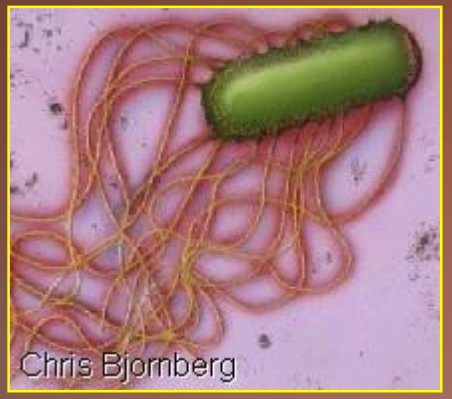
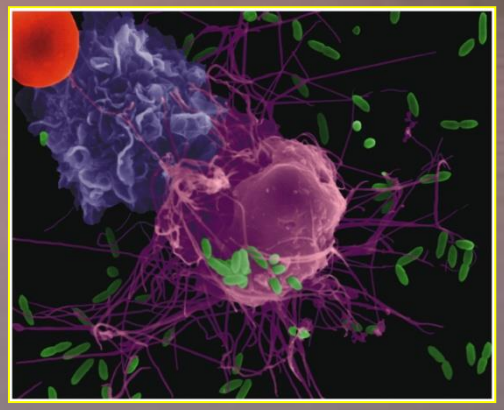


Introdução à Imunologia



Luis Tavares

Barreiras Naturais

Lisozima nas lágrimas e outras secreções das mucosas

Enzimas da Saliva

Microflora

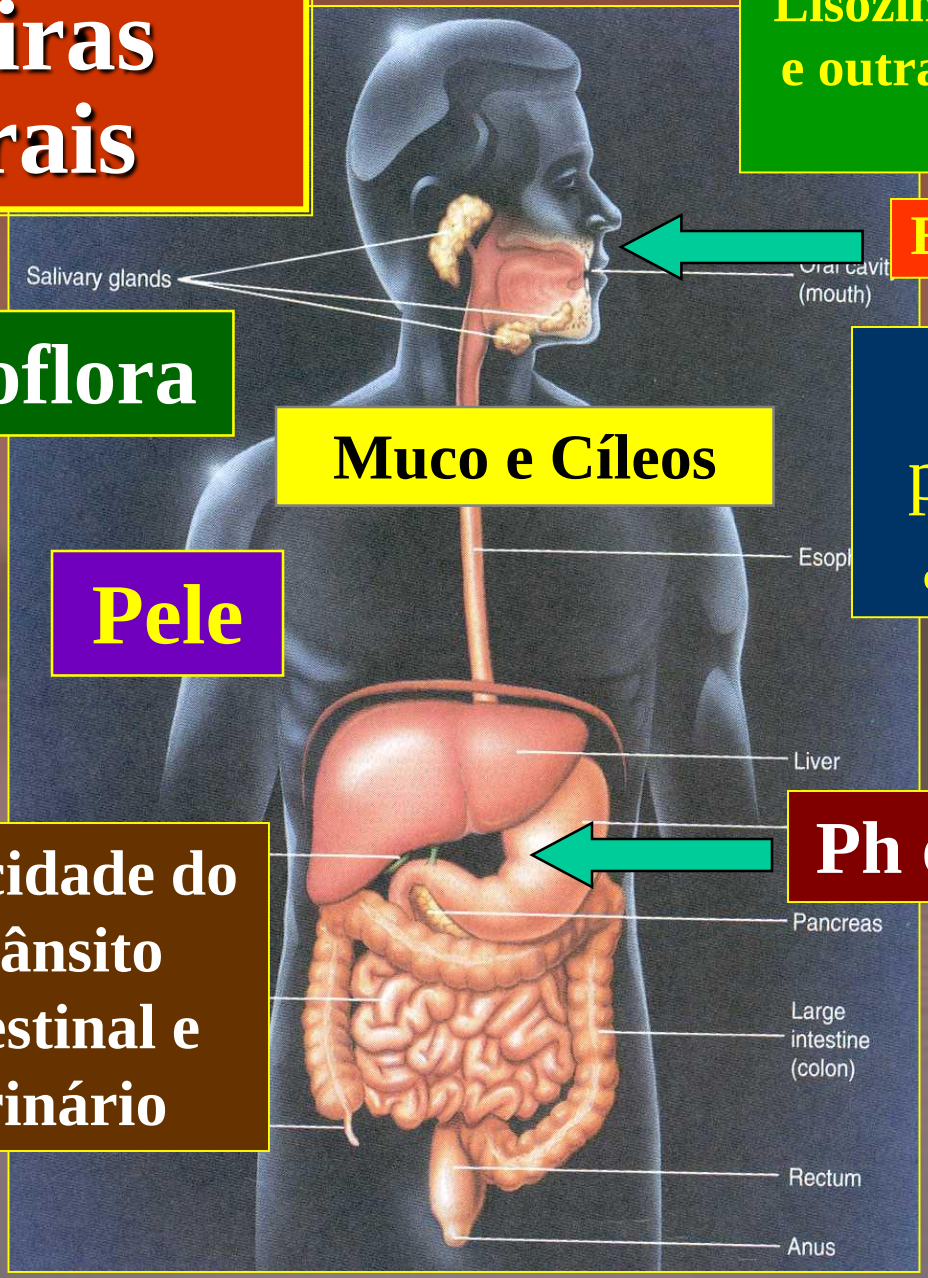
Muco e Cíleos

Rápida passagem do ar inspirado

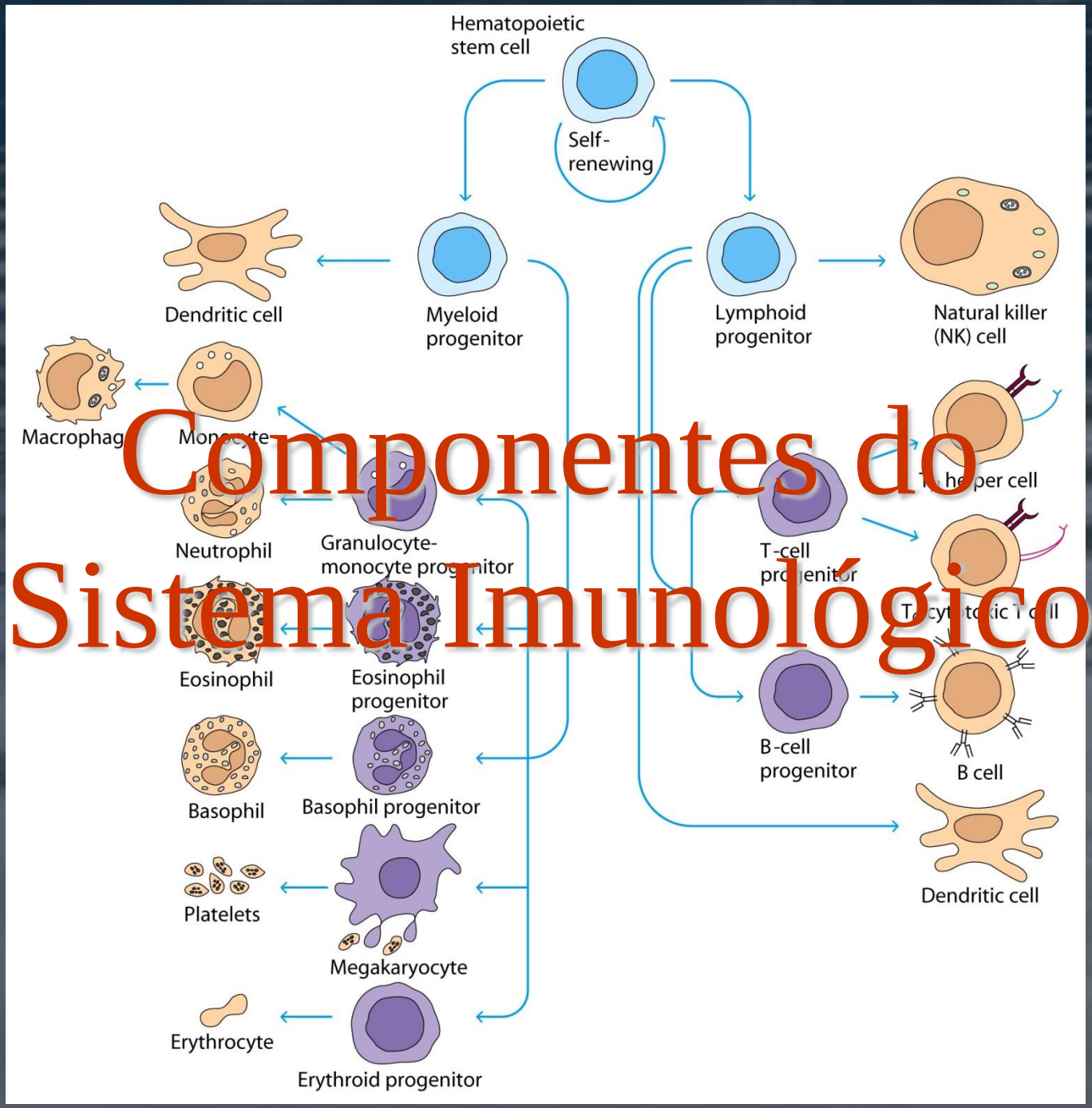
Pele

Ph do tracto G.I.

Velocidade do Trânsito Intestinal e Urinário



Componentes do Sistema Imunológico



Origin of cells of the immune system

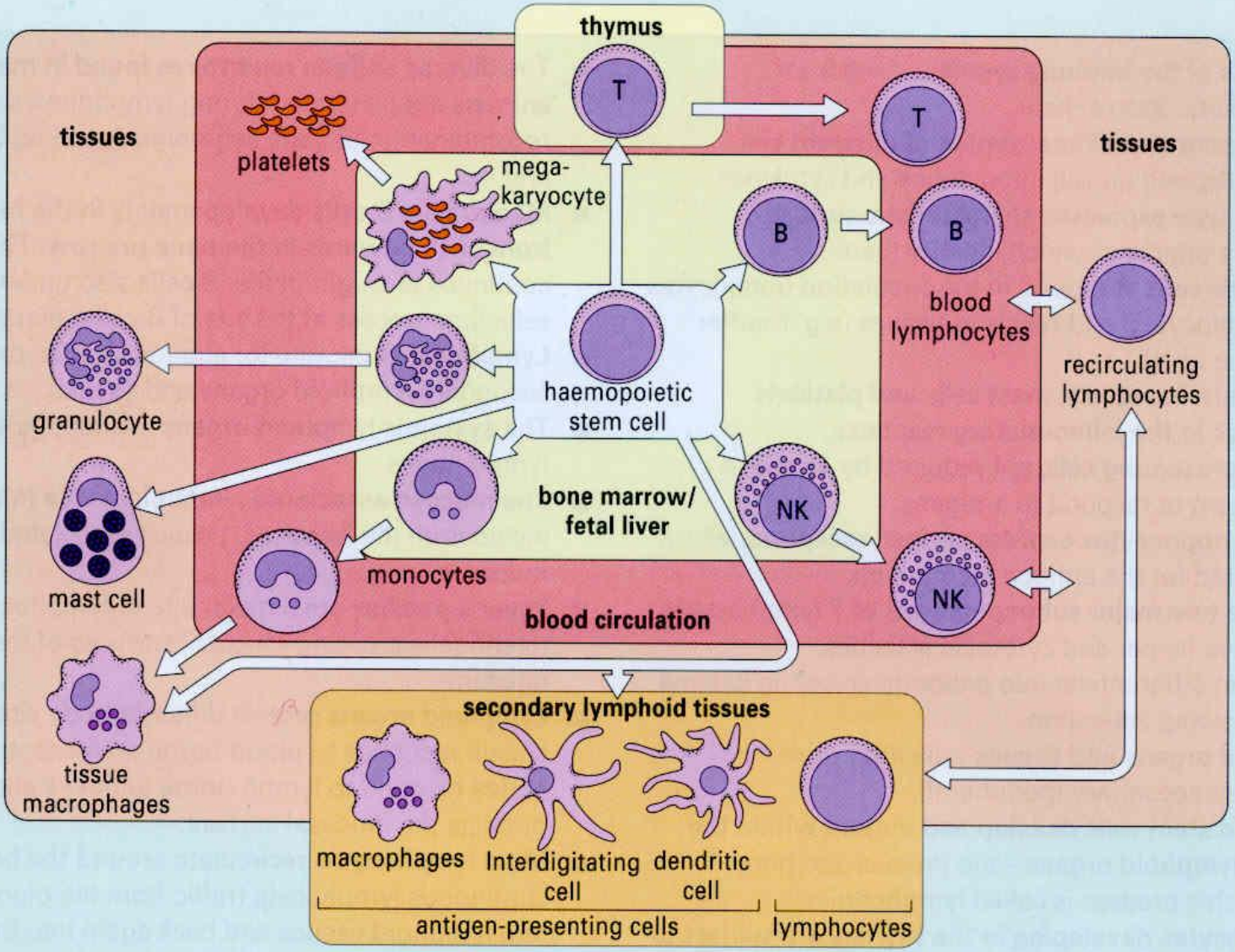
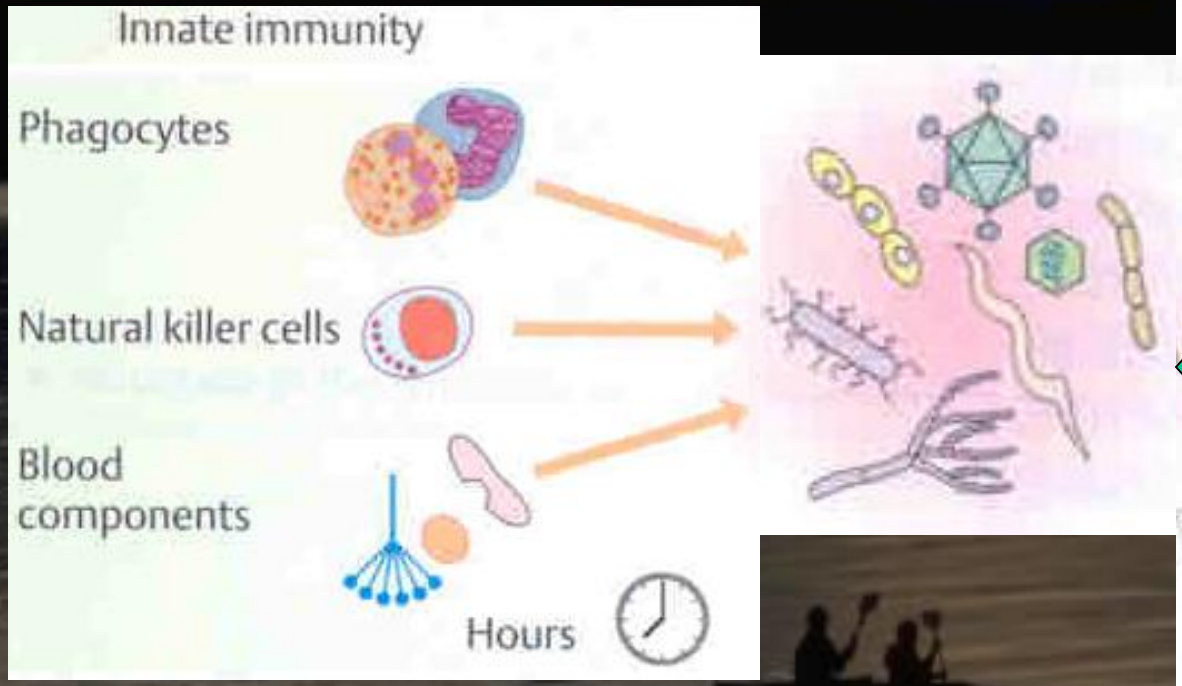
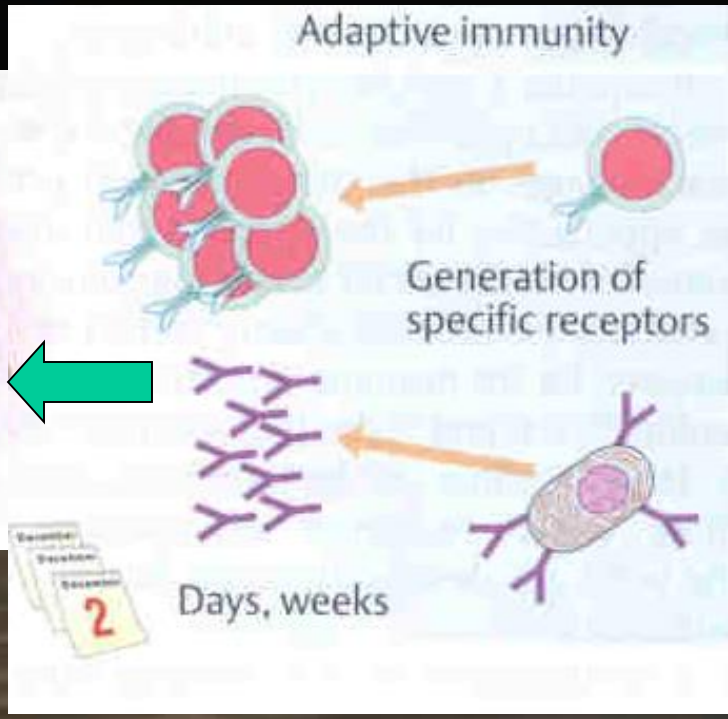


Fig. 2.1 All the cells shown arise from the haemopoietic stem cells mature in the thymus. The origin of the large granular

Imunidade


Innate immunity
Phagocytes
Natural killer cells
Blood components
Hours


Adaptive immunity
Generation of specific receptors
2
Days, weeks

Imunidade Inata

Inflamação

Febre

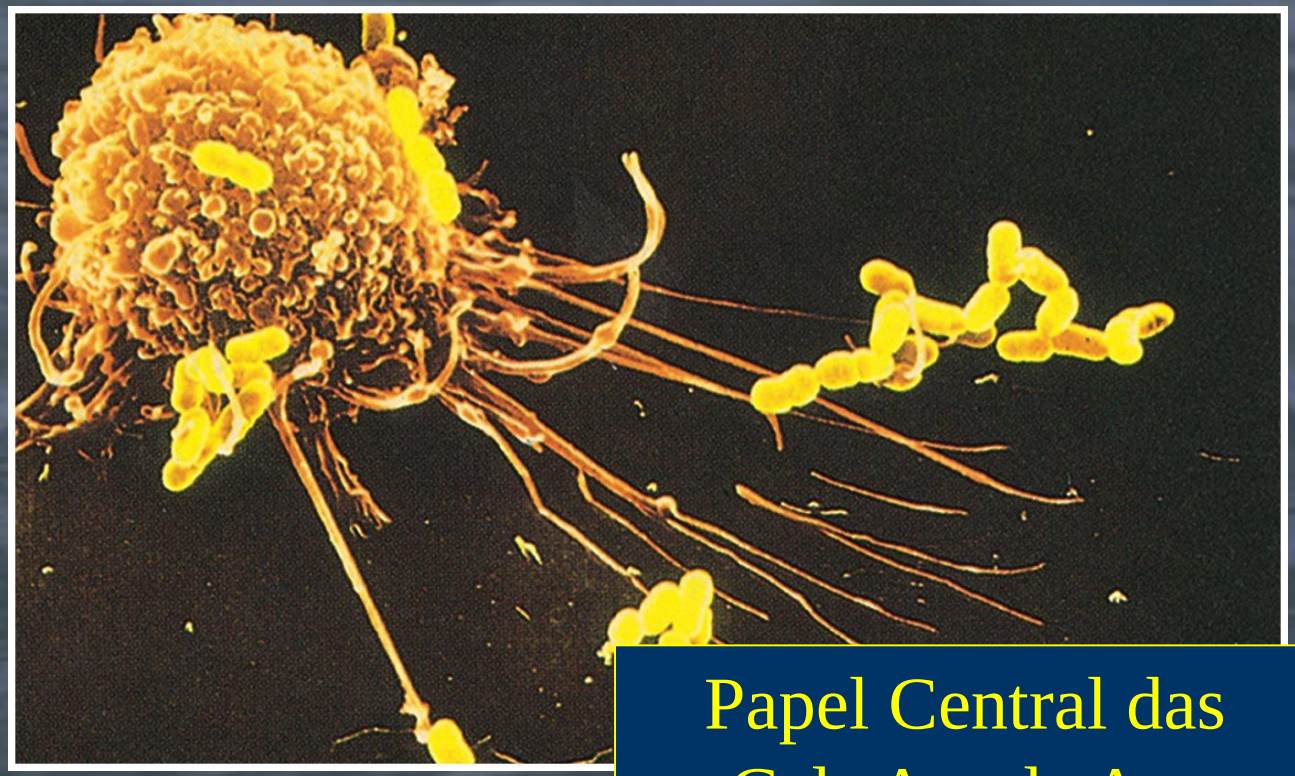
Células fagocitárias

Células NK (natural killer)

Componentes Sanguíneos

Complemento

Imunidade Adaptativa/ Adquirida



Papel Central das Cels Ap. de Ag: Macrófagos, DCs, etc

Cells of the mononuclear phagocyte lineage

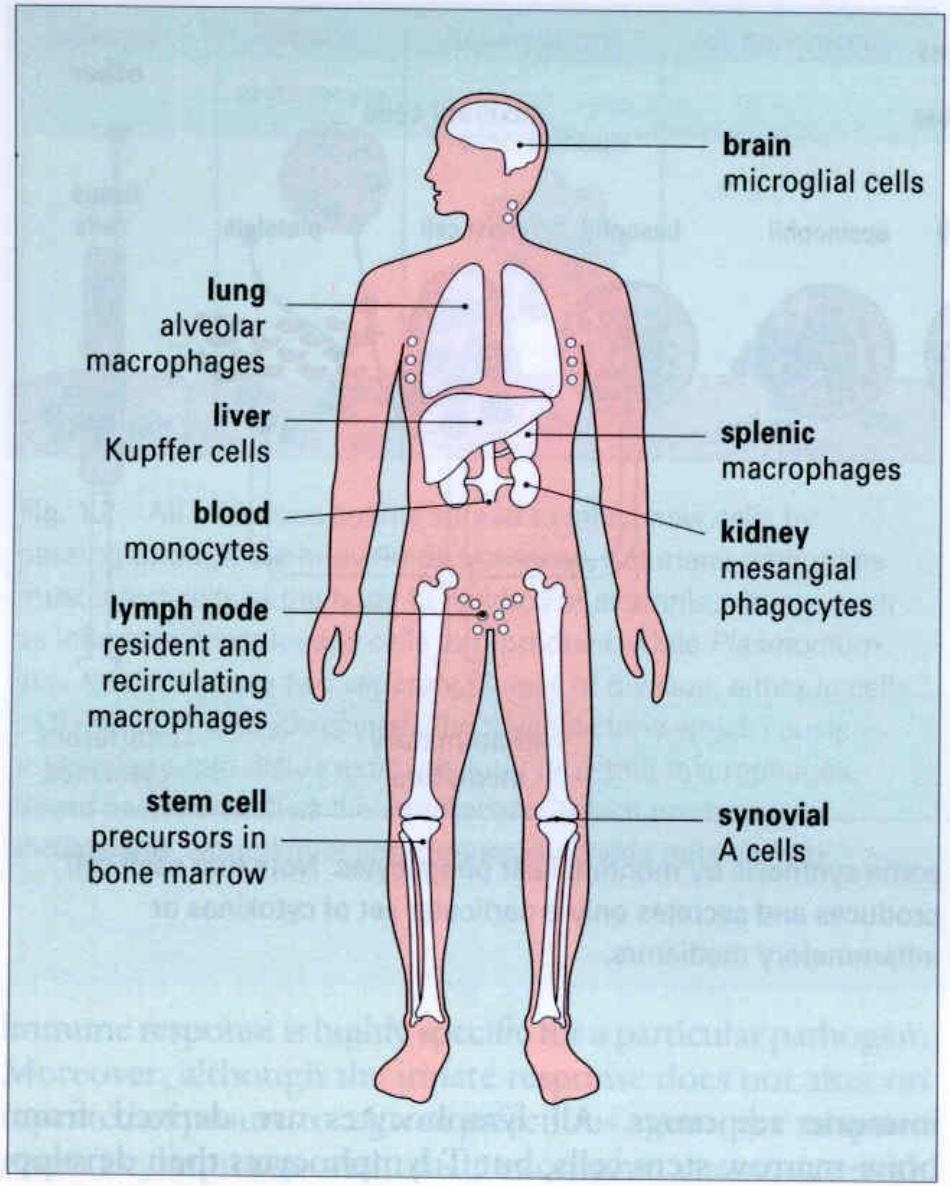
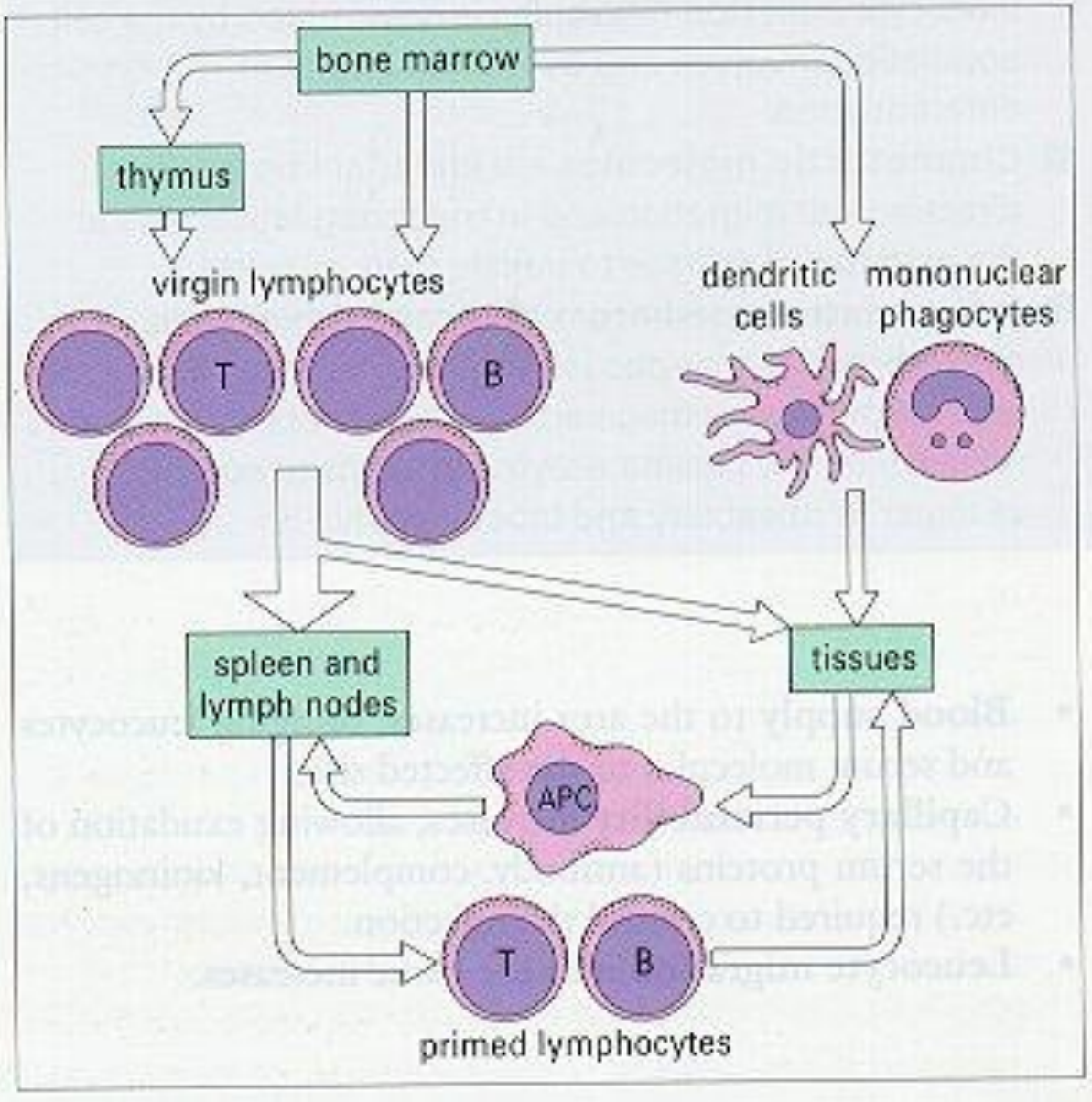


Fig. 1.5 Many organs contain phagocytic cells derived from

Recirculation of lymphocytes and antigen-presenting cells



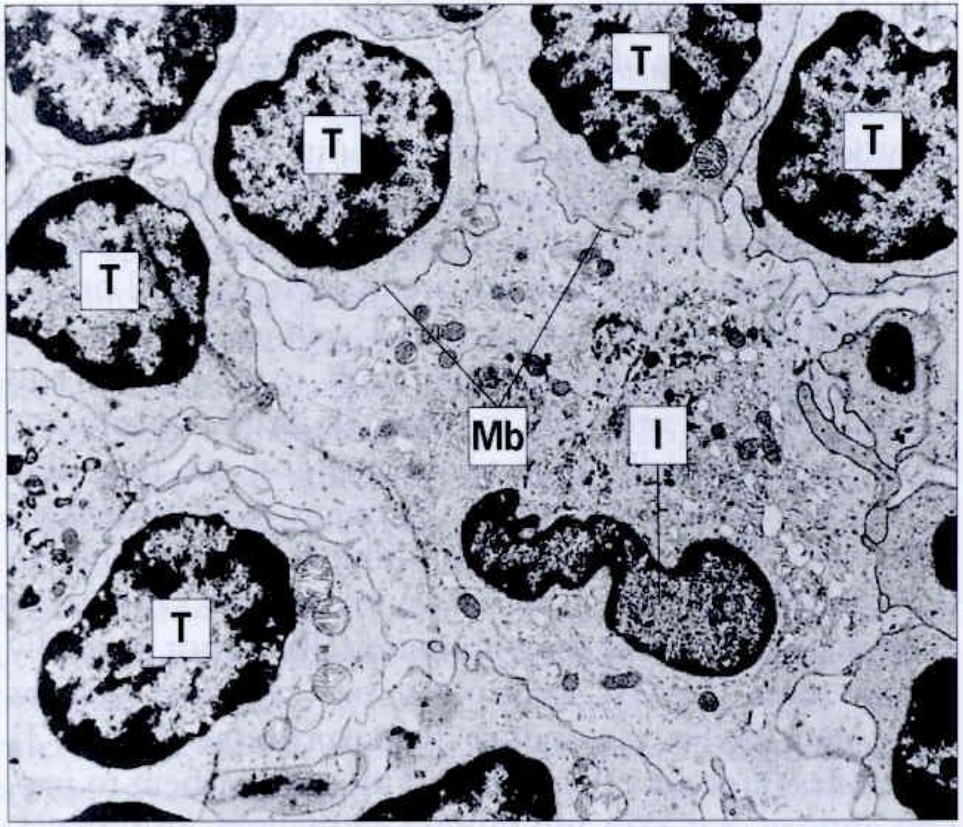
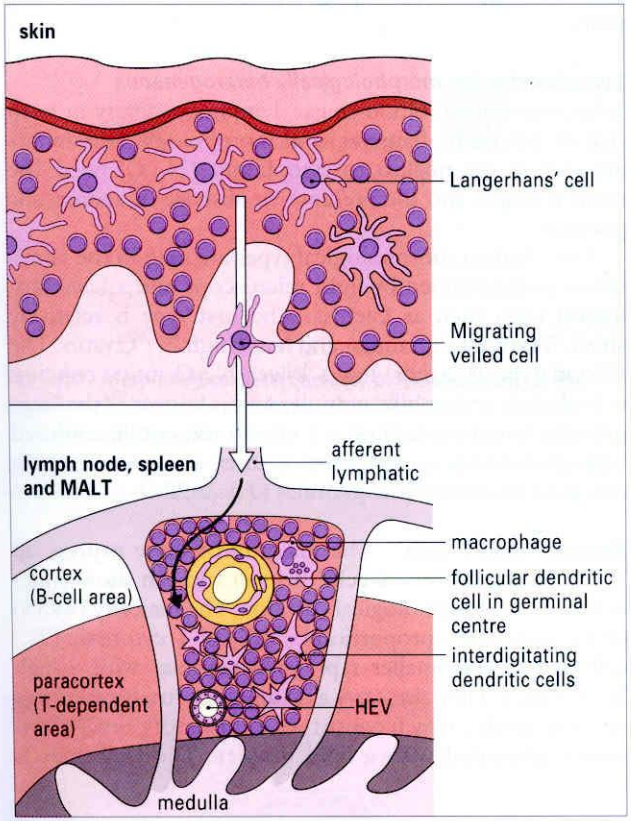


Fig. 2.19 Ultrastructure of an interdigitating dendritic cell (IDC)

Antigen-presenting cells



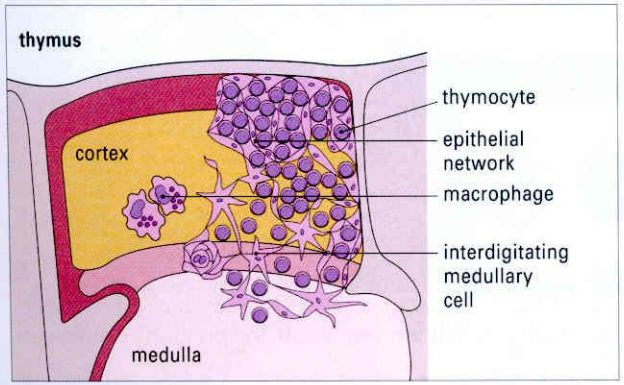


Fig. 2.18 Bone-marrow-derived antigen-presenting cells (APCs)

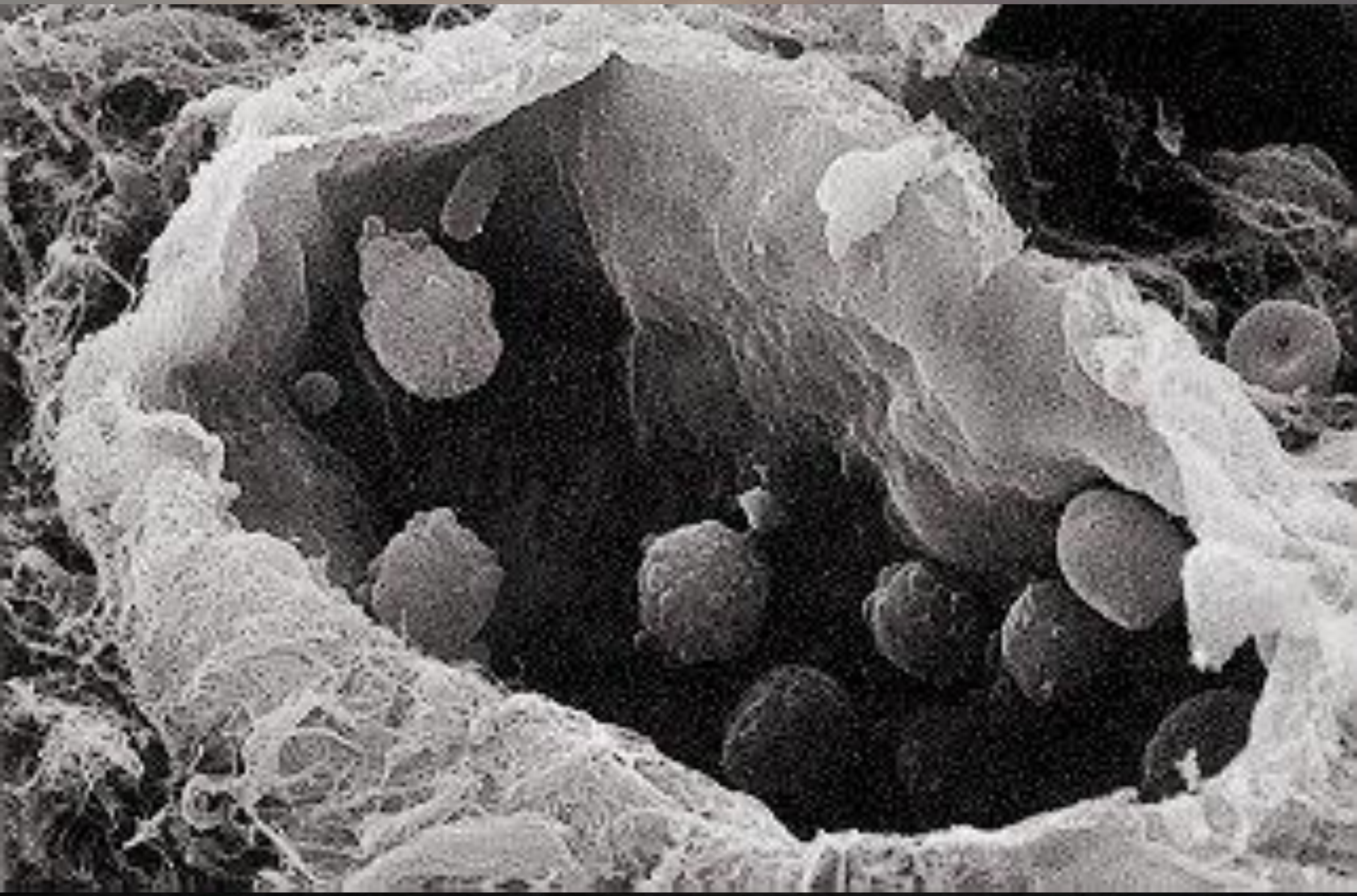
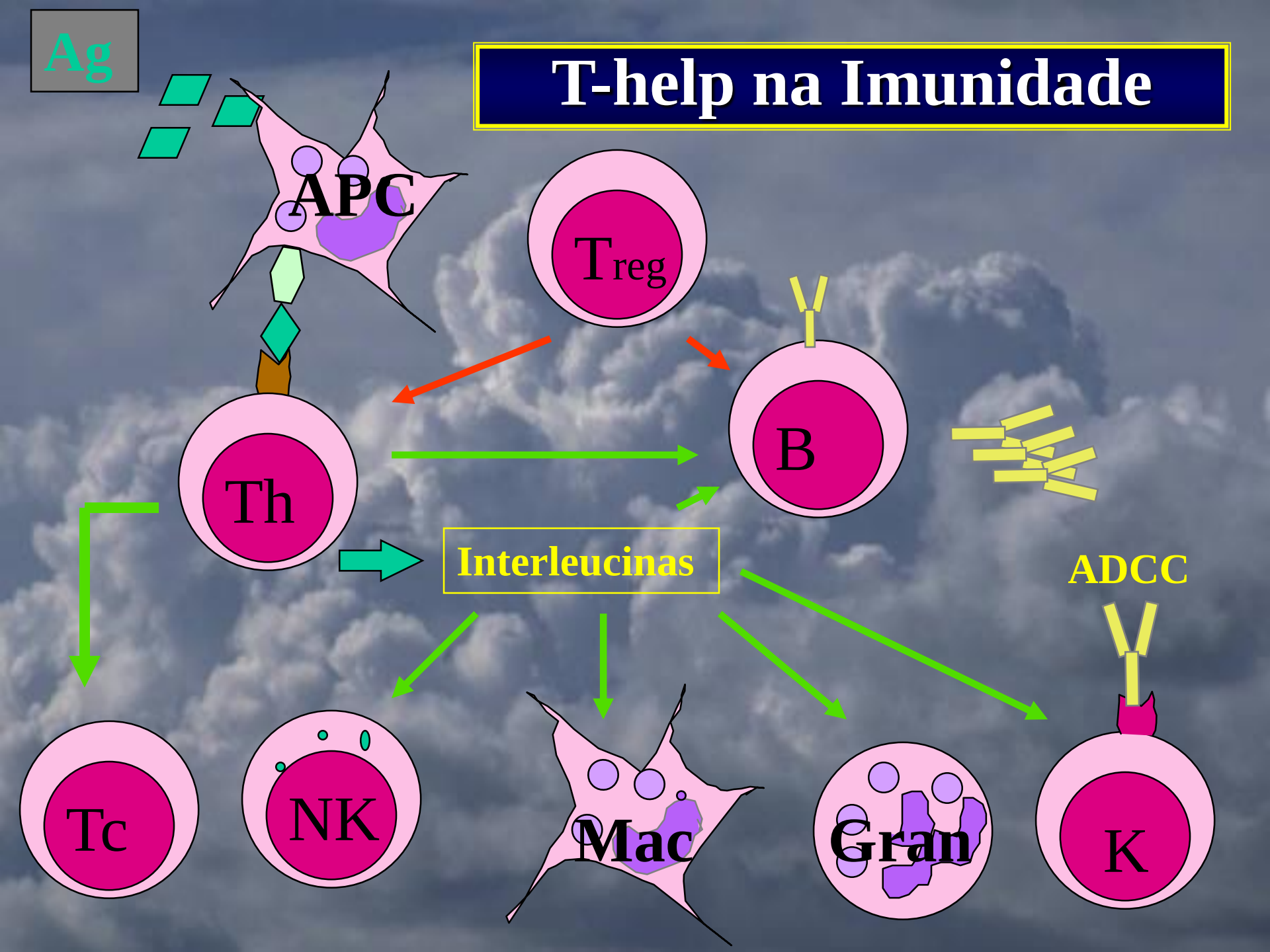
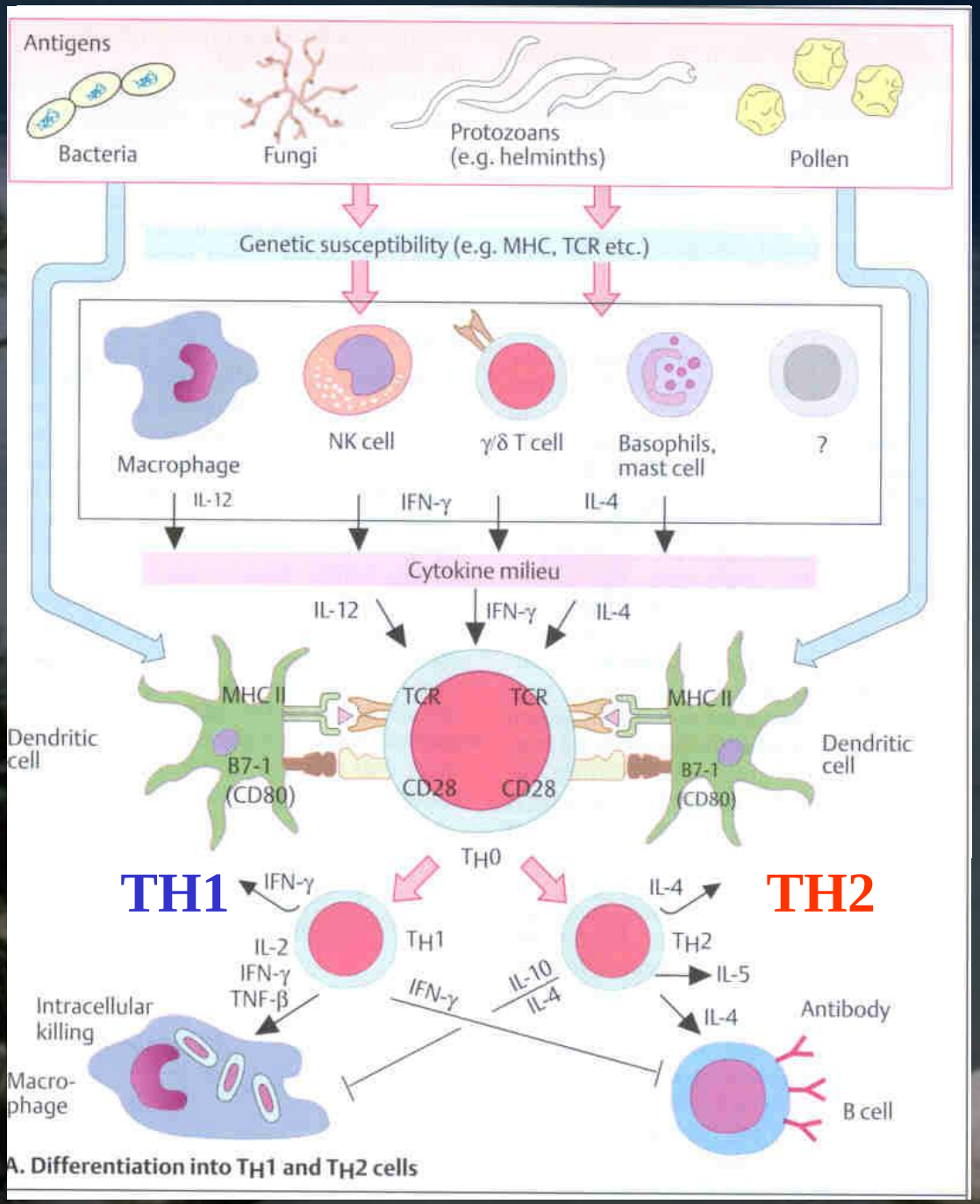


Fig. 1.16 Three phases of neutrophil migration across endothelium. (**1**) A neutrophil adheres to endothelium in a venule. (**2**) The cell extends its pseudopodia between the endothelial cells and migrates towards the basement membrane. (**3**) A neutrophil which has traversed the endothelium. The entire process is


Ag
T-help na Imunidade
APC
Treg
B
Th
Interleucinas
ADCC
Tc
NK
Mac
Gran
K


Antigens
Bacteria
Fungi
Protozoans
(e.g. helminths)
Pollen
Genetic susceptibility (e.g. MHC, TCR etc.)
Macrophage
NK cell
γ/δ T cell
Basophils,
mast cell
?
IL-12
IFN-γ
IL-4
Cytokine milieu
IL-12
IFN-γ
IL-4
MHC II
TCR
TCR
MHC II
Dendritic
cell
B7-1
(CD80)
CD28
CD28
B7-1
(CD80)
Dendritic
cell
TH0
TH1
IFN-γ
IL-4
TH2
IL-2
IFN-γ
TNF-β
TH1
IFN-γ
IL-10
IL-4
TH2
IL-5
IL-4
Intracellular
killing
Antibody
Macro-
phage
B cell
A. Differentiation into TH1 and TH2 cells

Resposta Celular:

Citotoxicidade

Reacções inflamatórias

Destruição de Mic. Intracelulares

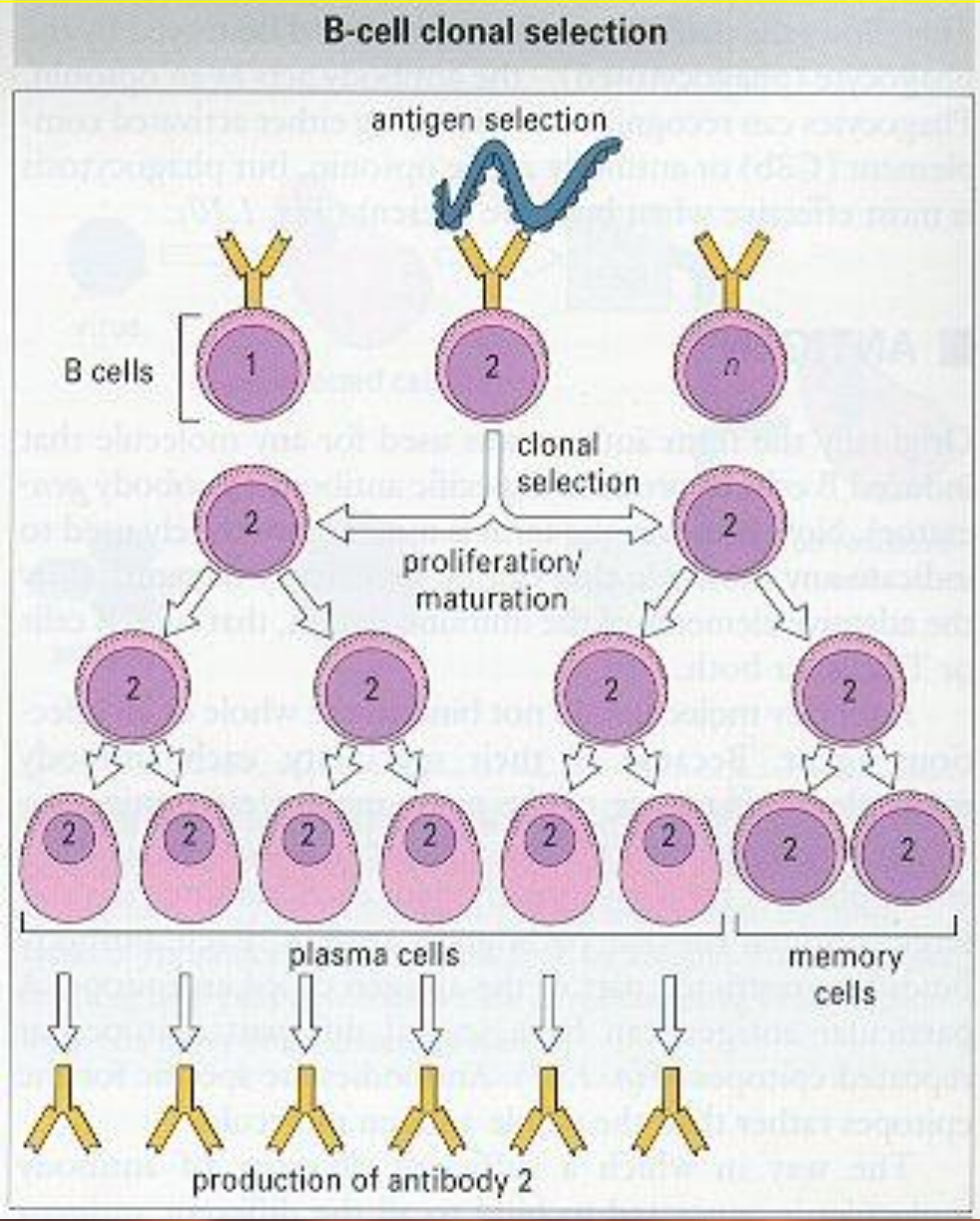
Resposta Humoral:

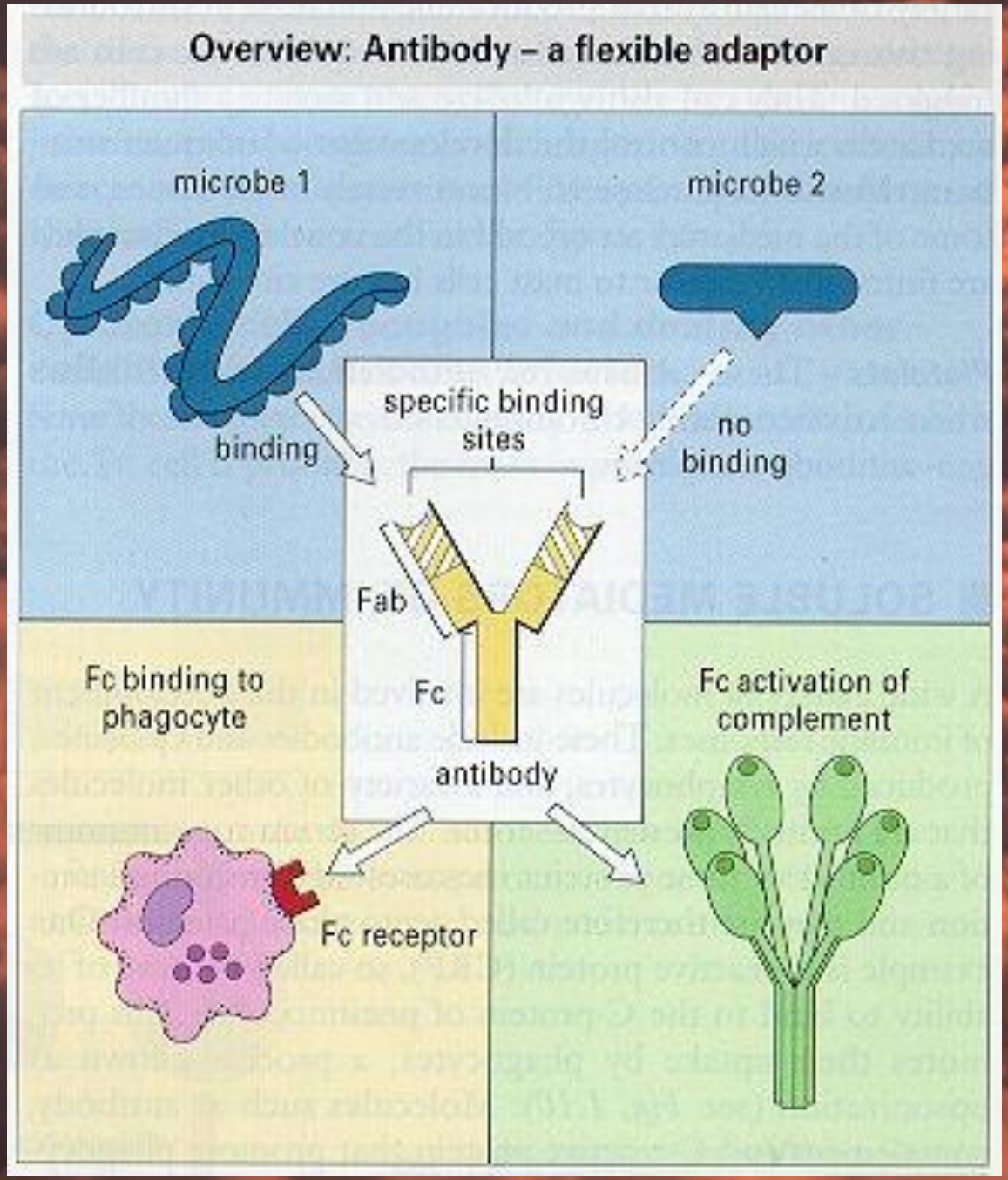
Produção de Anticorpos

IgM, IgG, IgA, IgE, IgD

Reacções alérgicas

Resposta Humoral

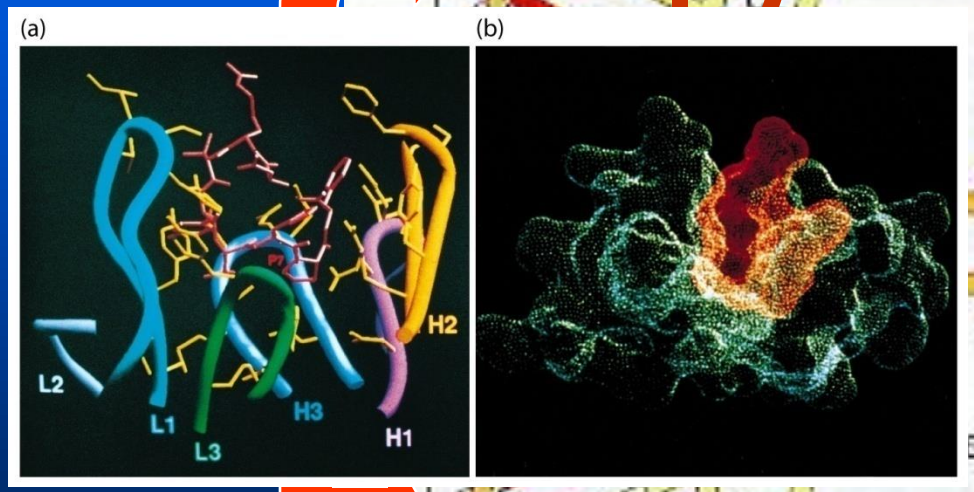


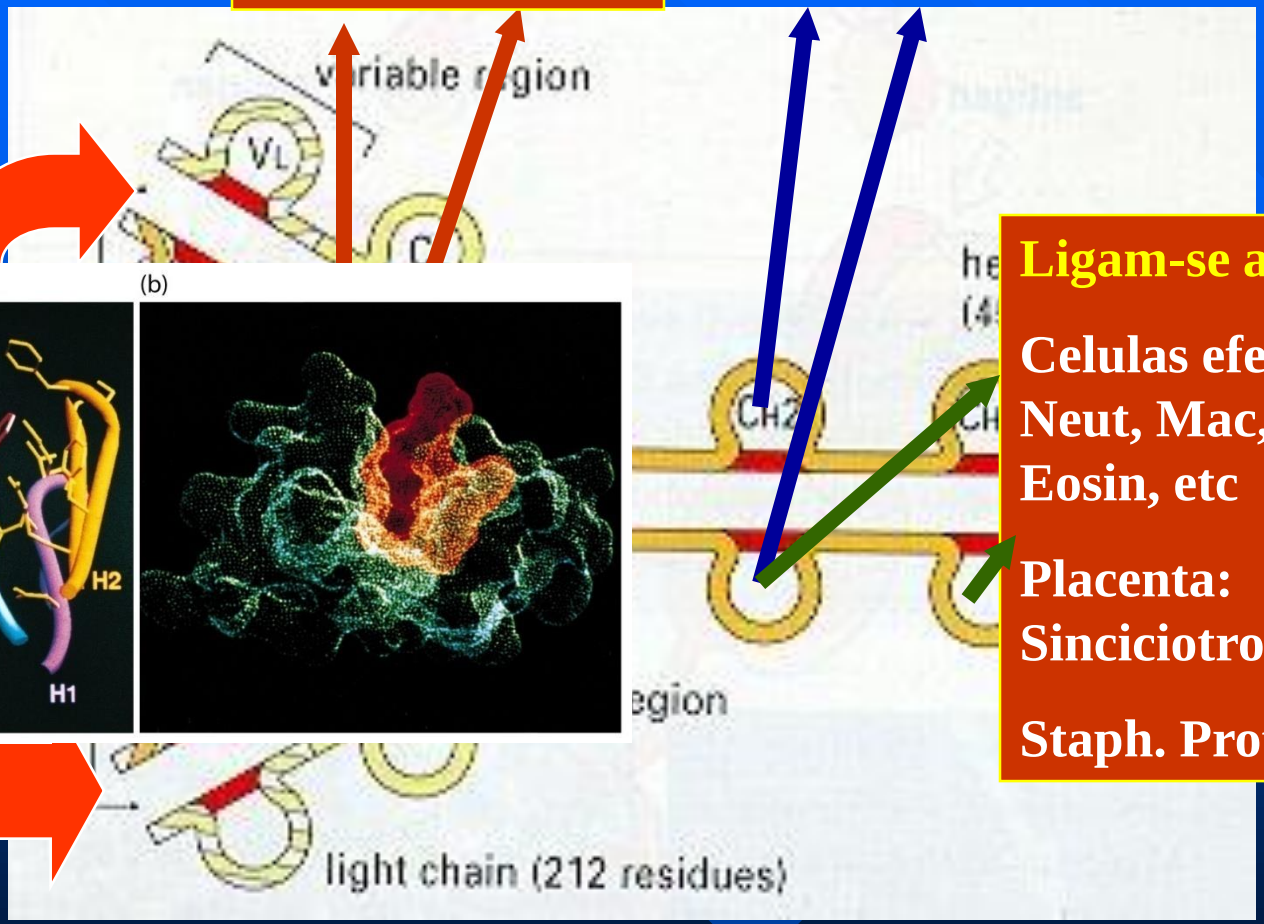

Overview: Antibody – a flexible adaptor
microbe 1
microbe 2
binding
specific binding sites
no binding
Fab
Fc
antibody
Fc binding to phagocyte
Fc activation of complement
Fc receptor

Funções

Liga-se C4b

Fixa C1q
Controle ritmo catabólico



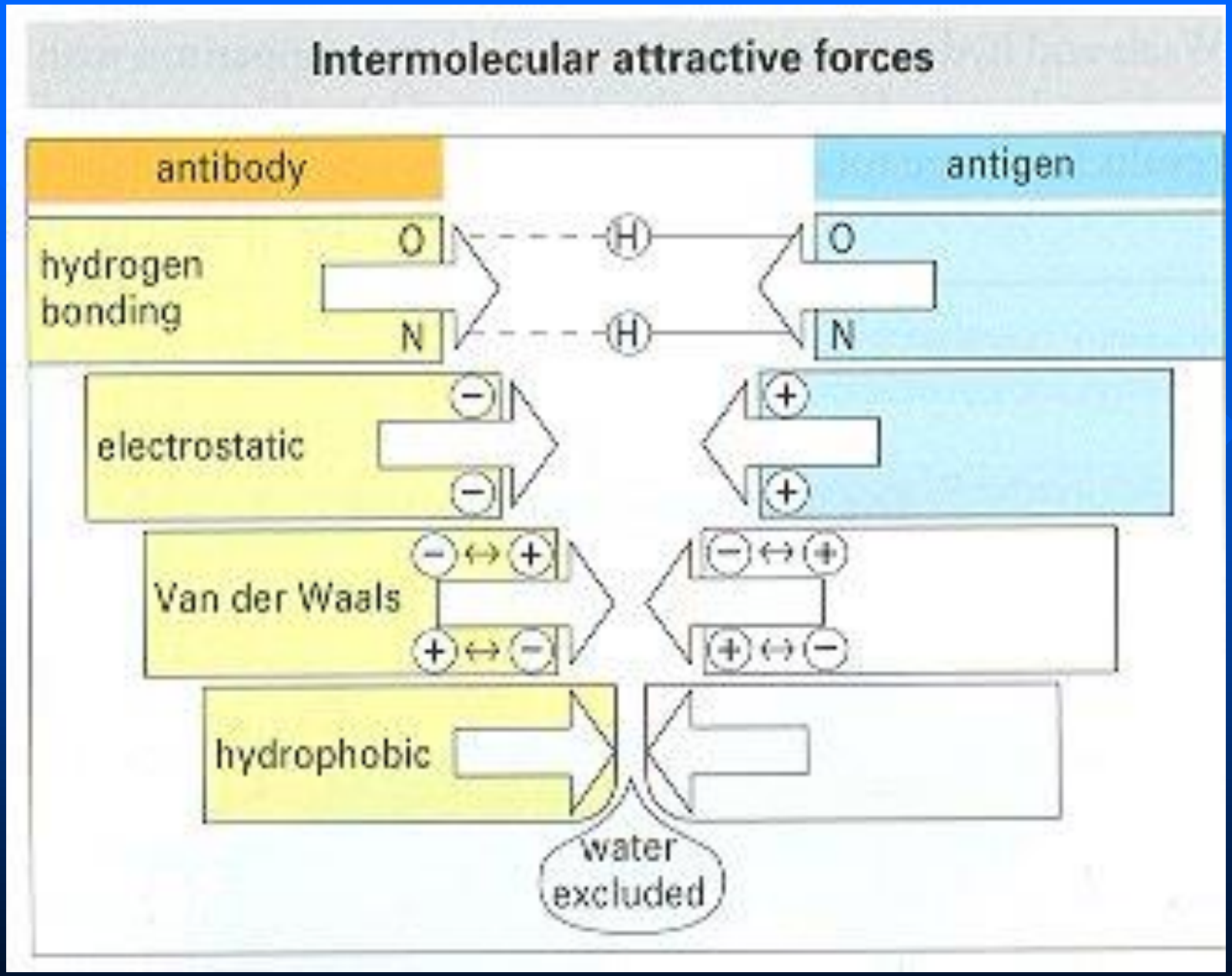


Ligam-se a:

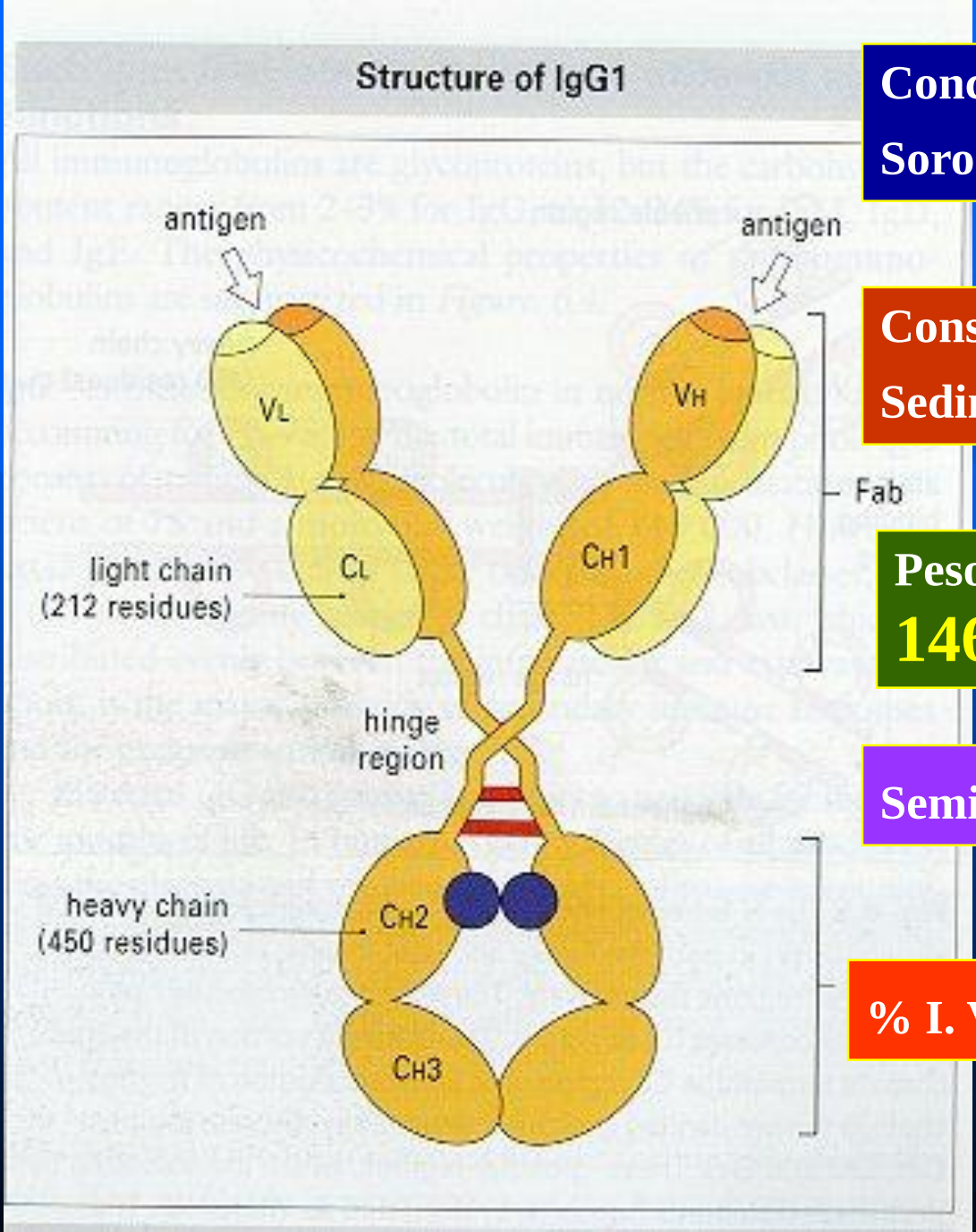
Celulas efectoras: Neut, Mac, Mast, Bas, Eosin, etc

Placenta: Sinciciotrofoblasto

Staph. Protein A


Intermolecular attractive forces
antibody
antigen
hydrogen bonding
O
H
O
N
H
N
electrostatic
Van der Waals
hydrophobic
water excluded

IgG



Concentração Soro: 9 mg/ml

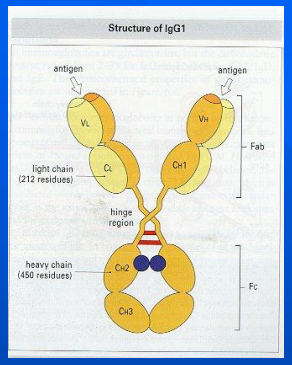
Constante de Sedimentação: 7s

Peso Molecular: 146 K

Semi-vida: 21d

% I. Vasc: 45%

IgG



Aprox.
150 kD

Opsonização

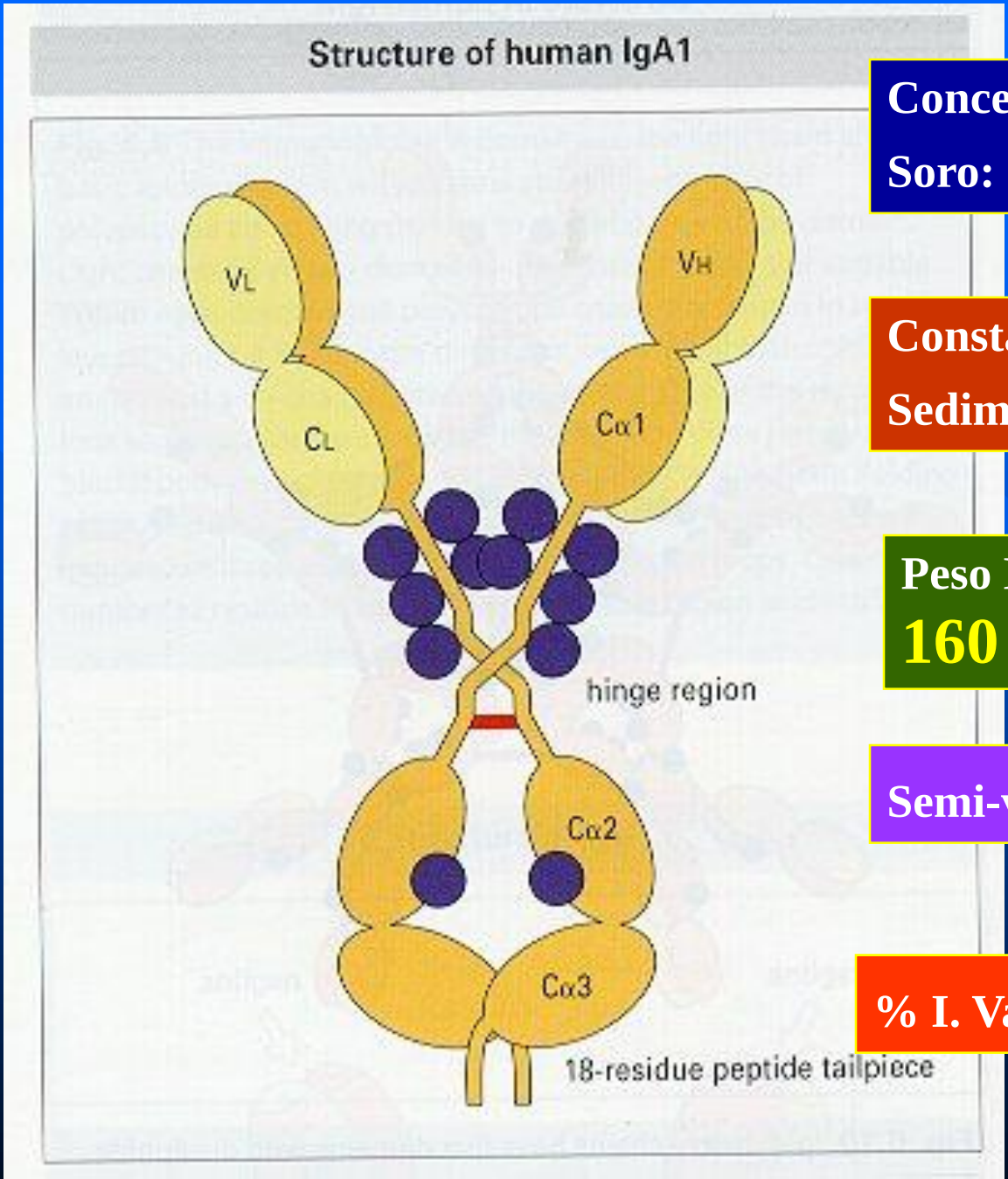
Neutralização

Aglutinação

Precipitação

(Activação do complemento)

IgA



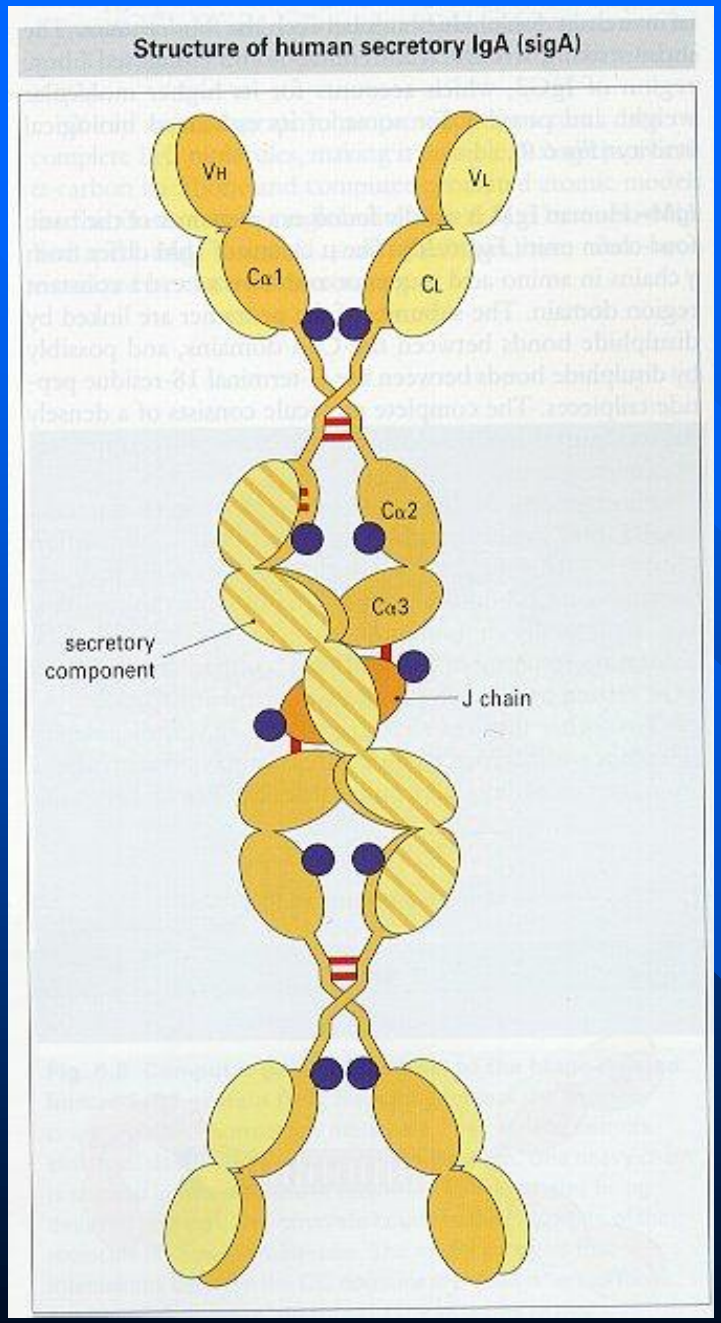
Concentração Soro: 3 mg/ml

Constante de Sedimentação: 7s

Peso Molecular: 160 K

Semi-vida: 6d

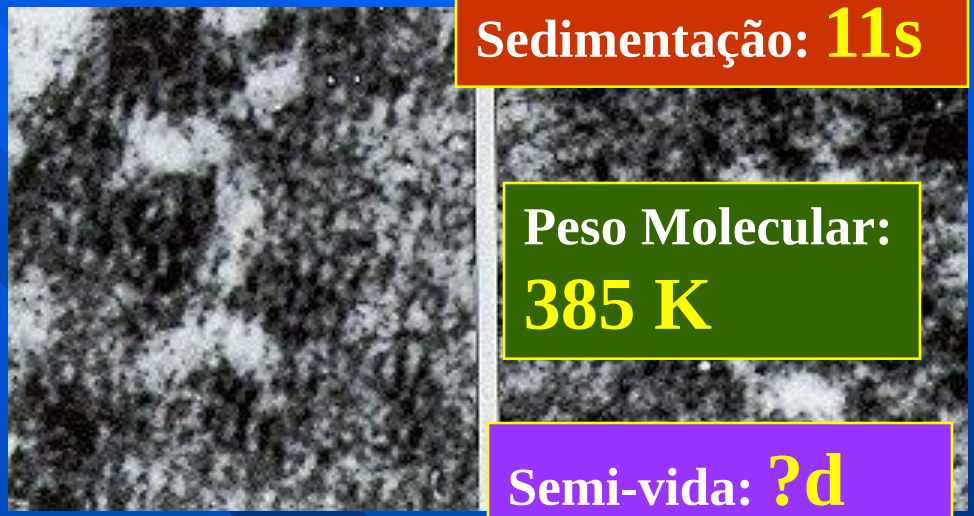
% I. Vasc: 42%



IgAs

Concentração Soro: 0,05 mg/ml

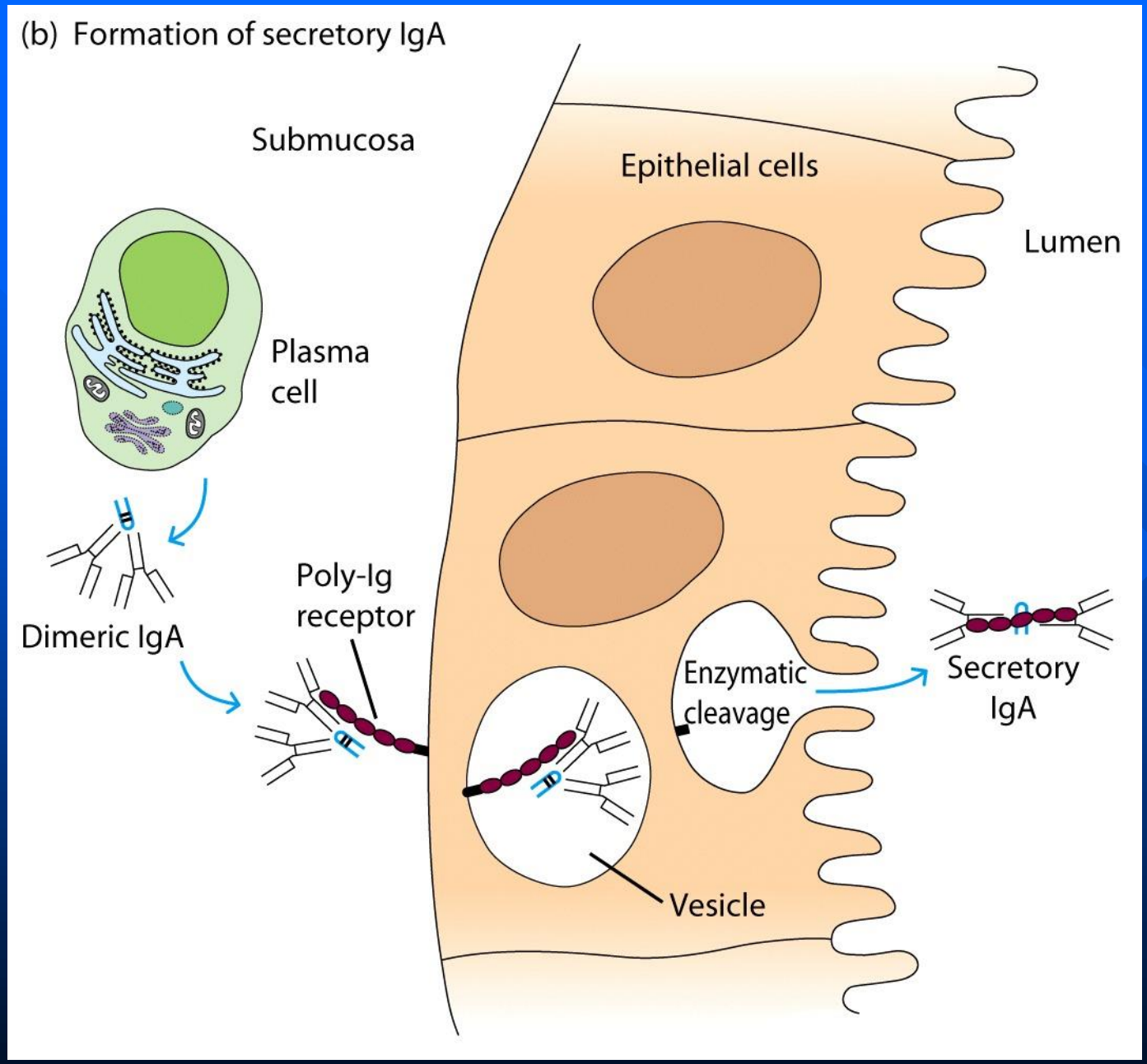
Constante de Sedimentação: 11s



Peso Molecular: 385 K

Semi-vida: ?d

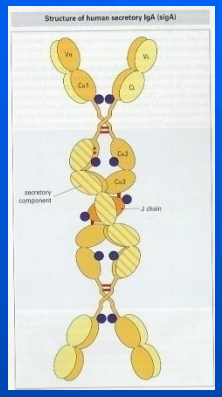
% I. Vasc: Vestigial


(b) Formation of secretory IgA
Submucosa
Epithelial cells
Lumen
Plasma cell
Dimeric IgA
Poly-Ig receptor
Enzymatic cleavage
Secretory IgA
Vesicle

Aglutinação

IgA

Neutralização de vírus



Previne aderência de antigénios às mucosas

(Intestino, Tracto Respiratório, Urinário, Pele e Glandula Mamária)

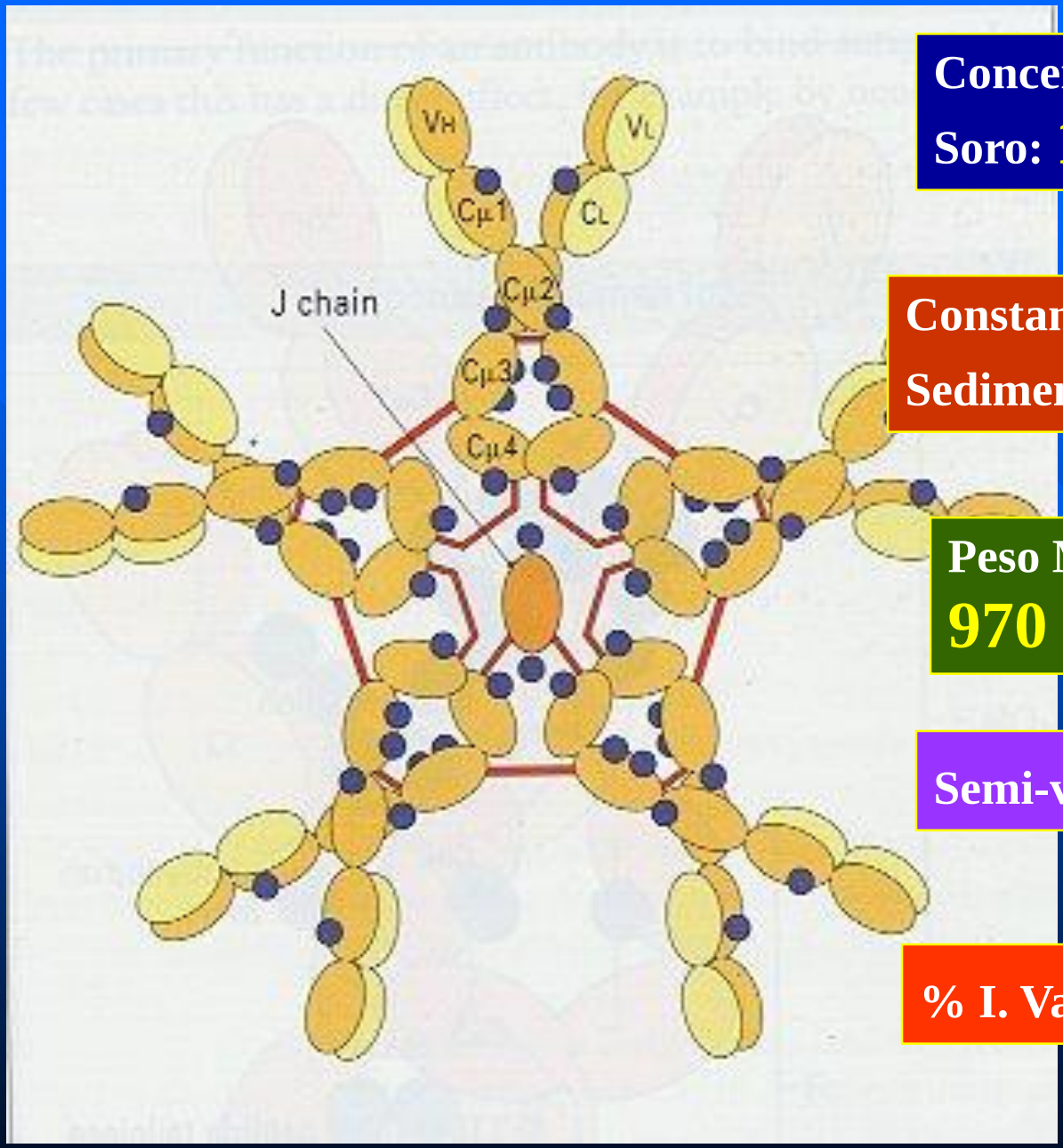
2 X 170 kD

Não Activa Complemento

cadeia J

Não Opsoniza – Previne aderência

IgM



Concentração Soro: 1,5 mg/ml

Constante de Sedimentação: 19s

Peso Molecular: 970 K

Semi-vida: 10d

% I. Vasc: 80%

IgM

IgM

5 X 180 kD

900 kD + J

1ª a ser produzida na resposta primária

Activação do complemento

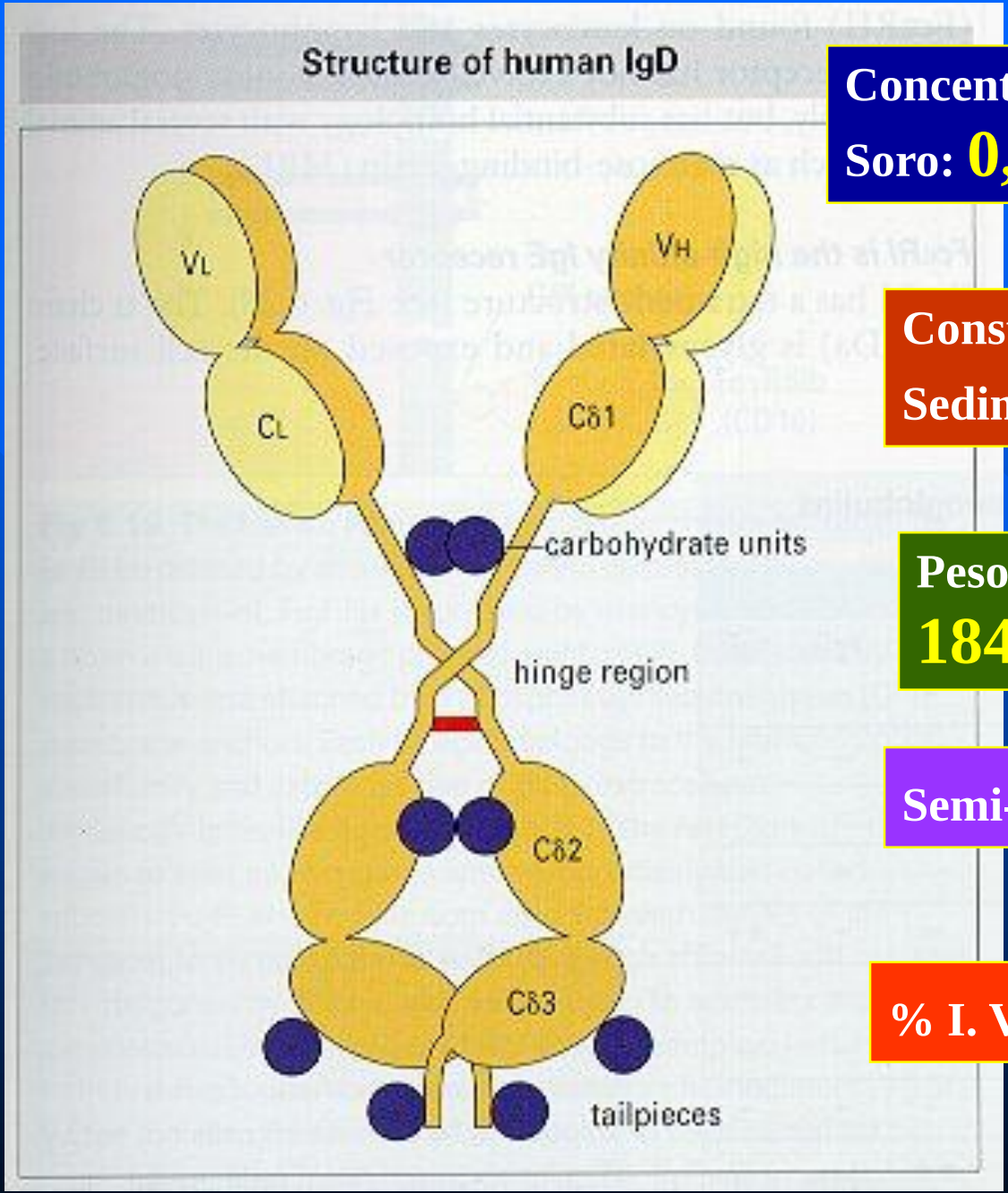
Opsonização

Neutralização de vírus

Aglutinação

Menor Mobilidade

IgD



Concentração Soro: 0,03 mg/ml

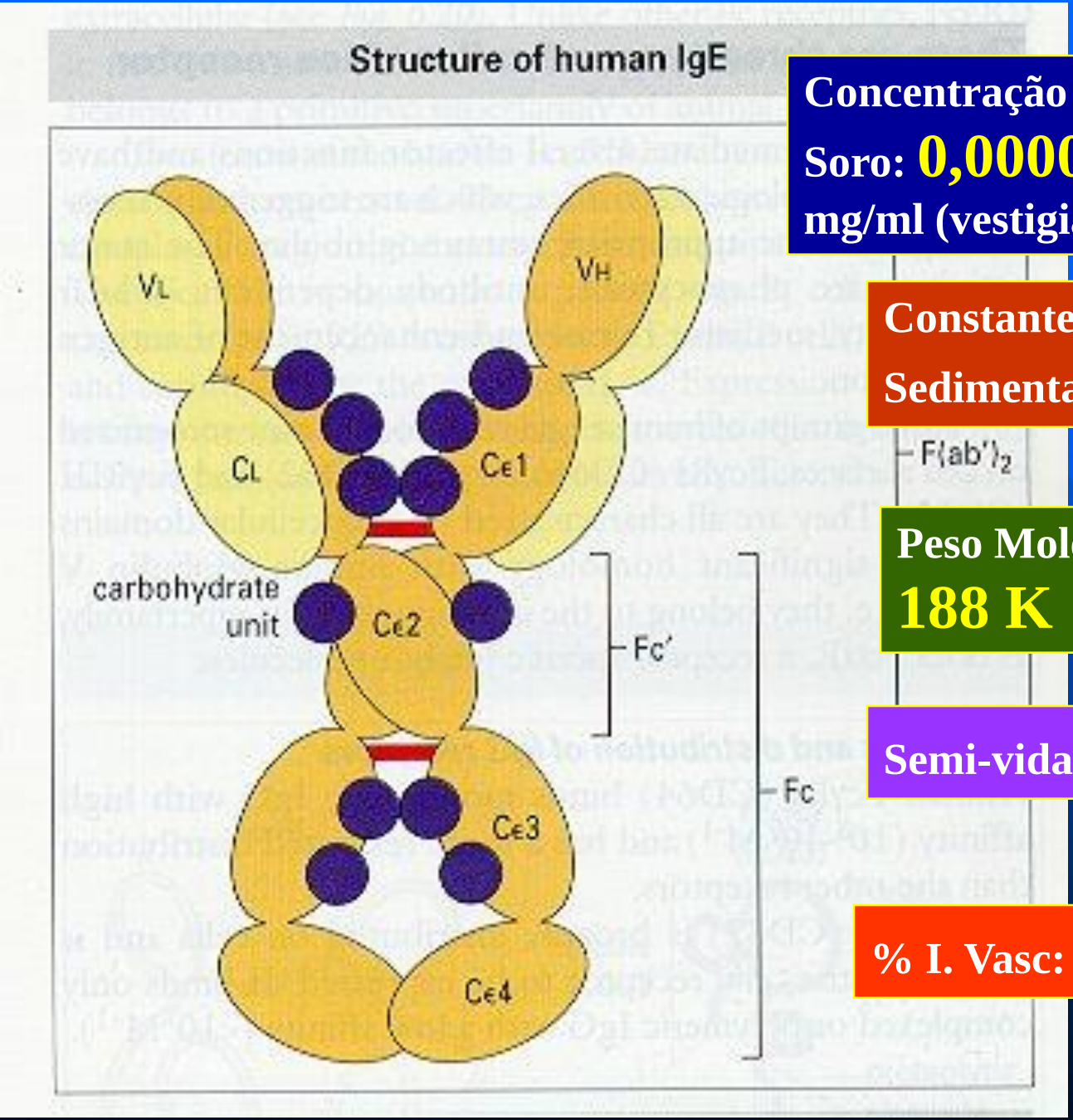
Constante de Sedimentação: 7s

Peso Molecular: 184 K

Semi-vida: 3d

% I. Vasc: 75%

IgE



Concentração
Soro: 0,00005 mg/ml (vestigial)

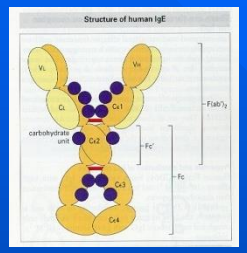
Constante de Sedimentação: 8s

Peso Molecular: 188 K

Semi-vida: 2d

% I. Vasc: 50%

IgE



200 kD

Localização sobretudo a nível das sub-mucosas, ligada a mastócitos e basófilos

Reacções de hipersensibilidade imediata - Alergias

Infecções parasitárias – Expulsão por reacção inflamatória intensa

Desgranulação dos mastócitos

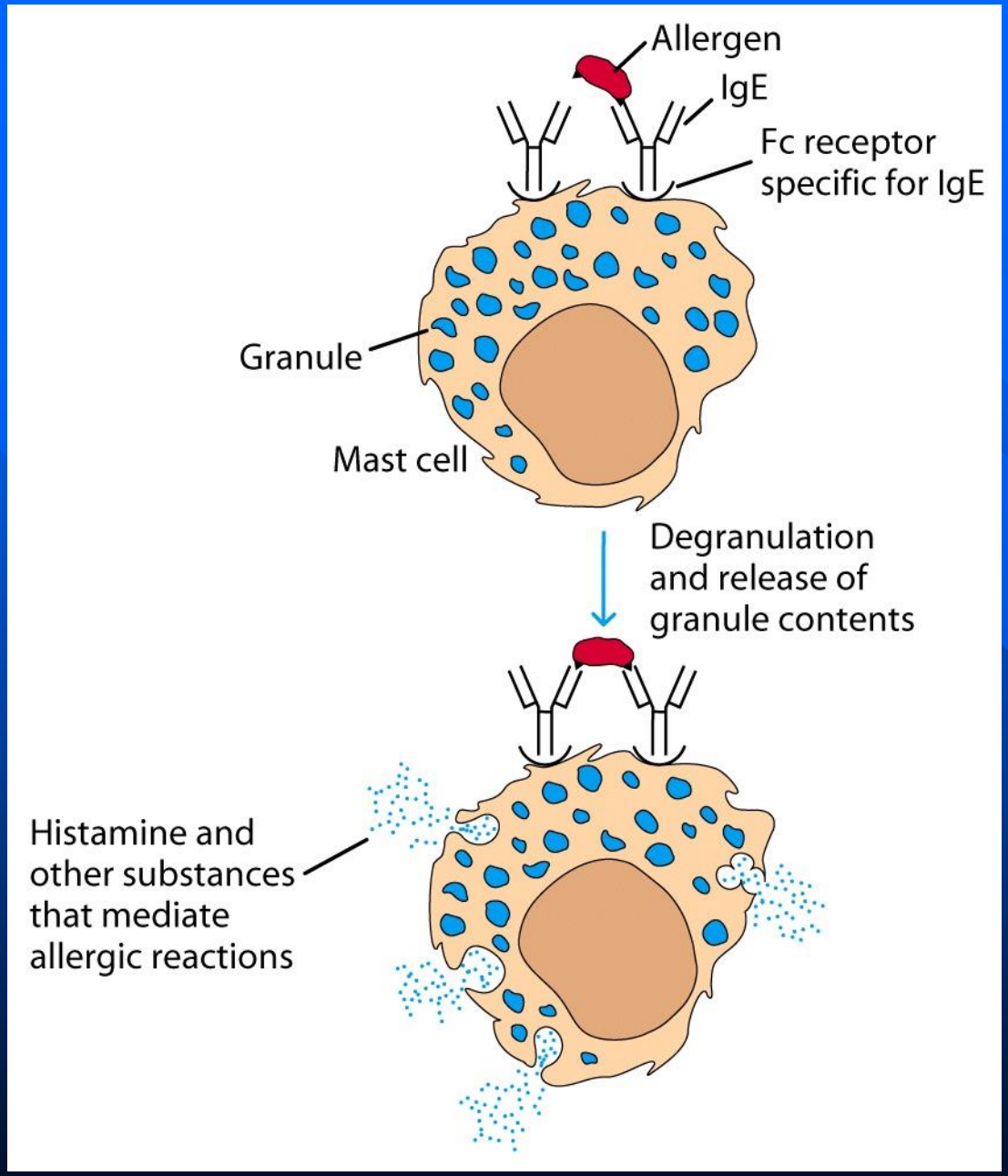
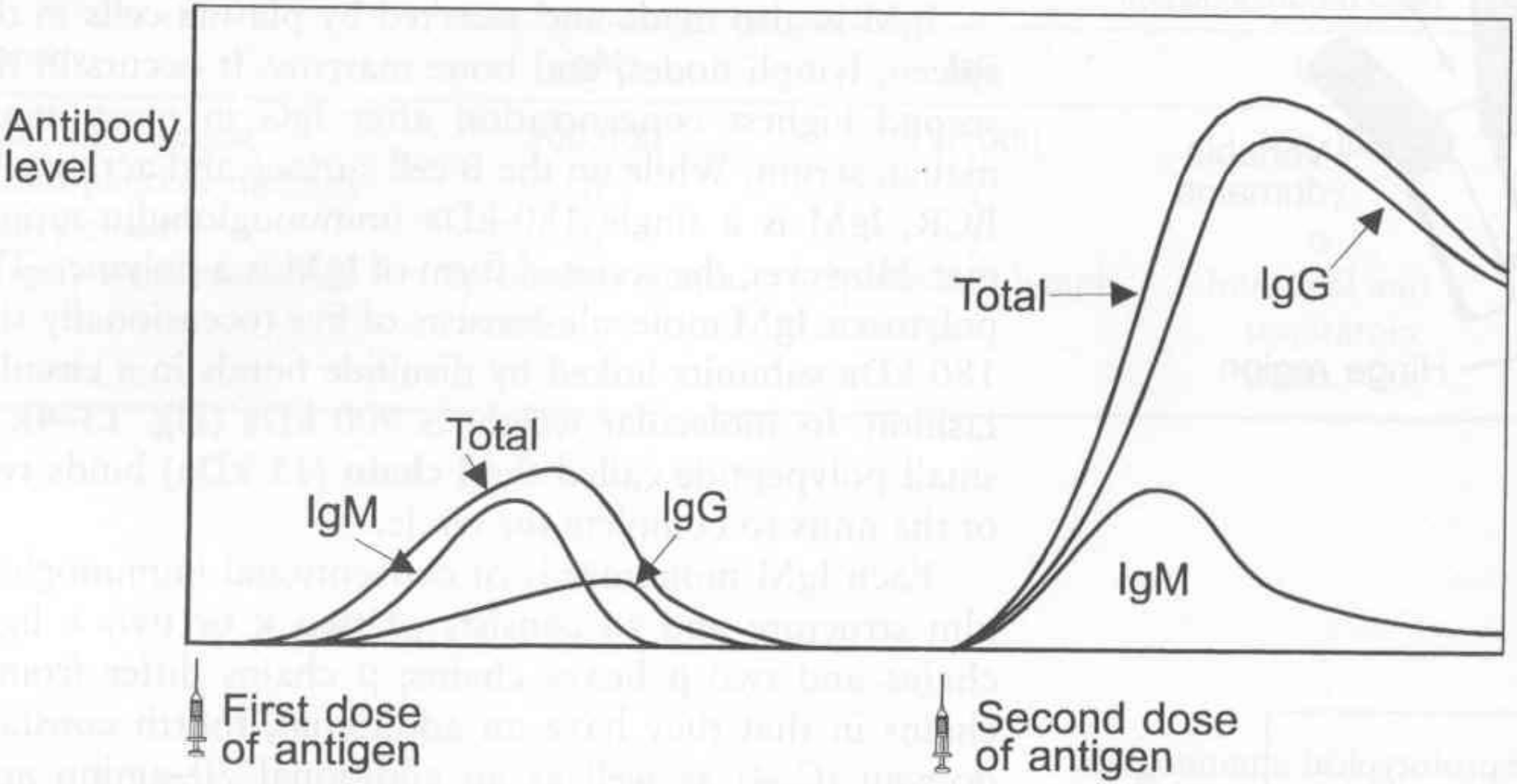

Allergen
IgE
Fc receptor
specific for IgE
Granule
Mast cell
Degranulation
and release of
granule contents
Histamine and
other substances
that mediate
allergic reactions

TABLE 13–3. *Immunoglobulin Classes and Subclasses in Domestic Mammals and Humans*

Species	Immunoglobulin Classes				
	IgG	IgA	IgM	IgE	IgD
Horse	Ga, Gb, Gc, G(B), G(T)a, G(T)b	A	M	E	?
Cattle	G1, G2 (G2a, G2b?)	A	M	E	—
Sheep	G1 (G1a?), G2, G3	A1, A2	M	E	—
Pig	G1, G2a, G2b, G3, G4	A	M	E	—
Dog	G1, G2, G3, G4	A	M	E1, E2	D
Cat	G1, G2, G3, (G4?)	(A1, A2?)	M	E	?
Chimpanzee	G1, G2, G3	A	M	E	D
Mouse	G1, G2a, G2b, G3	A1, A2	M	E	D
Human	G1, G2, G3, G4	A1, A2	M1, M2	E	D


Antibody level
Total
IgG
IgM
Total
IgM
IgG
First dose of antigen
Second dose of antigen

Immunoglobulins in the serum of the fetus and newborn child

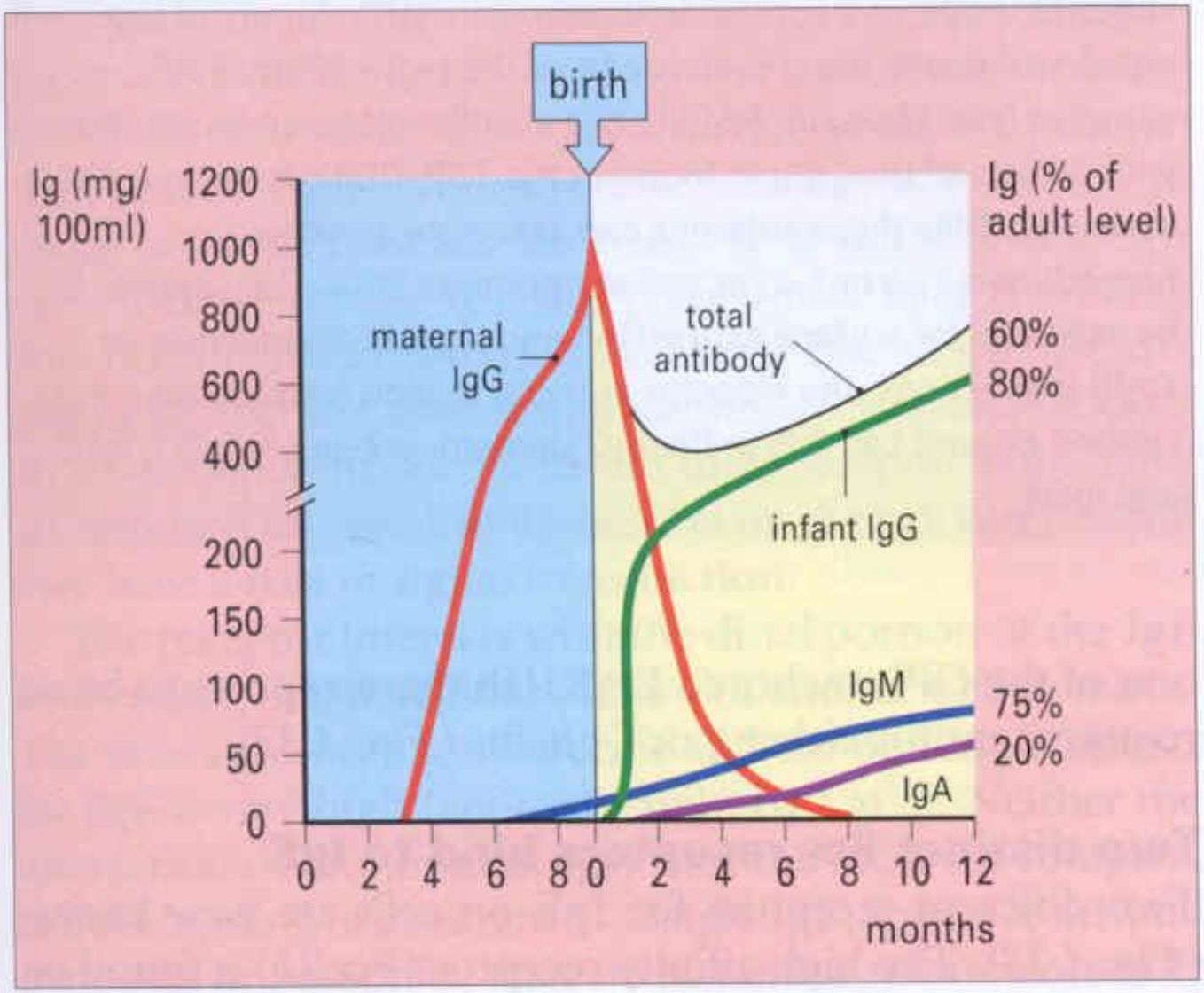


Fig. 4.20 IgG in the fetus and newborn infant is derived solely

Primatas e Hu - Placenta Hemocorial

Atravessa placenta – Titulo = mãe

Cão e Gato – Placenta Endoteliocorial

Apenas 5-10% IgG atravessa

Ruminantes – Placenta Sindesmocorial

Equinos e suínos – Placenta Epiteliocorial

IgG

(Não atravessa)

Imunidade Celular

Th1

Th2

Resposta Celular:

Citotoxicidade

Reacções inflamatórias

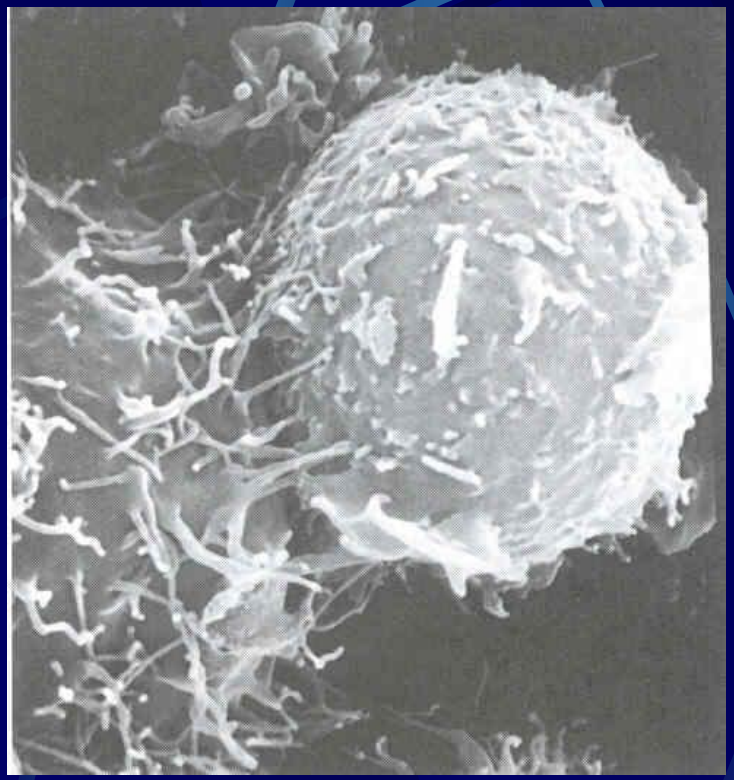
Destruição de Microorg. Intracelulares

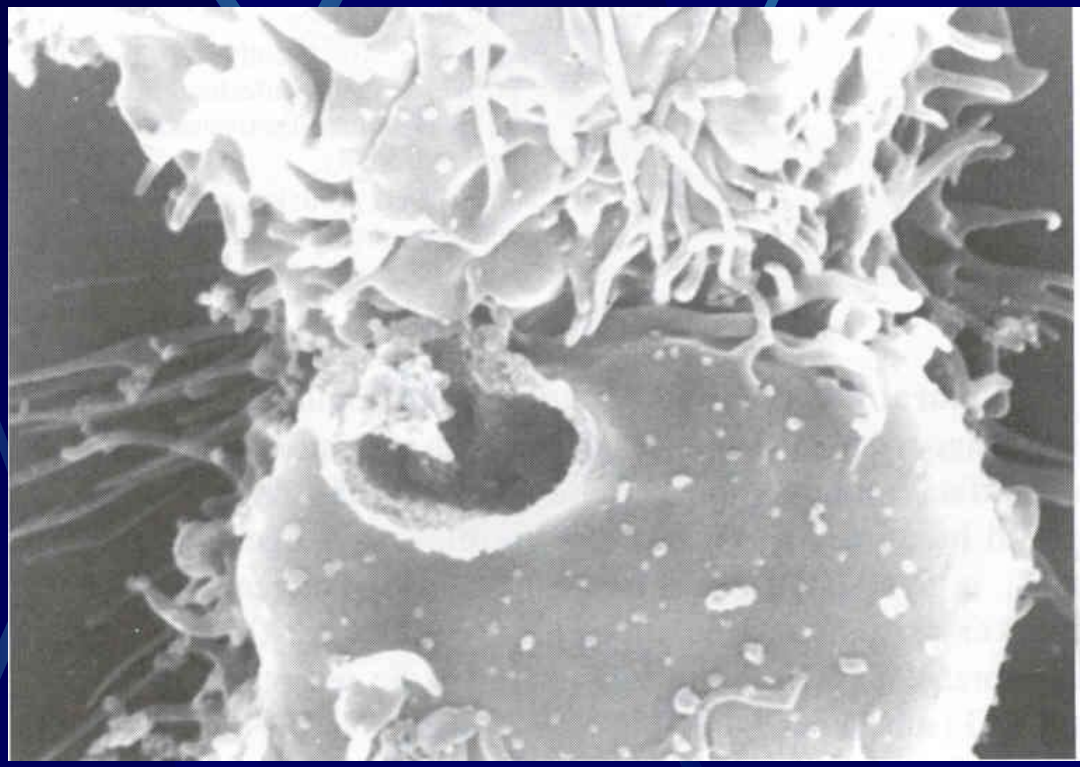
Resposta Humoral:

Produção de Anticorpos

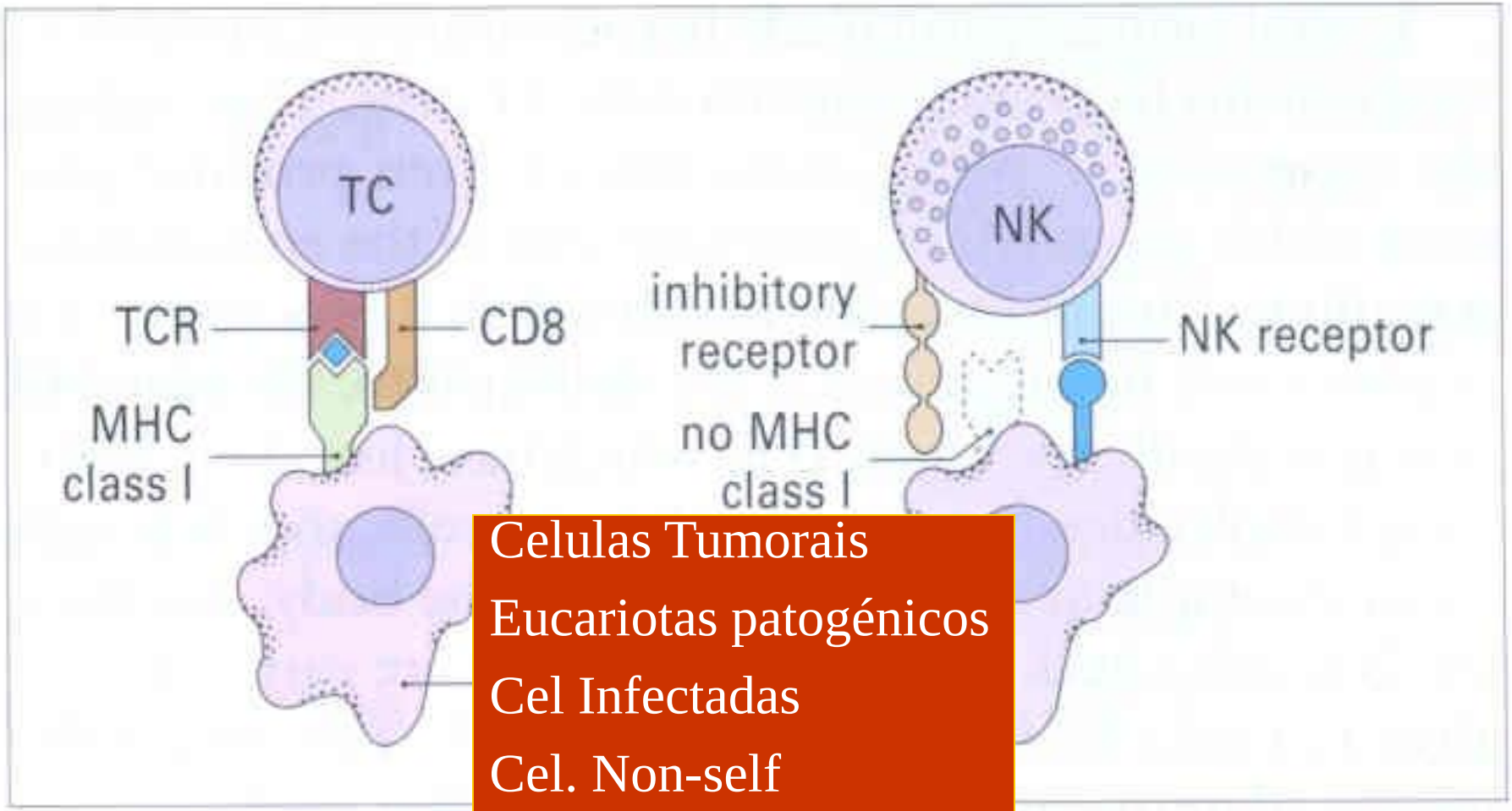
IgM, IgG, IgA, IgE

Reacções alérgicas

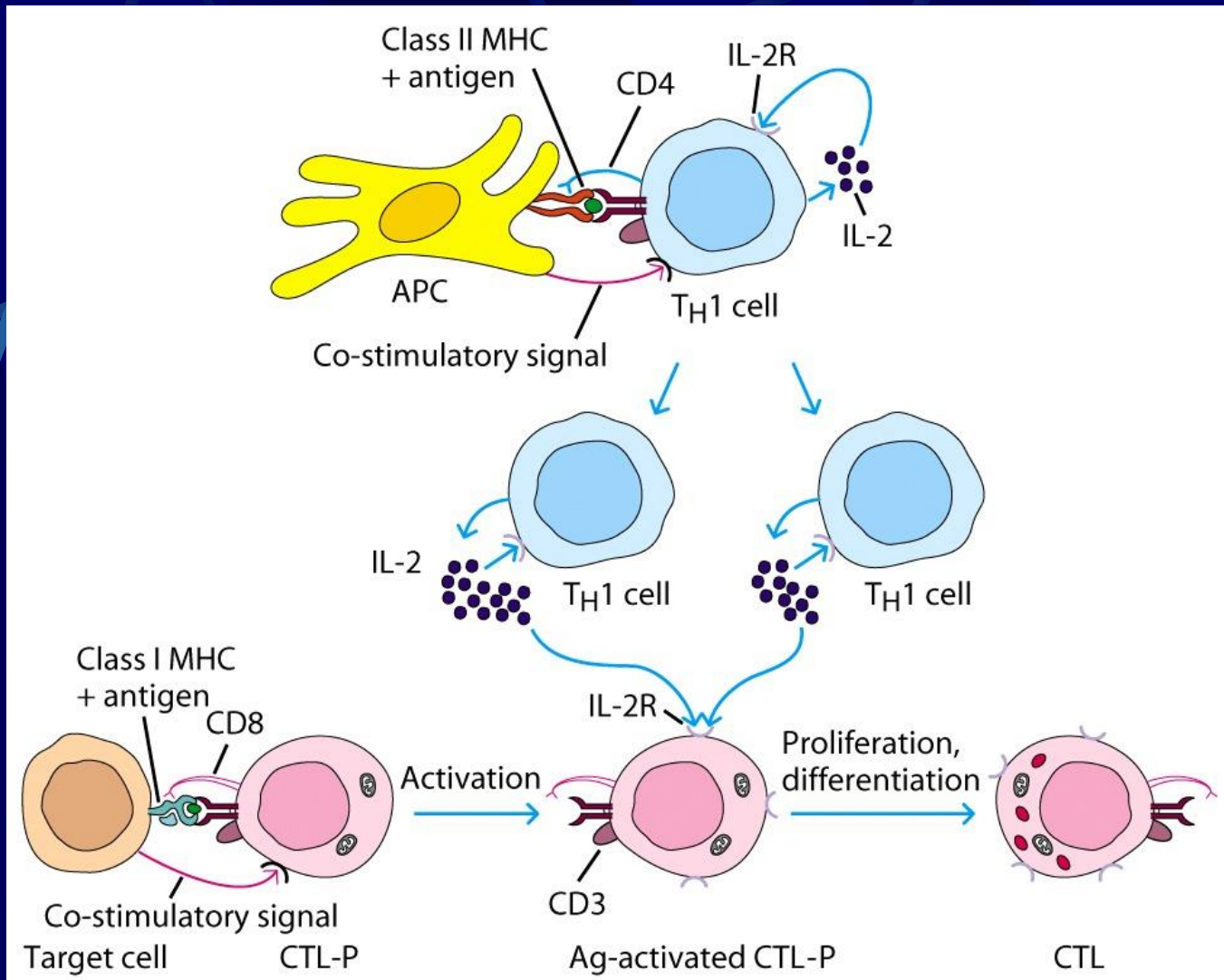




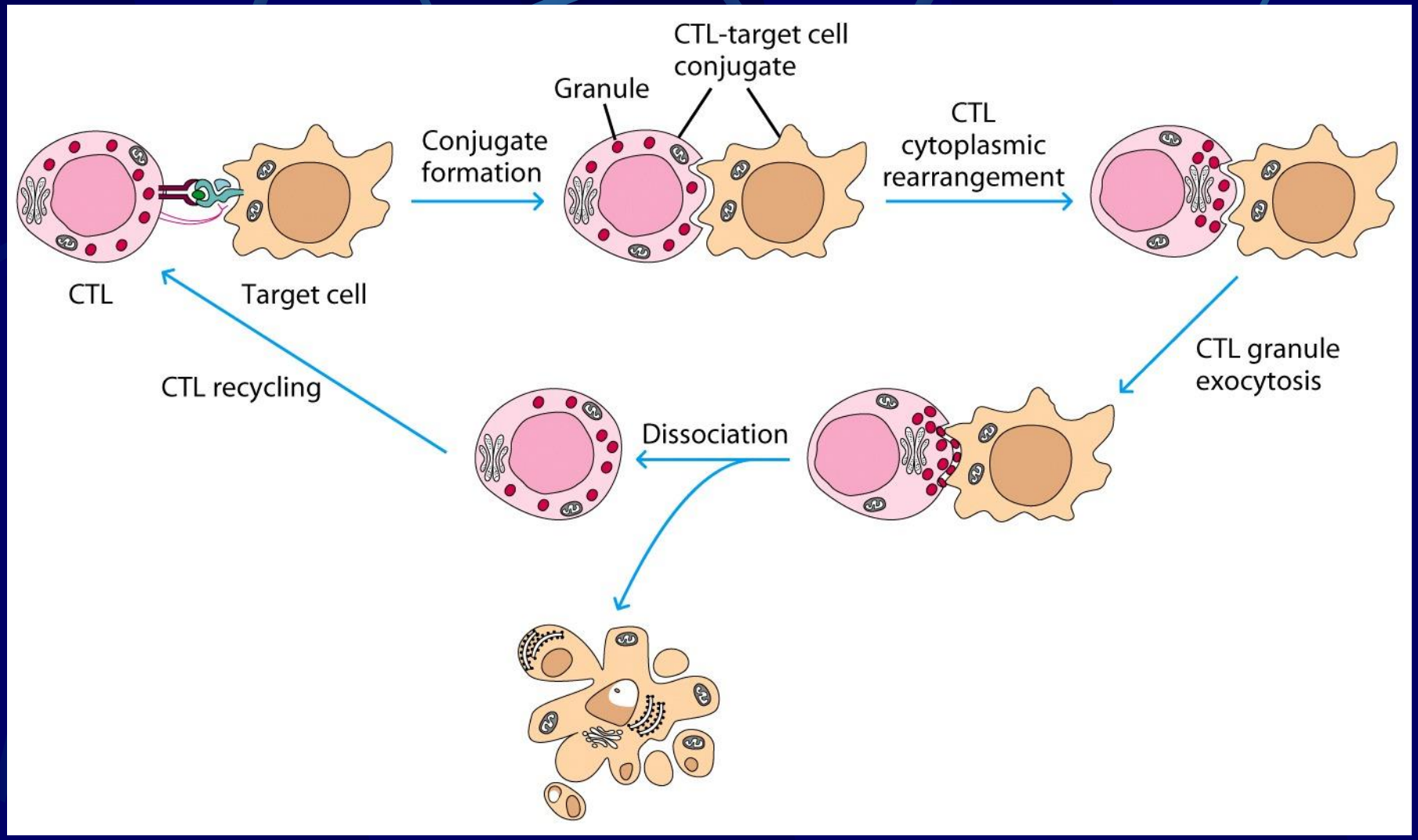
Recognition of target cells by Tc cells and NK cells

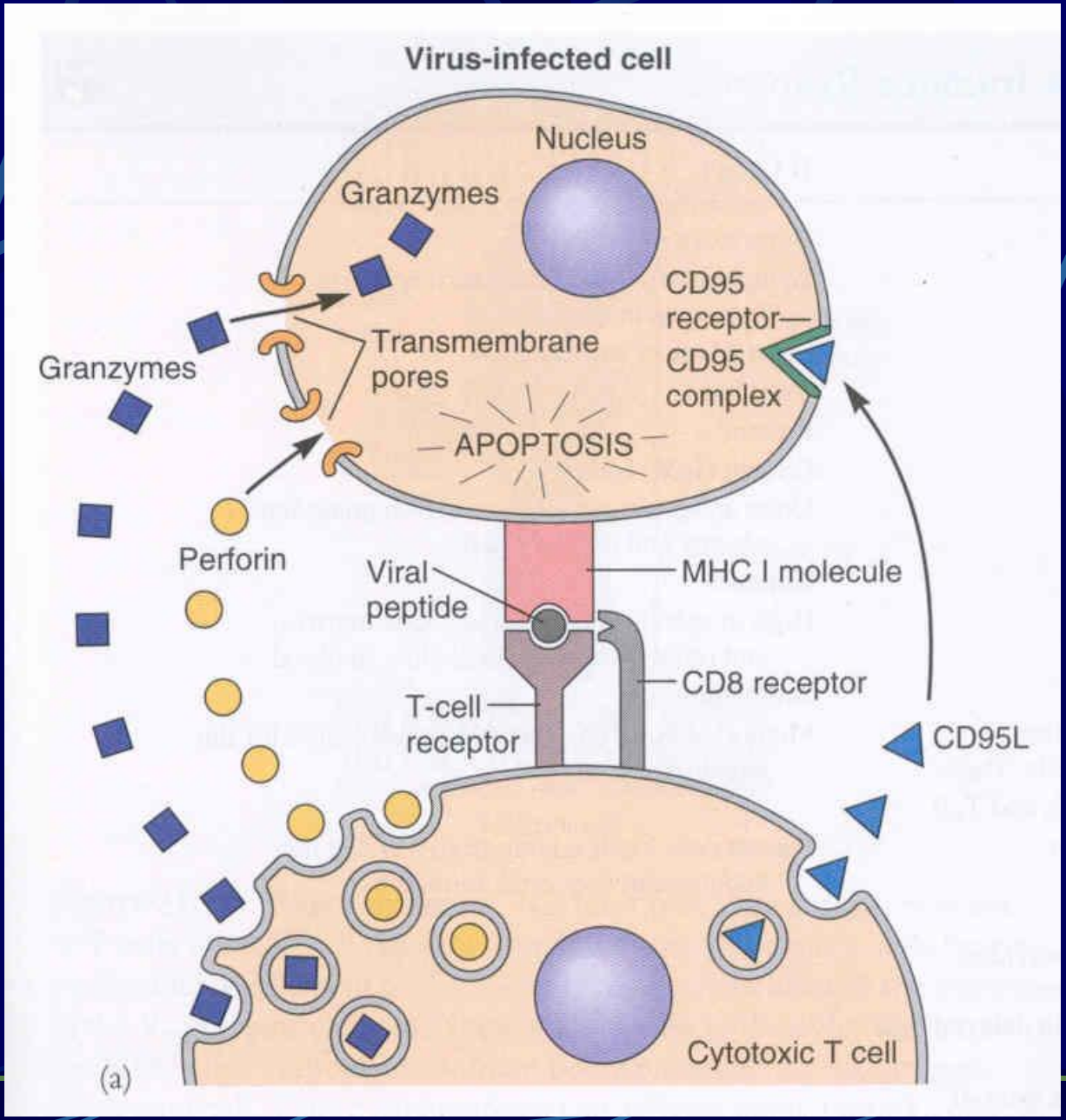


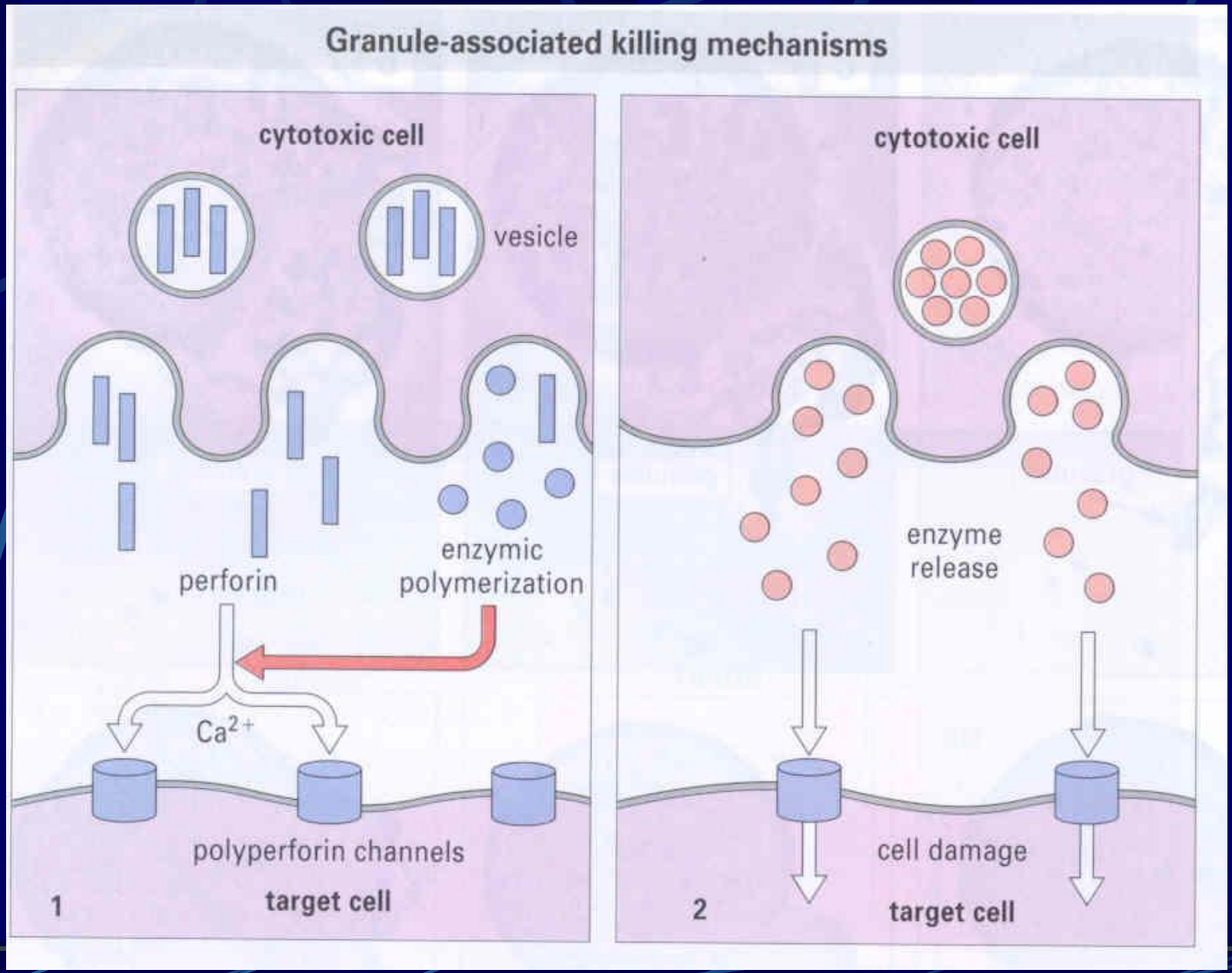
- Celulas Tumorais
- Eucariotas patogénicos
- Cel Infectadas
- Cel. Non-self
- Rejeição de enxertos

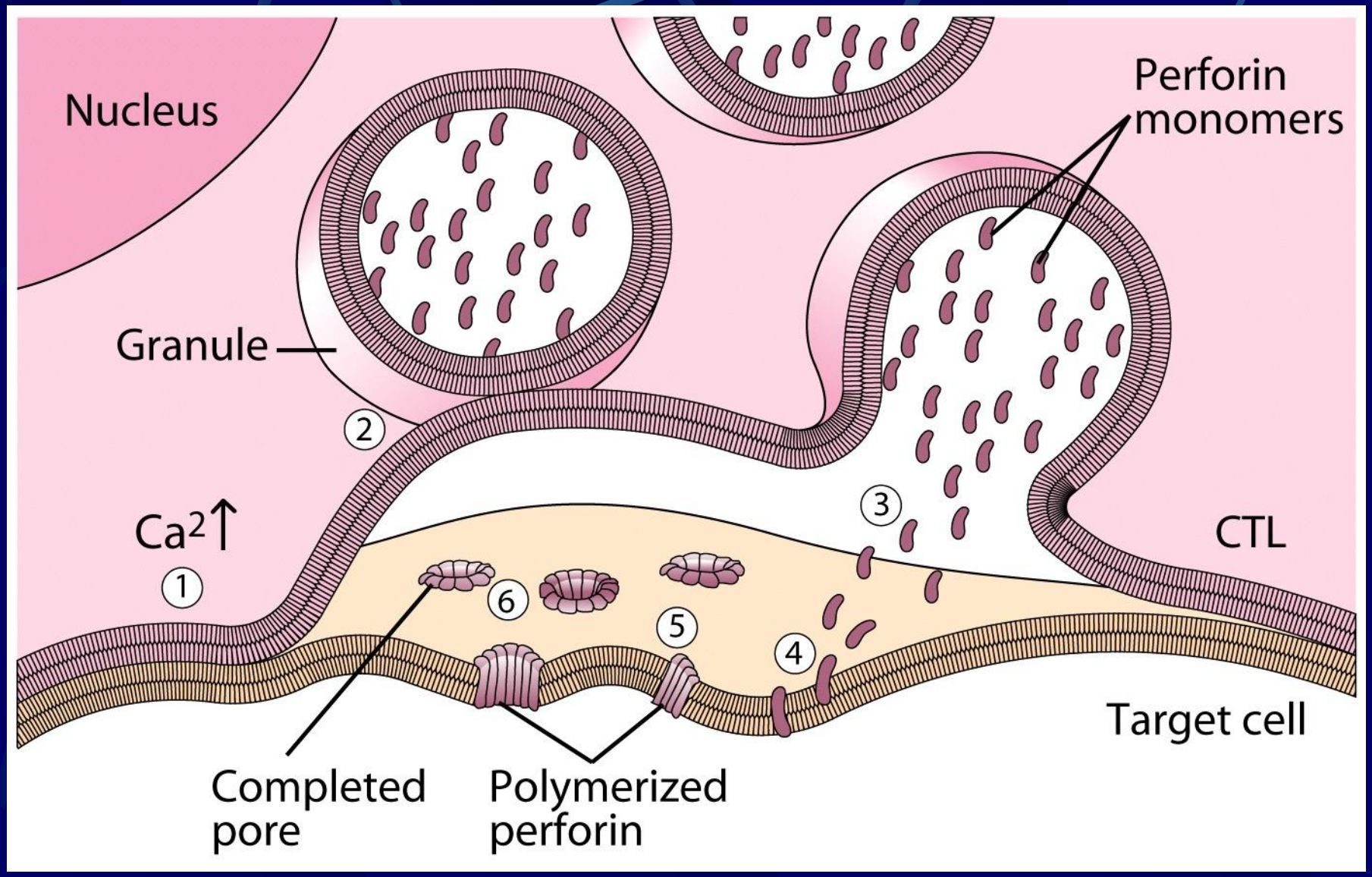


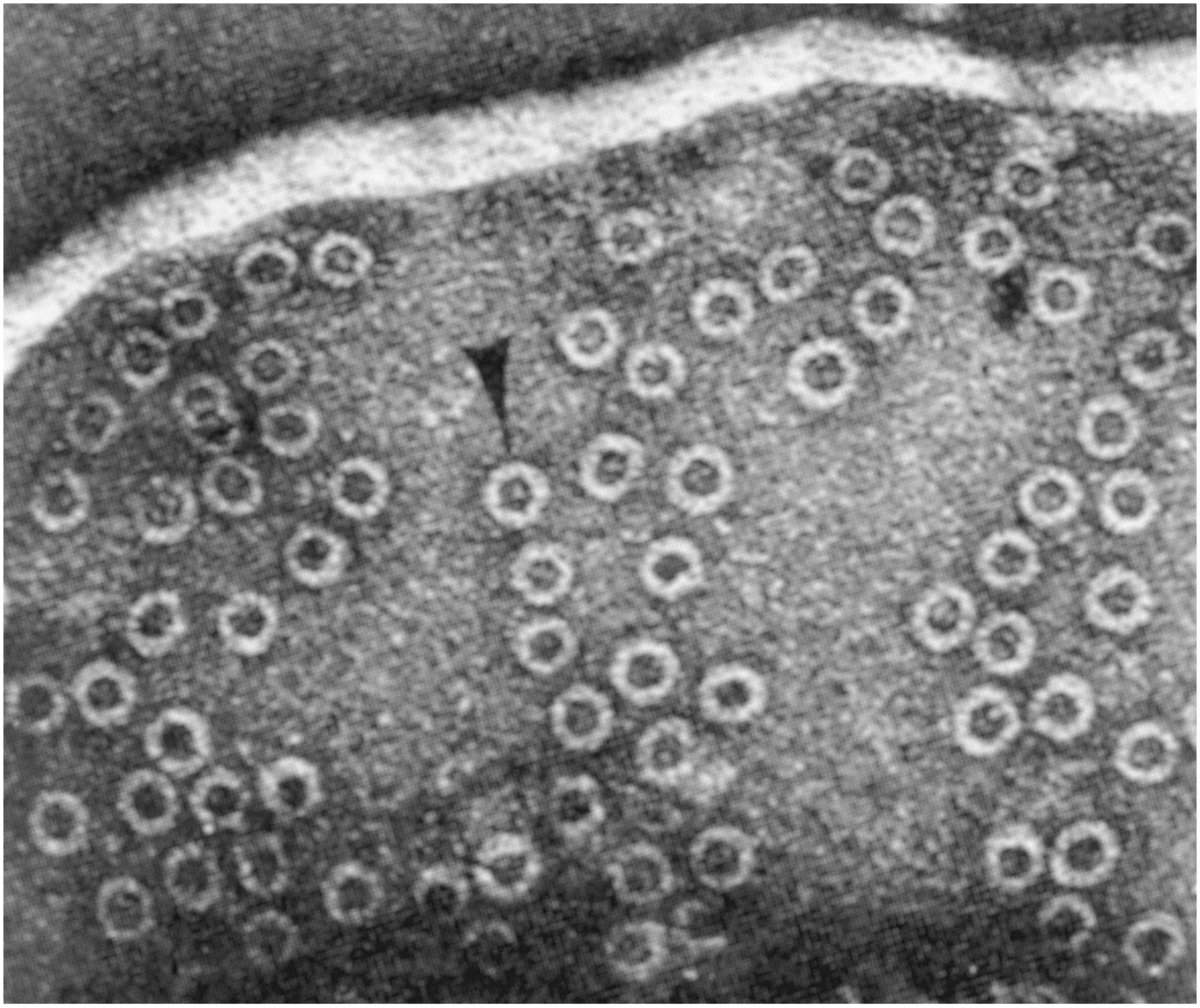
IL-2R expression	–	+	+
IL-2 expression	–	±	±
Proliferation	–	–	+
Effector cytotoxic function	–	–	+

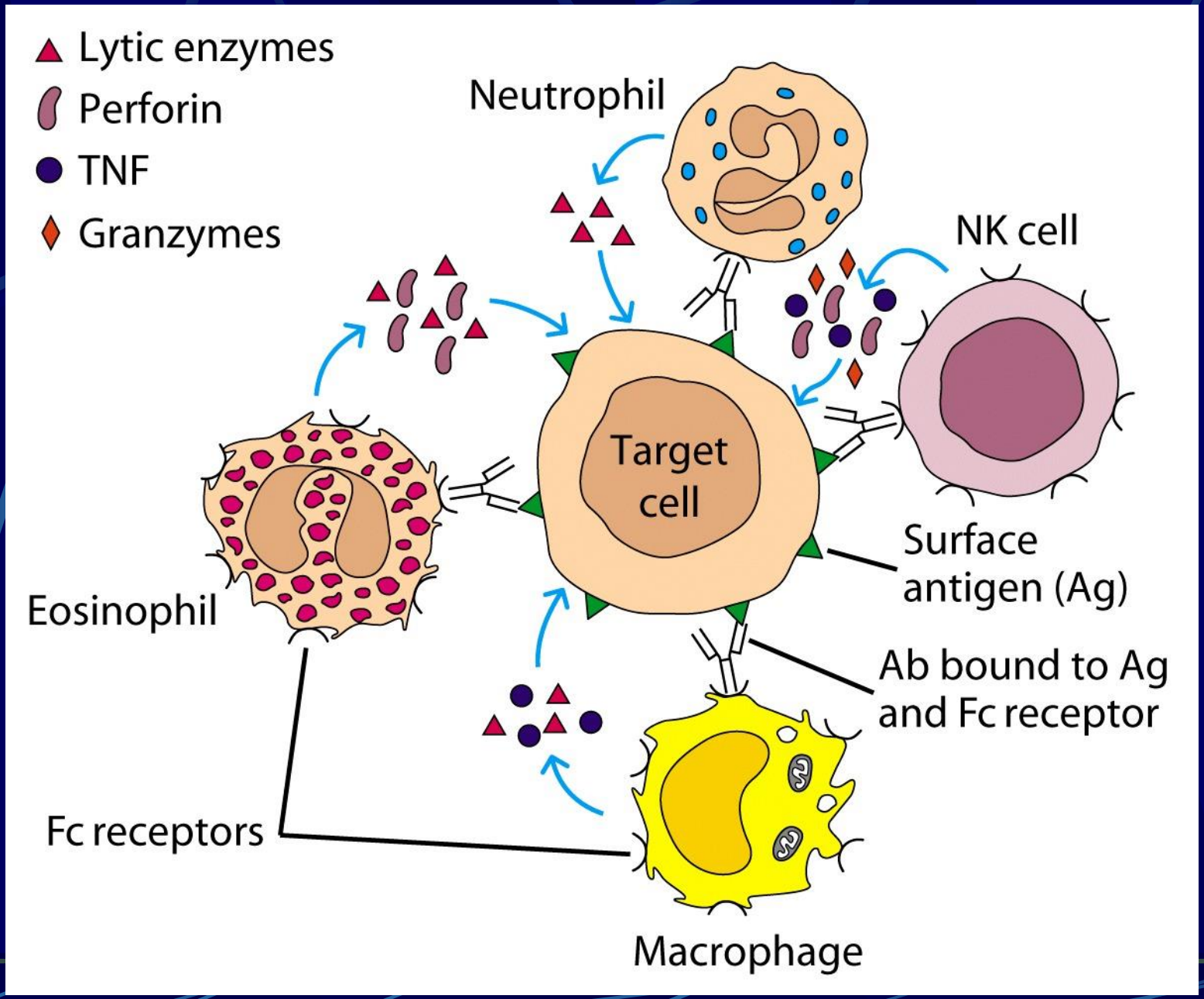

CTL-target cell conjugate
Granule
Conjugate formation
CTL cytoplasmic rearrangement
CTL
Target cell
CTL granule exocytosis
CTL recycling
Dissociation


Virus-infected cell
Nucleus
Granzymes
CD95 receptor
Granzymes
Transmembrane pores
CD95 complex
APOPTOSIS
Perforin
Viral peptide
MHC I molecule
CD8 receptor
T-cell receptor
CD95L
Cytotoxic T cell
(a)


Granule-associated killing mechanisms
cytotoxic cell
vesicle
perforin
enzymic polymerization
Ca^{2+}
polyperforin channels
1
target cell
cytotoxic cell
enzyme release
cell damage
2
target cell

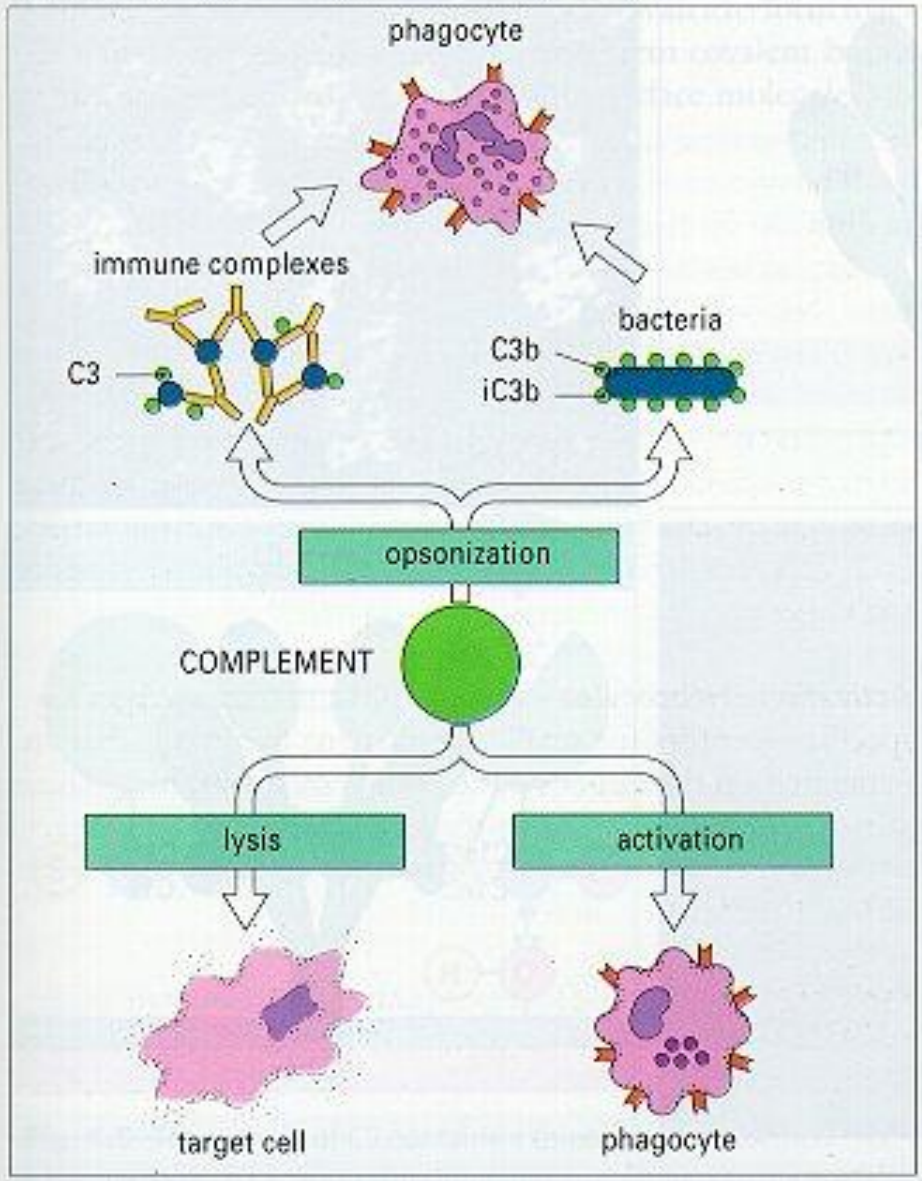

Nucleus
Perforin monomers
Granule
2
$Ca^{2}\uparrow$
1
3
CTL
6
5
4
Target cell
Completed pore
Polymerized perforin



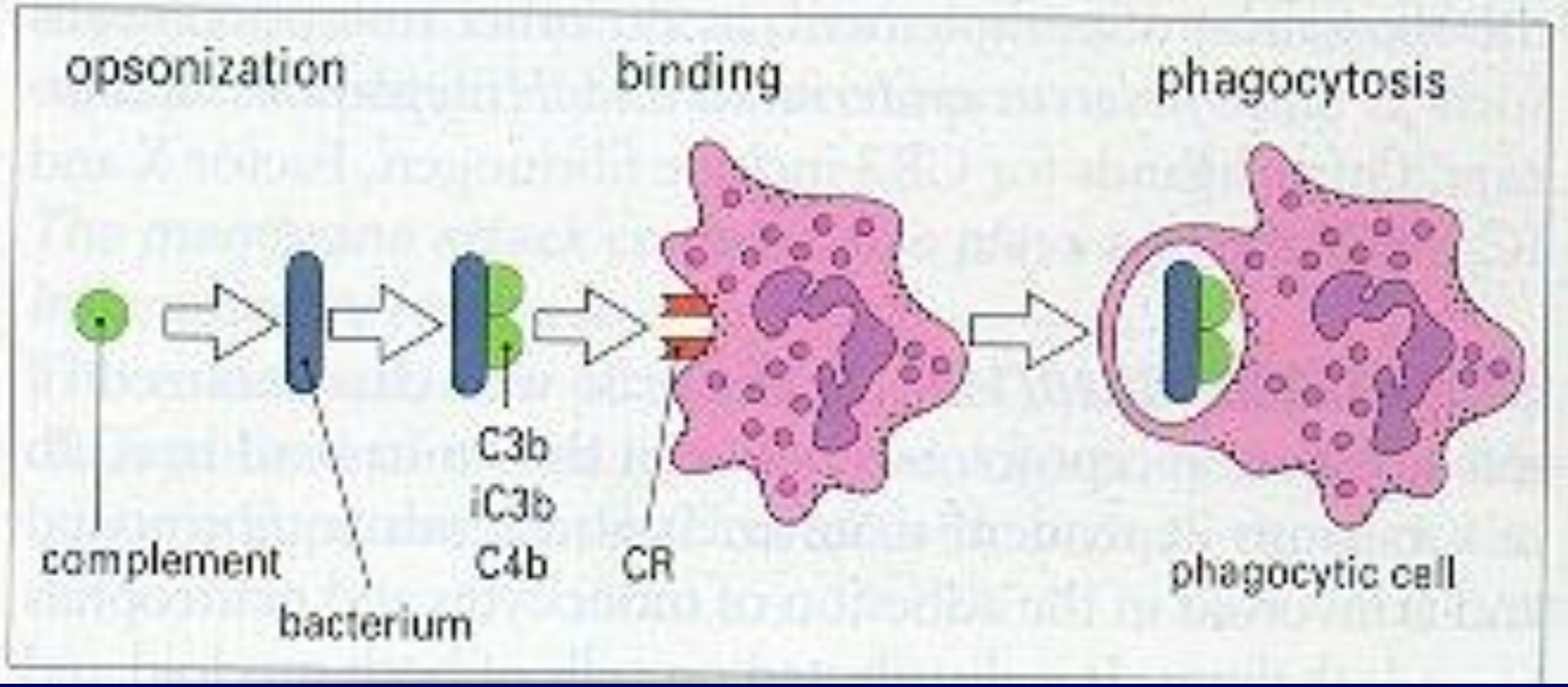

Lytic enzymes
Perforin
TNF
Granzymes
Neutrophil
NK cell
Target cell
Surface antigen (Ag)
Eosinophil
Ab bound to Ag and Fc receptor
Fc receptors
Macrophage

O Sistema Complemento

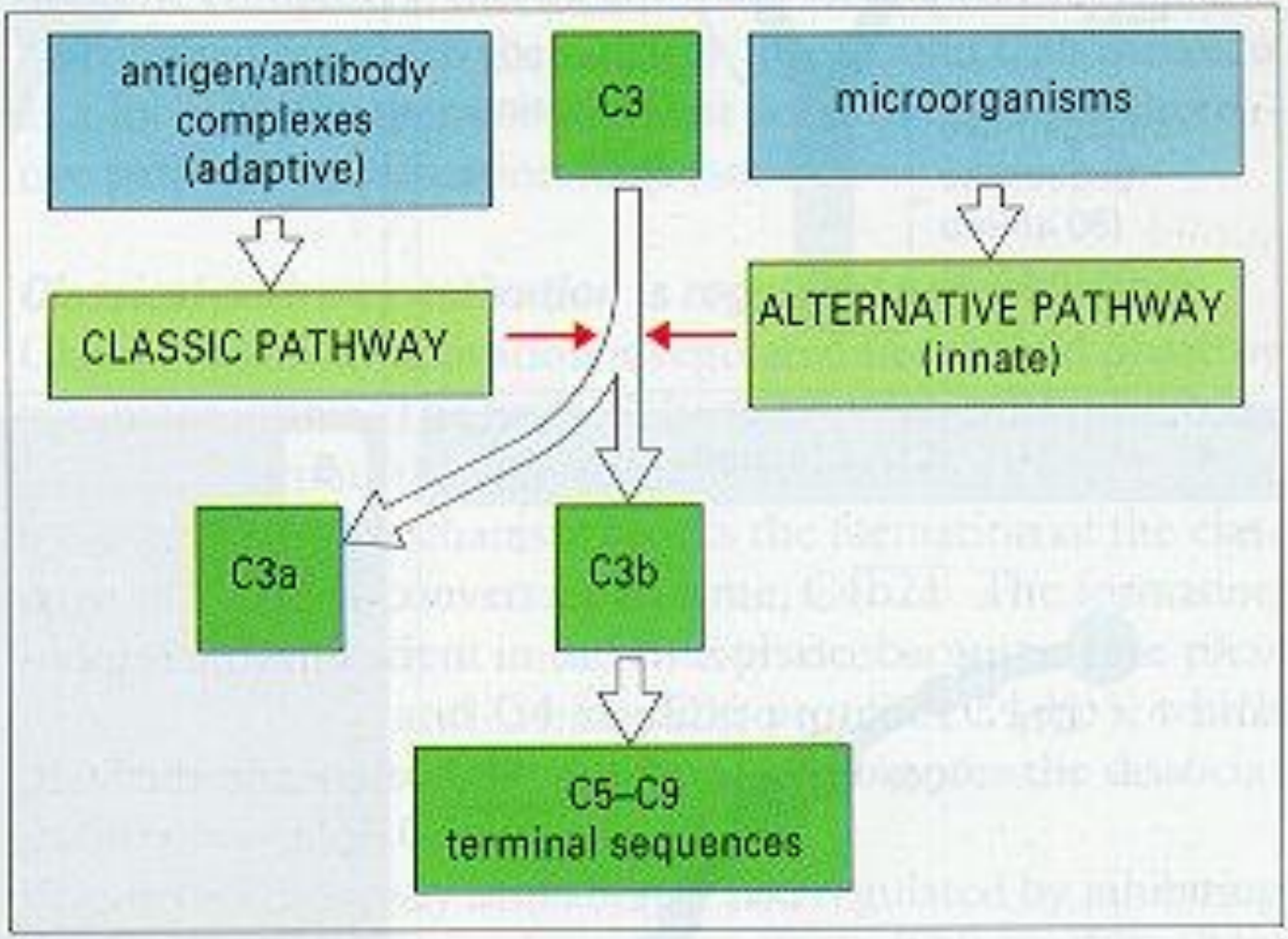
Three major biological activities of the complement system in inflammation



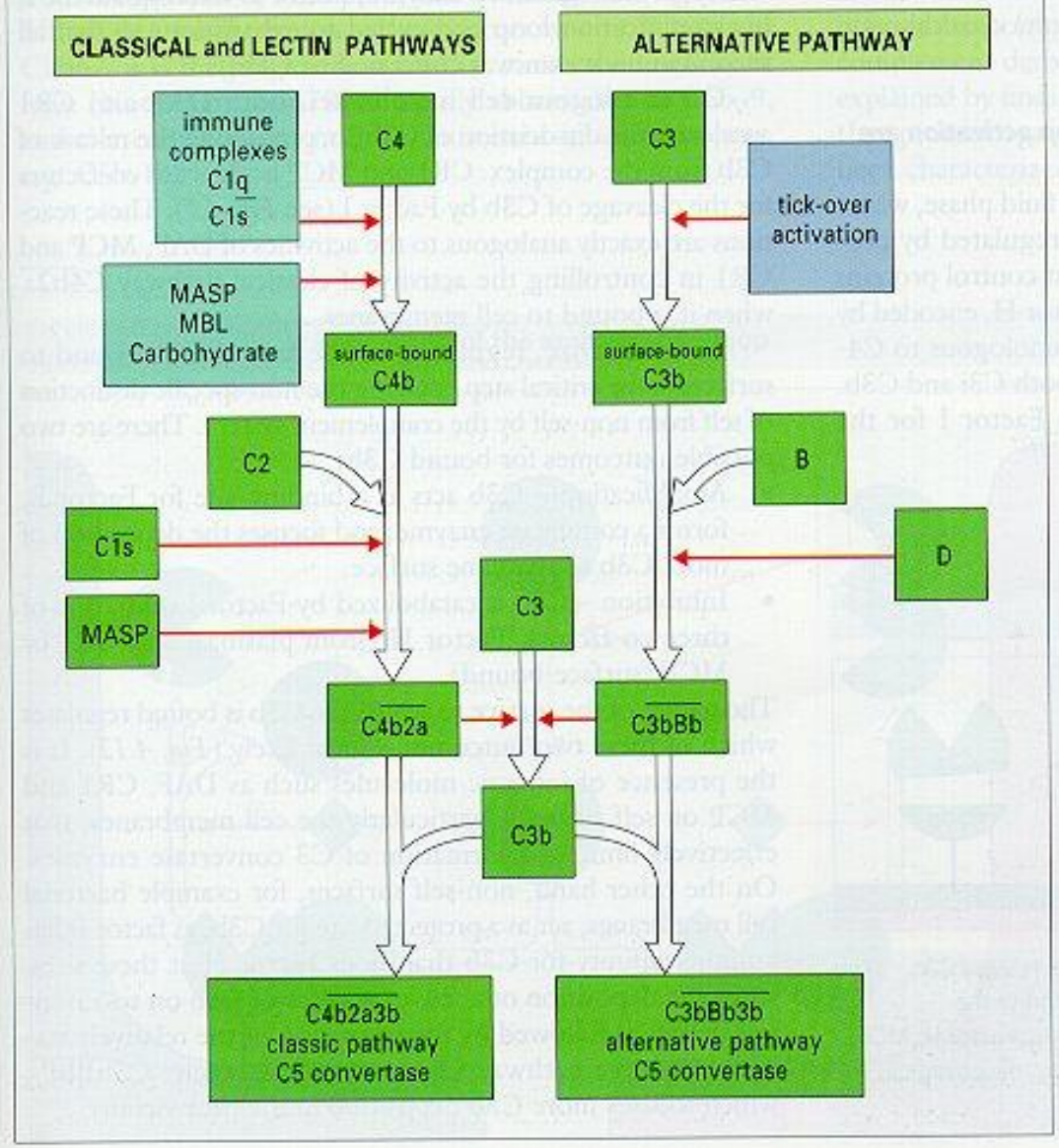
Opsonization and phagocytosis



Comparison of the classical and alternative complement pathways



Analogous action of the classical and lectin and alternative pathways



Complement functions

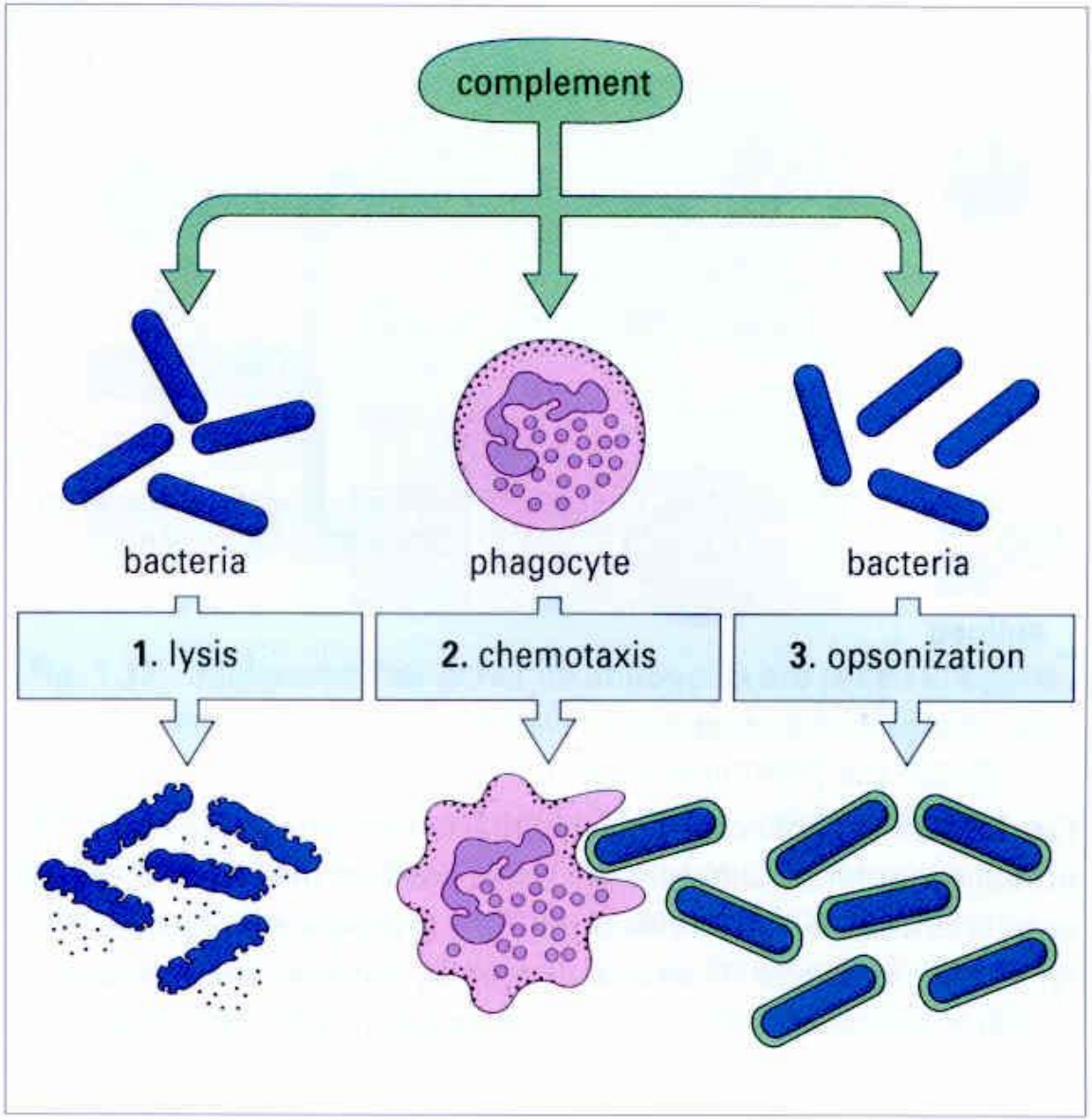


Fig. 1.7 (1) The complement system has an intrinsic ability to

Interferons (IFNs)

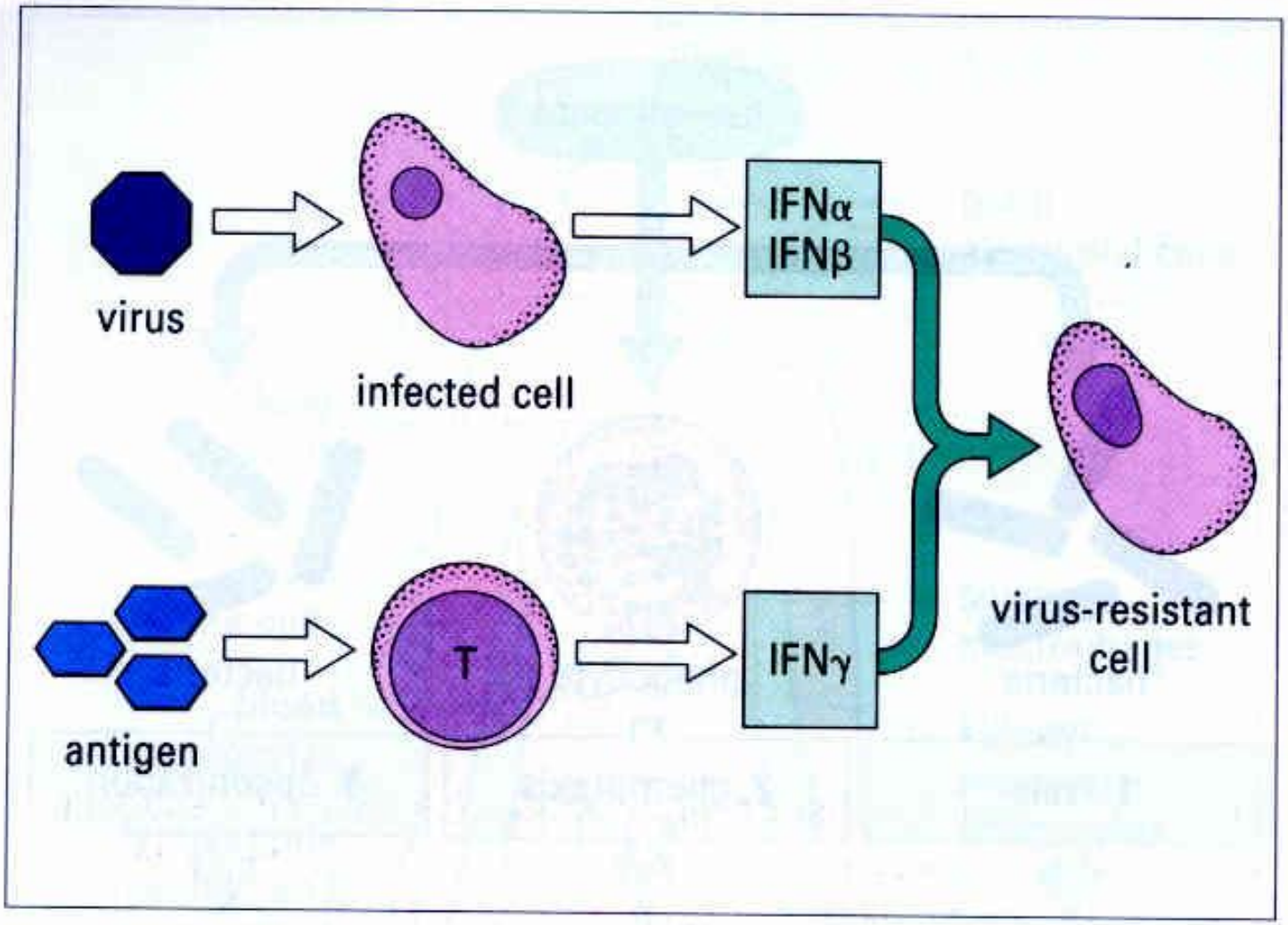


Fig. 1.8 When host cells become infected by virus, they may

Principle of vaccination

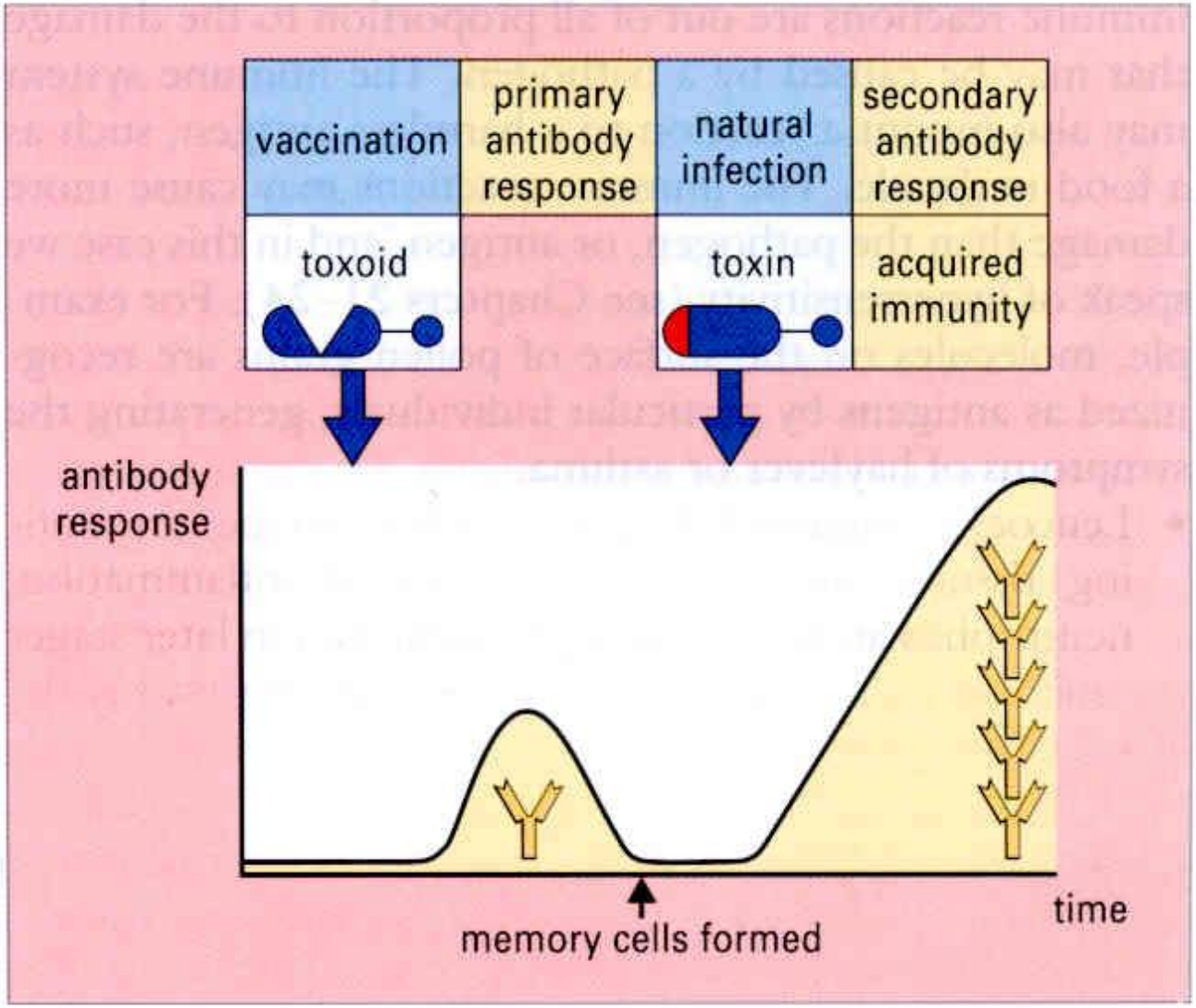
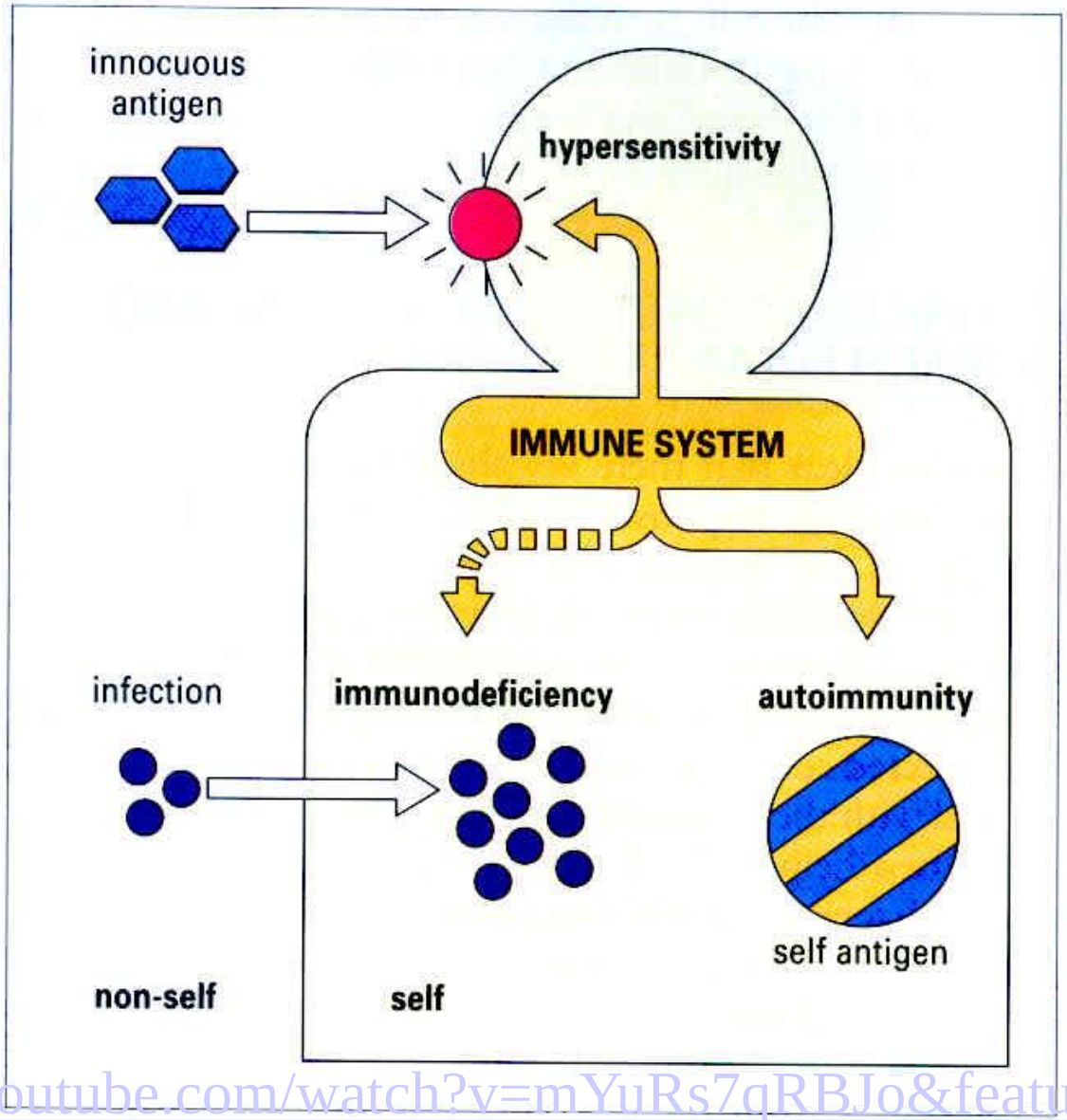


Fig. 1.19 The principle of vaccination is illustrated by

Failure of the immune system



http://www.youtube.com/watch?v=mYuRs7qRBJo&feature=related

Fig. 1.20 There are three principal ways in which the immune