IMMUNOLOGY LECTURE

Dr. Deep Chandan Chakraborty

Assistant Professor, Asutosh College

INNATE IMMUNITY

Immunity which is not intrinsically affected by prior contact with antigen, i.e. all aspects of immunity not directly mediated by lymphocytes.

Nonspecific – raises similar response against all types of pathogen

Prompt – acts immediately as it does not requires to built

No immunologic memory – does not produce memory cells

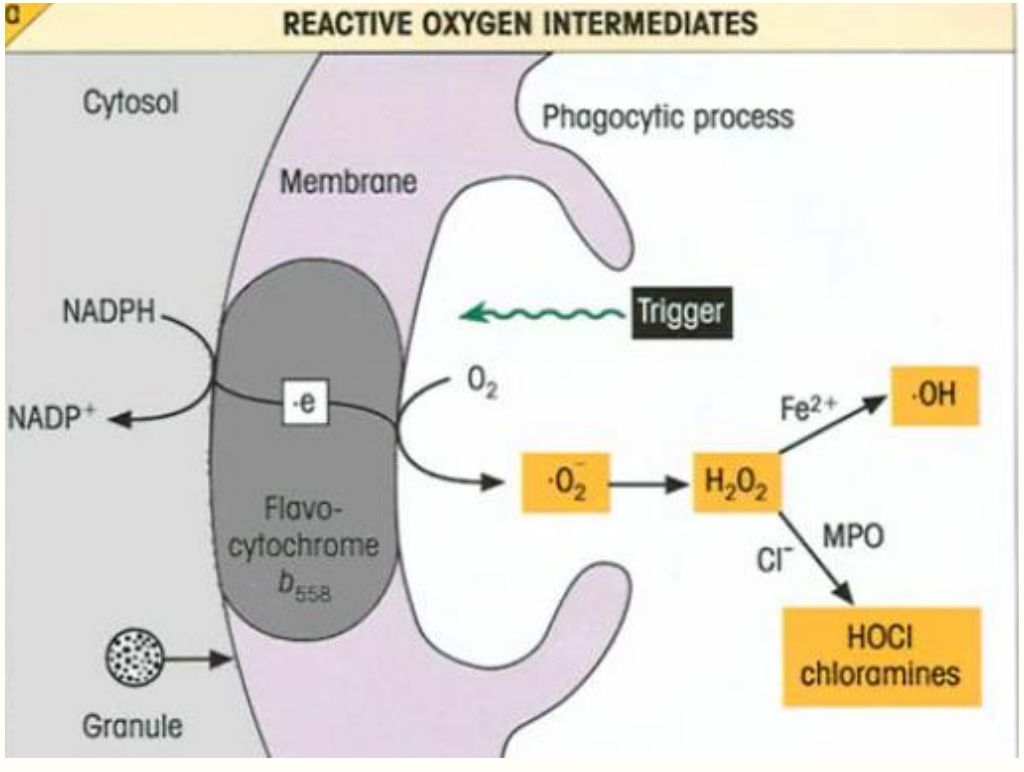
Cells involved – macrophages, dendritic cells, neutrophils, eosinophils etc.

Molecules involved – antimicrobials (Lysozymes, CRPs, Collectins), Complements, antivirals (Interferons)

Receptors – pattern recognition receptors (TLRs, NLRs), Lectins ctc.

Modes of pathogen killing - by roi, rni and antimicrobials, stomach acidity

Barriers - anatomical (skin, mucous membrane, cilia), inflammatory, physiological (temperature, pH, chemical - roi, rni and antimicrobials) and phagocytotic (monocytes, macrophages, dendritic cells, neutrophils, eosinophils and natural killer cells)



OXYGEN-INDEPENDENT MECHANISMS

Cathepsin G Low mol. wt defensins High mol. wt cationic proteins Bactericidal permeability increasing protein (BPI)	Damage to microbial membranes
Lysozyme	Splits mucopeptide in bacterial cell wall
Lactoferrin	Complex with iron
Proteolytic enzymes Variety of other hydrolytic enzymes	Digestion of killed organisms

Killing by reactive oxygen intermediates

$$NADPH + O_2 \xrightarrow{\text{oxidase}} NADP^+ + \cdot O_2^- \quad \text{(superoxide anion)}$$

Phagocytosis triggers production of NADPH

↓

Electron passes from NADPH to $cytb_{558}$

↓

This reduced molecular O_2 to superoxide anion.

↓

Reaction catalysed by this NADPH oxidase, and initiates the formation of reactive oxygen intermediates (ROI)

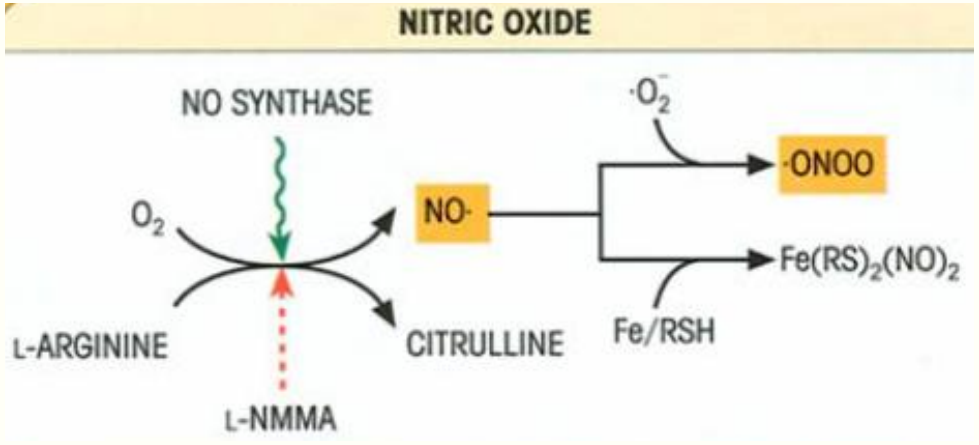
↓

The superoxide anion undergoes conversion to hydrogen peroxide under the influence of superoxide dismutase, and subsequently to hydroxyl radicals (*OH)

↓

H_2O_2 and the halogenated compounds are more stable and therefore diffuse further, making them toxic to microorganisms in the extracellular spaces.

Killing by reactive nitrogen intermediates



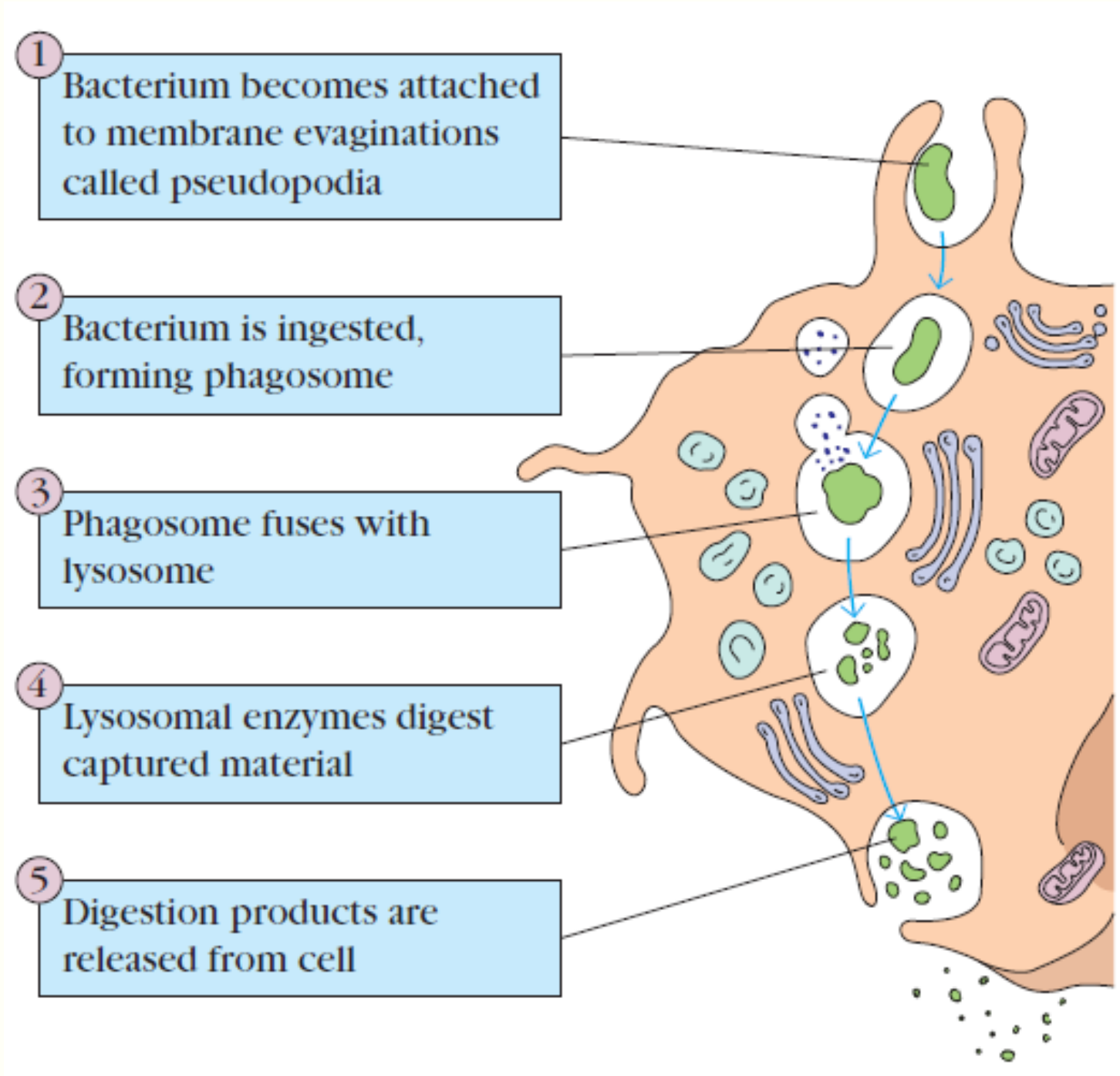
Nitric oxide induces formation of inducible NO- synthase (iNOS) within most cells, particularly macrophages and human neutrophils, thereby generating a powerful antimicrobial system

Whereas the NADPH oxidase is dedicated to the killing of extracellular organisms taken up by phagocytosis and cornered within the phagocytic vacuole, the NO.

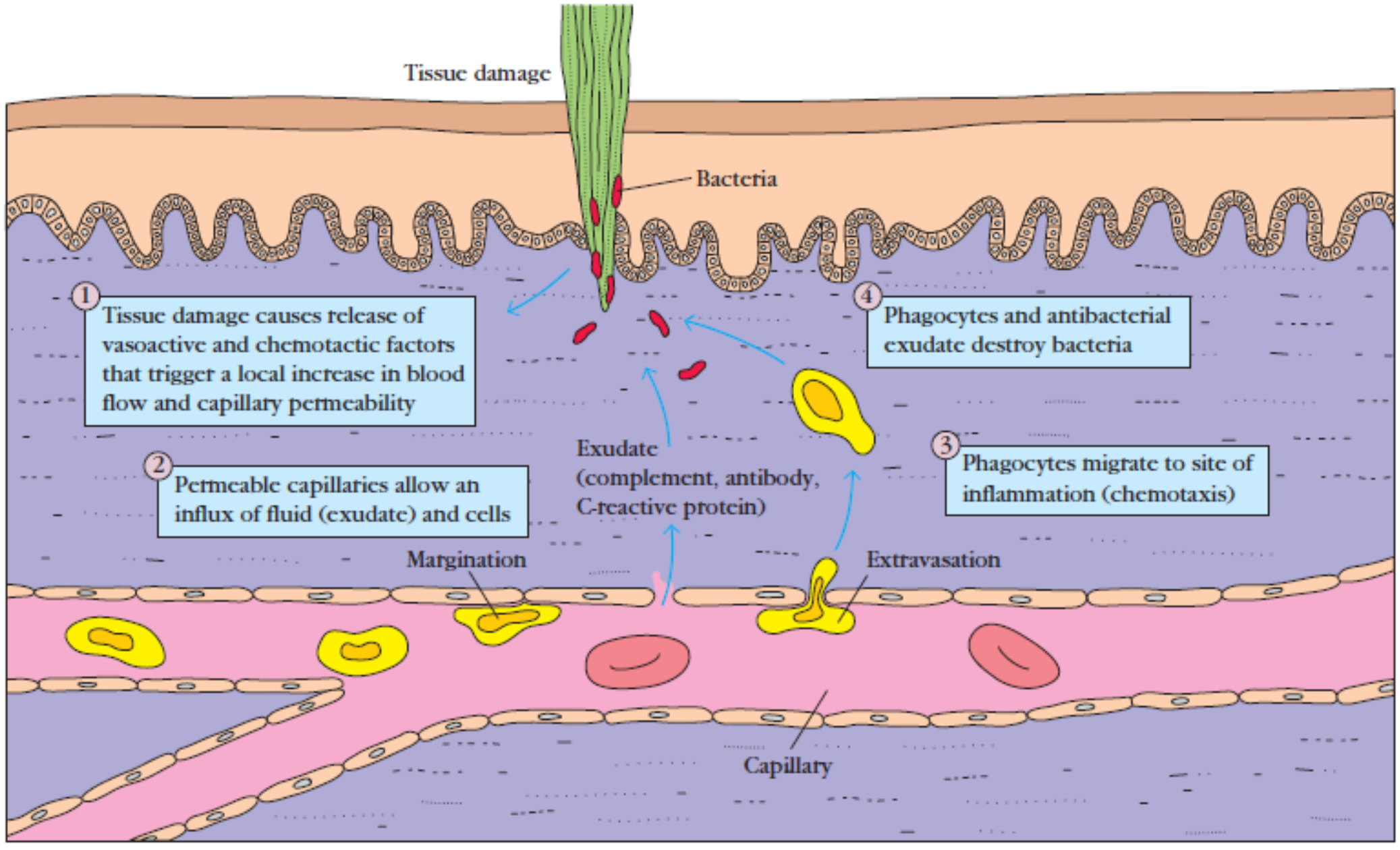
Mechanism can operate against microbes which invade the cytosol; so, it is not surprising that the majority of nonphagocytic cells which may be infected by viruses and other parasites are endowed with an iNOS capability.

The mechanism of action may be through degradation of the Fe-S prosthetic groups of certain electron transport enzymes, depletion of iron and production of toxic -ONO0 radicals.

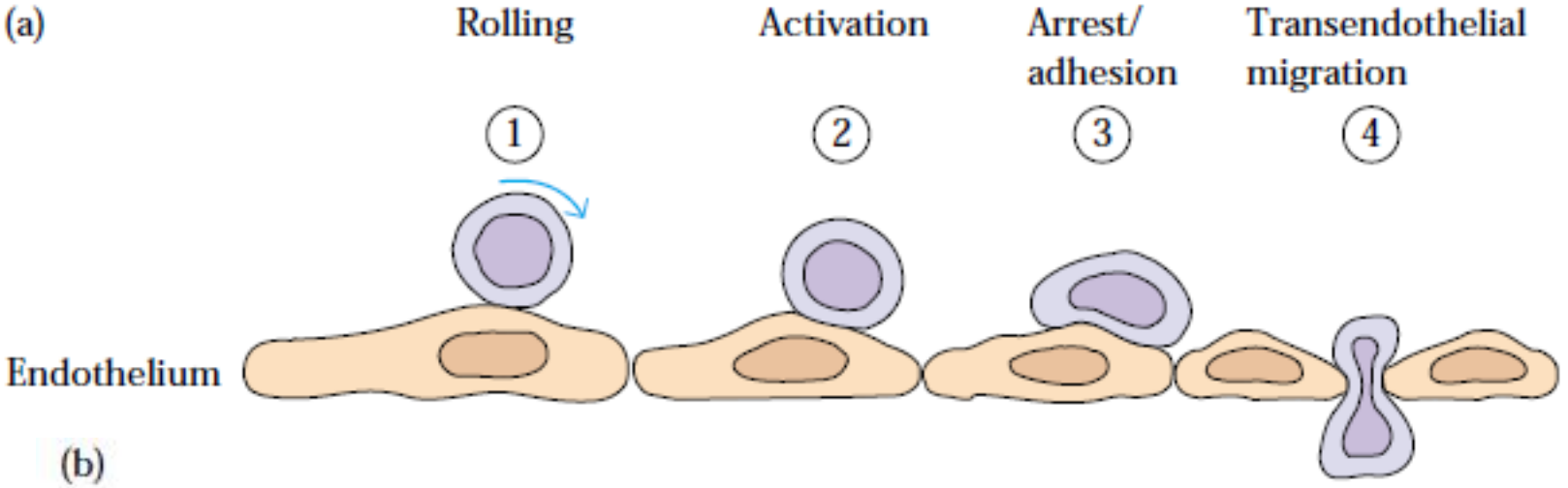
PHAGOCYTOTIC BARRIER



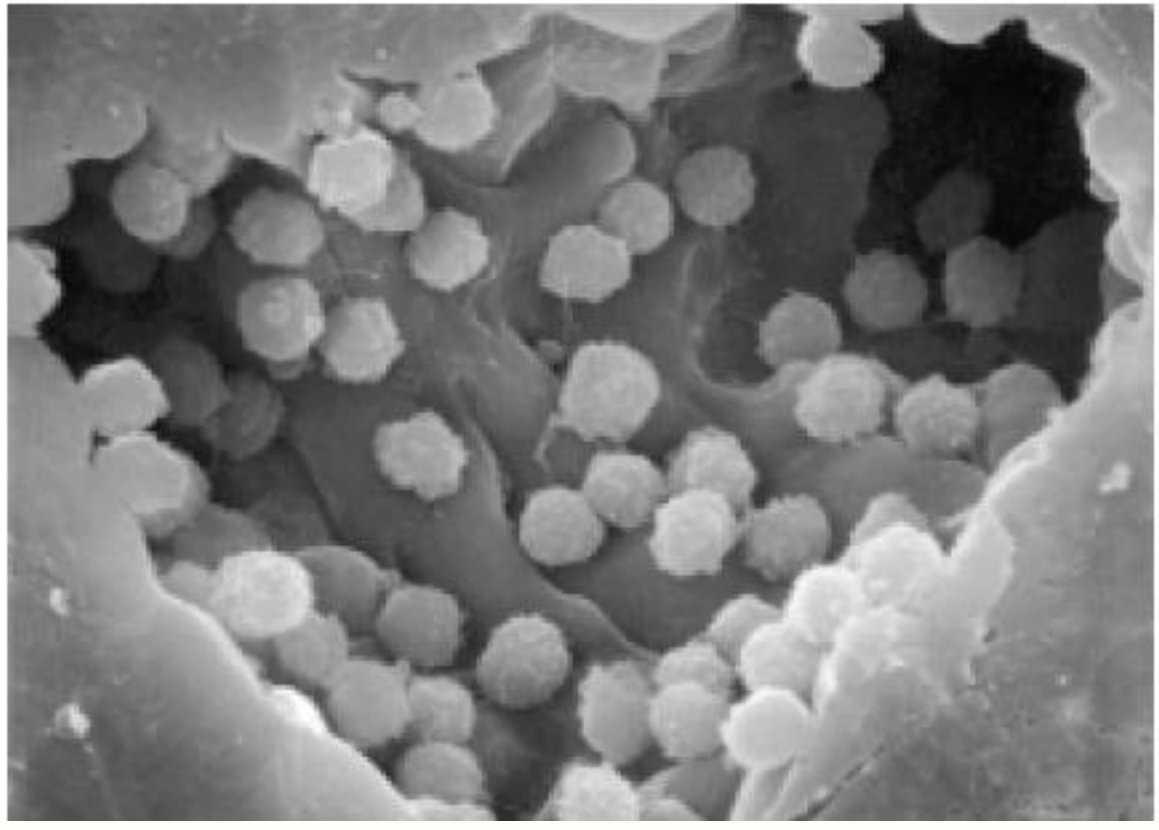
INFLAMMATORY BARRIER



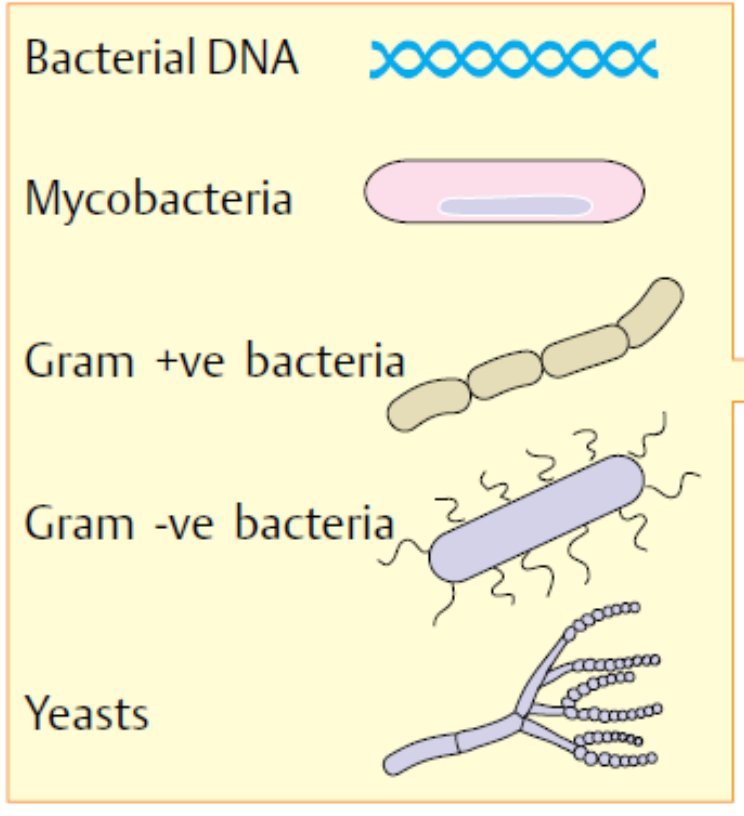
(a)


Rolling
Activation
Arrest/
adhesion
Transendothelial
migration
1
2
3
4
Endothelium

(b)



Toll-like Receptors



PAMPs	PRR
– CpG	Toll-like-receptor 9
– LPS	Scavenger receptors, LBP, CD14, Toll-like receptors 4
– Lipoproteins	Toll-like-receptor 2
– Peptidoglycans	CD14, Toll-like-receptor 2
– Lipoarabinomannan	CD1, Toll-like-receptor 2
– Mannan	Mannose receptor Mannose-binding protein
– Zymosan	Mannose receptor, β-glucan receptors, Toll-like receptor 2

A. Pathogen-Associated Molecular Patterns and Pattern Recognition Receptors

C-reactive protein - An acute phase protein which is able to bind to the surface of microorganisms where it functions as a stimulator of the classical pathway of complement activation, and as an opsonin for phagocytosis.

Lysozyme - Anti-bacterial enzyme present in phagocytic cell granules, tears and saliva, which digests peptidoglycans in bacterial cell walls.

Pathogen-associated molecular pattern (PAMP): Molecules such as lipopolysaccharide, peptidoglycan, lipoteichoic acids and mannans, which are widely expressed by microbial pathogens as repetitive motifs but are not present on host tissues. They are therefore utilized by the pattern recognition receptors (PRRs) of the immune system to distinguish pathogens from self antigens.

Pattern recognition receptor (PRR): Receptors on professional antigen-presenting cells and phagocytes which enable them to recognize pathogen associated molecular patterns (PAMPs).

ADAPTIVE IMMUNITY

Immunity mediated by lymphocytes and characterized by antigen specificity and memory.

Antigenic specificity (B and T cell receptors; clonal selection - distinguish antigens even with difference in single amino acid)

Diversity (Variable domains or CDRs of immunoglobulins)

Immunologic memory (secondary antibodies from memory B and T lymphocytes)

Self/non self recognition (spares self proteins, learns to target foreign antigens)

Types - Cellular (B and T lymphocytes, antigen presenting cells) and **Humoral** (secreted antibodies)

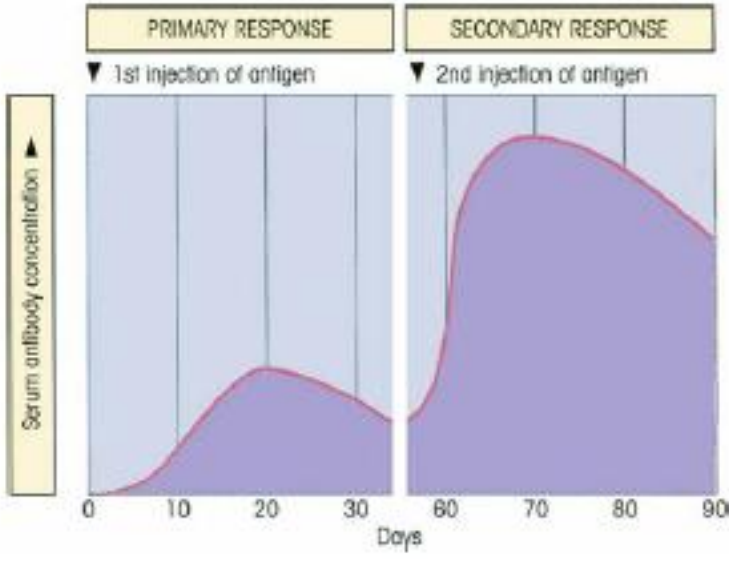


Figure 2.12. Primary and secondary response. A rabbit is injected on two separate occasions with tetanus toxoid. The antibody response on the second contact with antigen is more rapid and more intense.

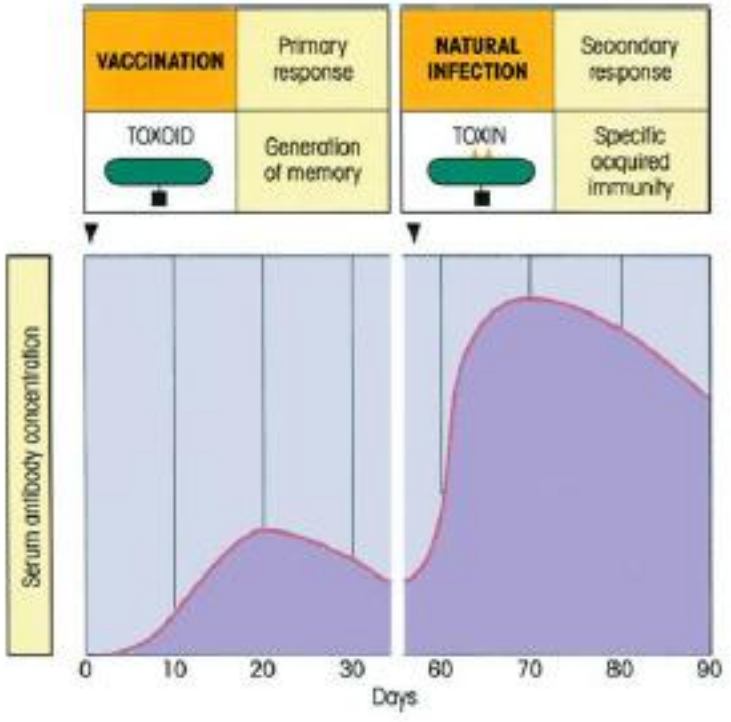
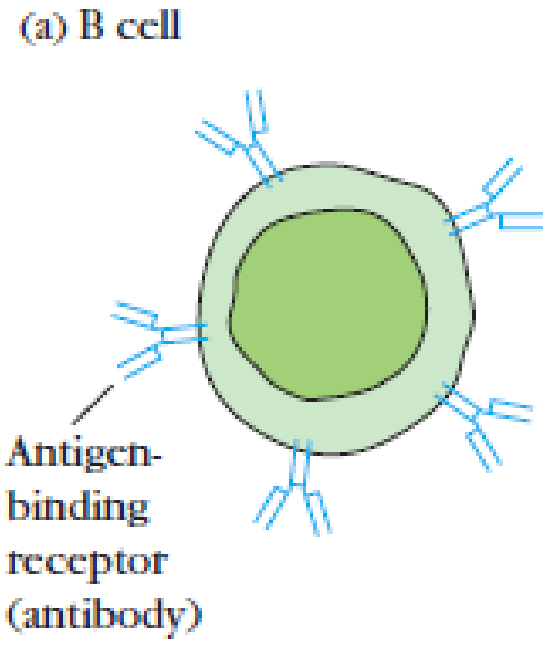


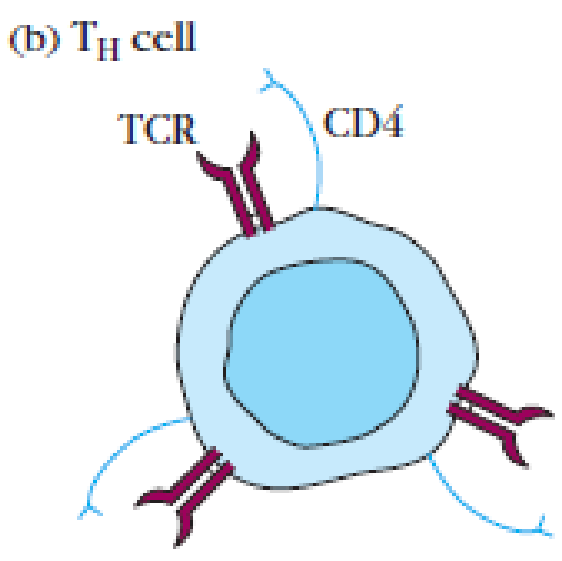
Figure 2.14. The basis of vaccination illustrated by the response to tetanus toxoid. Treatment of the bacterial toxin with formaldehyde destroys its toxicity (associated with ▲▲) but retains antigenicity. Exposure to toxin in a subsequent natural infection boosts the memory cells, producing high levels of neutralizing antibody which are protective.

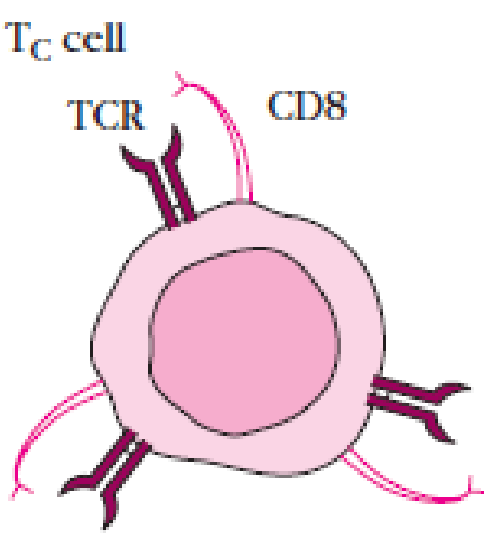
Immunological Memory – difference between primary and secondary immune response

Vaccination – generation of immunologic memory for combating deadly diseases

CELLS OF IMMUNE SYSTEM





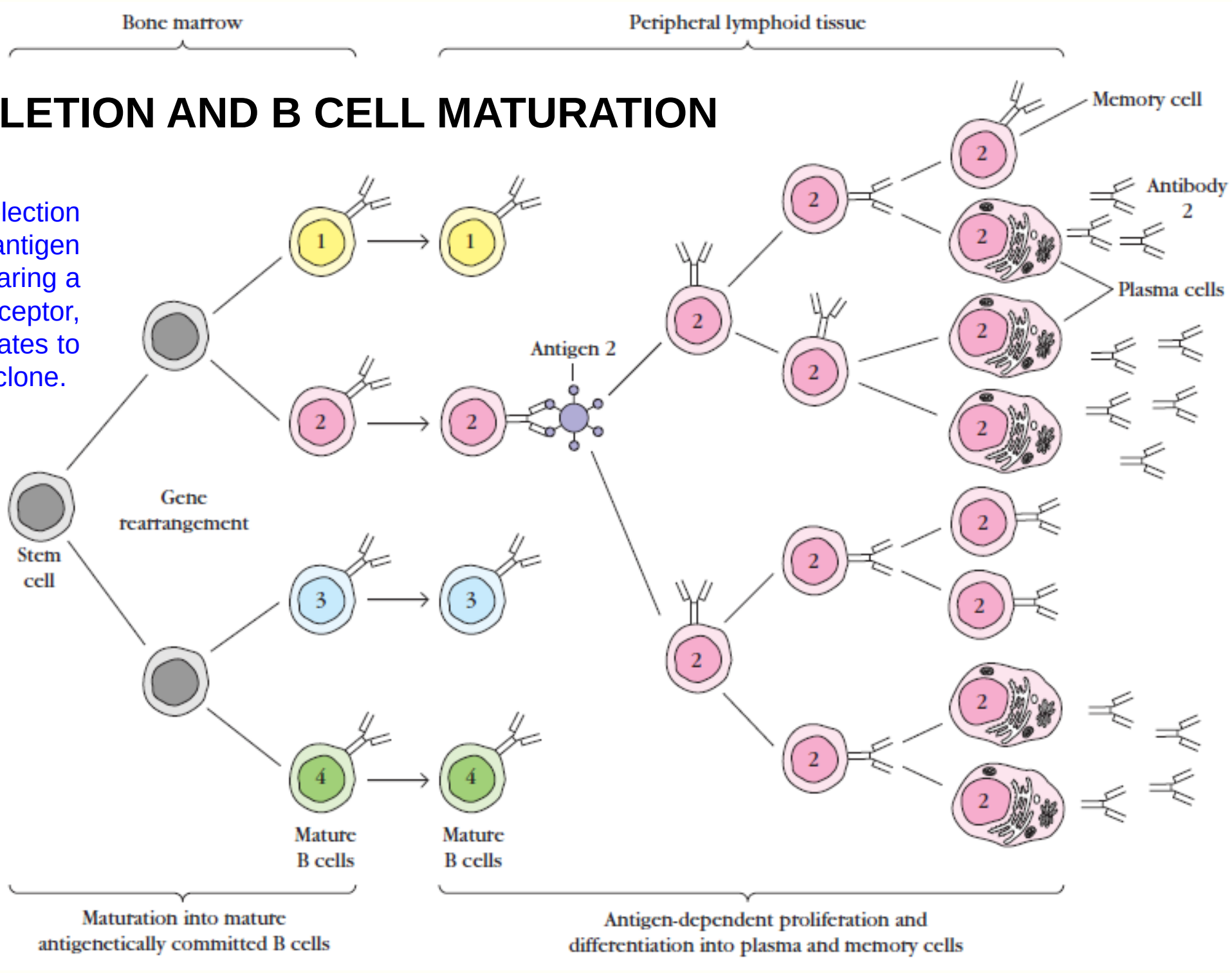


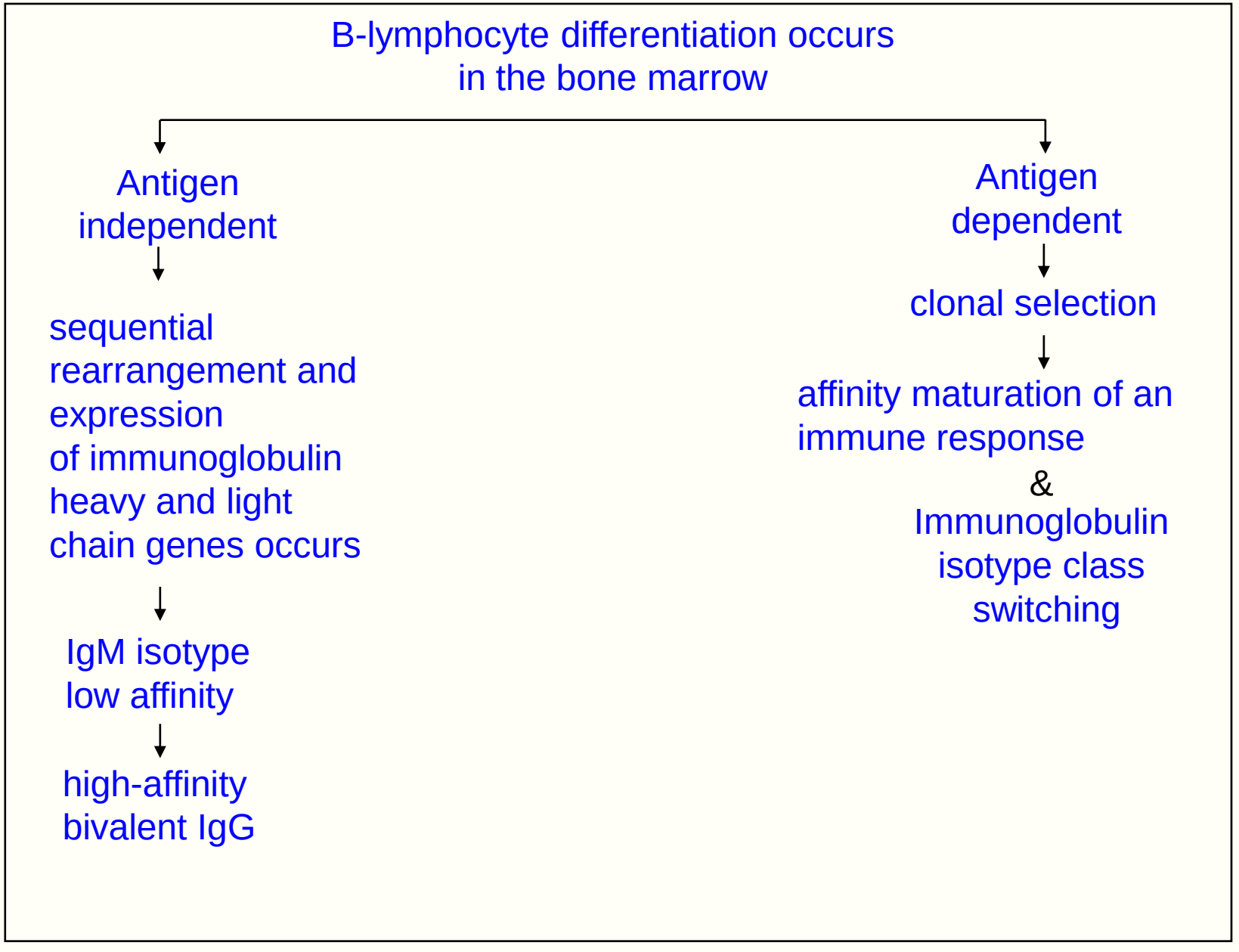
Helper T Lymphocyte (T_h)
A subclass of T-cells which provide help (in the form of cytokines and/or cognate interactions) necessary for the expression of effector function by other cells in the immune system.

Cytotoxic T Lymphocyte (T_c)
T-cells (usually CD8') which kill target cells following recognition of foreign peptide-MHC molecules on the target cell membrane.

CLONAL SELETION AND B CELL MATURATION

Definition: The selection and activation by antigen of a lymphocyte bearing a complementary receptor, which then proliferates to form an expanded clone.



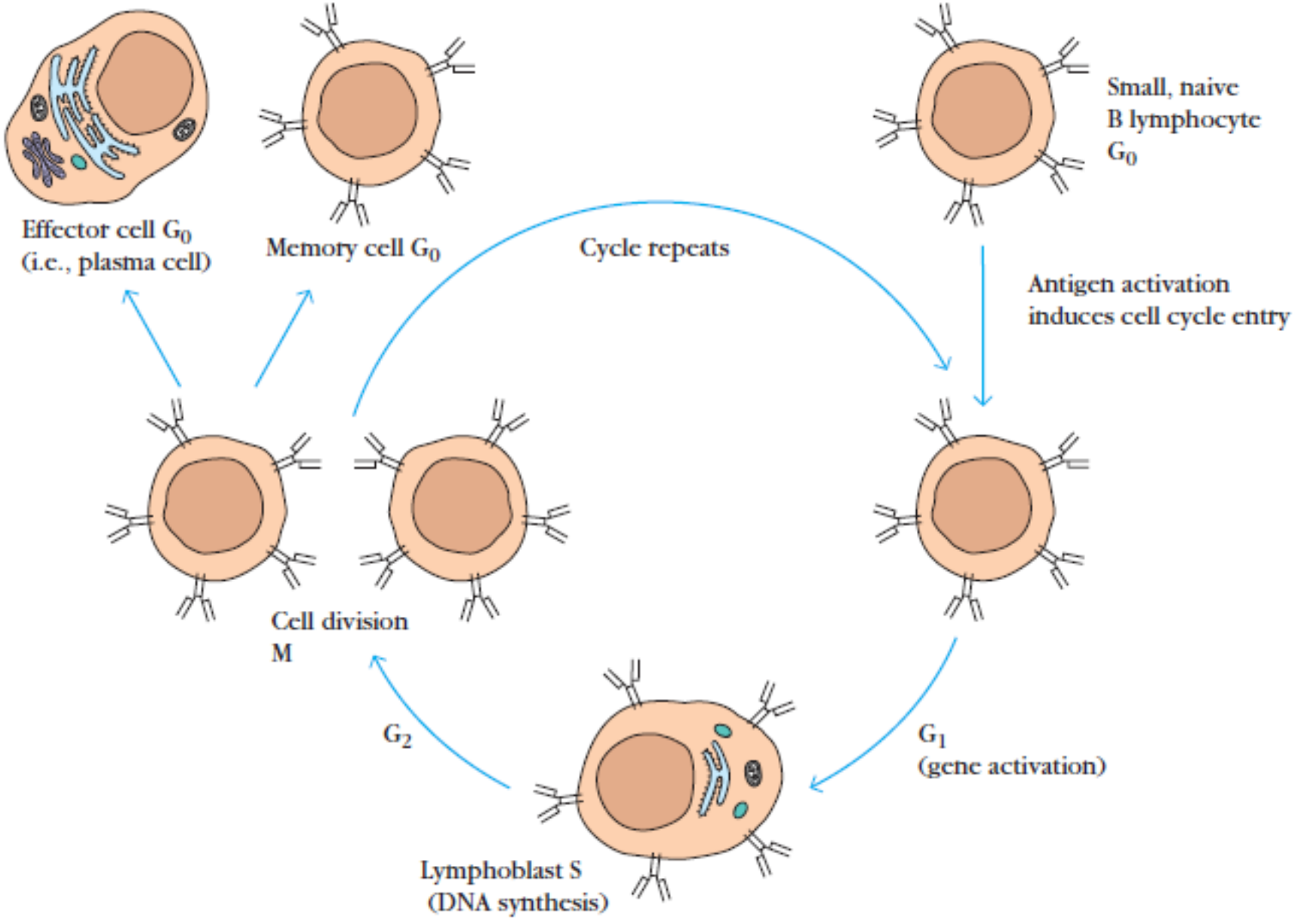

B-lymphocyte differentiation occurs
in the bone marrow
Antigen
independent
sequential
rearrangement and
expression
of immunoglobulin
heavy and light
chain genes occurs
IgM isotype
low affinity
high-affinity
bivalent IgG
Antigen
dependent
clonal selection
affinity maturation of an
immune response
&
Immunoglobulin
isotype class
switching

B-CELL MATURARION

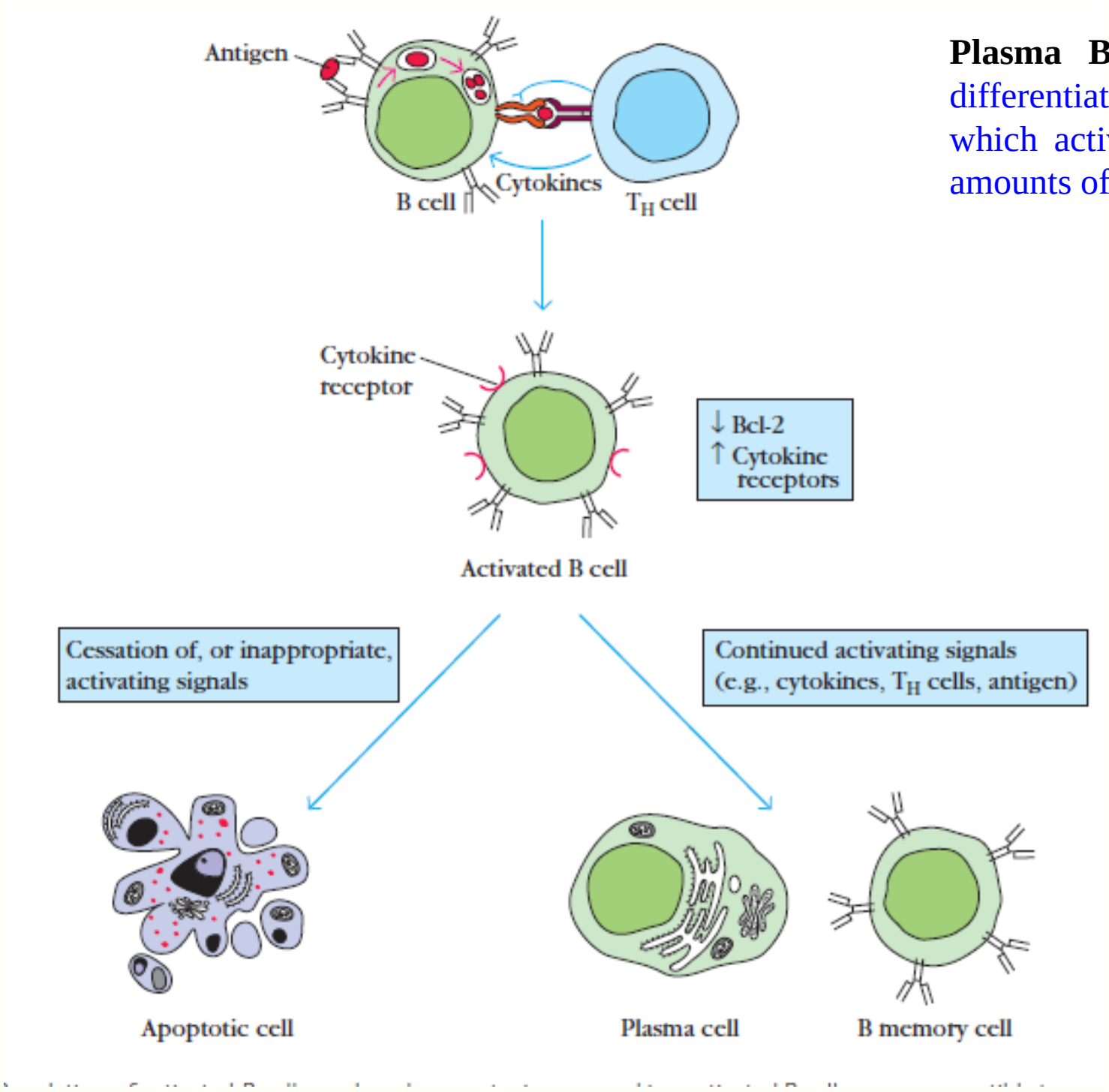
The **affinity maturation** of an immune response is achieved by the mechanism of somatic hypermutation. This mechanism generates nucleotide substitutions within heavy and light chain variable region genes that can result in amino acid substitutions affecting the affinity of the antibody combining site.

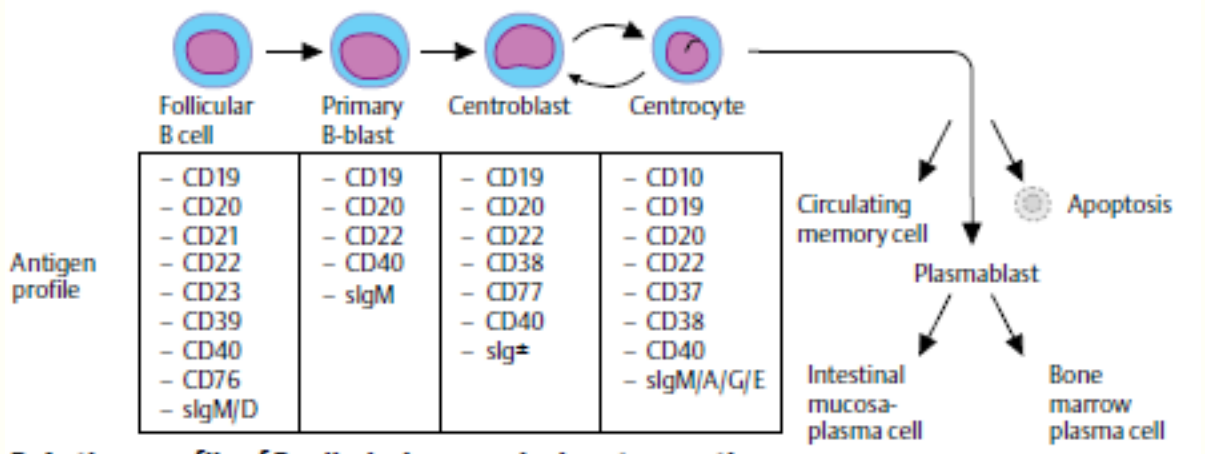
Immunoglobulin isotype class switching results in the association of different heavy chain constant region domains with the same variable region domain. Progeny B-lymphocytes switch from IgM, the first isotype expressed in all primary immune responses, to another heavy chain class or subclass resulting in populations of antibody molecules that have the same antigen binding specificities associated with different isotypes such as IgG, IgA, or IgE. The different isotypes or constant regions of the antibody molecule carry distinct recognition sites for receptors of a variety of effector systems.

B CELL CELL CYCLE

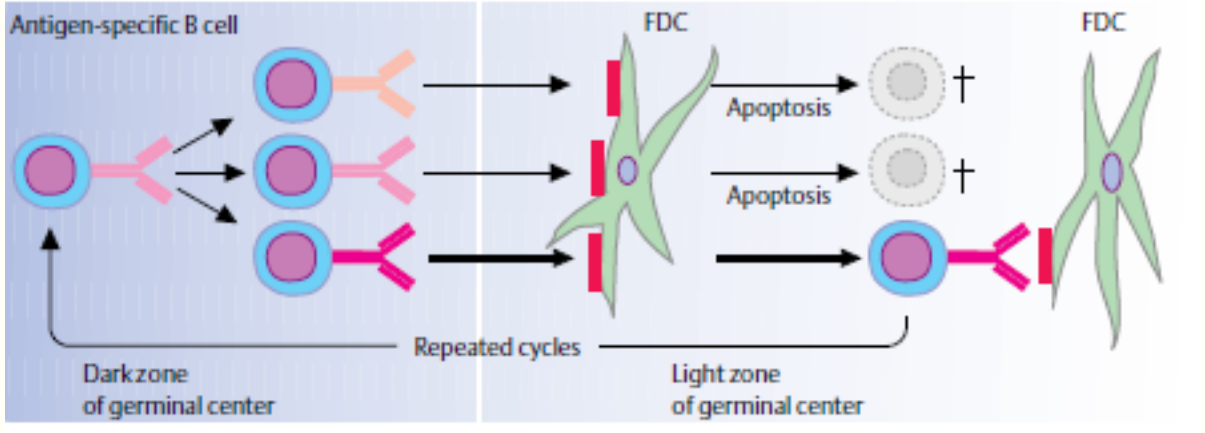


Plasma B cell: Terminally differentiated B lymphocyte which actively secretes large amounts of antibody.





B. Antigen profile of B cells during germinal center reaction



Immunoglobulin structure

Early studies showed the bulk of the antibody activity in serum to be in the slow electrophoretic fraction termed **gamma globulin** (subsequently immunoglobulin).

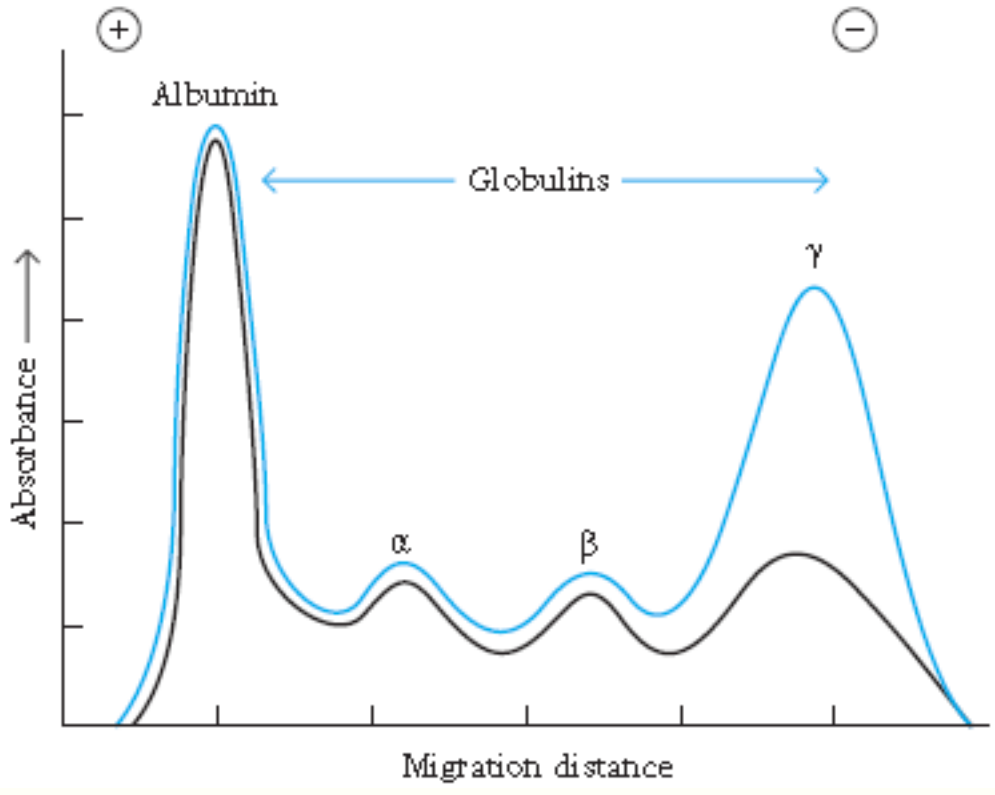
Antibody molecules have a common structure of four peptide chains. This structure consists of two identical **light (L) chains** and two identical **heavy (H) chains.** Each light chain is bound to a heavy chain by a disulfide bond, and by such noncovalent interactions as salt linkages, hydrogen bonds, and hydrophobic bonds.

To **Rodney Porter** and **Gerald Edelman** must go the credit for unlocking the secrets of the basic structure of the immunoglobulin molecule.

Hinge region, is rich in proline residues and is flexible, giving IgG, IgD, and IgA segmental flexibility. As a result, the two Fab arms can assume various angles to each other when antigen is bound.

Hypervariable regions of the VH and VL domains form the antigen binding site of the antibody molecule. Because the antigen binding site is complementary to the structure of the epitope, these areas are now more widely called **complementarity determining regions (CDRs).**

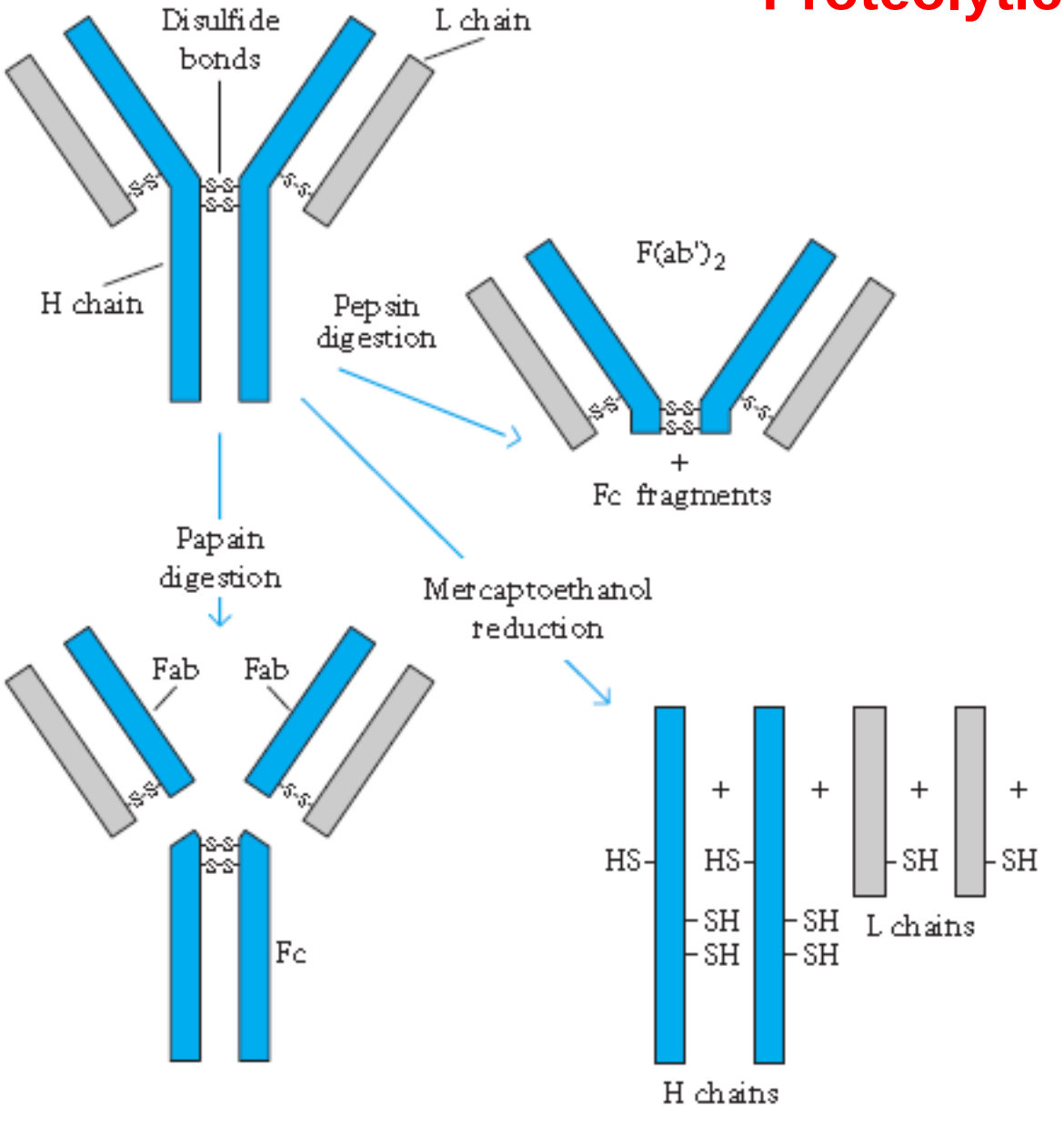
The remainder of the VL and VH domains exhibit far less variation; these stretches are called the **framework regions (FRs).**



F(ab)$_2$ - Bivalent antigen-binding fragment obtained following pepsin digestion of immunoglobulin. Consists of both light chains and the N-terminal part of both heavy chains linked by disulfide bonds.

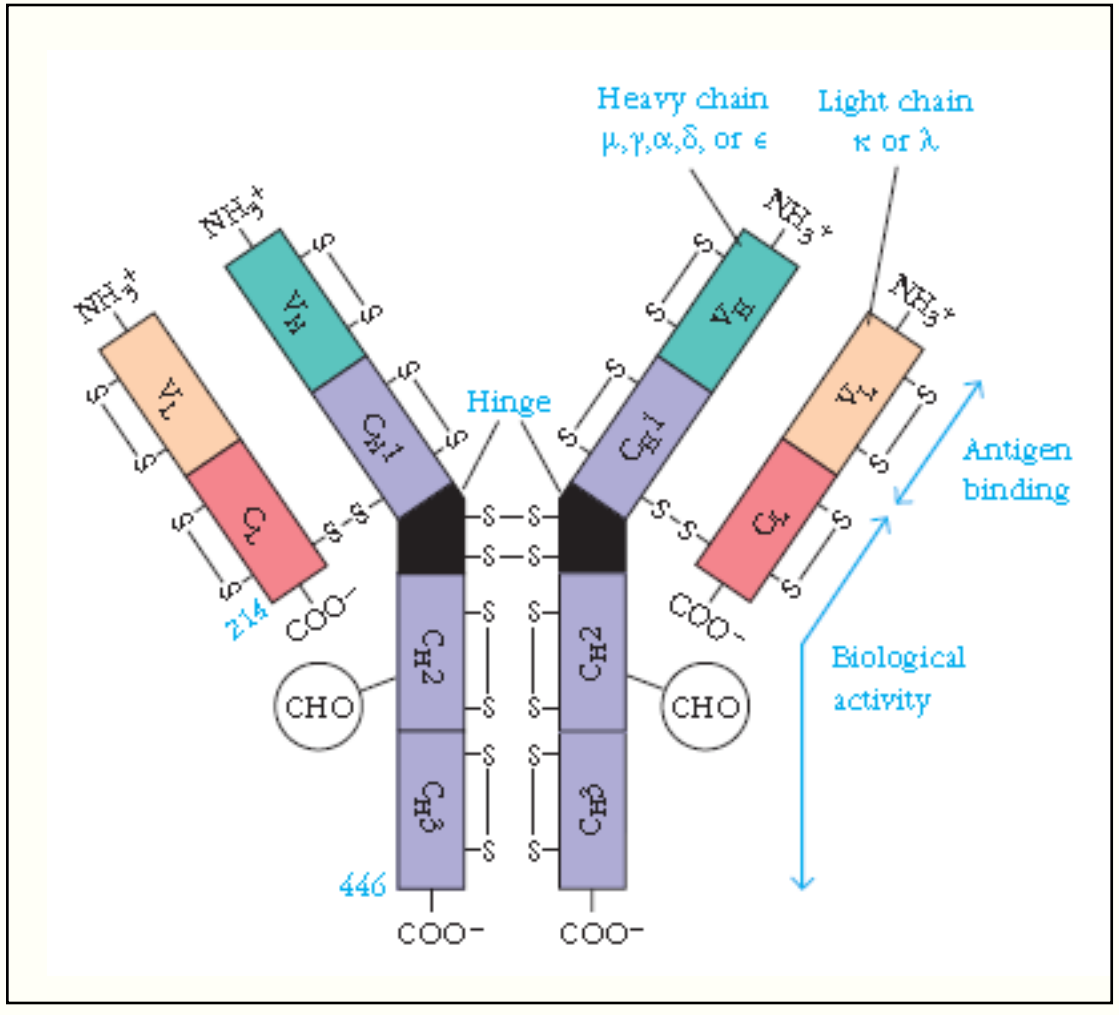
Fc: Crystallizable, non-antigen binding fragment of an immunoglobulin molecule obtained following papain digestion. Consists of the C-terminal portion of both heavy chains

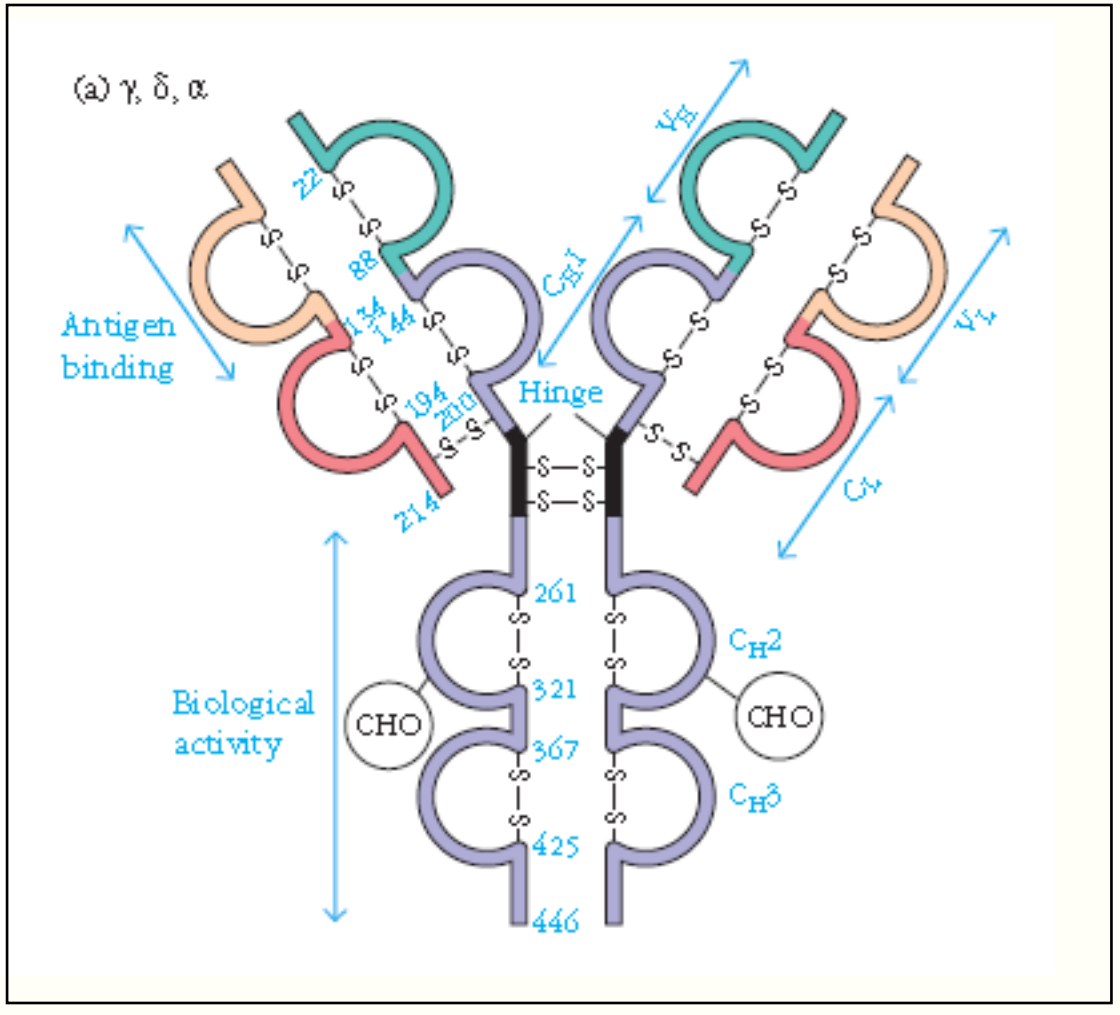
Proteolytic cleavage



Treatment	Result	Remark
Papain+Ig	two univalent Fab (*fragment antigen binding)* fragments and the remaining fragment had no affinity for antigen called Fc *(fragment crysfullizable).*	destroyed the precipitating power 2 bands in gel
Pepsin+Ig	$F(ab')_2$, was isolated; it still precipitated antigen and so retained both binding sites, but the Fc portion was further degraded.	2 bands in gel

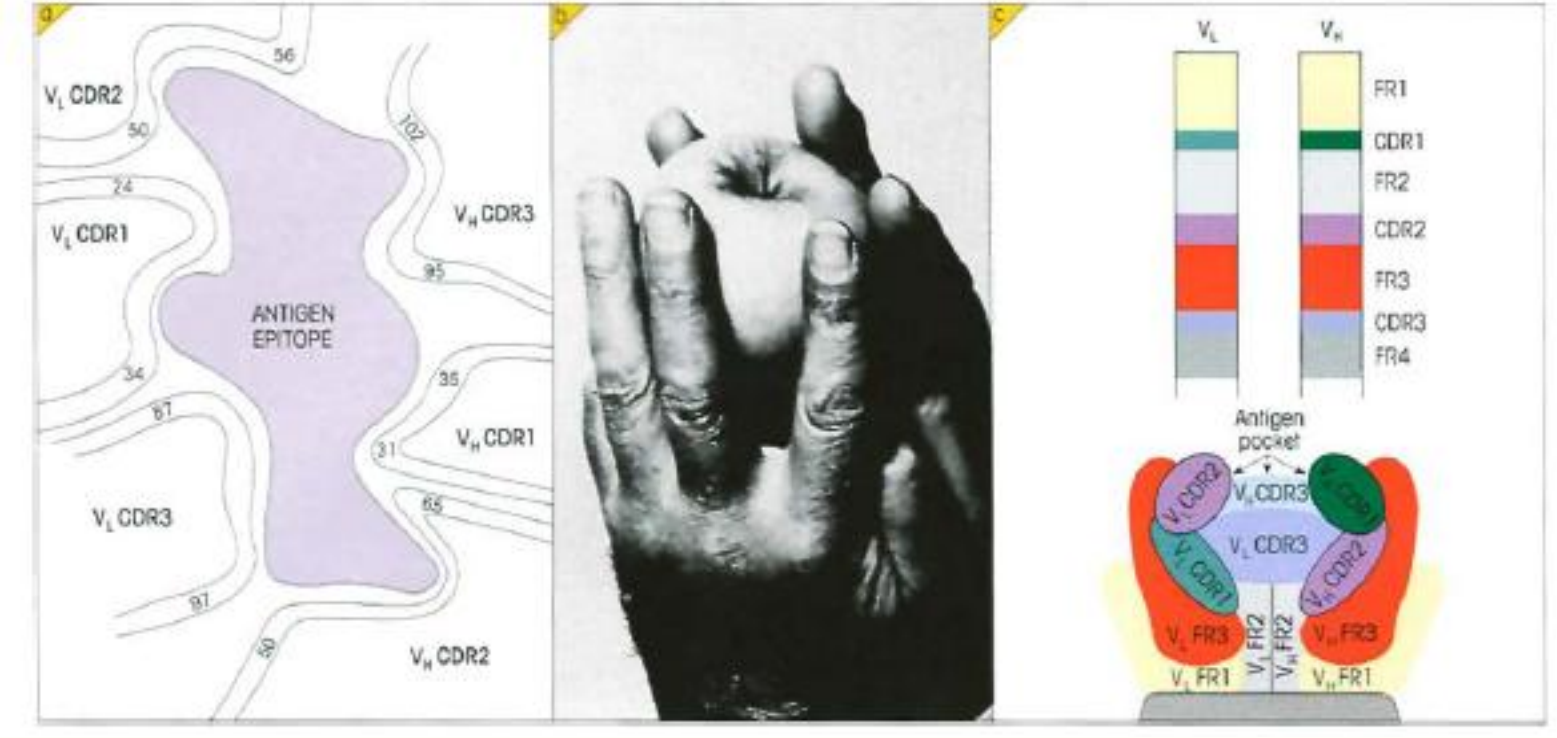
Immunoglobulin G structure



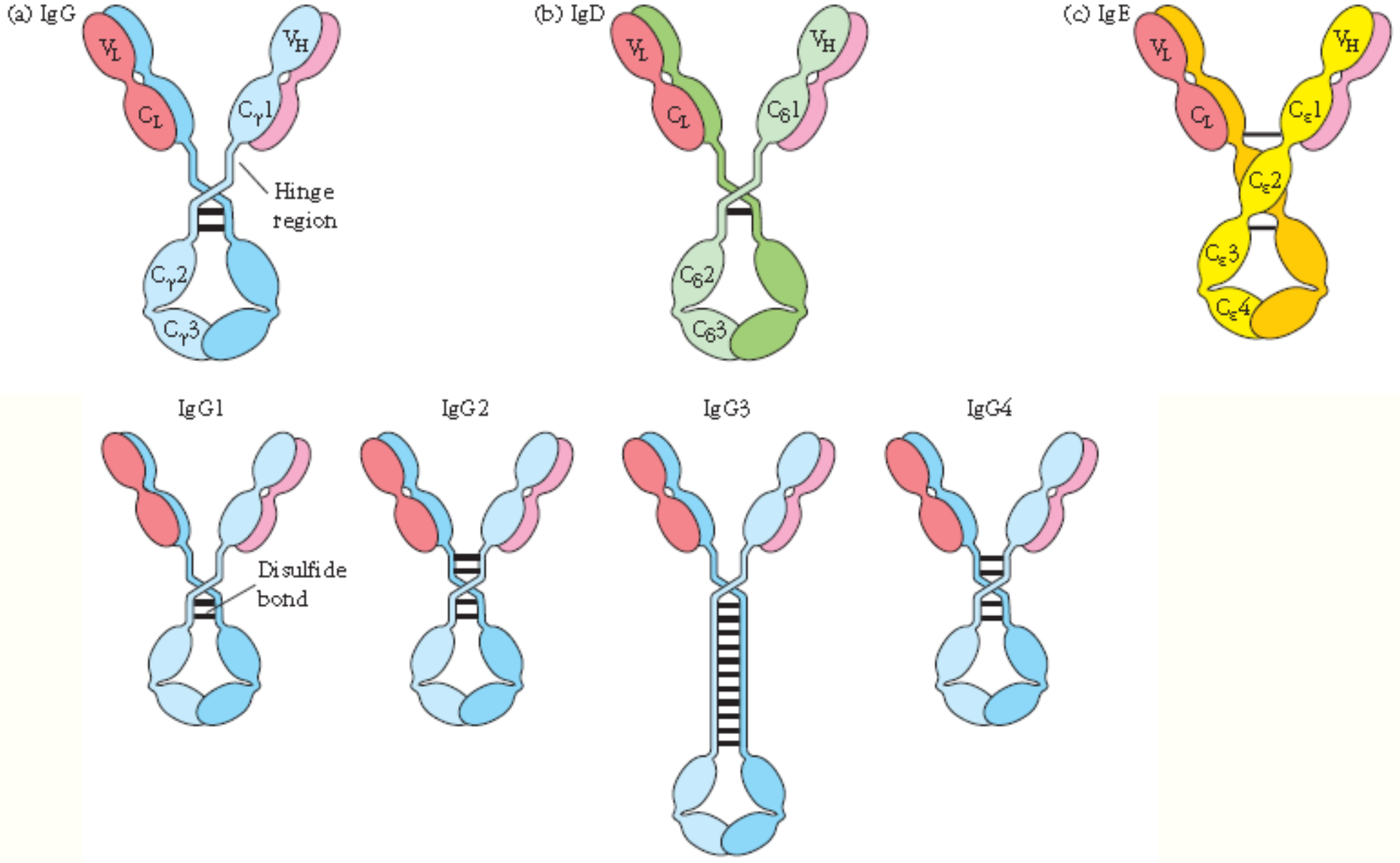


16 disulfide linkages = 12 intrachain + 4 interchain bonds
Light chain types – κ or λ
Heavy chain types –γ, α, δ, ξ and μ

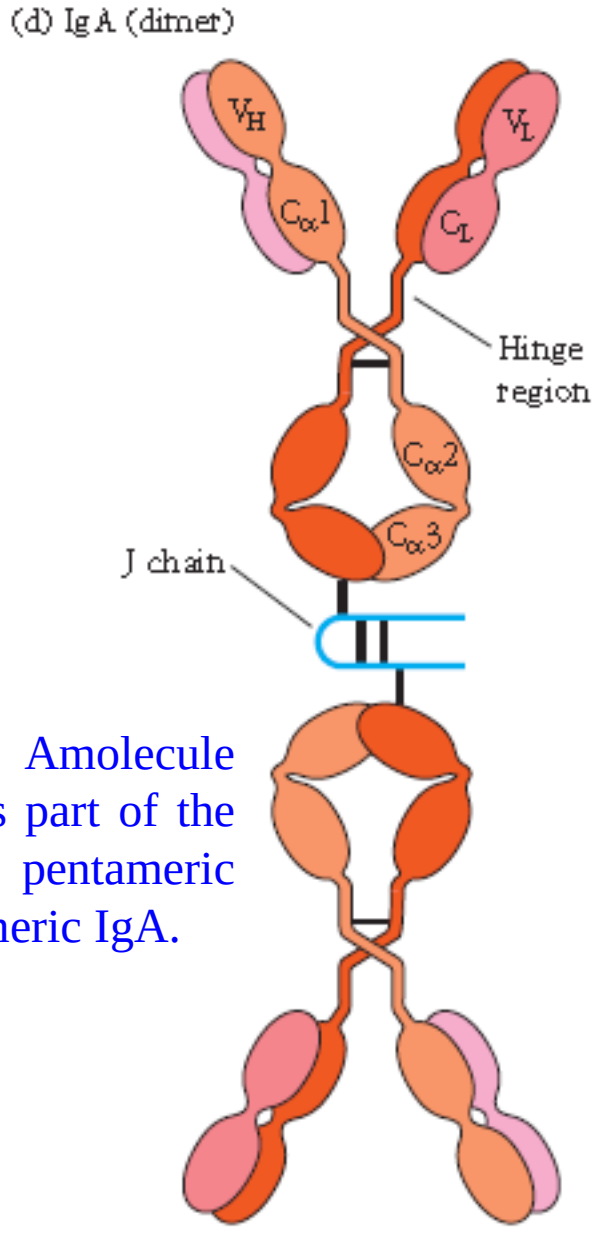
Antigen and antibody binding -

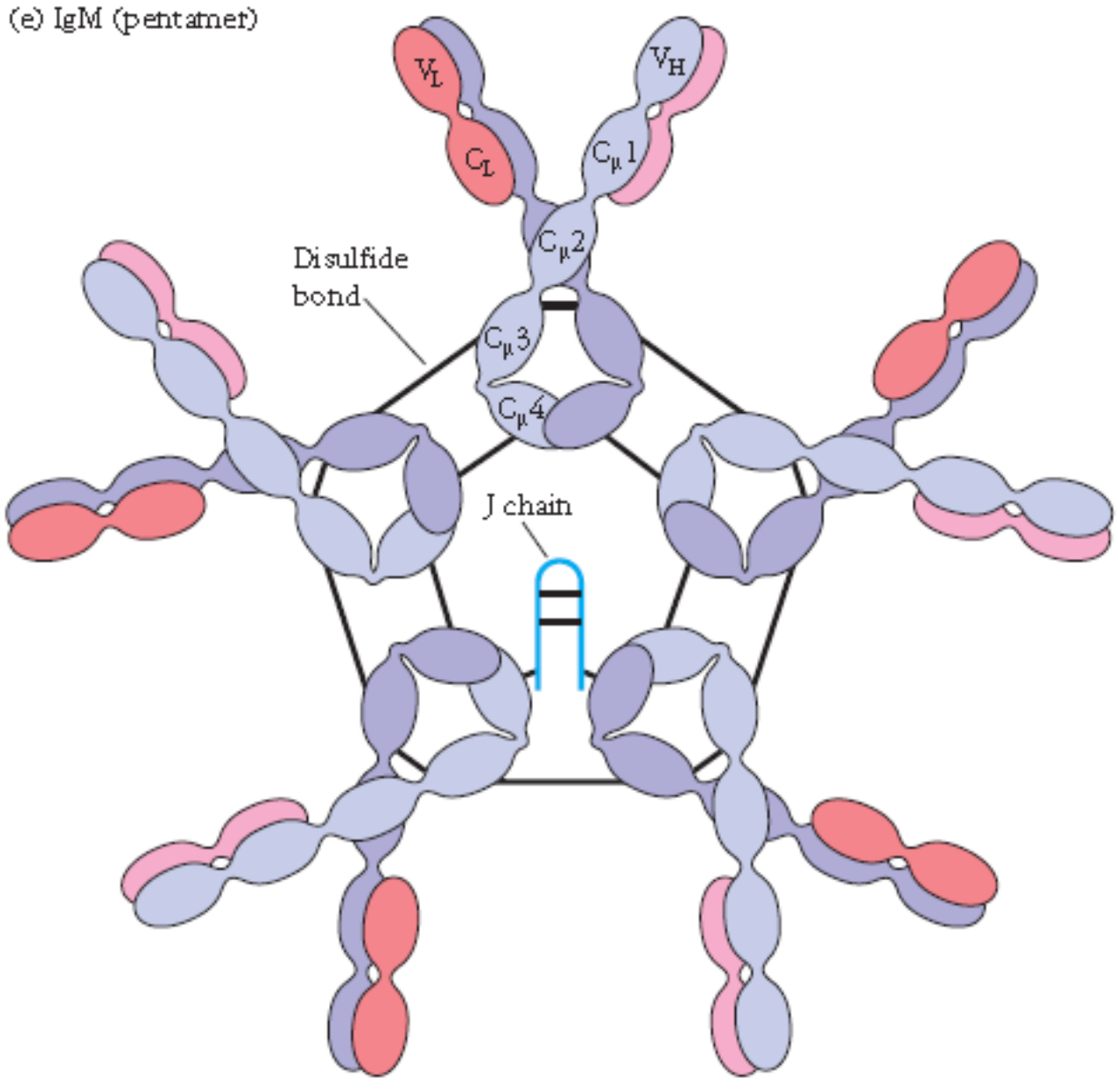


Immunoglobulin classes – IgG, IgD, IgE



Immunoglobulin classes – IgA, IgM





J chain: Amolecule which forms part of the structure of pentameric IgM and dimeric IgA.

TABLE 4-2 Properties and biological activities* of classes and subclasses of human serum immunoglobulins

Property/Activity	IgG1	IgG2	IgG3	IgG4	IgA1	IgA2	IgM‡	IgE	IgD
Molecular weight†	150,000	150,000	150,000	150,000	150,000–600,000	150,000–600,000	900,000	190,000	150,000
Heavy-chain component	γ1	γ2	γ3	γ4	α1	α2	μ	ε	δ
Normal serum level (mg/ml)	9	3	1	0.5	3.0	0.5	1.5	0.0003	0.03
In vivo serum half life (days)	23	23	8	23	6	6	5	2.5	3
Activates classical complement pathway	+	+/−	++	−	−	−	+++	−	−
Crosses placenta	+	+/−	+	+	−	−	−	−	−
Present on membrane of mature B cells	−	−	−	−	−	−	+	−	+
Binds to Fc receptors of phagocytes	++	+/−	++	+	−	−	?	−	−
Mucosal transport	−	−	−	−	++	++	+	−	−
Induces mast-cell degranulation	−	−	−	−	−	−	−	+	−

*Activity levels indicated as follows: ++ = high; + = moderate; +/− = minimal; − = none; ? = questionable.

†IgG, IgE, and IgD always exist as monomers; IgA can exist as a monomer, dimer, trimer, or tetramer. Membrane-bound IgM is a monomer, but secreted IgM in serum is a pentamer.

‡IgM is the first isotype produced by the neonate and during a primary immune response.

Role of IgE in allergy

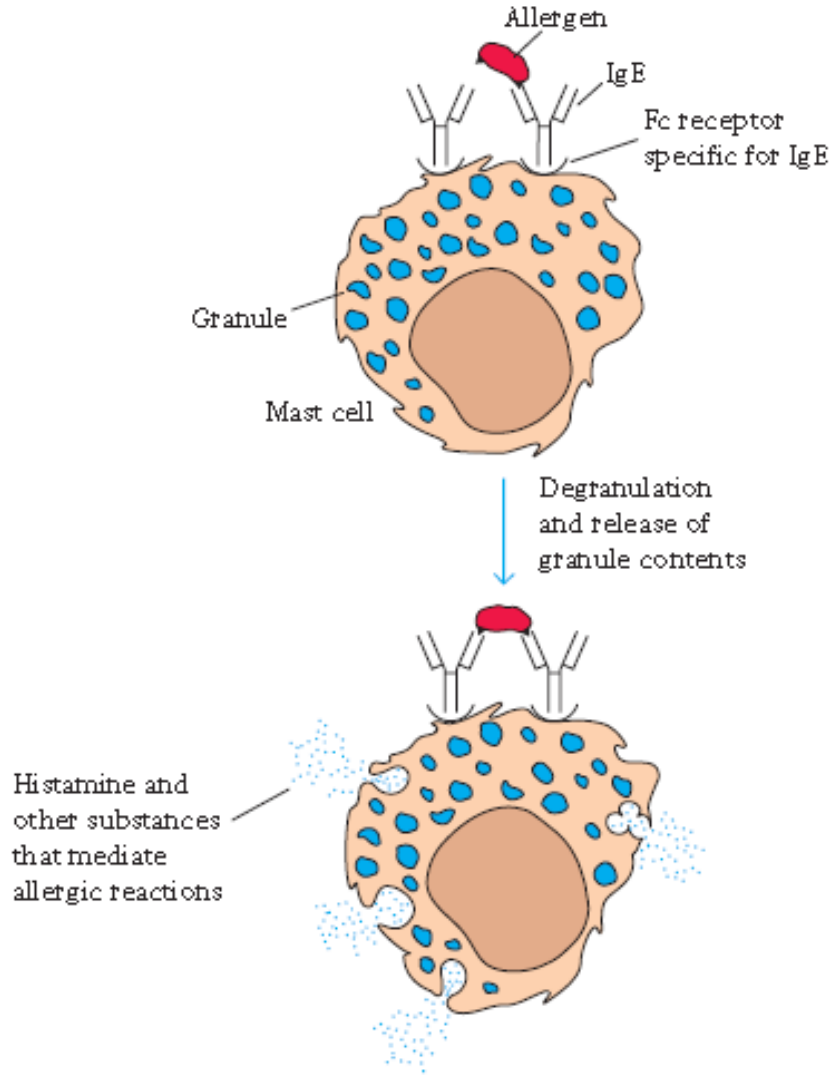
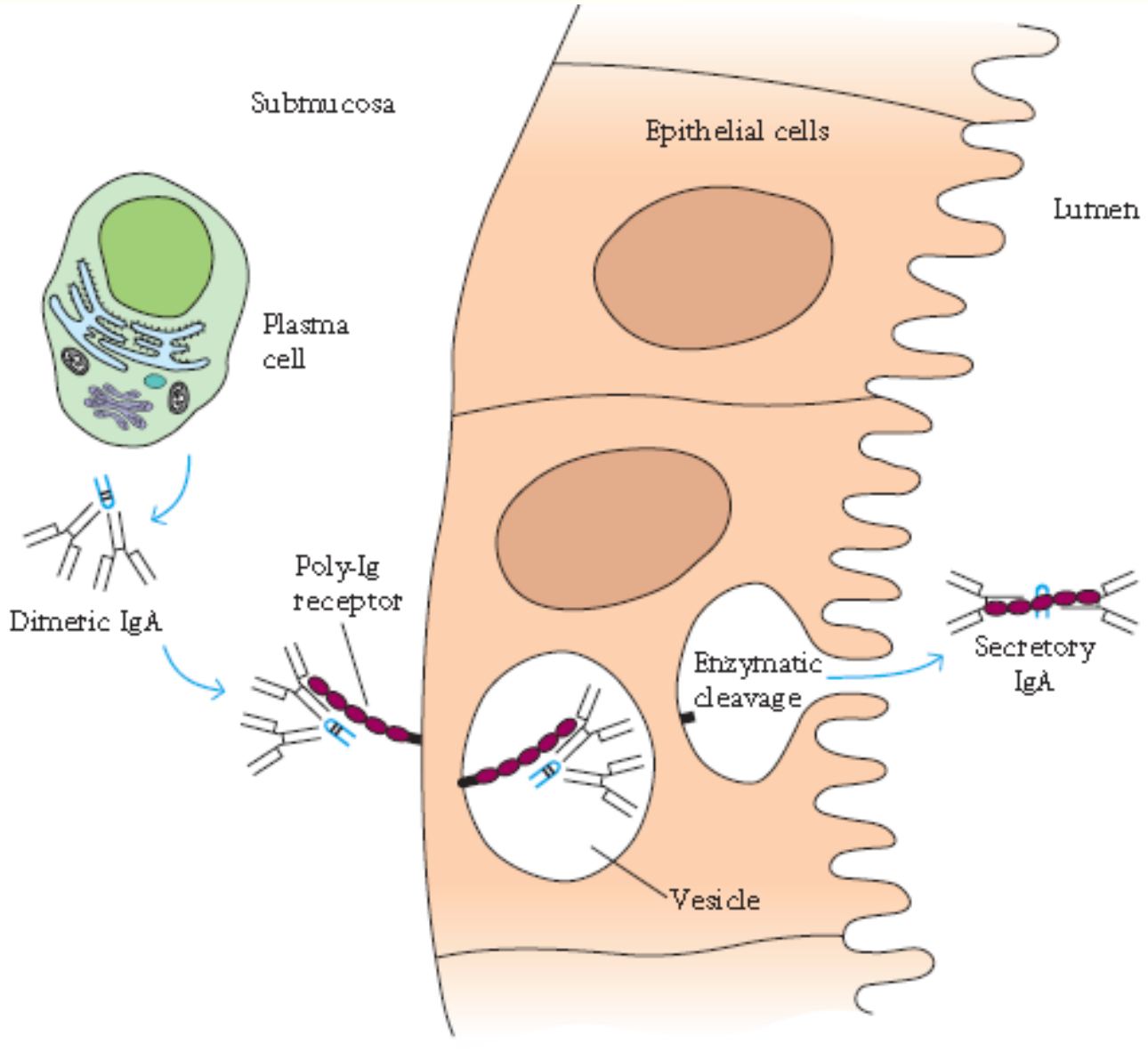


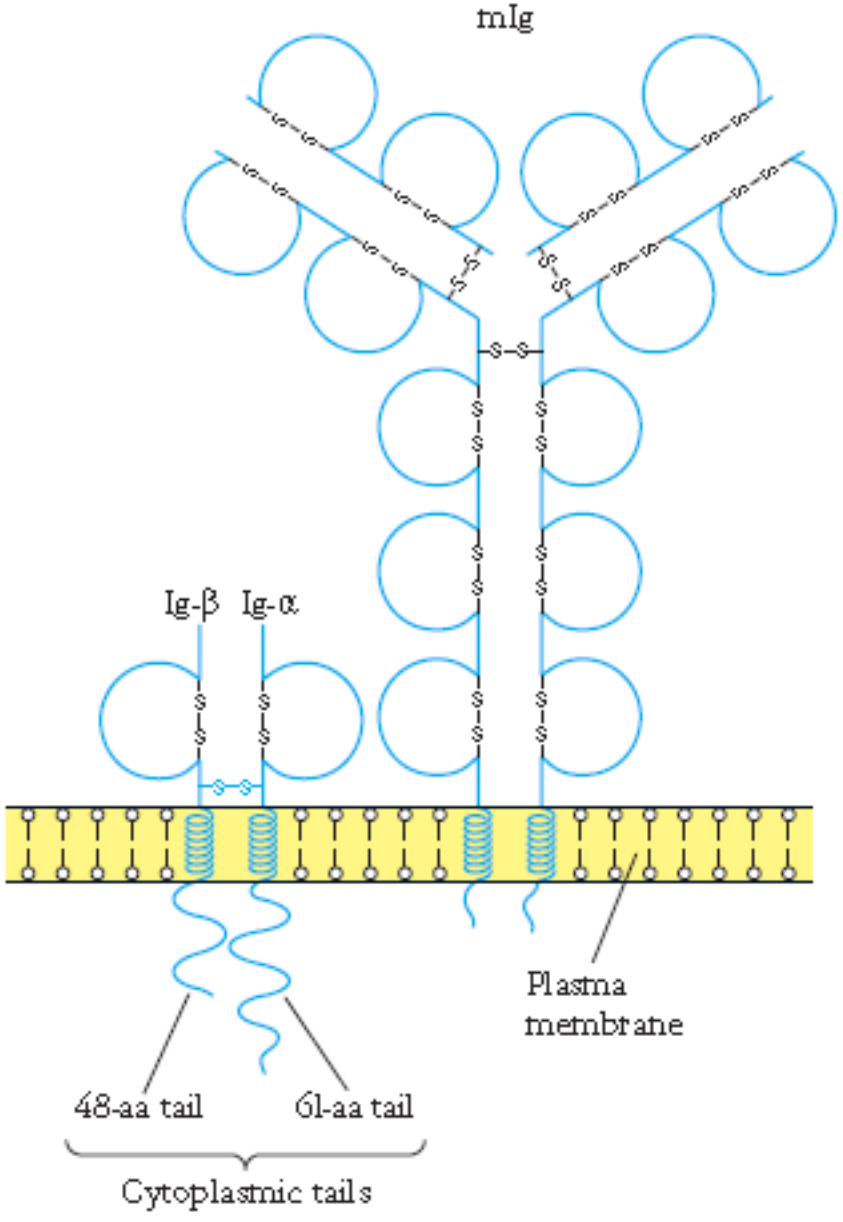
FIGURE 4-16 Allergen cross-linkage of receptor-bound IgE on mast cells induces degranulation, causing release of substances (blue dots) that mediate allergic manifestations.

Role of IgA as secretory antibody



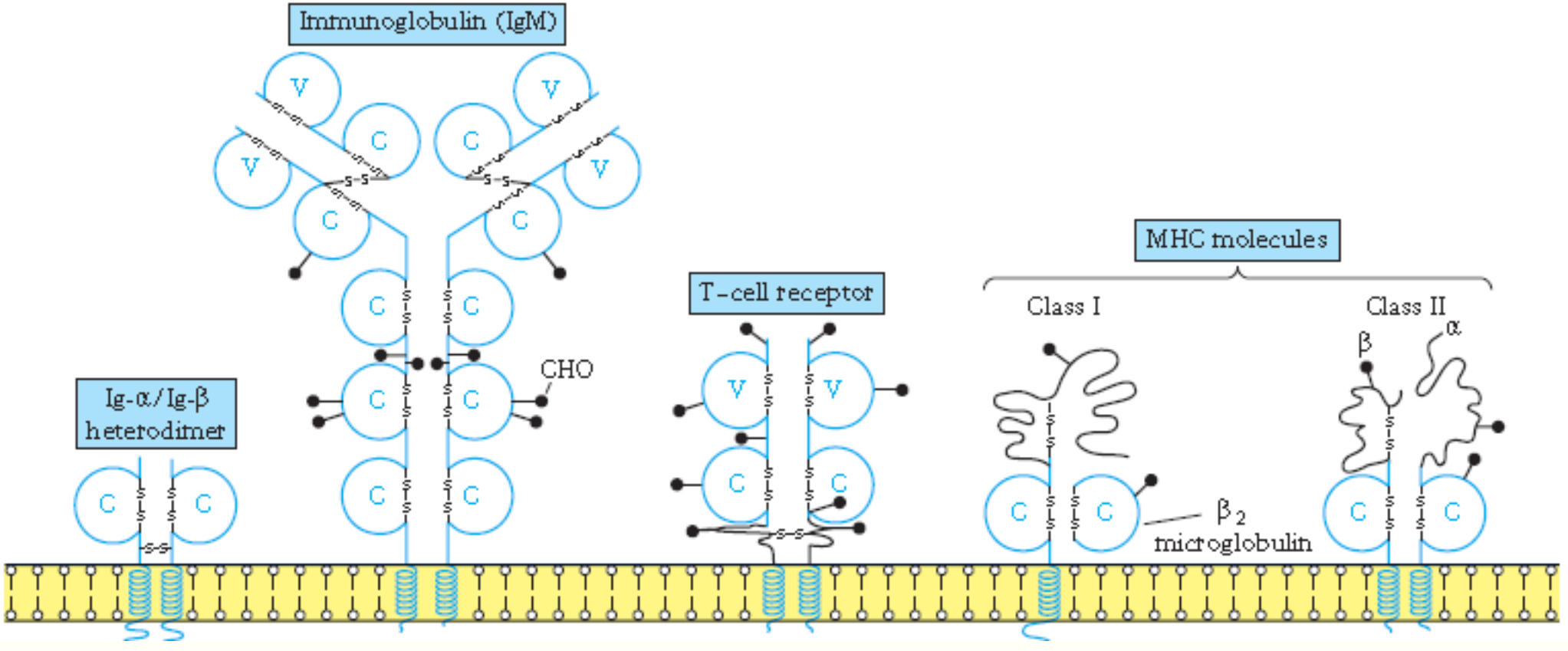
B cell receptor (BCR)

A transmembrane protein complex composed of mIg and disulfide-linked heterodimers called Ig-/Igβ molecules of this heterodimer associates with an mIg molecule to form a BCR.

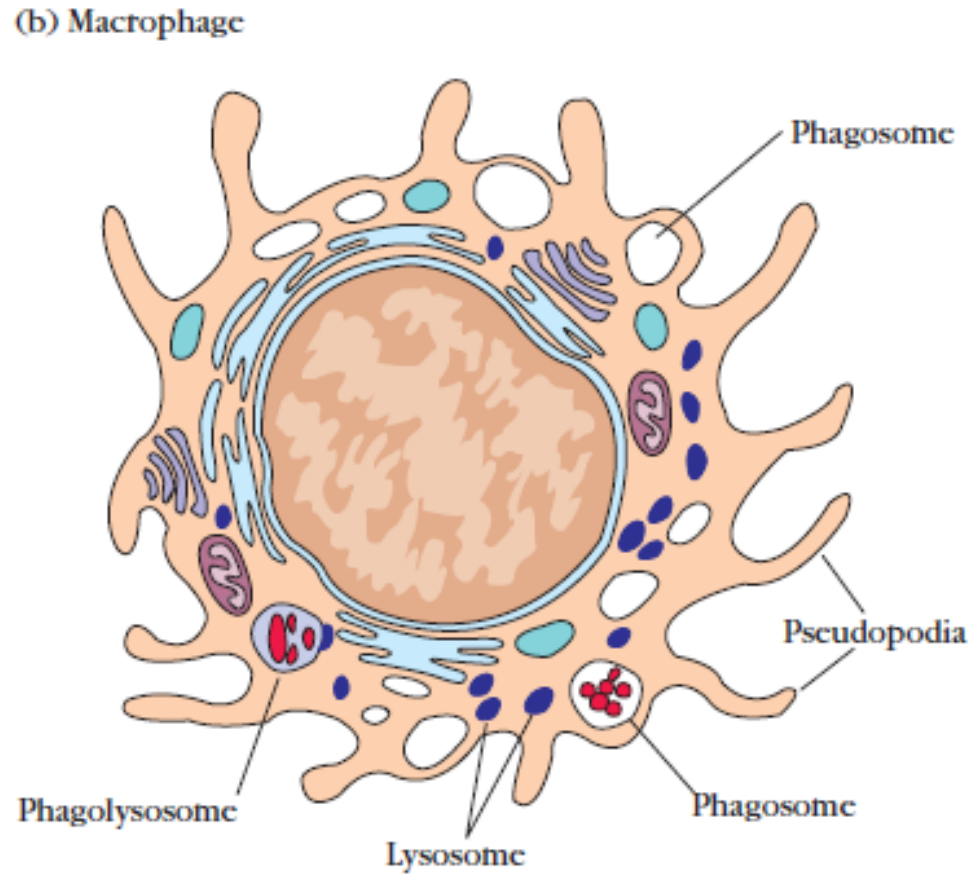


THE IMMUNOGLOBULIN SUPERFAMILY

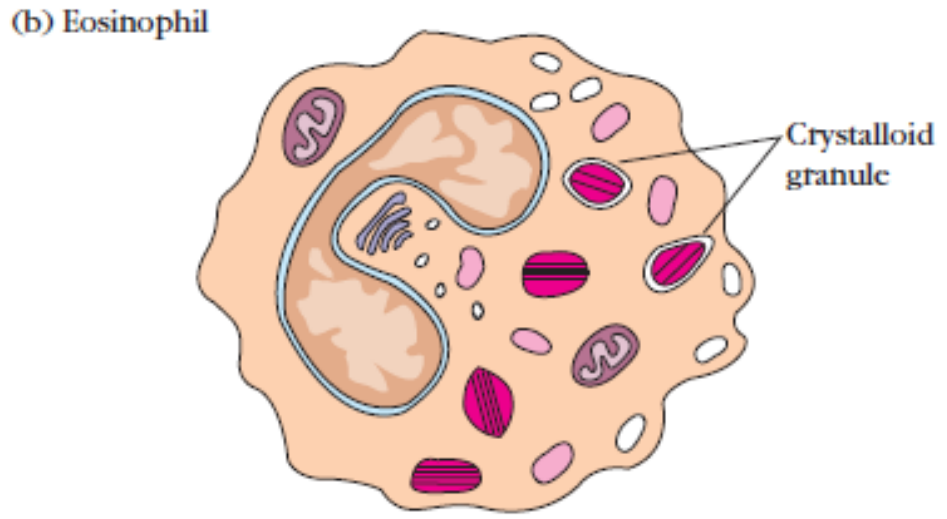
Ig-/Igβ heterodimer, part of the B-cell receptor
Poly-Ig receptor, which contributes the secretory component to secretory IgA and IgM
T-cell receptor
T-cell accessory proteins, including CD2, CD4, CD8, CD28, and the gamma, delta, and chains of CD3
Class I and class II MHC molecules 2-microglobulin, an invariant protein associated with class I MHC molecules
Various cell-adhesion molecules, including VCAM-1, ICAM-1, ICAM-2, and LFA-3
Platelet-derived growth factor



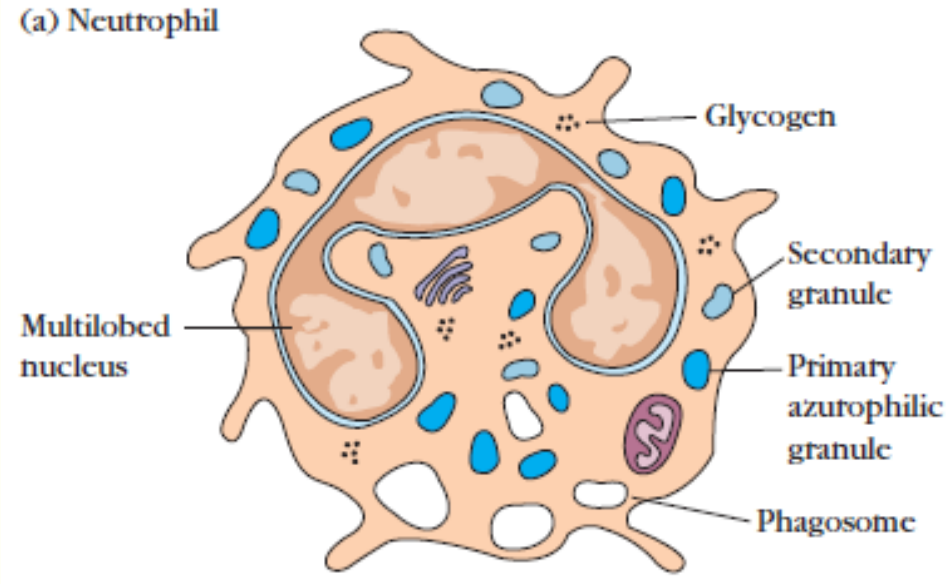
PHAGOCYTIC CELLS



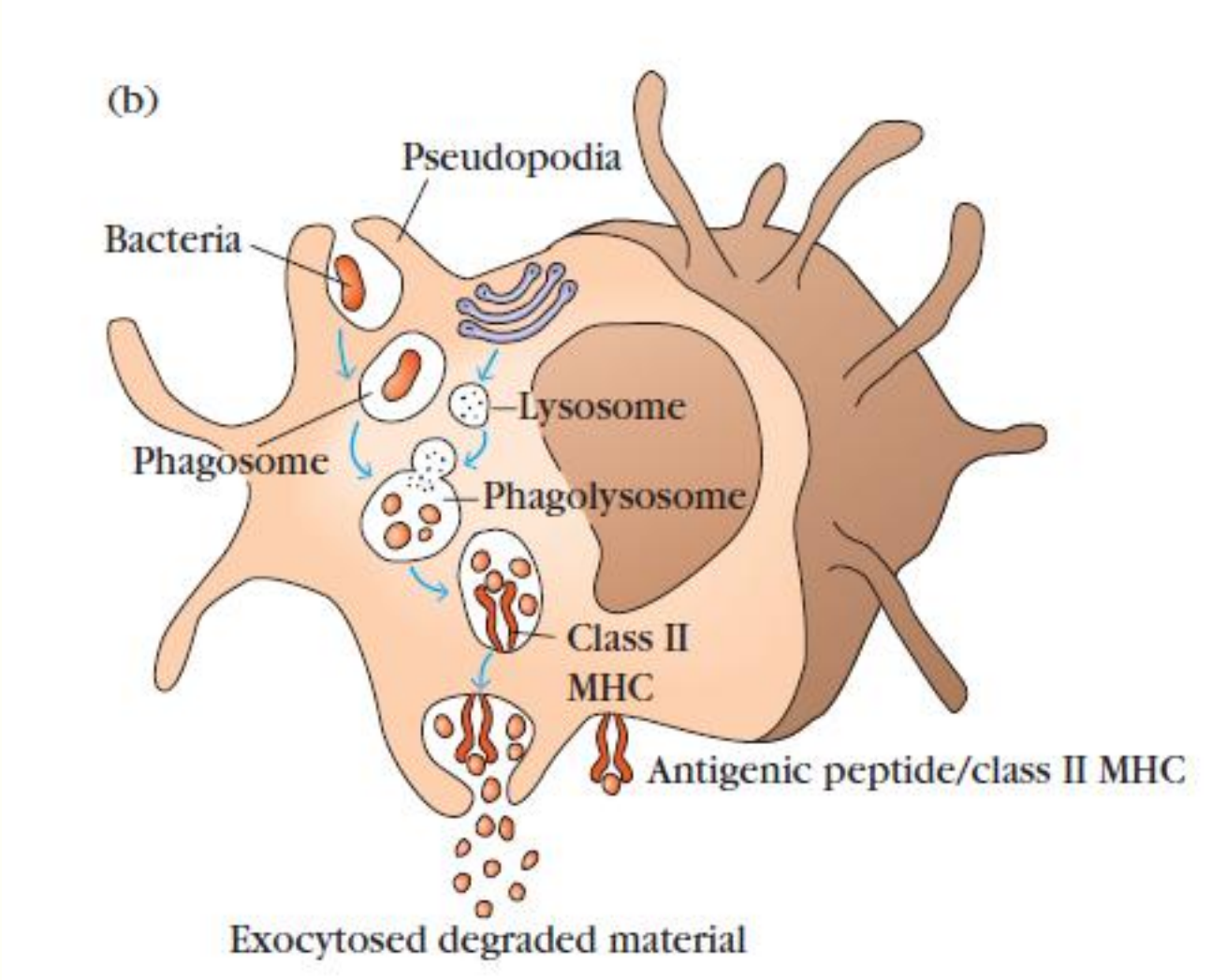
Macrophage: Large phagocytic cell, derived from the blood monocyte, which also functions as an antigen presenting cell and can mediate ADCC.



Eosinophil: A class of granulocyte, the granules of which contain toxic cationic proteins.



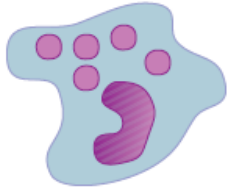
Neutrophil: The major circulating phagocytic polymorphonuclear granulocyte. Enters tissues early in an inflammatory response and is also able to mediate antibody-dependent cellular cytotoxicity (ADCC).


(b)
Pseudopodia
Bacteria
Lysosome
Phagosome
Phagolysosome
Class II
MHC
Antigenic peptide/class II MHC
Exocytosed degraded material

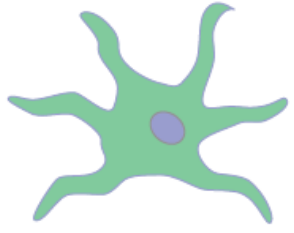
ANTIGEN PRESENTING CELLS

Cells that present, processed antigenic peptide with the help of MHC class II molecules to the T-cell receptor on $CD4^+$ T cells, Note, however, that most types of cell are able to present antigenic peptides with MHC class I to $CD8^+$ T cells, e.g. as occurs with virally infected cells.

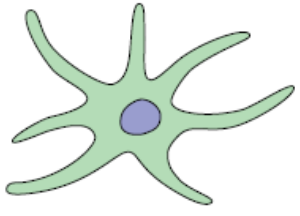
Professional antigen-presenting cells	Nonprofessional antigen-presenting cells	
Dendritic cells (several types)	Fibroblasts (skin)	Thymic epithelial cells
Macrophages	Glial cells (brain)	Thyroid epithelial cells
B cells	Pancreatic beta cells	Vascular endothelial cells



Macrophage



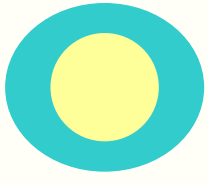
Mature dendritic cell



Langerhans' cell

B cell

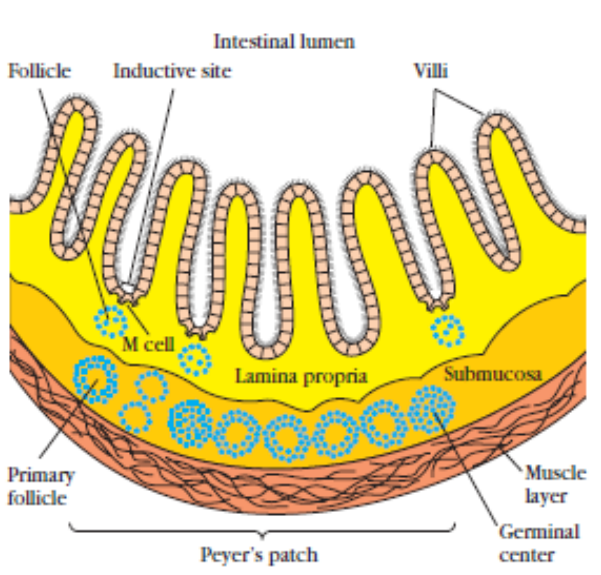
Interdigitating dendritic cell

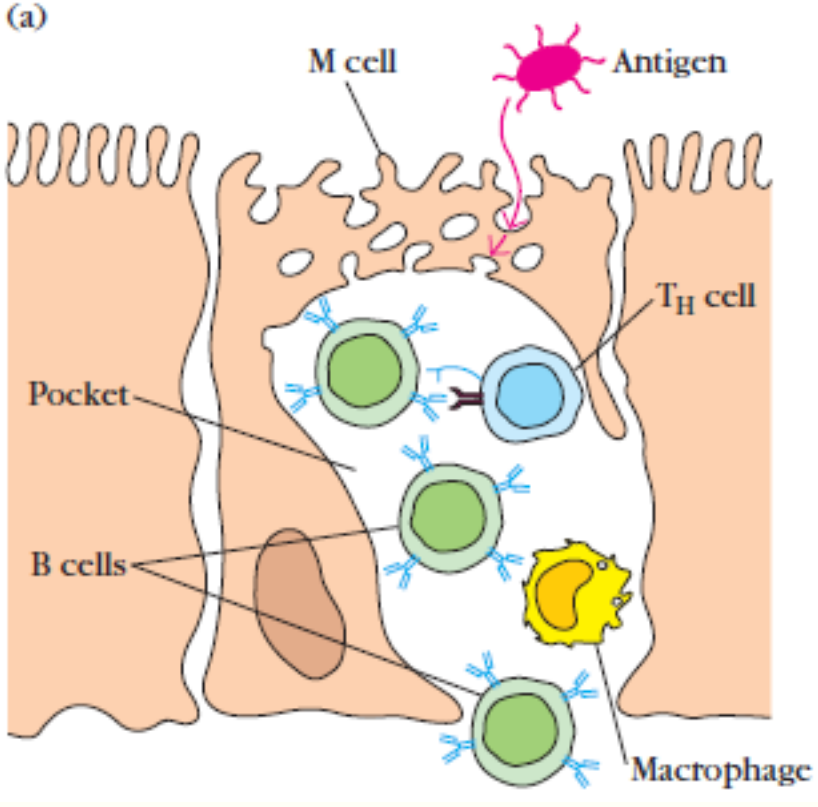


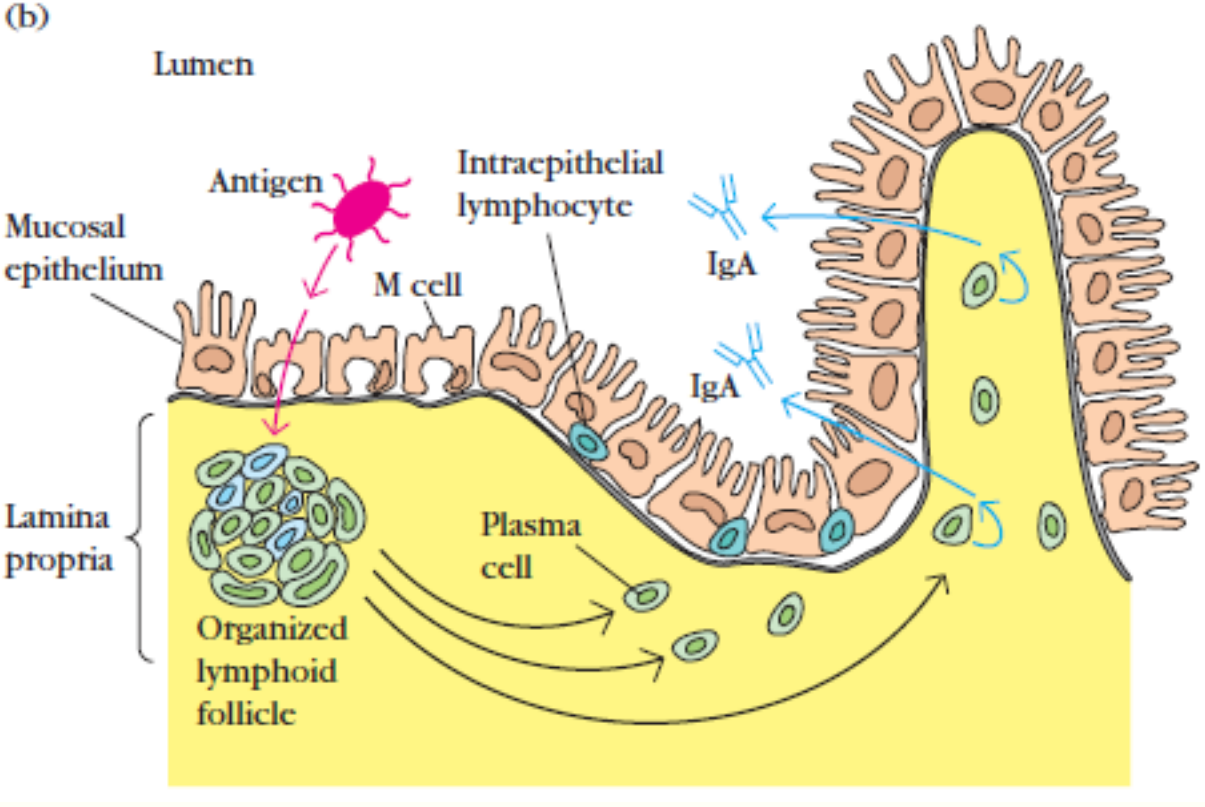
No immune cells

MUCOSAL IMMUNITY

Peyer's patches: Part of the gut associated lymphoid tissue (GALT) and found as distinct lymphoid nodules mainly in the small intestine.
Mucosal-associated lymphoid tissue (MALT): Lymphoid tissue present in the surface mucosa of the respiratory, gastrointestinal and genitourinary tracts.
Gut-associated lymphoid tissue (GALT): Includes Peyer's patches, appendix, and solitary lymphoid nodules in the submucosa.







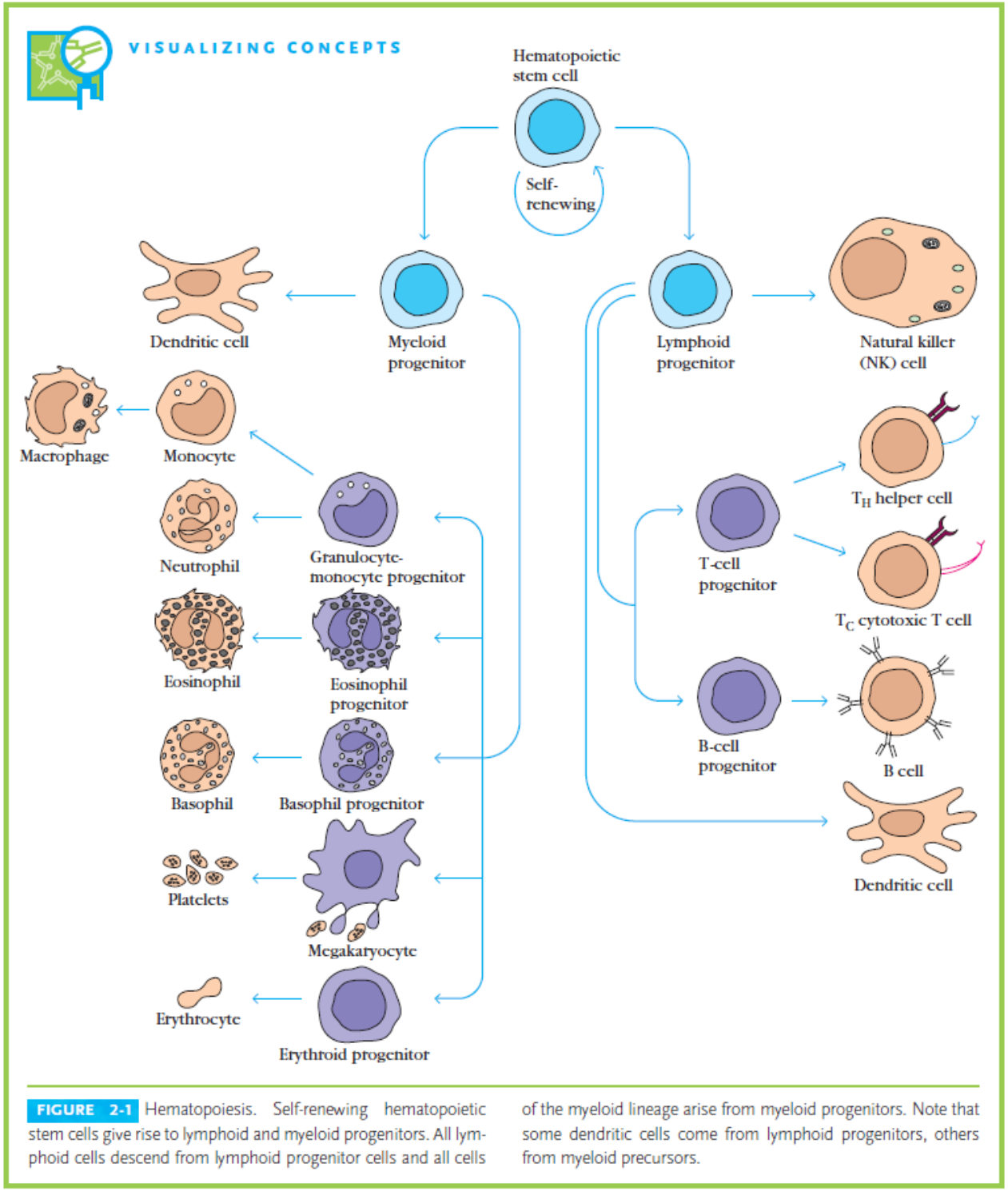
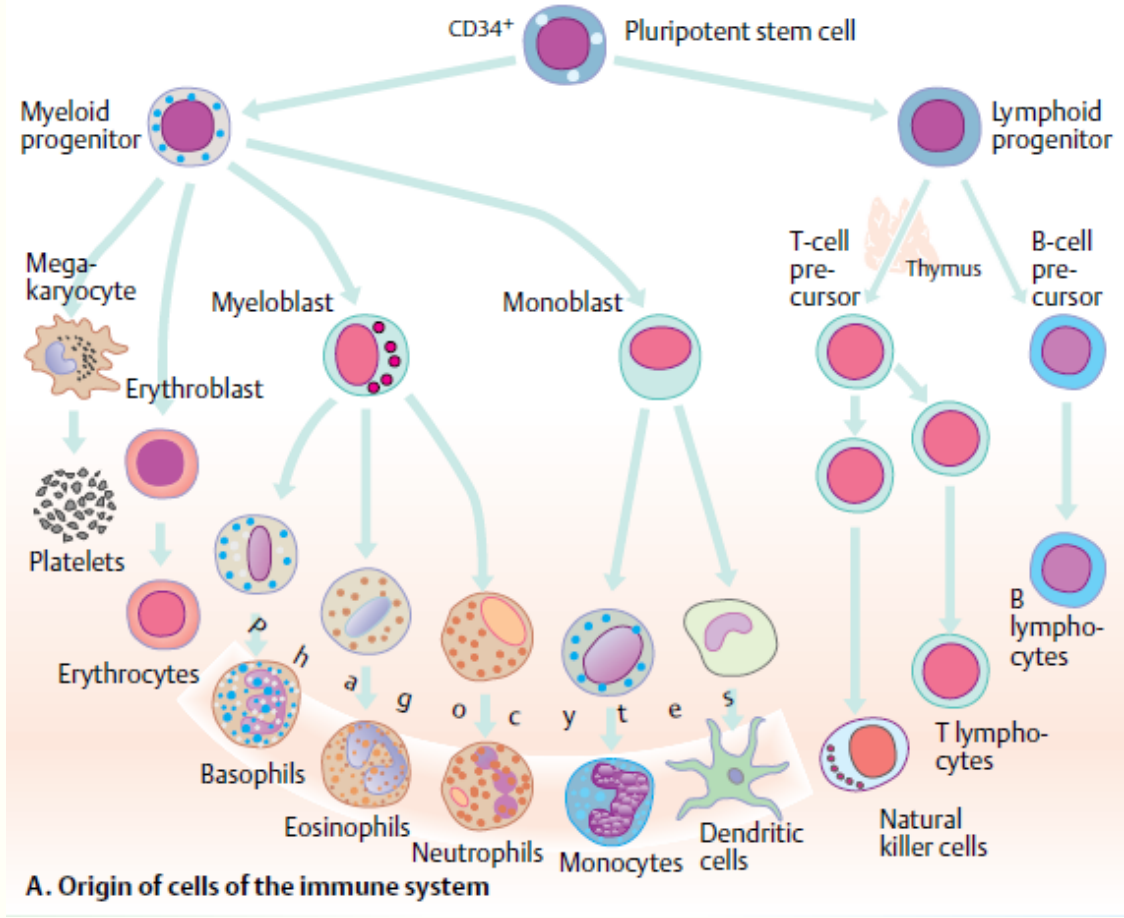
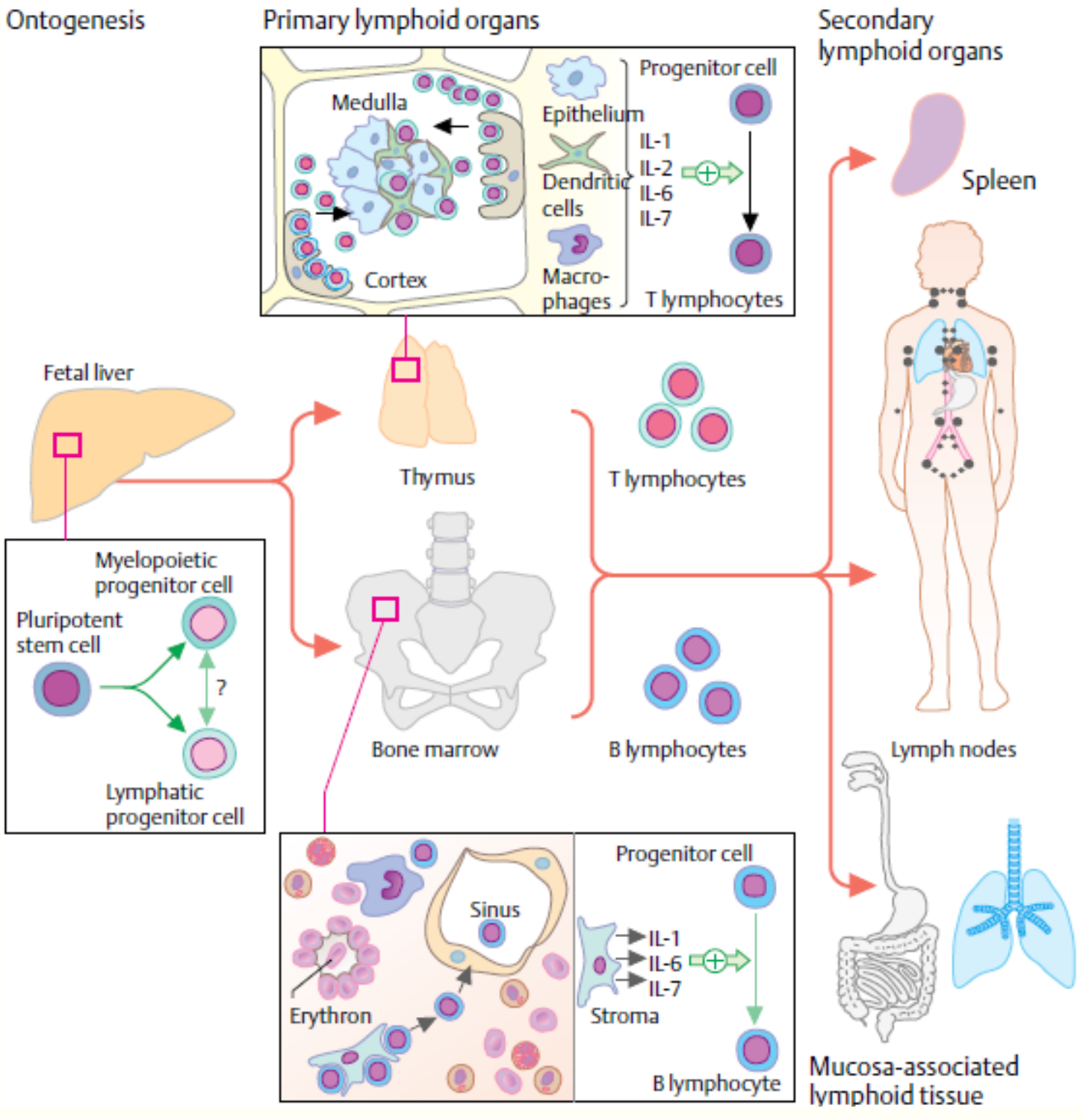


FIGURE 2-1 Hematopoiesis. Self-renewing hematopoietic stem cells give rise to lymphoid and myeloid progenitors. All lymphoid cells descend from lymphoid progenitor cells and all cells of the myeloid lineage arise from myeloid progenitors. Note that some dendritic cells come from lymphoid progenitors, others from myeloid precursors.



HEMATOPOESIS

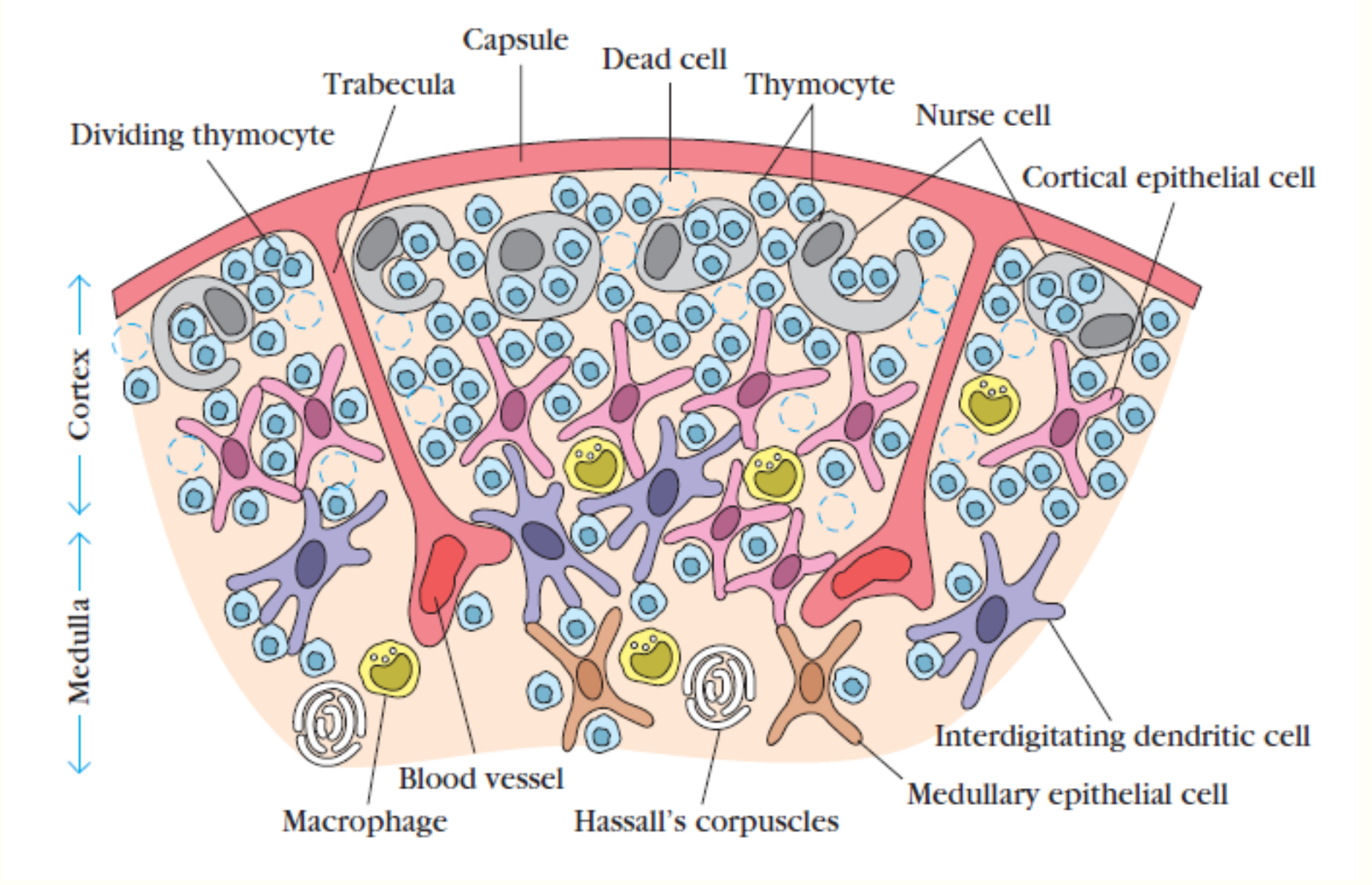

Ontogenesis
Primary lymphoid organs
Secondary lymphoid organs
Medulla
Cortex
Epithelium
Dendritic cells
Macro-phages
Progenitor cell
IL-1
IL-2
IL-6
IL-7
T lymphocytes
Spleen
Fetal liver
Thymus
T lymphocytes
Myelopoietic progenitor cell
Pluripotent stem cell
?
Lymphatic progenitor cell
Bone marrow
B lymphocytes
Lymph nodes
Sinus
Erythron
Progenitor cell
IL-1
IL-6
IL-7
Stroma
B lymphocyte
Mucosa-associated lymphoid tissue

Primary Lymphoid Organ

The sites at which immunocompetent lymphocytes develop.

THYMUS, BONE MARROW

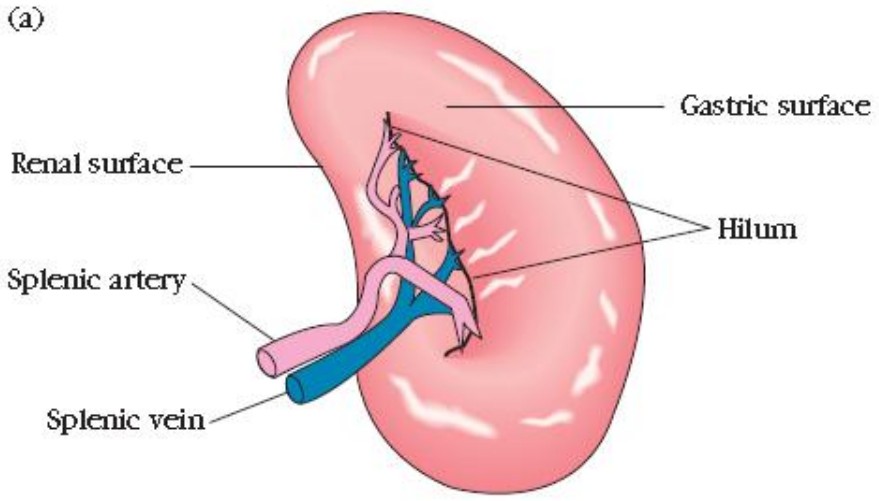
THYMUS


Capsule
Dead cell
Trabecula
Thymocyte
Dividing thymocyte
Nurse cell
Cortical epithelial cell
Cortex
Medulla
Interdigitating dendritic cell
Blood vessel
Medullary epithelial cell
Macrophage
Hassall's corpuscles

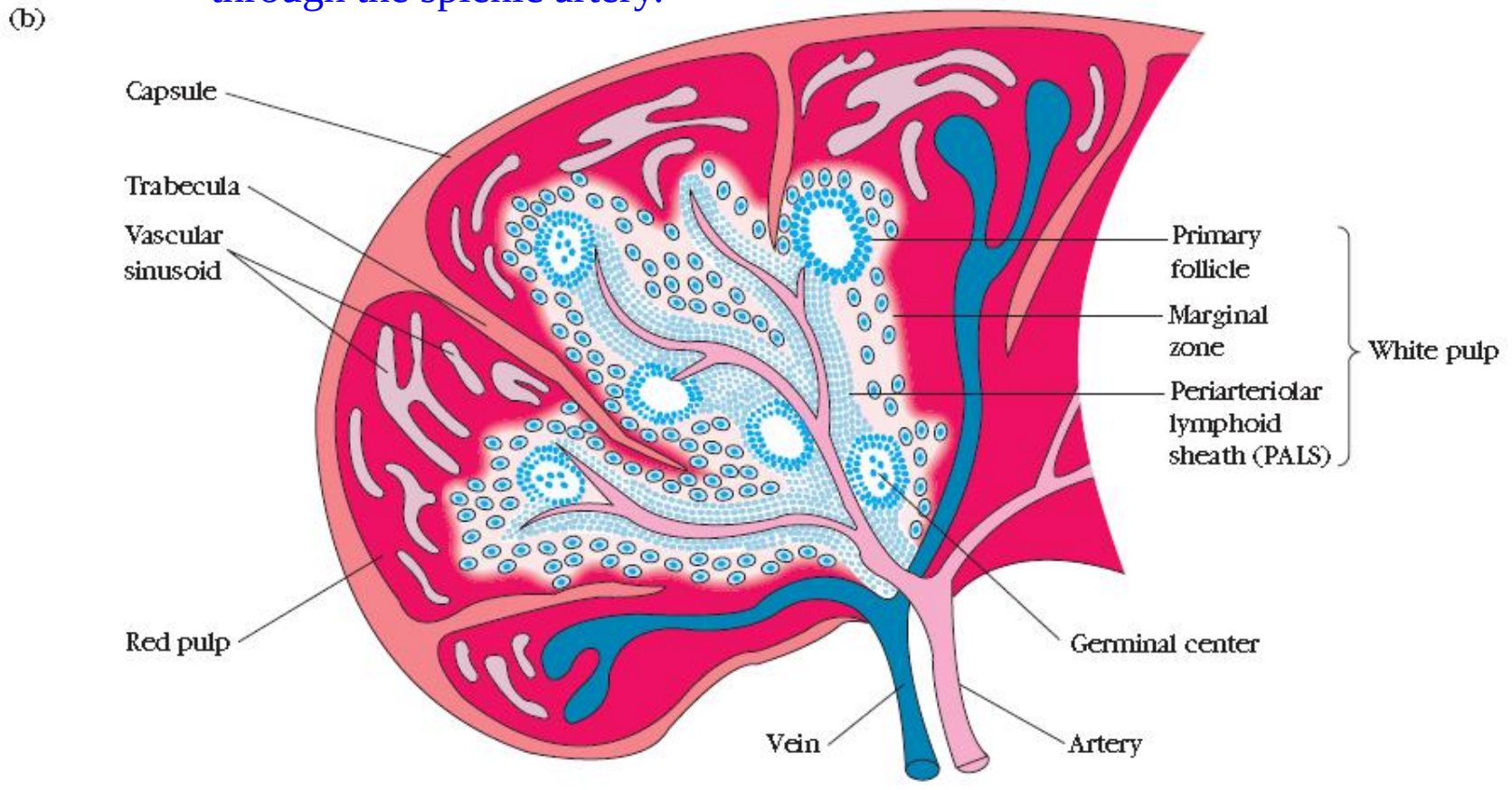
Secondary Lymphoid Organs

The qualitatively and quantitatively improved immune response which occurs upon the second encounter of primed lymphocytes with a given antigen.

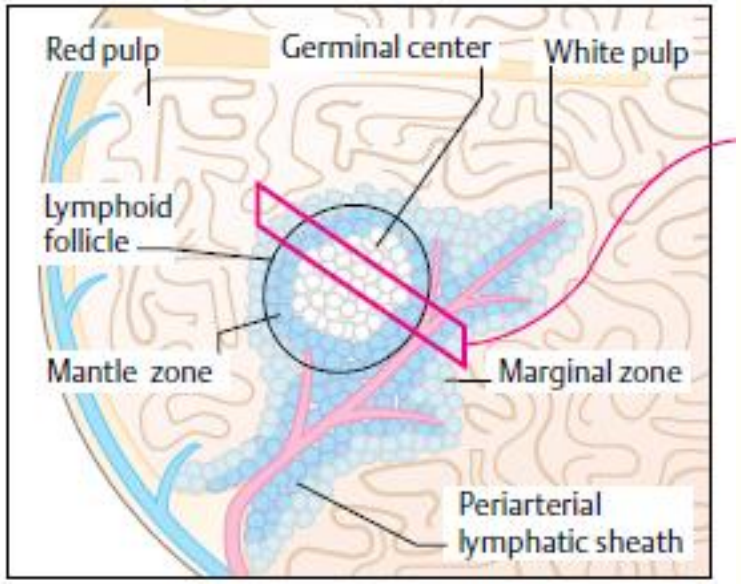
Spleen



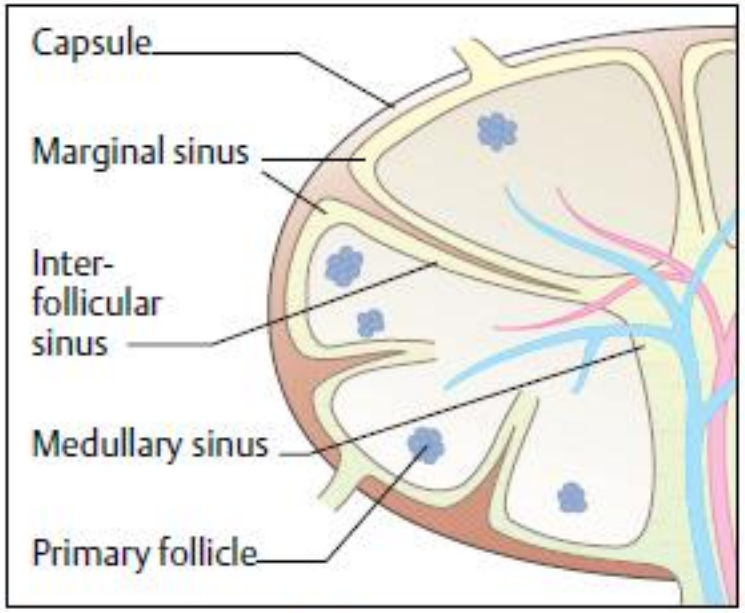
The spleen plays a major role in mounting immune responses to antigens in the blood stream.
It is a large, ovoid secondary lymphoid organ situated high in the left abdominal cavity.
While lymph nodes are specialized for trapping antigen from local tissues, the spleen specializes in filtering blood and trapping blood-borne antigens; thus, it can respond to systemic infections.
Unlike the lymph nodes, the spleen is not supplied by lymphatic vessels. Instead, bloodborne antigens and lymphocytes are carried into the spleen through the splenic artery.

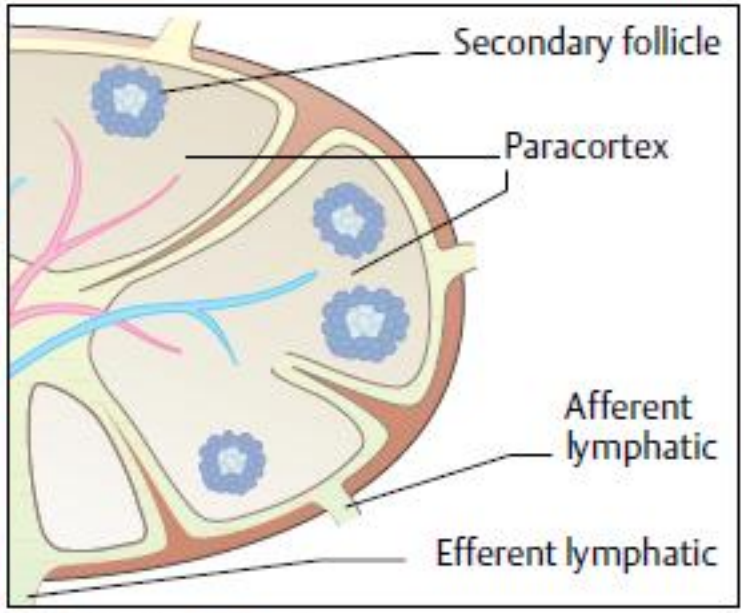


A. Structure of the spleen



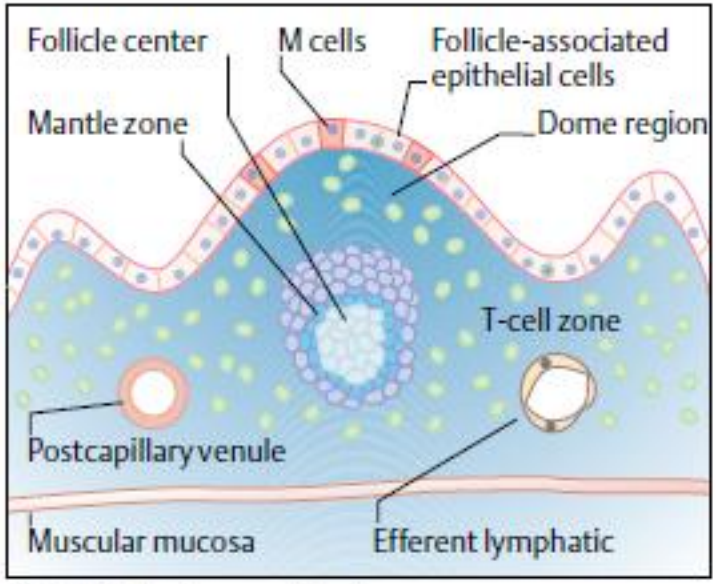
1. Anatomic structure



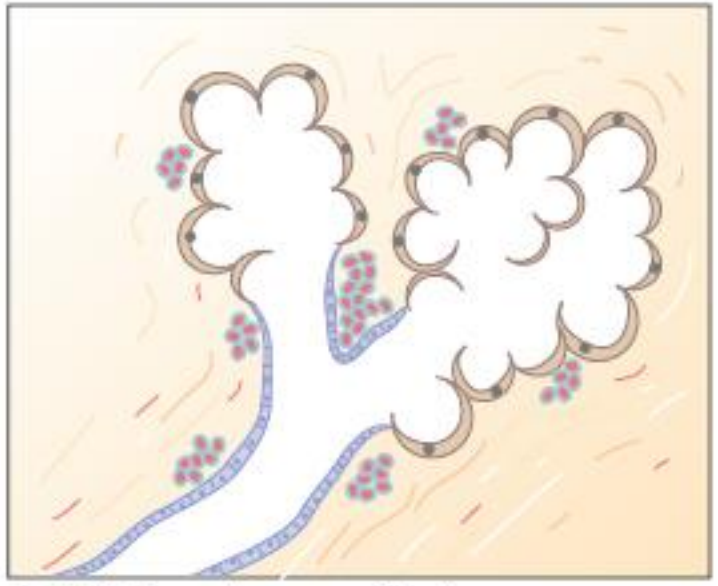


2. Active lymph node

B. Structure of the lymph node

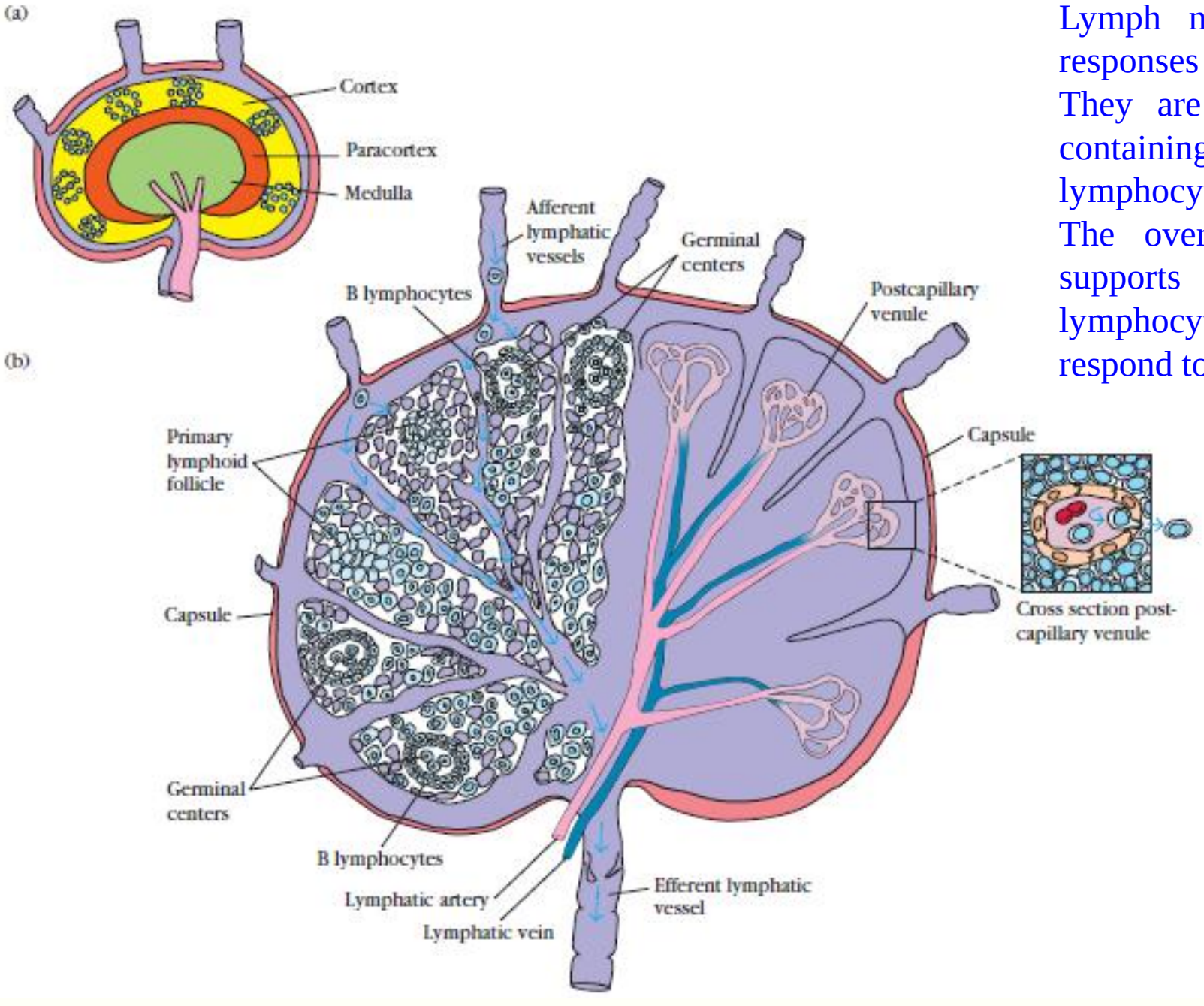


1. GALT: Gut-associated lymphoid tissue; Peyer's patch



2. BALT: Bronchus-associated lymphoid tissue

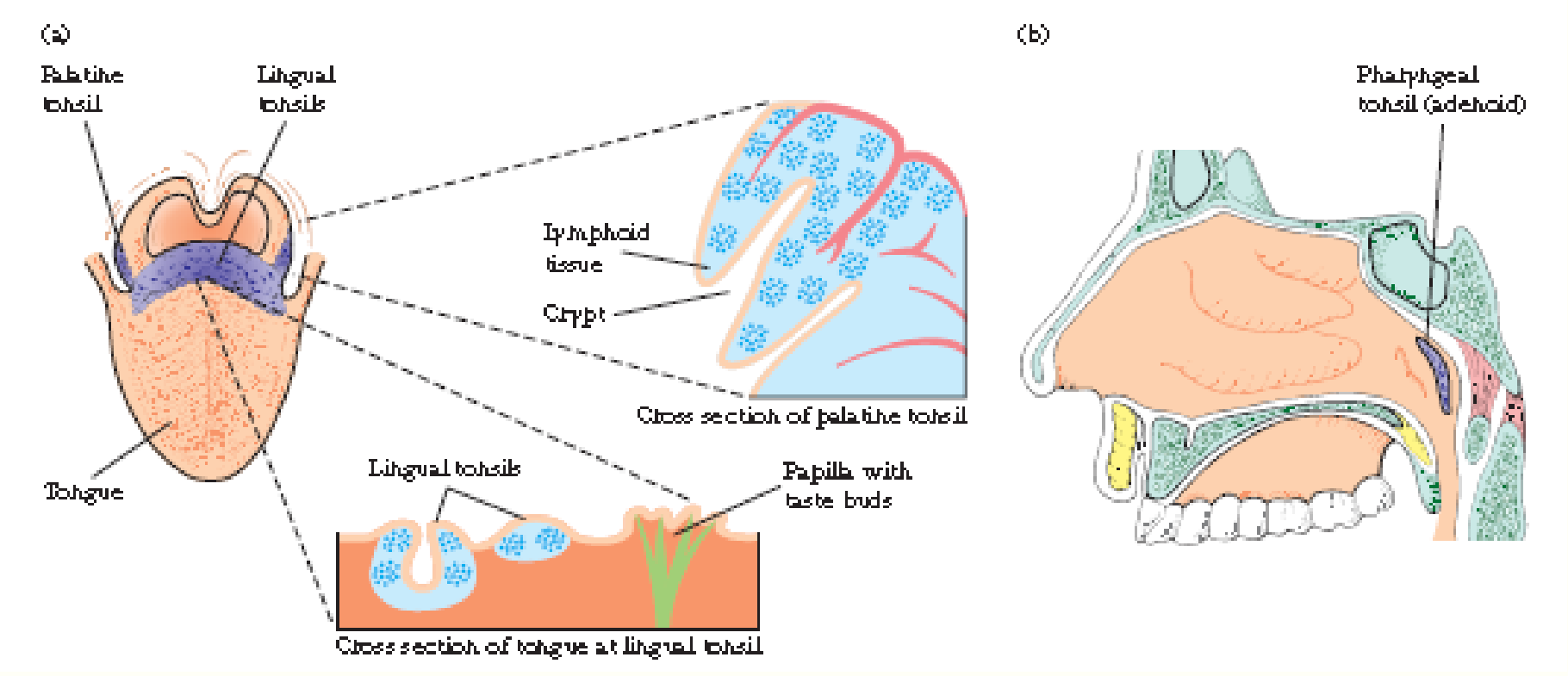
C. Mucosa-associated lymphoid tissue

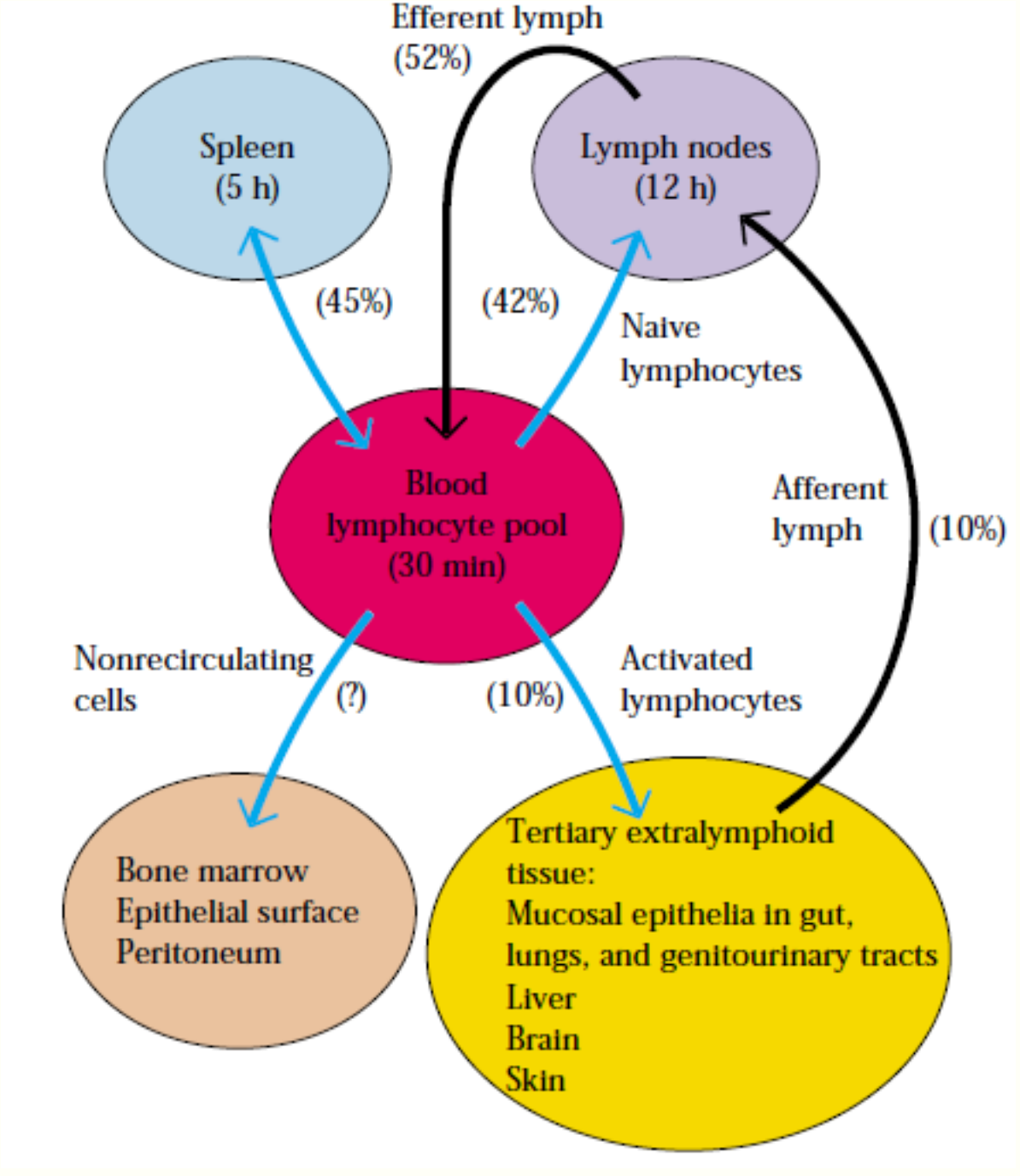


Lymph nodes are the sites where immune responses are mounted to antigens in lymph.
They are encapsulated beanshaped structures containing a reticular network packed with lymphocytes, macrophages, and dendritic cells.
The overall architecture of a lymph node supports an ideal microenvironment for lymphocytes to effectively encounter and respond to trapped antigens.

Lymph nodes

TONSIL


(a)
Palatine tonsil
Lingual tonsils
Lymphoid tissue
Crypt
Cross section of palatine tonsil
Tongue
Lingual tonsils
Papilla with taste buds
Cross section of tongue at lingual tonsil
(b)
Pharyngeal tonsil (adenoid)

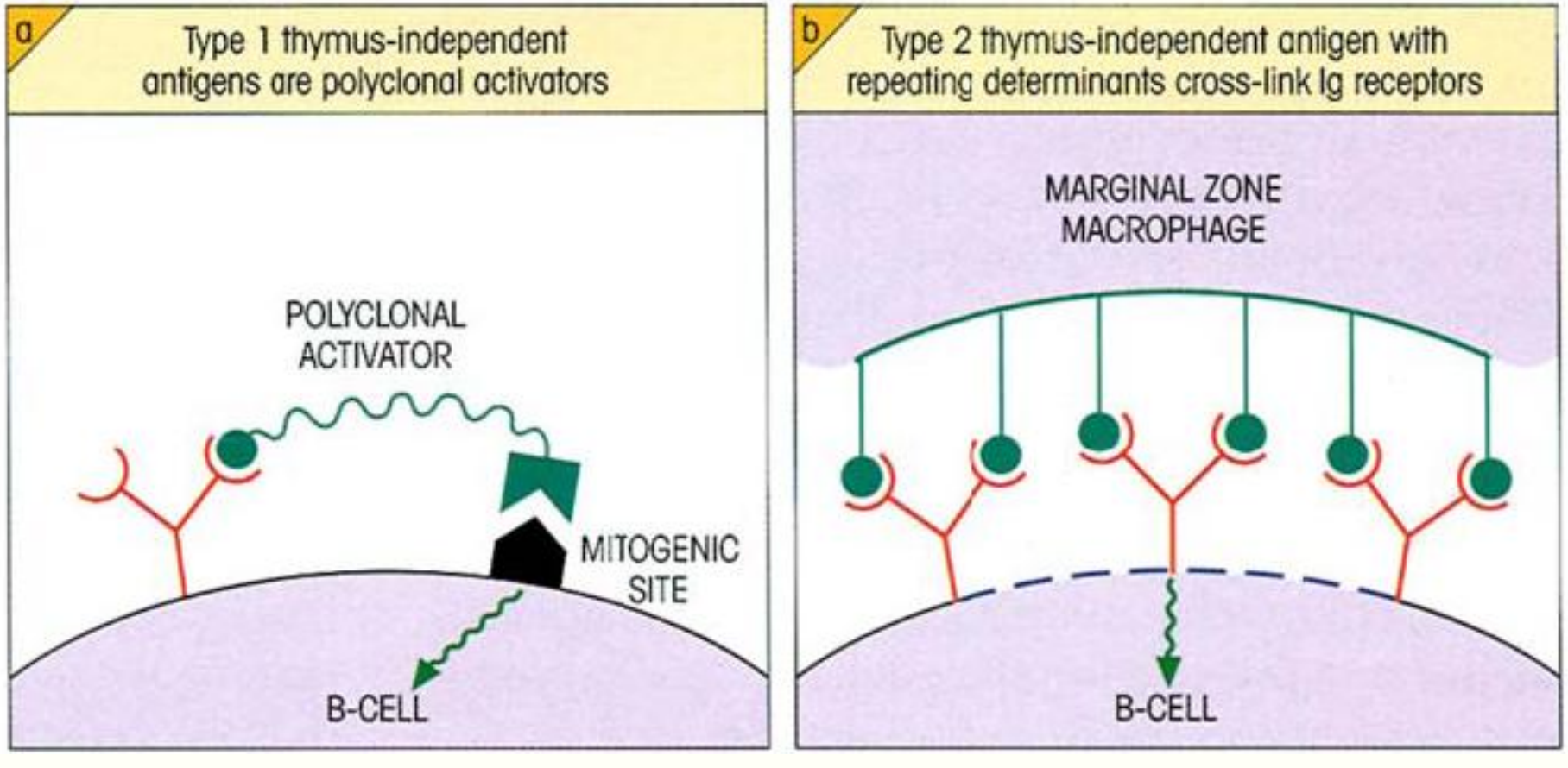

Efferent lymph
(52%)
Spleen
(5 h)
Lymph nodes
(12 h)
(45%)
(42%)
Naive
lymphocytes
Blood
lymphocyte pool
(30 min)
Afferent
lymph
(10%)
Nonrecirculating
cells
(?)
(10%)
Activated
lymphocytes
Bone marrow
Epithelial surface
Peritoneum
Tertiary extralymphoid
tissue:
Mucosal epithelia in gut,
lungs, and genitourinary tracts
Liver
Brain
Skin

ANTIGENS

Thymus independent antigen type1- Certain antigens, such as bacterial LPS, at a high enough concentration, have the ability to activate a substantial proportion of the B-cell polyclonally.

Thymus independent antigen type2-

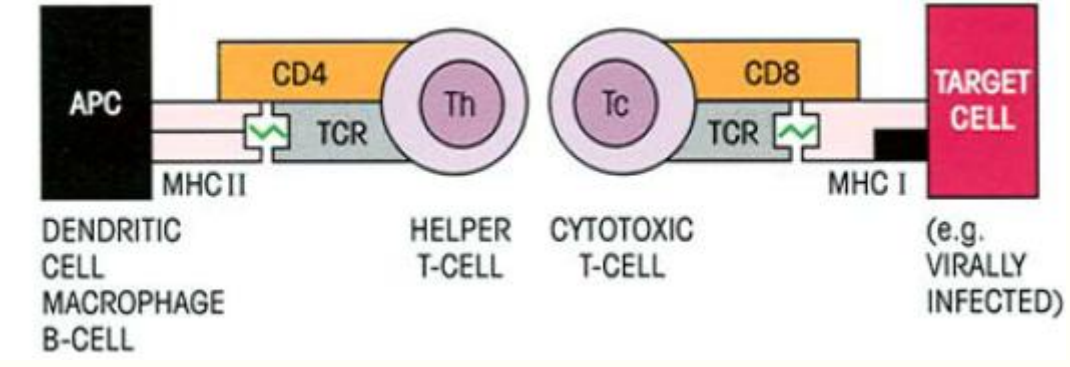
Thymus dependent antigen (The need for collaboration with T-helper cells) Many antigens are thymus-dependent in that they provoke little or no antibody response

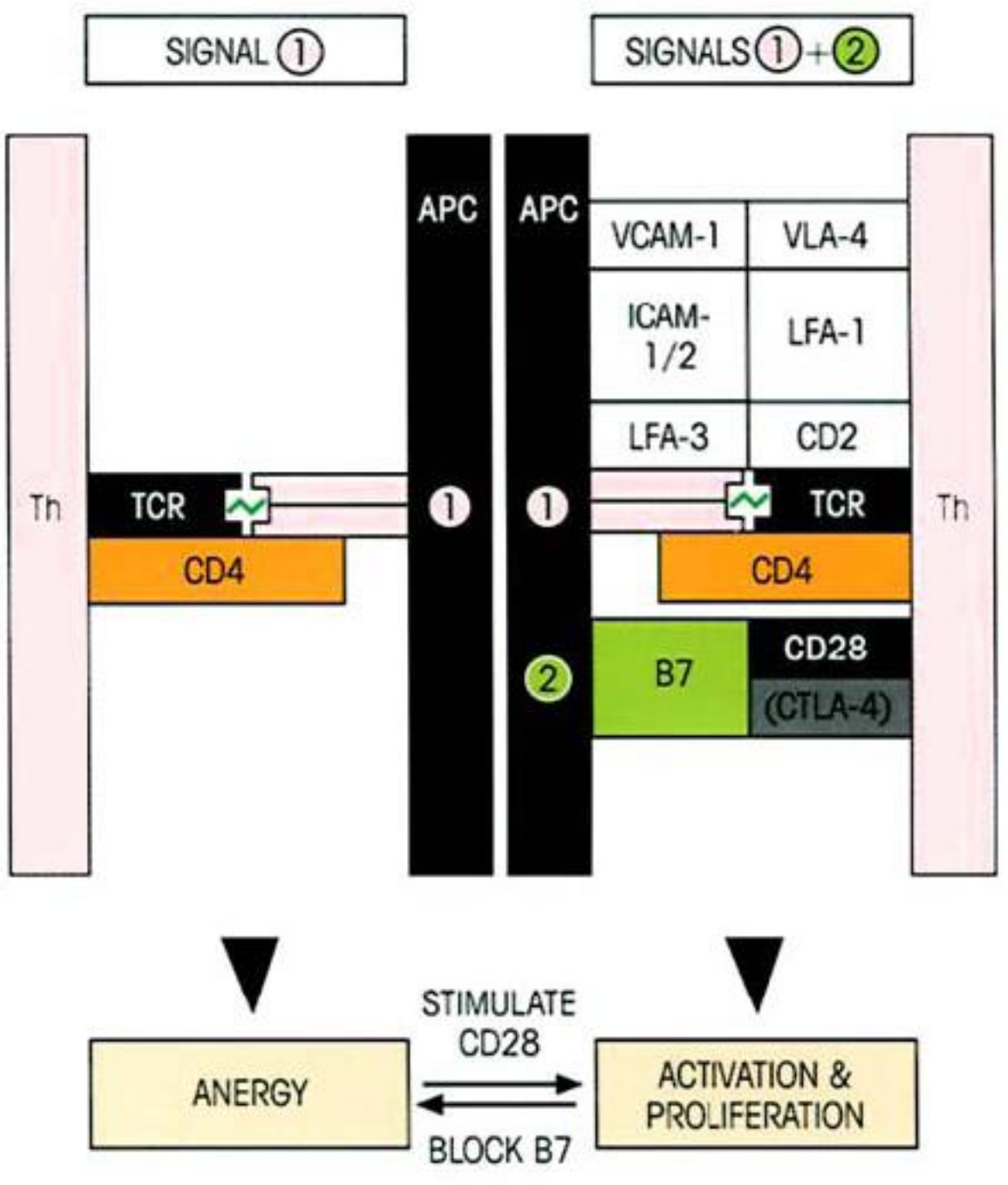


ANTIGEN PRESENTATION

To T cell

1. TCR-MHC-II
2. Co-stimulatory signaling





CYTOKINES

These low molecular weight secreted proteins, usually 15-25 kDa
Mediate cell growth, inflammation, immunity, differentiation, migration and repair.
Acts at femtomolar (10-l5 M) concentrations
Short half-life
Act locally in a paracrine or even autocrine fashion
Certain cytokines, including IL-1 and TNF, also exist in membrane forms which can exert their stimulatory effects without becoming soluble
Combines with small numbers of high affinity cell surface receptors

CYTOKINE	SOURCE	EFFECTOR FUNCTION
INTERLEUKINS		
IL-1α, IL-1β	Mono, Mϕ, DC, NK, B, Endo	Costimulates T activation by enhancing production of cytokines including IL-2 and its receptor; enhances B proliferation and maturation; NK cytotoxicity; induces IL-1,-6,-8, TNF, GM-CSF and PGE_2 by Mϕ; proinflammatory by inducing chemokines and ICAM-1 and VCAM-1 on endothelium; induces fever, APP, bone resorption by osteoclasts
IL-2	Th1	Induces proliferation of activated T- and B-cells; enhances NK cytotoxicity and killing of tumor cells and bacteria by monocytes and Mϕ
IL-3	T, NK, MC	Growth and differentiation of hematopoietic precursors; MC growth
IL-4	Th2, Tc2, NK, NK-T, γδ T, MC	Induces Th2 cells; stimulates proliferation of activated B, T, MC; upregulates MHC class II on B and Mϕ, and CD23 on B; downregulates IL-12 production and thereby inhibits Th1 differentiation; increases Mϕ phagocytosis; induces switch to IgG1 and IgE
IL-5	Th2, MC	Induces proliferation of eosino and activated B; induces switch to IgA
IL-6	Th2, Mono, Mϕ, DC, BM stroma	Differentiation of myeloid stem cells and of B into plasma cells; induces APP; enhances T proliferation
IL-7	BM and thymic stroma	Induces differentiation of lymphoid stem cells into progenitor T and B; activates mature T
IL-8	Mono, Mϕ, Endo	Mediates chemotaxis and activation of neutrophils
IL-9	Th	Induces proliferation of thymocytes; enhances MC growth; synergizes with IL-4 in switch to IgG1 and IgE
IL-10	Th (Th2 in mouse), Tc, B, Mono, Mϕ	Inhibits IFNγ secretion by mouse, and IL-2 by human, Th1 cells; downregulates MHC class II and cytokine (including IL-12) production by mono, Mϕ and DC, thereby inhibiting Th1 differentiation; inhibits T proliferation; enhances B differentiation
IL-11	BM stroma	Promotes differentiation of pro-B and megakaryocytes; induces APP
IL-12	Mono, Mϕ, DC, B	Critical cytokine for Th1 differentiation; induces proliferation and IFNγ production by Th1, $CD8^+$ and γδ T and NK; enhances NK and $CD8^+$ T cytotoxicity
IL-13	Th2, MC	Inhibits activation and cytokine secretion by Mϕ; co-activates B proliferation; upregulates MHC class II and CD23 on B and mono; induces switch to IgG1 and IgE; induces VCAM-1 on endo

IL-15	T, NK, Mono, Mϕ, DC, B	Induces proliferation of T-, NK and activated B and cytokine production and cytotoxicity in NK and $CD8^+$ T; chemotactic for T; stimulates growth of intestinal epithelium
IL-16	Th, Tc	Chemoattractant for CD4 T, mono and eosino; induces MHC class II
IL-17	T	Proinflammatory; stimulates production of cytokines including TNF,IL-1β,-6,-8, G-CSF
IL-18	Mϕ, DC	Induces IFNγ production by T; enhances NK cytotoxicity
IL-19	Mono	Modulation of Th1 activity
IL-20	Keratinocytes?	Regulation of inflammatory responses to skin?
IL-21	Th	Regulation of hematopoiesis; NK differentiation; B activation; T costimulation
IL-22	T	Inhibits IL-4 production by Th2
IL-23	DC	Induces proliferation and IFNγ production by Th1; induces proliferation of memory cells
COLONY STIMULATING FACTORS		
GM-CSF	Th, Mϕ, Fibro, MC, Endo	Stimulates growth of progenitors of mono, neutro, eosino and baso; activates Mϕ
G-CSF	Fibro, Endo	Stimulates growth of neutro progenitors
M-CSF	Fibro, Endo, Epith	Stimulates growth of mono progenitors
SLF	BM stroma	Stimulates stem cell division (c-*kit* ligand)
TUMOR NECROSIS FACTORS		
TNF (TNFα)	Th, Mono, Mϕ, DC, MC, NK, B	Tumor cytotoxicity; cachexia (weight loss); induces cytokine secretion; induces E-selectin on endo; activates Mϕ; antiviral
Lymphotoxin (TNFβ)	Th1 Tc	Tumor cytotoxicity; enhances phagocytosis by neutro and Mϕ; involved in lymphoid organ development; antiviral
INTERFERONS		
IFNα	Leukocytes	Inhibits viral replication; enhances MHC class I
IFNβ	Fibroblasts	Inhibits viral replication; enhances MHC class I
IFNγ	Th1, Tc1, NK	Inhibits viral replication; Enhances MHC class I and II; activates Mϕ; induces switch to IgG2a; antagonizes several IL-4 actions; inhibits proliferation of Th2
OTHERS		
TGFβ	Th3, B, Mϕ, MC	Proinflammatory by, e.g., chemoattraction of mono and Mϕ but also anti-inflammatory by, e.g. inhibiting lymphocyte proliferation; induces switch to IgA; promotes tissue repair
LIF	Thymic epith, BM stroma	Induces APP
Eta-1	T	Stimulates IL-12 production and inhibits IL-10 production by Mϕ
Oncostatin M	T, Mϕ	Induces APP