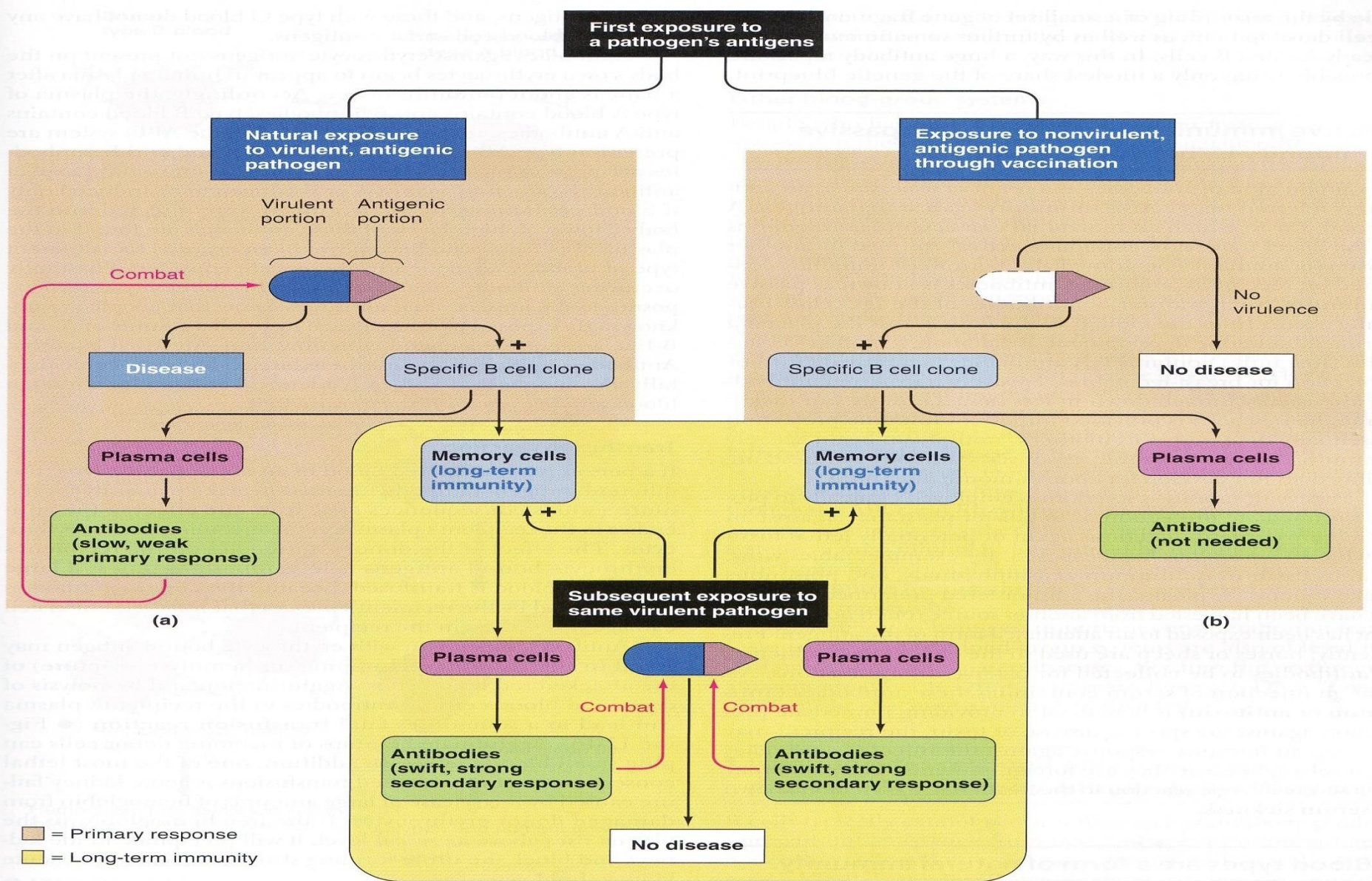
Second exposure to antigen

Stronger and more rapid response



Primary response

Secondary response

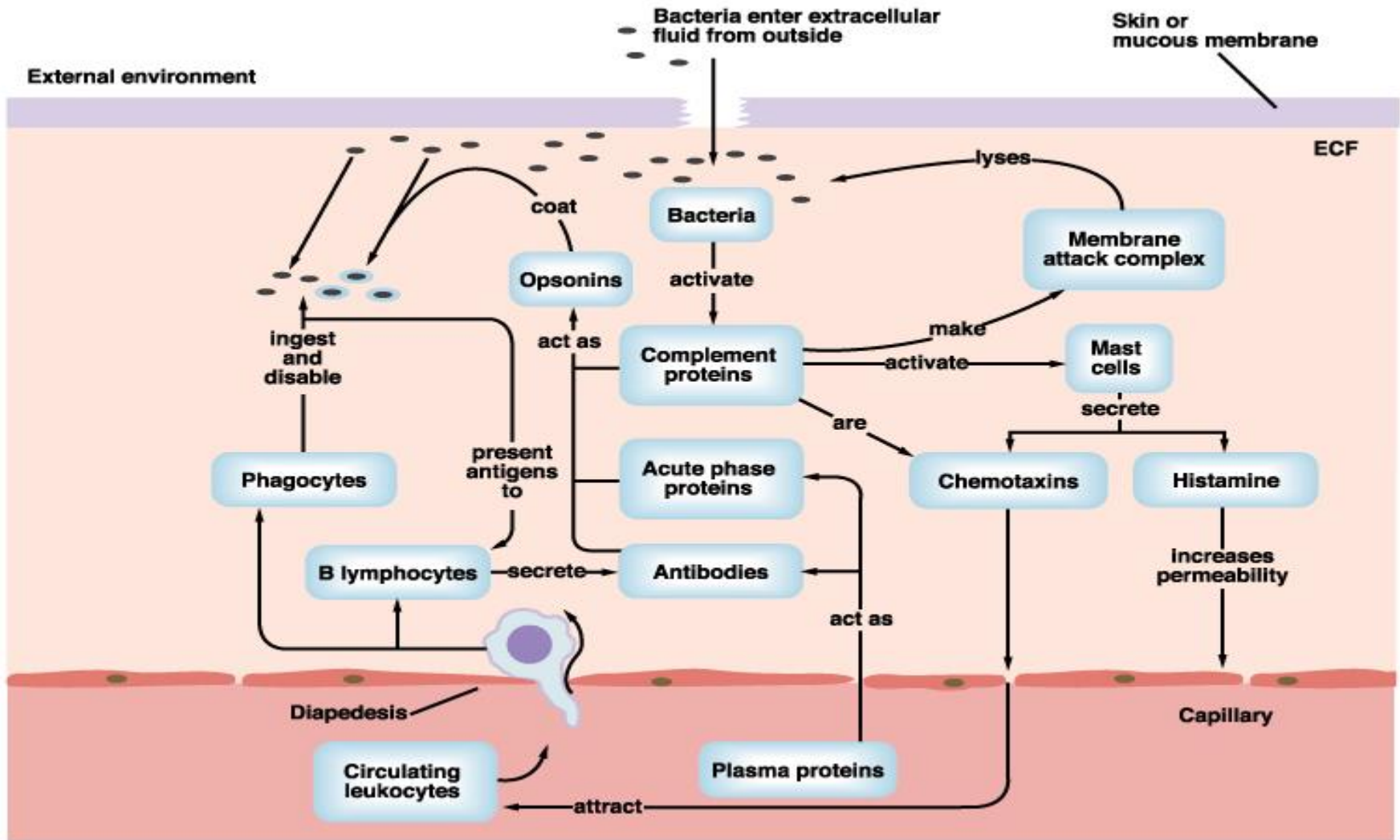


● FIGURE 12-15

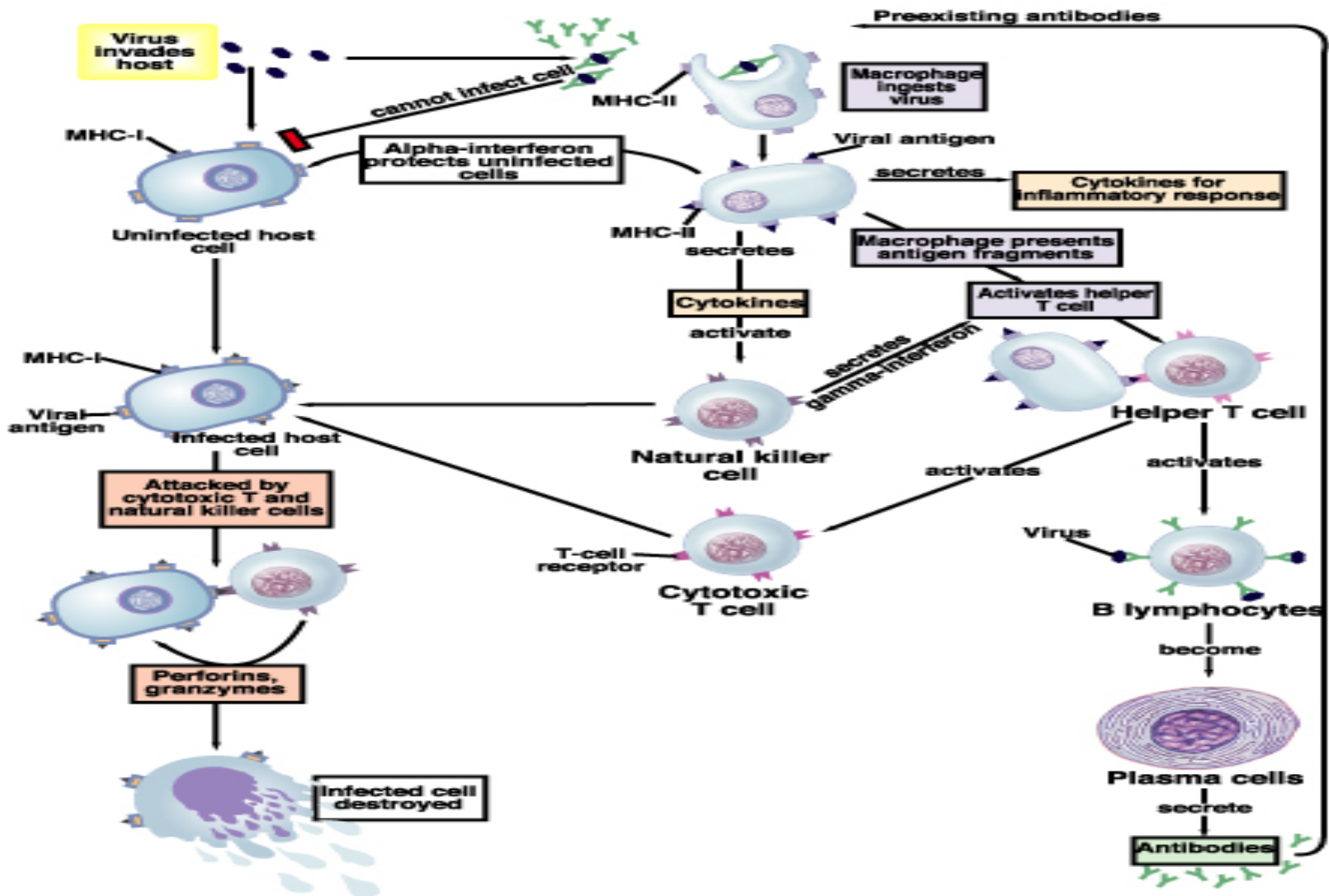
Means of acquiring long-term immunity

Long-term immunity against a pathogen can be acquired through having the disease or being vaccinated against it. (a) Exposure to a virulent (disease-producing) pathogen. (b) Vaccination with a modified pathogen that is no longer virulent (that is, can no longer produce disease) but is still antigenic. In both cases, long-term memory cells are produced that mount a swift, secondary response that prevents or minimizes symptoms on a subsequent natural exposure to the same virulent pathogen.

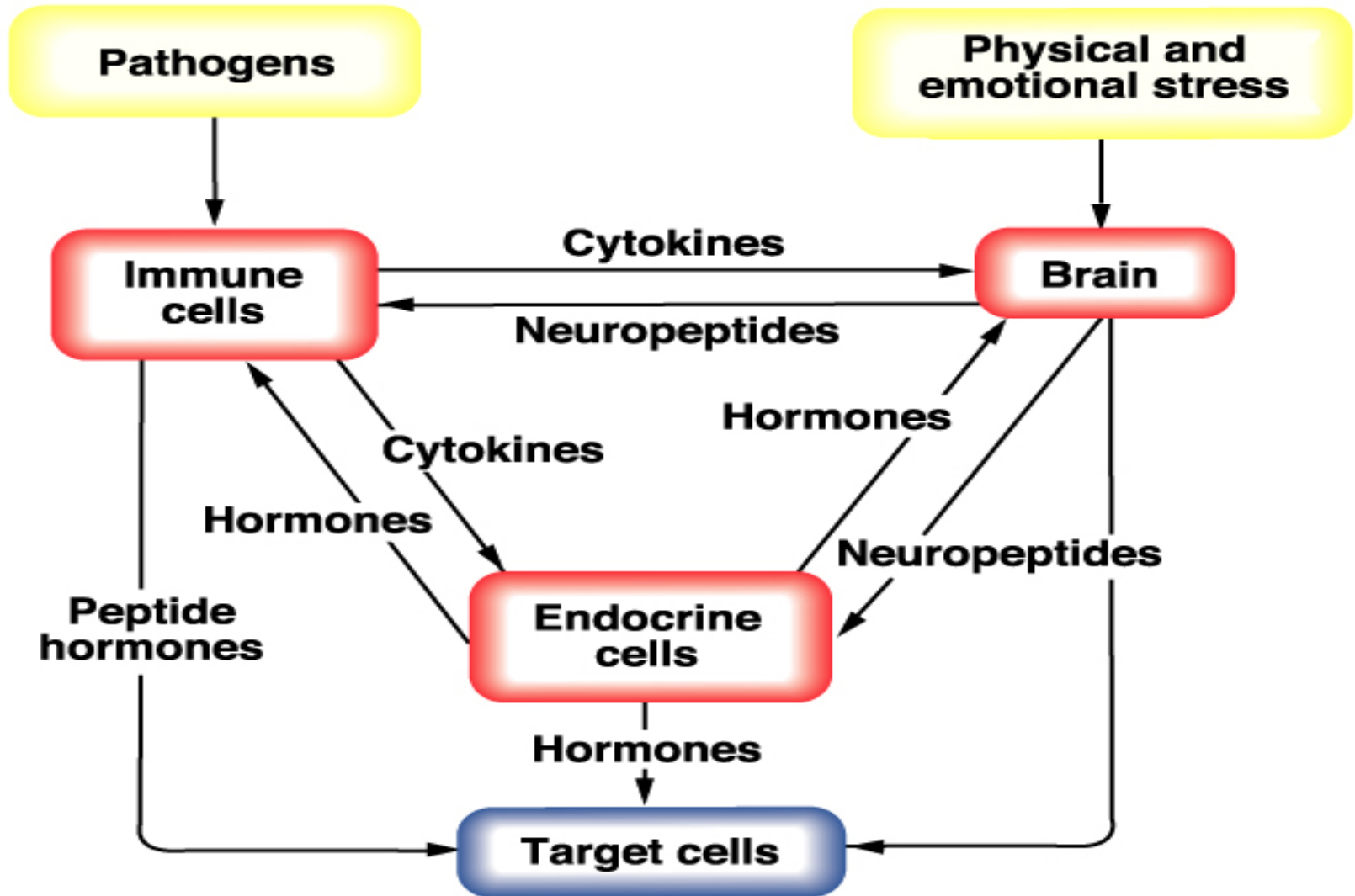
Respons Immun thd Invasi Bakteri



Respons Immun thd Invasi Virus



Interaksi Sistem Imun-Saraf- Endokrin



Gangguan sistem imun

1. *Lack of response* (imunodefisiensi)
contoh: AIDS, leukemia
2. *Incorrect response* (peny. autoimun)
contoh: DM tipe I, miastenia gravis,
multiple sclerosis; penyakit Graves.
3. *Overactive response* (alergi/
hipersensitivitas)
contoh: asma, *rhinitis allergic*, rx
transfusi