II Curso Educativo
Sociedad Peruana de Hematología

Manejo de las Urgencias en el Niño con trastornos de la Coagulación

Erick Mattos Villena

APPENDIX 52 Reference Ranges for Global Coagulation Assays in Children and Adolescents

Assay	Method	1-6 Months N = 29† (14M/15F)	7-12 Months N = 25‡ (19M/6F)	1-5 Years N = 57 (35M/22F)	6-10 Years N = 56 (29M/27F)	11-18 Years N = 50§ (24M/26F)	> 19 Years N = 52 (27F/25M)
PT (sec)	Thromborel S	12.5/12.8*‖	12.2/12.4*‖	12.1/12.2*‖	12.6/12.6*‖	12.8/12.6*‖	11.7/11.8*
	BCS	11.2-15.5	11.4-13.5	11.2-13.4	11.5-14.0	11.4-13.8	10.7-12.9
	Innovin	10.7/10.7 *	10.6/10.6*	10.6/10.6 *	10.9/10.9*‖	10.8/10.9*‖	10.5/10.6*
	CA-1500	10.0-12.7	9.5-12.8	10.0-11.4	10.2-11.6	10.1-11.9	9.7-11.4
PT (%)	Thromborel S	92/89*‖	95/93*‖	97/96*‖	91/91*‖	89/91*‖	101/101*
	BCS	64-108	81-105	81-108	76-104	78-105	88-116
	Innovin	103/104*	106/106*	106/106*	100/100*‖	101/100*	108/108*
	CA-1500	72-122	71-128	89-121	86-116	81-118	89-129
APTT (sec)	Pathromtin SL	41/42*‖	39/39*‖	36/37*‖	37/37*‖	35/36*‖	34/34*
	BCS	33-56	32-49	31-44	31-44	30-43	27-40
	Actin FS	29/29*‖	28/28*‖	27/27*‖	28/28*‖	27/27*‖	25/25*
	CA-1500	21-33	24-33	24-30	25-32	25-30	22-28
TT (sec)	Thromboclotin	19.2/20.0‖	18.0/18.0	17.0/17.2	17.5/17.4	17.4/17.8	17.4/17.5
	CA-1500	16.2-24.9	15.4-21.1	15.3-19.7	14.5-19.9	15.2-24.0	15.5-20.5
BT (sec)	Batroxobin	21.0/21.4‖	20.2/20.5	20.2/20.3	20.2/20.2	19.8/19.9	20.1/20.1
	Reagent CA-1500	19.7-25.0	19.1-24.0	18.8-22.7	19.1-21.5	18.8-21.5	18.7-22.4

Grimminck B, Geerts J, et al: Age dependency of coagulation parameters during childhood and puberty. J Thromb Haemost *10:2254–2263, 2012.*

APTT, Activated partial thromboplastin time; *BCS,* Behring Coagulation System; *BT,* batroxobin time; *CA-1500,* Sysmex CA-1500 Analyzer; *F,* female; *M,* male; *PT,* prothrombin time; *sec,* seconds; *TT,* thrombin time.

*Indicates statistically significant difference between devices for the student's t-test.

†n = 28 for APTT with the BCS.

‡n = 24 for PT, TT, and BT with the CA-1500.

§n = 49 for batroxobin time (one sample was excluded because of an extremely outlying result of 13.3 seconds). Data are presented as median/mean with t-test results of between methods and age comparisons in the first row, whereas the second row shows the boundaries including 90% of the central population.

‖Indicates statistically significant difference between child groups and adults for the student's t-test.

APPENDIX 60 Coagulation Screening Tests and Factor Levels in Fetuses and Full-Term Newborns

	FETUSES (WEEKS' GESTATION)				
Parameter	**19-23 (N = 20)**	**24-29 (N = 22)**	**30-38 (N = 22)**	**Newborns (N = 60)**	**Adults (N = 40)**
PT (s)	32.5 (19-45)	32.3 (19-44)†	22.6 (16-30)*	16.7 (12.0-23.5)*	13.5 (11.4-14.0)
PT (INR)	6.4 (1.7-11.1)	6.2 (2.1-10.6)†	3.0 (1.5-5.0)*	1.7 (0.9-2.7)*	1.1 (0.8-1.2)
APTT (s)	168.6 (83-250)	154.0 (87-210)†	104.8 (76-128)†	44.3 (35-52)*	33.0 (25-39)
TCT (s)	34.2 (24-44)*	26.2 (24-28)*	21.4 (17.0-23.3)	20.4 (15.2-25.0)†	14.0 (12-16)
Factor					
I (g/L Von Clauss)	0.85 (0.57-1.50)	1.12 (0.65-1.65)	1.35 (1.25-1.65)	1.68 (0.95-2.45)†	3.0 (12-16)
I Ag (g/L)	1.08 (0.75-1.50)	1.93 (1.56-2.40)	1.94 (1.30-2.40)	2.65 (1.68-3.60)†	3.5 (2.50-5.20)
IIc(%)	16.9 (10-24)	19.9 (11-30)*	27.9 (15-50)†	43.5 (27-64)†	98.7 (70-125)
VIIc (%)	27.4 (17-37)	33.8 (18-48)*	45.9 (31-62)	52.5 (28-78)†	101.3 (68-130)
IXc (%)	10.1 (6-14)	9.9 (5-15)	12.3 (5-24)†	31.8 (15-50)†	104.8 (70-142)
Xc (%)	20.5 (14-29)	24.9 (16-35)	28.0 (16-36)†	39.6 (21-65)†	99.2 (75-125)
Vc (%)	32.1 (21-44)	36.8 (25-50)	48.9 (23-70)†	89.9 (50-140)	99.8 (65-140)
VIIIc (%)	34.5 (18-50)	35.5 (20-52)	50.1 (27-78)†	94.3 (38-150)	101.8 (55-170)
XIc (%)	13.2 (8-19)	12.1 (6-22)	14.8 (6-26)†	37.2 (13-62)*	100.2 (70-135)
XIIc (%)	14.9 (6-25)	22.7 (6-40)	25.8 (11-50)†	69.8 (25-105)†	101.4 (65-144)
PK (%)	12.8 (8-19)	15.4 (8-26)	18.1 (8-28)†	35.4 (21-53)†	99.8 (65-135)
HMWK (%)	15.4 (10-22)	19.3 (10-26)	23.6 (12-34)†	38.9 (28-53)†	98.8 (68-135)

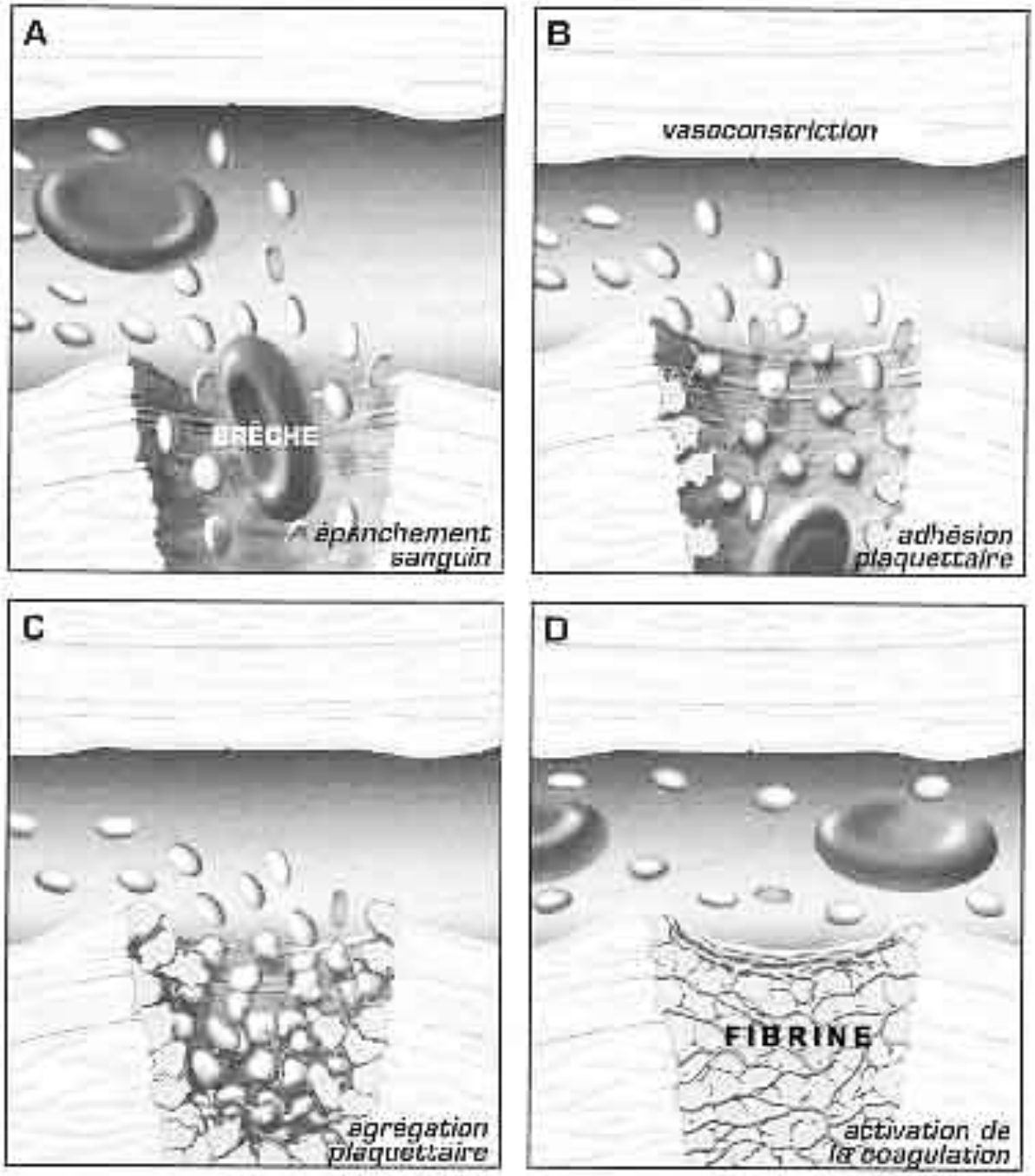
From Reverdiau Moalic P, Delahouse B, Body G, et al: Evaluation of blood coagulation activators and inhibitors in the healthy human fetus. Blood *88:900, 1996.*

Ag, Antigenic value; *c*, coagulant activity.

Values are the mean, followed in parentheses by the lower and upper boundaries including 95% of the population.

*$P < .05$

†$P < .01$



Introduction à l'étude de l'hémostase et de la thrombose - B. Boneu, J-P. Cazenave - 1997

Recordar:

- H Primaria: **células endoteliales** y **plaquetas**.
- H Secundaria: **16 factores de la coagulación** que están en la circulación sanguínea.
  - Casi todos son sintetizados en el **hígado**, y algunos en las células endoteliales, en las plaquetas y en los monocitos.
    - 8 son proenzimas (cimógenos)
    - 6 son cofactores
    - 6 son glucoproteínas que actúan como anticoagulantes

Rodak; Hematología Fundamentos y Aplicaciones Clínicas, 2da Ed pág 618

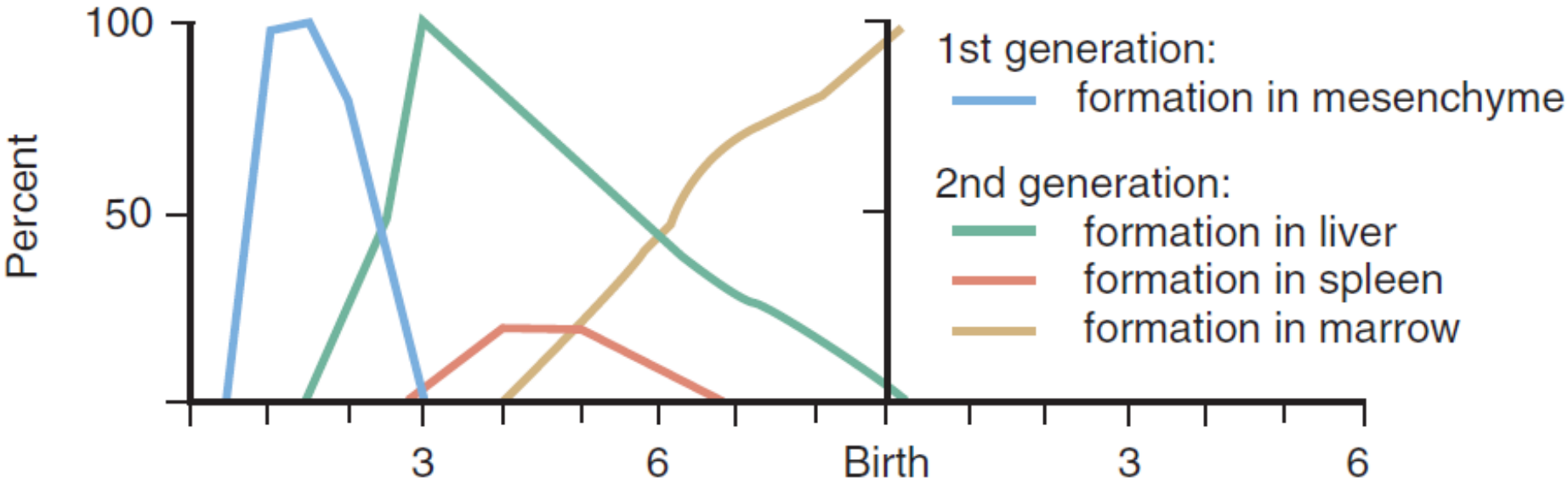
TABLE 26-1 General Properties of Blood Coagulation Proteins

Protein	Molecular Weight	PLASMA CONCENTRATION nmol/L	PLASMA CONCENTRATION µg/mL	Plasma $t_{1/2}$ (Days)	Chromosome* (Gene Location)	Functional Classification
INTRINSIC PATHWAY PROTEINS						
Factor XII	80,000	500 (265)	40 (21)	2-3	Chr 5 (176 Mb)	Zymogen
Factor XI	160,000	30 (11)	4.8 (2)	2.5-3.3	Chr 4 (187 Mb)	Zymogen
Prekallikrein	85/88,000	486 (180)	42 (16)		Chr 4 (187 Mb)	Zymogen
HMW kininogen	120,000	670 (362)	80 (43)		Chr 3 (188 Mb)	Cofactor
LMW kininogen	66,000	1300	90		Chr 3 (188 Mb)	Cofactor
EXTRINSIC PATHWAY PROTEINS						
Prothrombin (factor II)	72,000	1400 (672)	100 (48)	2.5	Chr 11 (47 Mb)	VKD zymogen
α-Thrombin	37,000					Serine protease
Factor VII	50,000	10 (7)	0.5 (0.3)	0.25	Chr 13 (113 Mb)	VKD zymogen
Factor IX	55,000	90 (48)	5 (3)	1	X Chr (138 Mb)	VKD zymogen
Factor X	59,000	170 (68)	10 (4)	1. 5	Chr 13 (113 Mb)	VKD zymogen
Protein C	62,000	65 (23)	4 (1)	.33	Chr 2 (128 Mb)	VKD zymogen
Protein S	69,000	300 (108)	20 (7)	1.75	Chr 3 (95 Mb)	VKD protein
Protein Z	62,000	47	3	2.5	Chr 13 (113 Mb)	VKD protein
Factor V	330,000	20 (14)	6.6 (5)	0.5	1q21-q25	Procofactor
Factor VIII	285,000	0.7 (0.7)	0.2 (0.2)	0.3-0.5	X Chr (154 Mb)	Procofactor
VWF	255,000 (monomer)	Varies	10		Chr 12 (6 Mb)	Platelet adhesion, factor VIII carrier
Tissue factor	44,000	—	—	—	Chr 1 (9 Mb)	Cell-associated cofactor
Thrombomodulin	100,000	—	—	—	Chr 20 (23 Mb)	Cofactor
Fibrinogen	340,000	7400 (8380)	2500 (2830)	3-5	Chr 4 (156 Mb)	Structural protein cell adhesion
Aα	66,500					
Bβ	52,000					
γ	46,500					
Factor XIII	320,000	94 (72)	30 (23)	9-10		Transglutaminase zymogen
A chain	83,200				Chr 6 (6 Mb)	
B chain	79,700				Chr 1 (195 Mb)	
Tissue factor pathway inhibitor	40,000	1-4	0.1	6.4×10^{-4}-1.4×10^{-3}	Chr 2 (188 Mb)	Kunitz inhibitor
Antithrombin	58,000	2400 (1510)	140 (88)	2.5-3	Chr 1 (172 Mb)	Serpin inhibitor
Heparin cofactor II	66,000	950 (408)	62 (26)	2.5	Chr 22 (19 Mb)	Serpin inhibitor
Protein C inhibitor	57,000	90	5	1	Chr 14 (94 Mb)	Serpin inhibitor

*Chromosome number. Numbers in parentheses are approximate positions in megabases (from human genome build 36.2 www.ncbi.nlm.nih.gov).
HMW, high molecular weight; LMW, low molecular weight; VKD, vitamin K dependent; VWF, von Willebrand factor.

Hígado, Plaquetas y Endotelio

Hígado



Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 2-Volume Set, 8e 2014

Desórdenes en las **Organelos**:
MYH9
Plaquetas Grises

Plaquetas

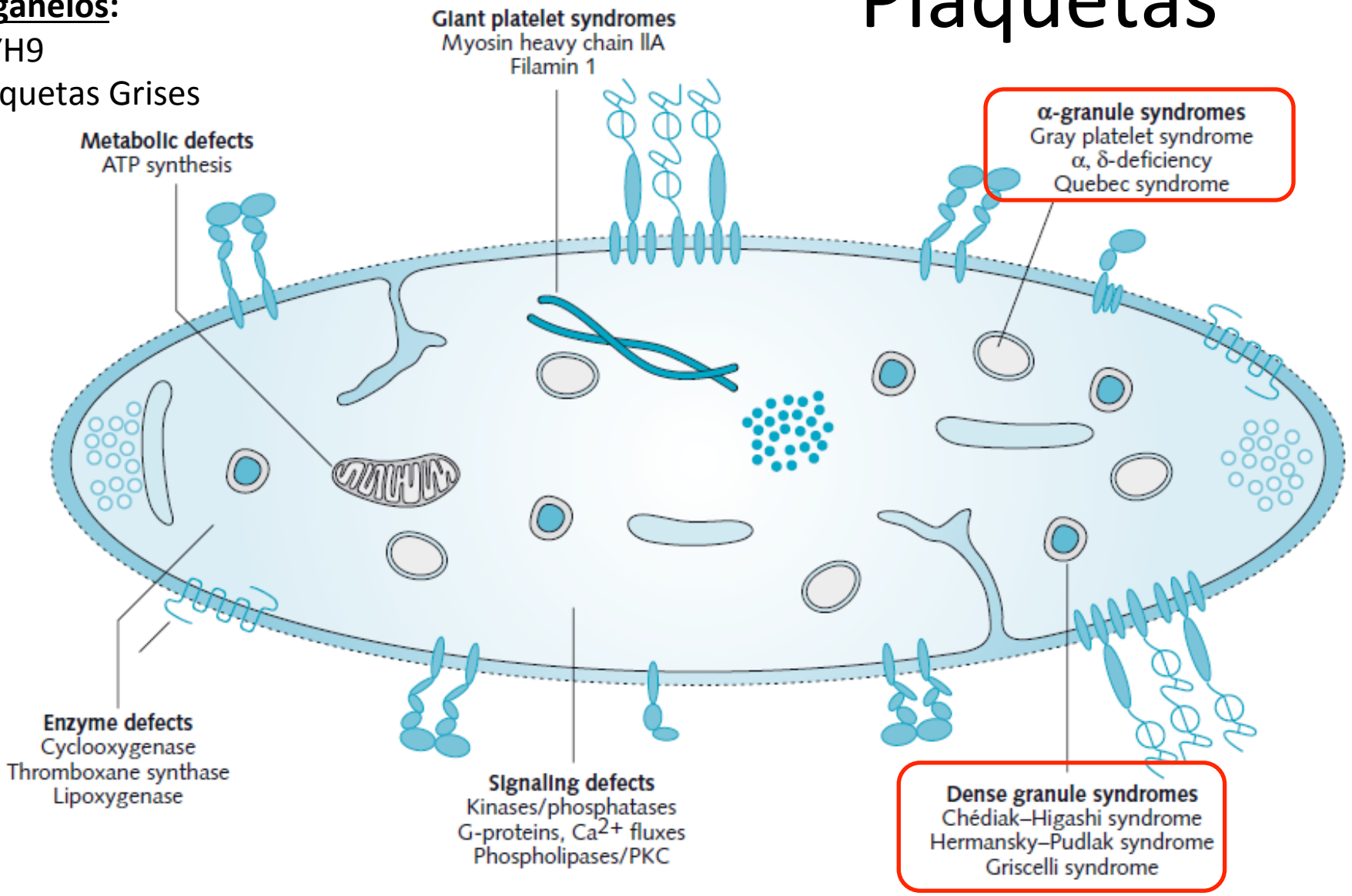
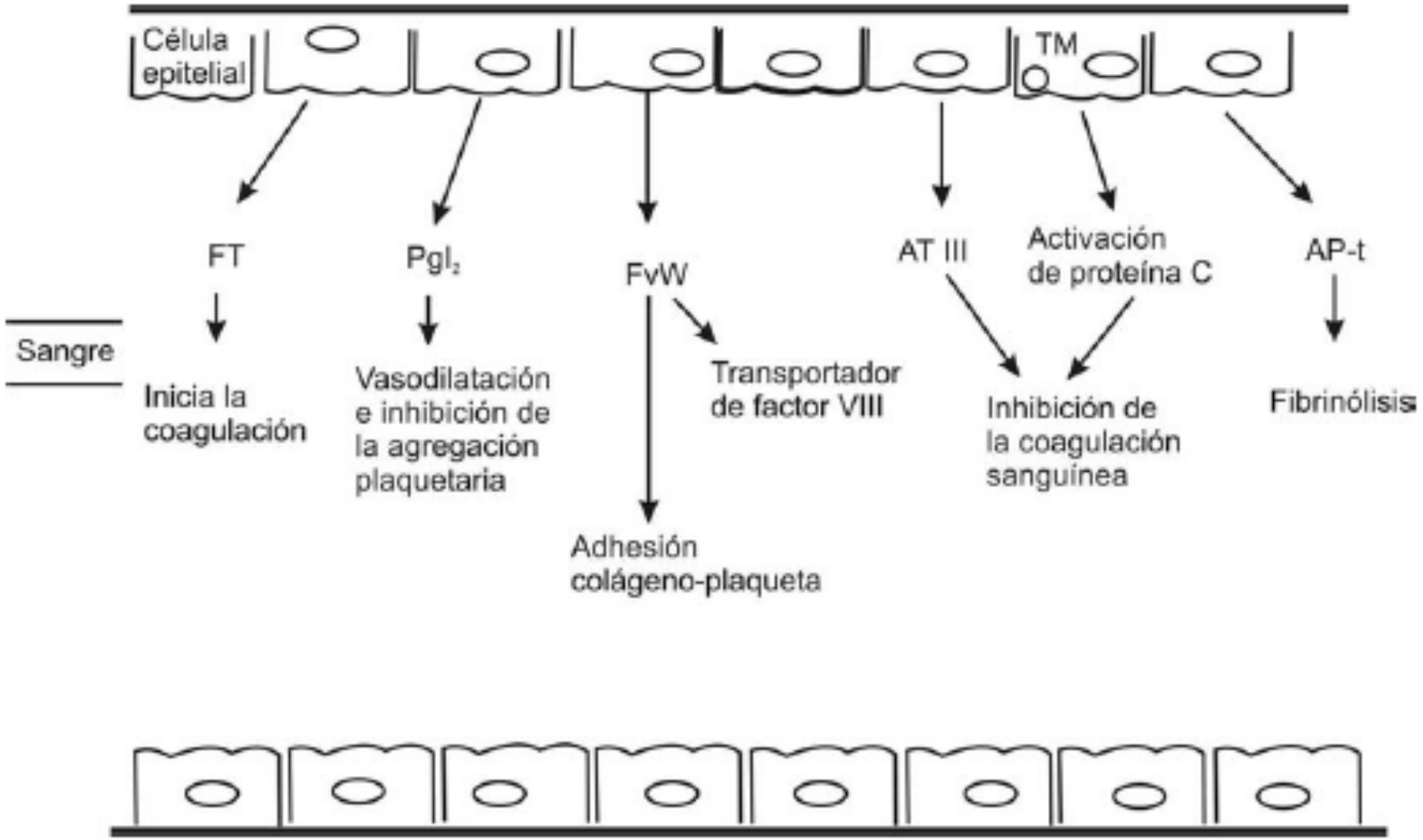
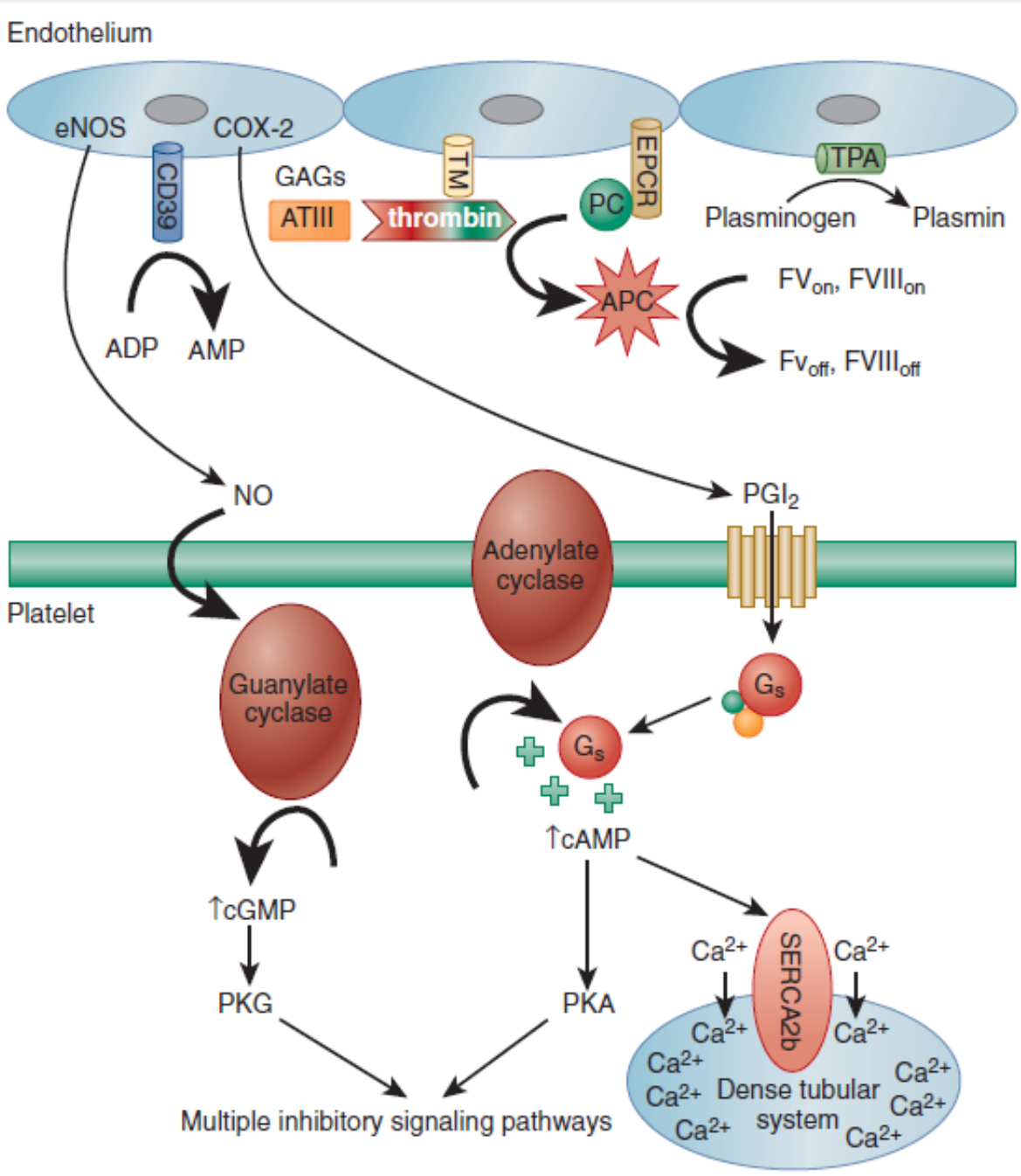


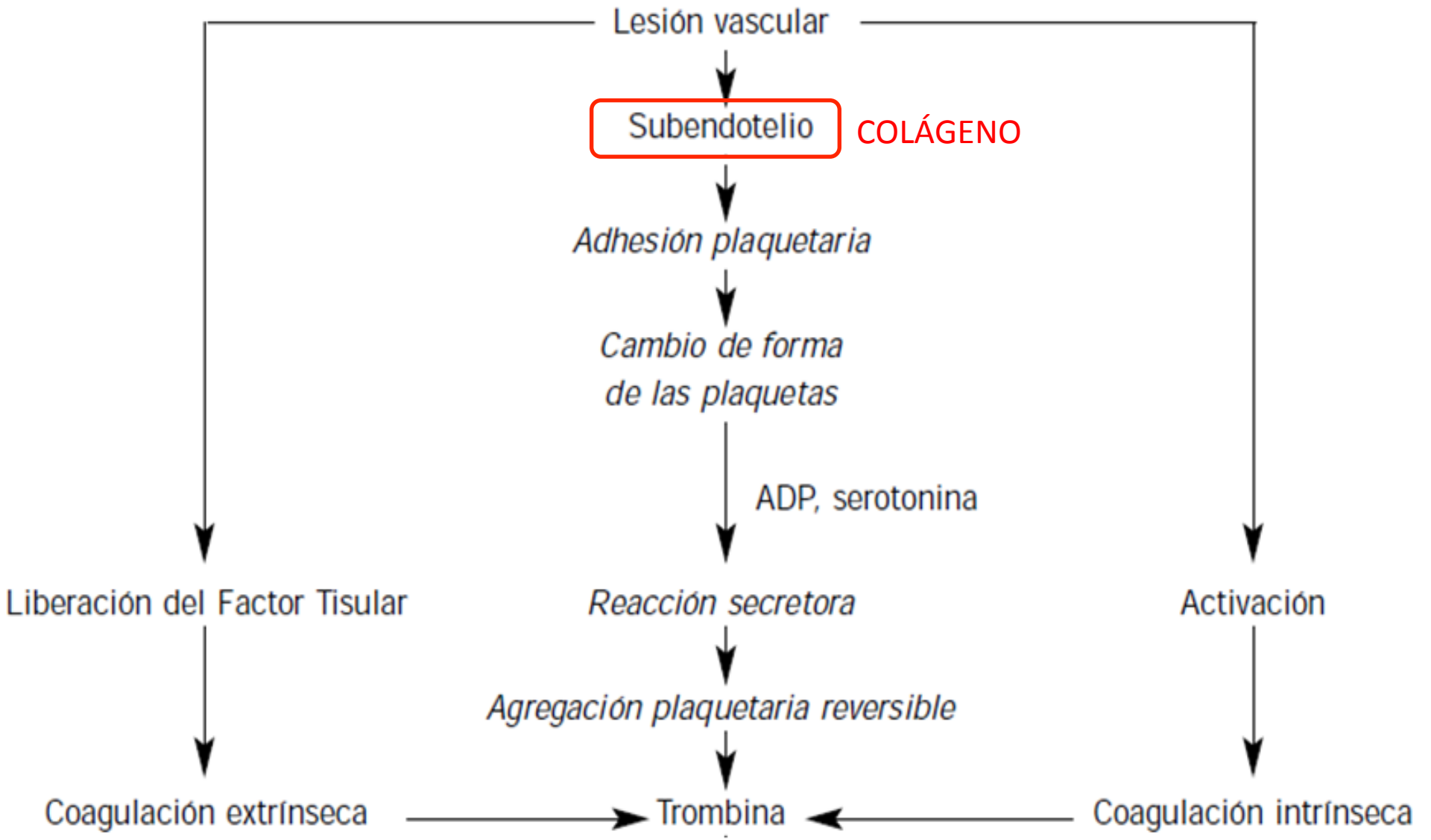
Fig. 20.2 Diagram of a resting platelet indicating the major internal organelles and other structures implicated in inherited bleeding disorders

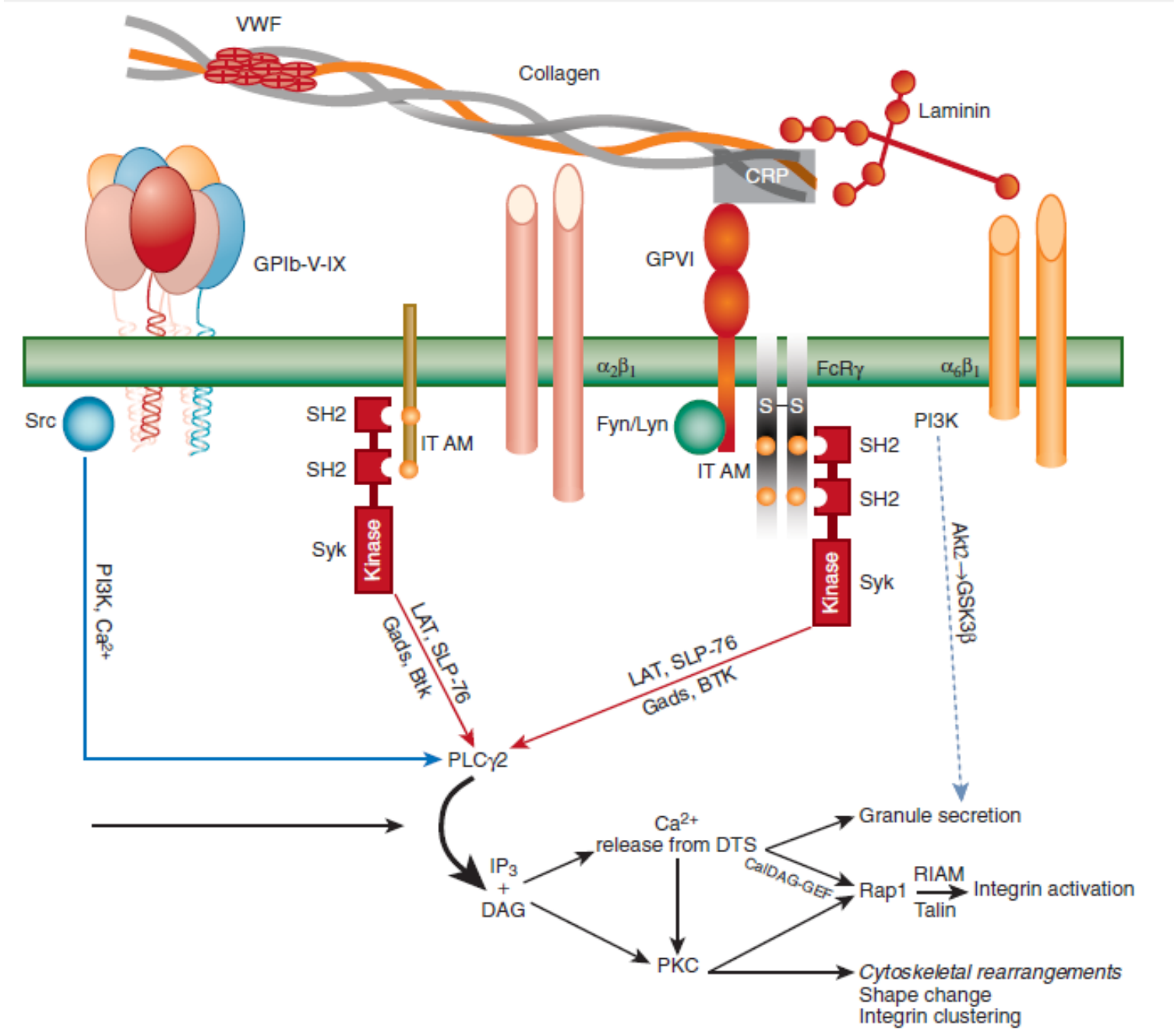
Endotelio


Célula epitelial
TM
FT
PgI_2
FvW
AT III
Activación de proteína C
AP-t
Sangre
Inicia la coagulación
Vasodilatación e inhibición de la agregación plaquetaria
Transportador de factor VIII
Adhesión colágeno-plaqueta
Inhibición de la coagulación sanguínea
Fibrinólisis



Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 2-Volume Set, 8e


Lesión vascular
Subendotelio
COLÁGENO
Adhesión plaquetaria
Cambio de forma
de las plaquetas
ADP, serotonina
Liberación del Factor Tisular
Reacción secretora
Activación
Agregación plaquetaria reversible
Coagulación extrínseca
Trombina
Coagulación intrínseca



Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 2-Volume Set, 8e

Coagulopatías en Niños

TABLE 29-3 Acquired Bleeding Disorders

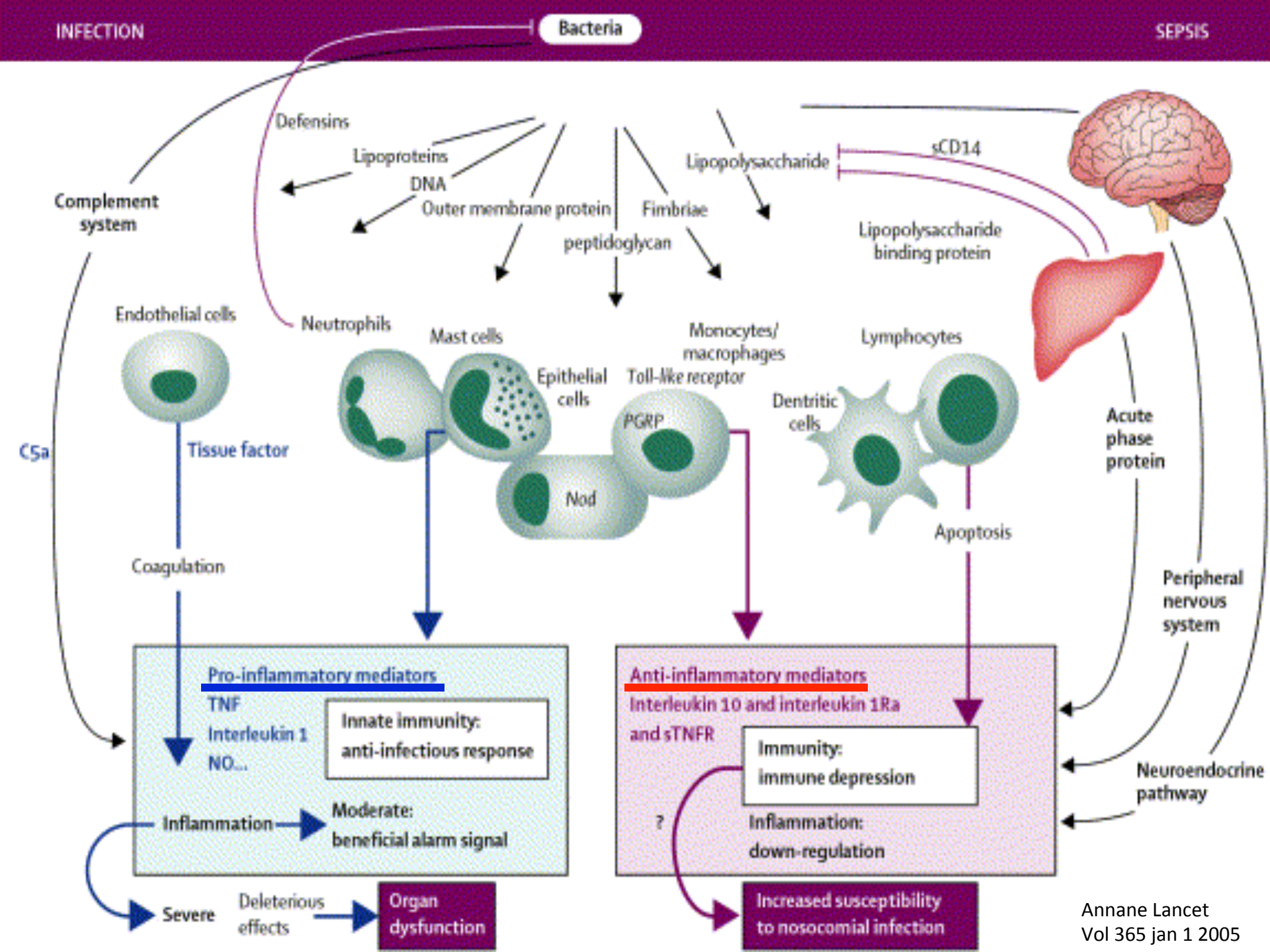
Underlying Bleeding Disorder	Hemostatic Defect	Cause
Overwhelming sepsis	Acute DIC	Initiation of coagulation, damage to the endothelium; decrease in clotting and anticlotting factors
Liver disease	Multiple coagulation factor deficiency	Decreased hepatic synthesis Increased fibrinolysis Decreased clearance of plasminogen activators Hypercoagulable state Decreased production of natural anticoagulants Thrombocytopenia Hypersplenism
Malabsorption syndrome	Decreased production of factors II, VII, IX, and X and proteins C and S	Vitamin K deficiency
Cyanotic congenital heart disease	Mild to moderate thrombocytopenia	Shortened platelet survival Abnormal platelet function Acquired defects in platelet aggregation
Acyanotic congenital heart disease (e.g., ASD, PDA)	Decreased high-molecular-weight VWF multimers	Consumption
ECMO and CPB platelet dysfunction	Platelet activation in the oxygenator and physical damage to the platelet membrane	Coagulation factor deficiency Consumption of coagulation factors in the circuit Hyperfibrinolysis Increase in tPA and decrease in α_2-antiplasmin
Acute promyelocytic leukemia	Thrombocytopenia Decreased production in bone marrow and increased consumption	Disseminated intravascular coagulation Release of procoagulant material from the leukemic cells Hyperfibrinolysis Increased synthesis of plasminogen activators

ASD, Atrial septal defect; *CPB*, cardiopulmonary bypass; *ECMO*, extracorporeal membrane oxygenation; *PDA*, patent ductus arteriosus; *tPA*, tissue plasminogen activator; *VWF*, von Willebrand factor.

Sepsis

	Estimated frequency*
Gram-positive bacteria	30–50%
Meticillin-susceptible *S aureus*	14–24%
Meticillin-resistant *S aureus*	5–11%
Other *Staphylococcus* spp	1–3%
Streptococcus pneumoniae	9–12%
Other *Streptococcus* spp	6–11%
Enterococcus spp	3–13%
Anaerobes	1–2%
Other gram-positive bacteria	1–5%
Gram-negative bacteria	25–30%
E coli	9–27%
Pseudomonas aeruginosa	8–15%
Klebsiella pneumoniae	2–7%
Other *Enterobacter* spp	6–16%
Haemophilus influenzae	2–10%
Anaerobes	3–7%
Other gram-negative bacteria	3–12%
Fungus	
Candida albicans	1–3%
Other *Candida* spp	1–2%
Yeast	1%
Parasites	1–3%
Viruses	2–4%

Annane Lancet
Vol 365 jan 1 2005



Annane Lancet
Vol 365 jan 1 2005

Basic Bacterial Cell Structure

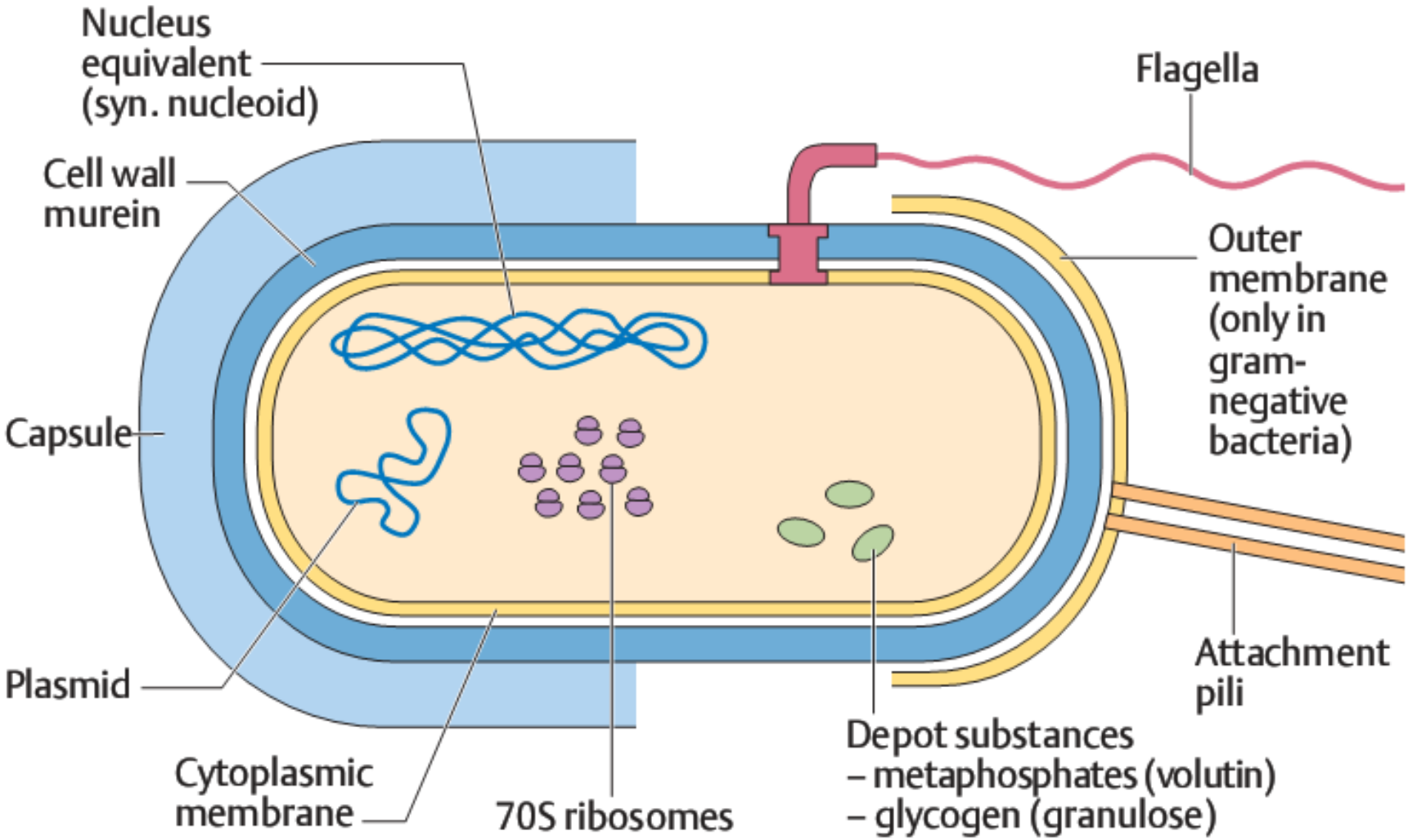
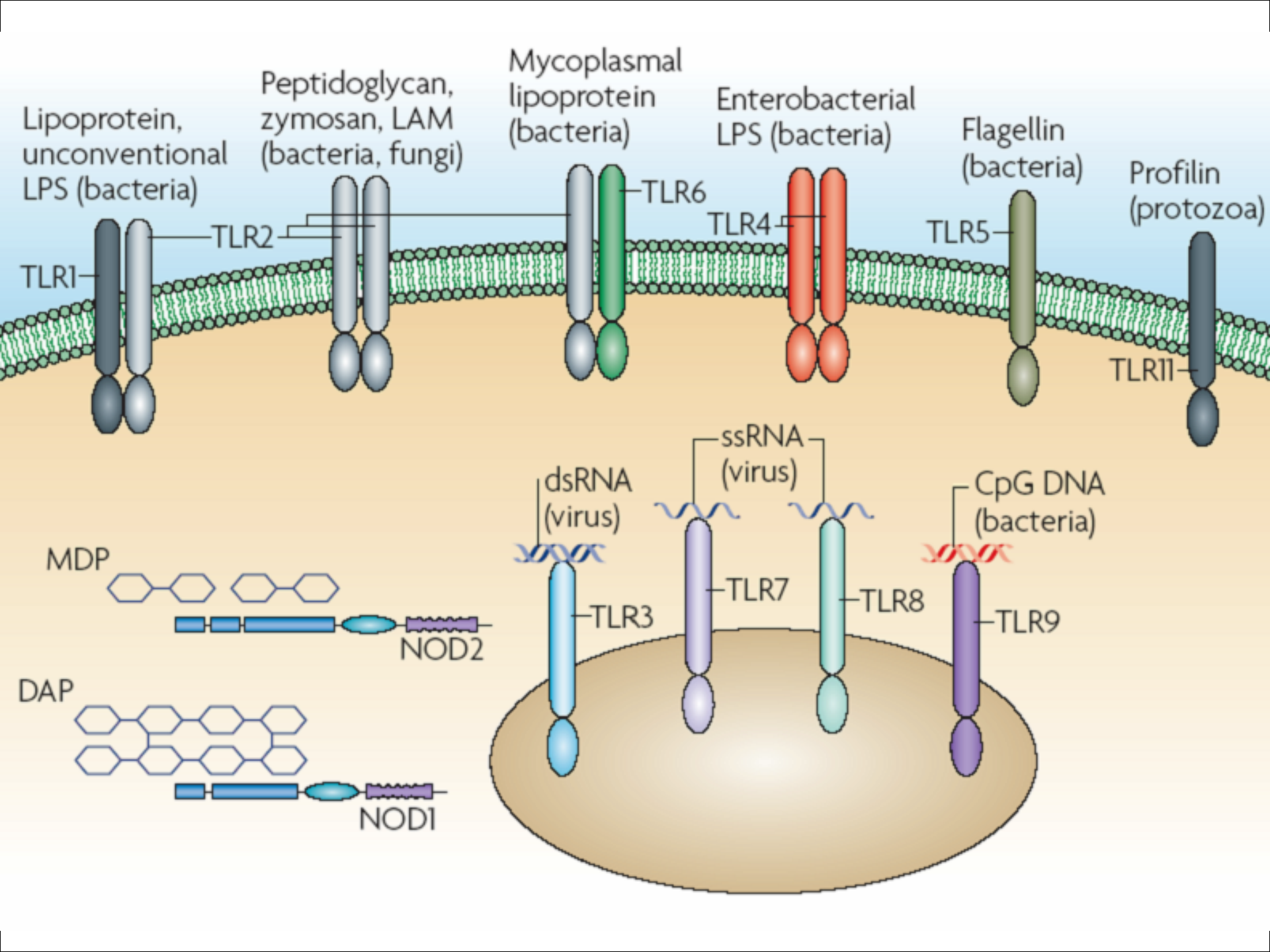


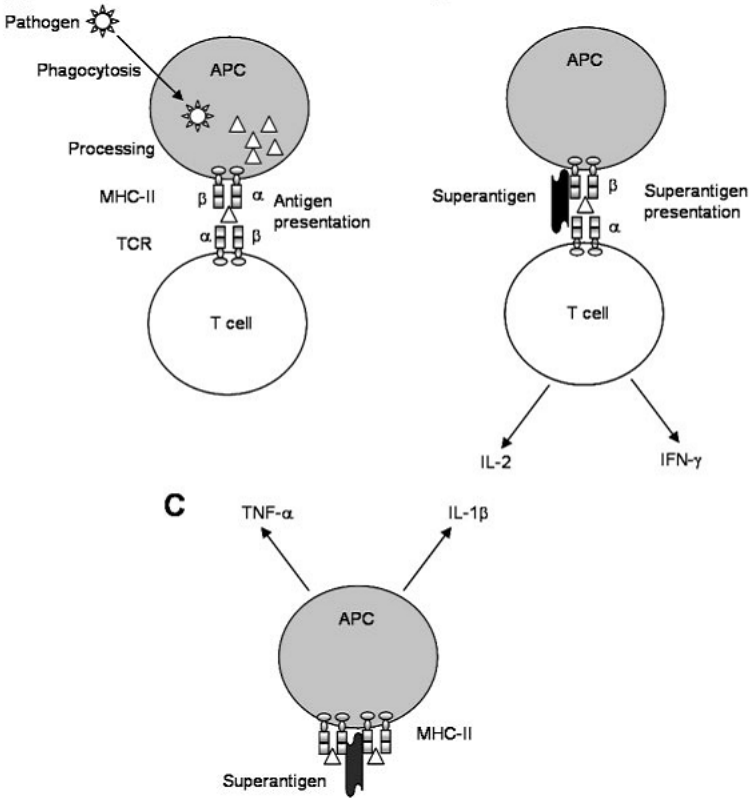
Fig. 3.7 All bacteria have the same basic structure (not to scale).

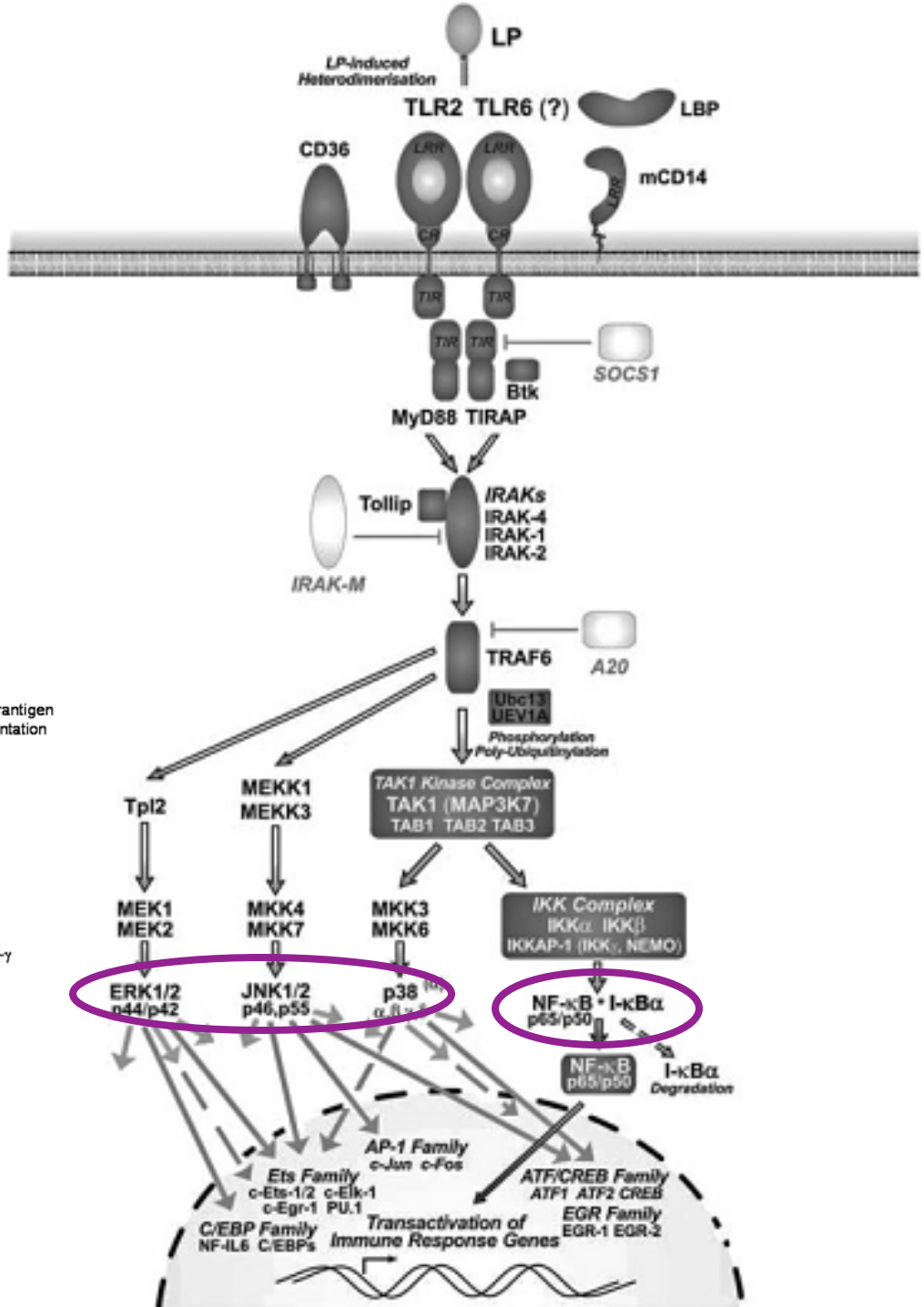
Gram (+) Gram (-)


Lipoprotein, unconventional LPS (bacteria)
Peptidoglycan, zymosan, LAM (bacteria, fungi)
Mycoplasmal lipoprotein (bacteria)
Enterobacterial LPS (bacteria)
Flagellin (bacteria)
Profilin (protozoa)
TLR1
TLR2
TLR6
TLR4
TLR5
TLR11
dsRNA (virus)
ssRNA (virus)
CpG DNA (bacteria)
MDP
NOD2
DAP
NOD1
TLR3
TLR7
TLR8
TLR9

PAMP Gram (+)

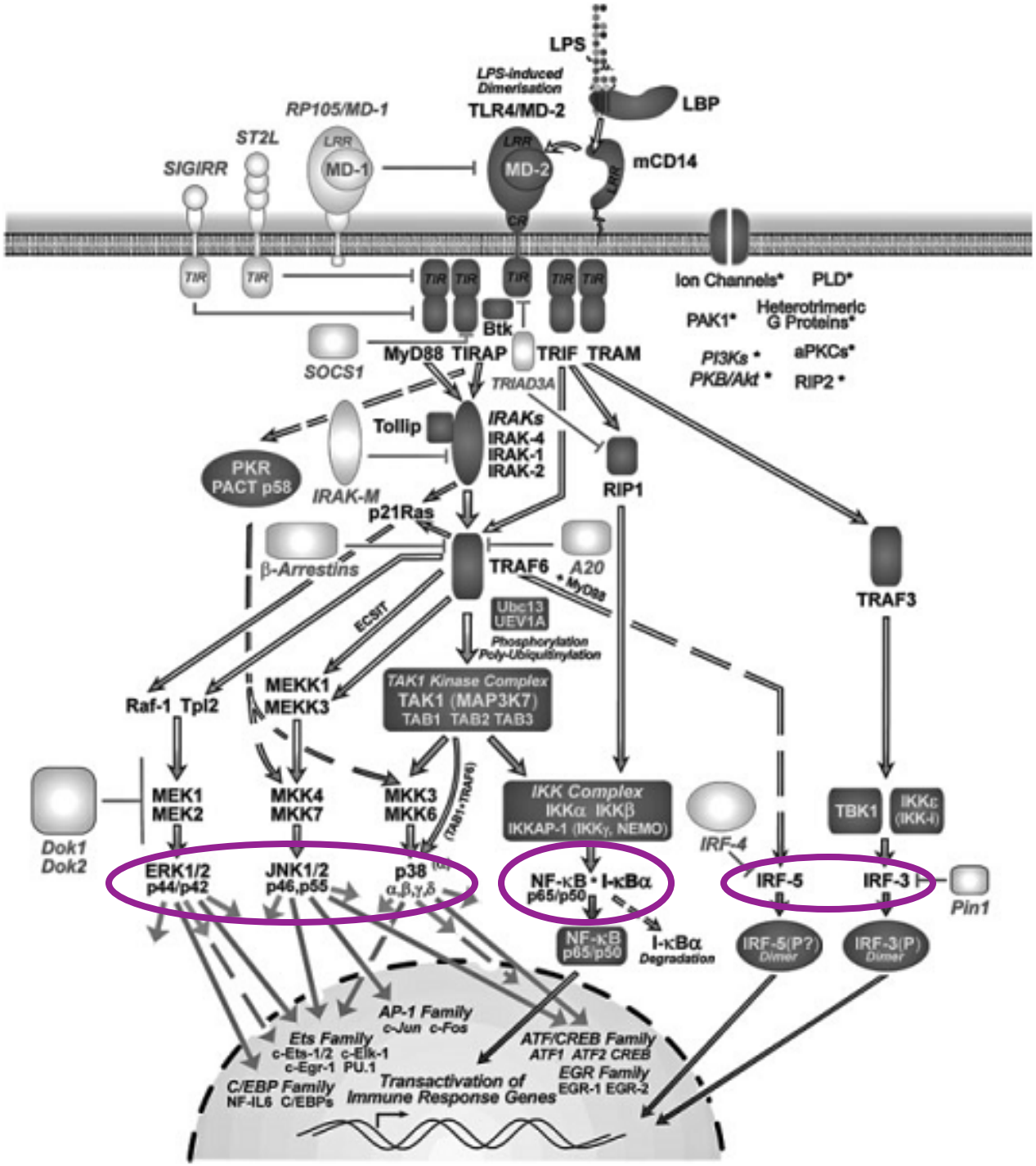
TOLL 2

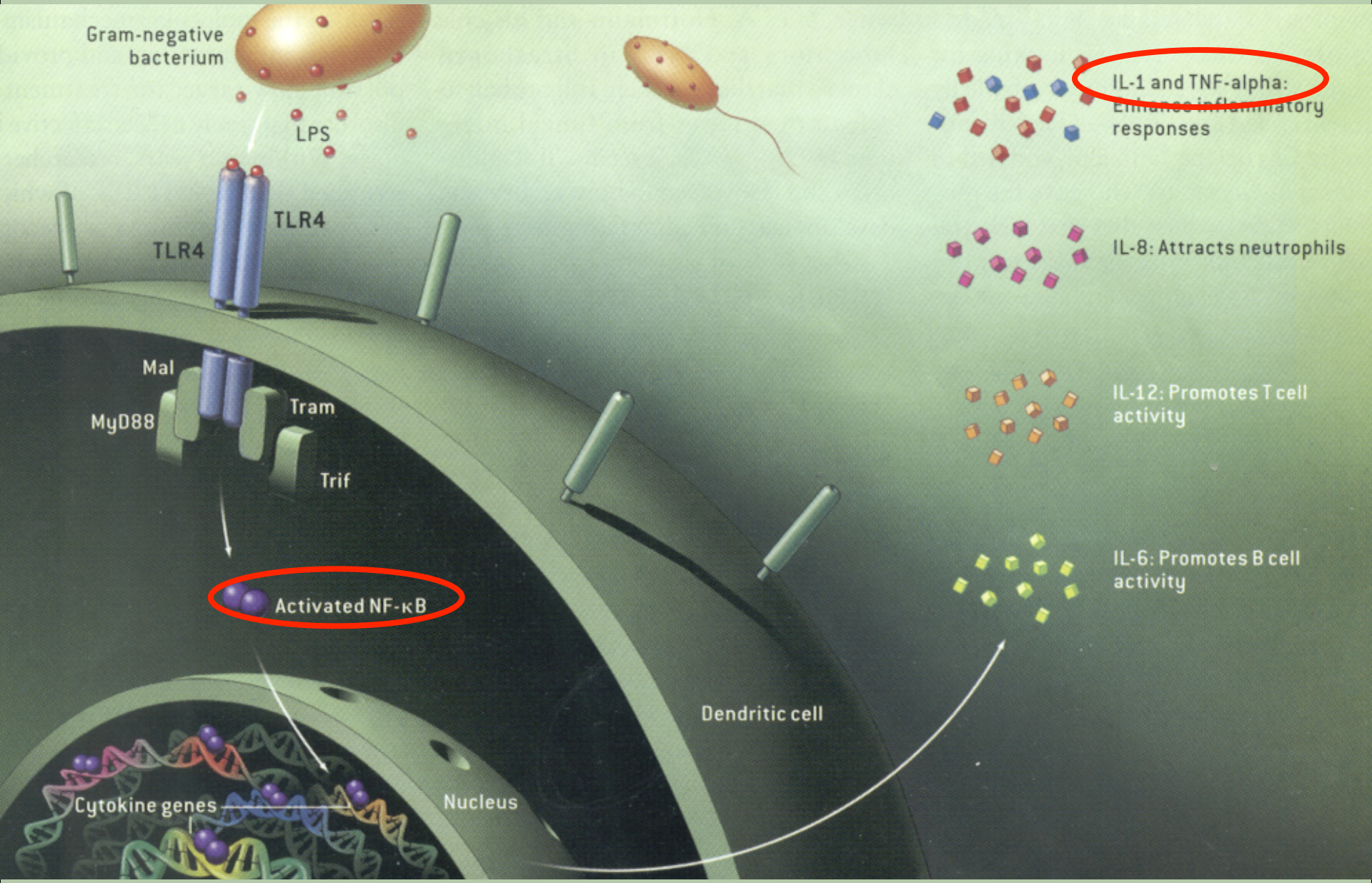




PAMP Gram (-)

TOLL 4

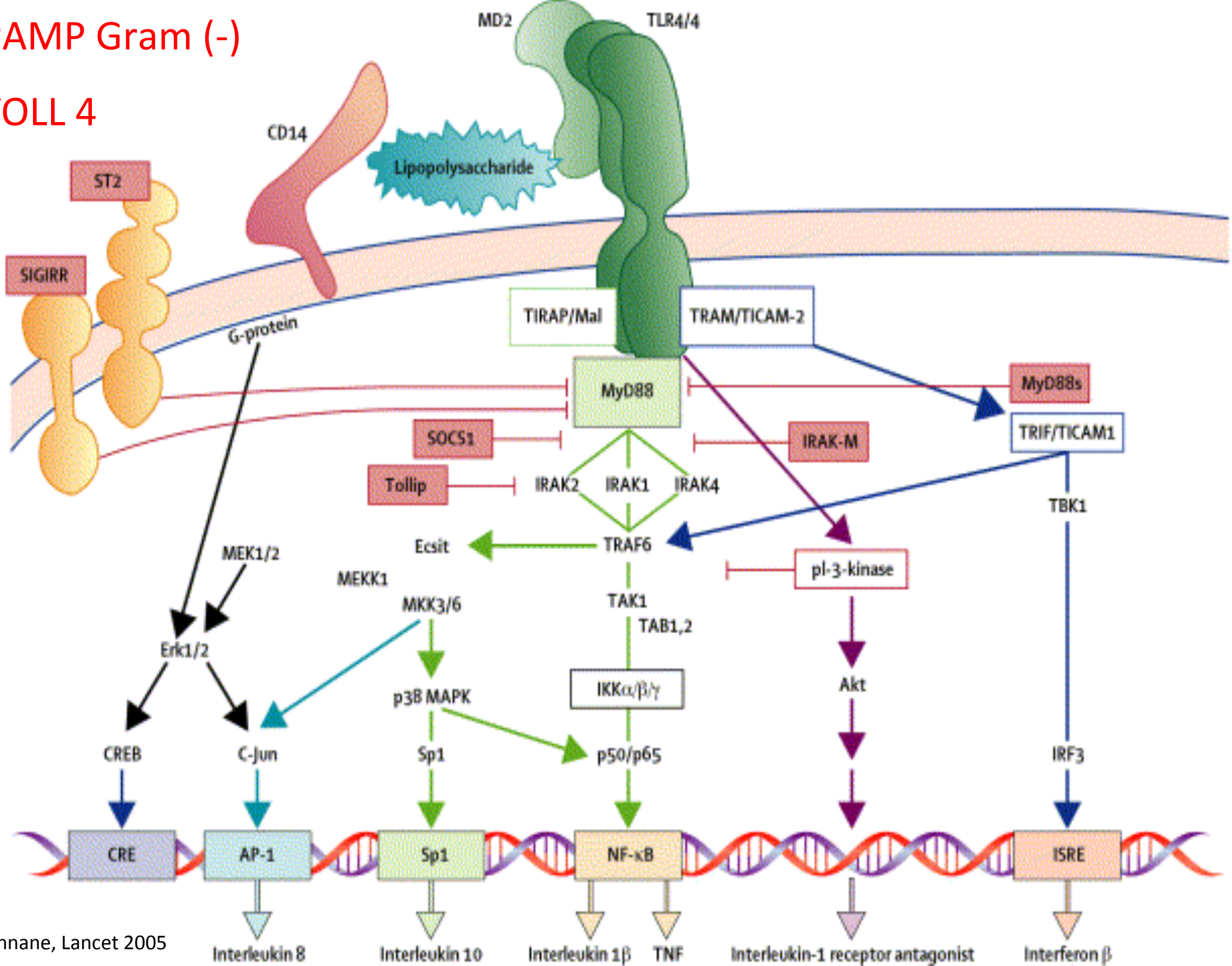




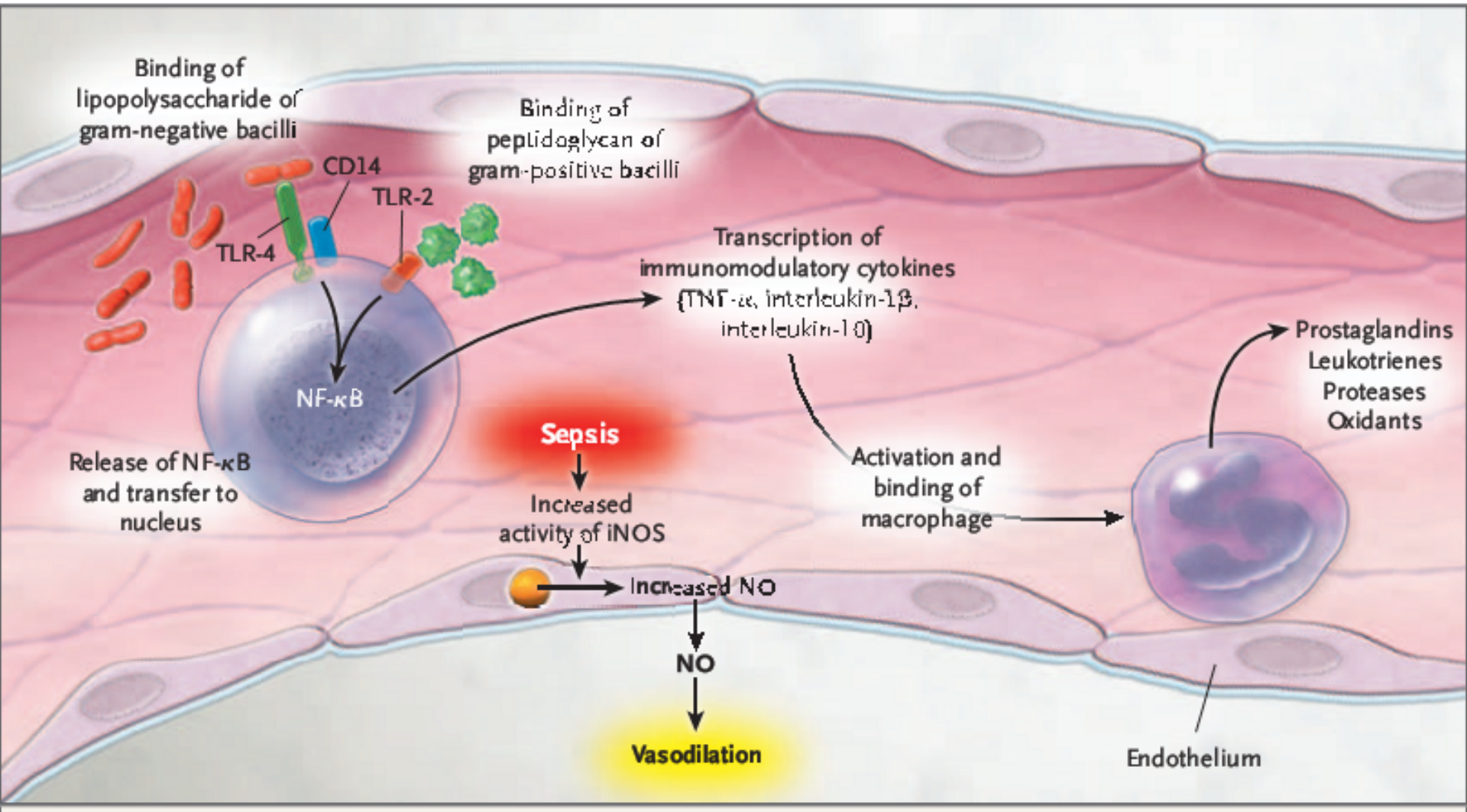
O'Neill, Luke A.J. "Immunity's Early-Warning System". Scientific American, Jan (2005), 38-45.

PAMP Gram (-)

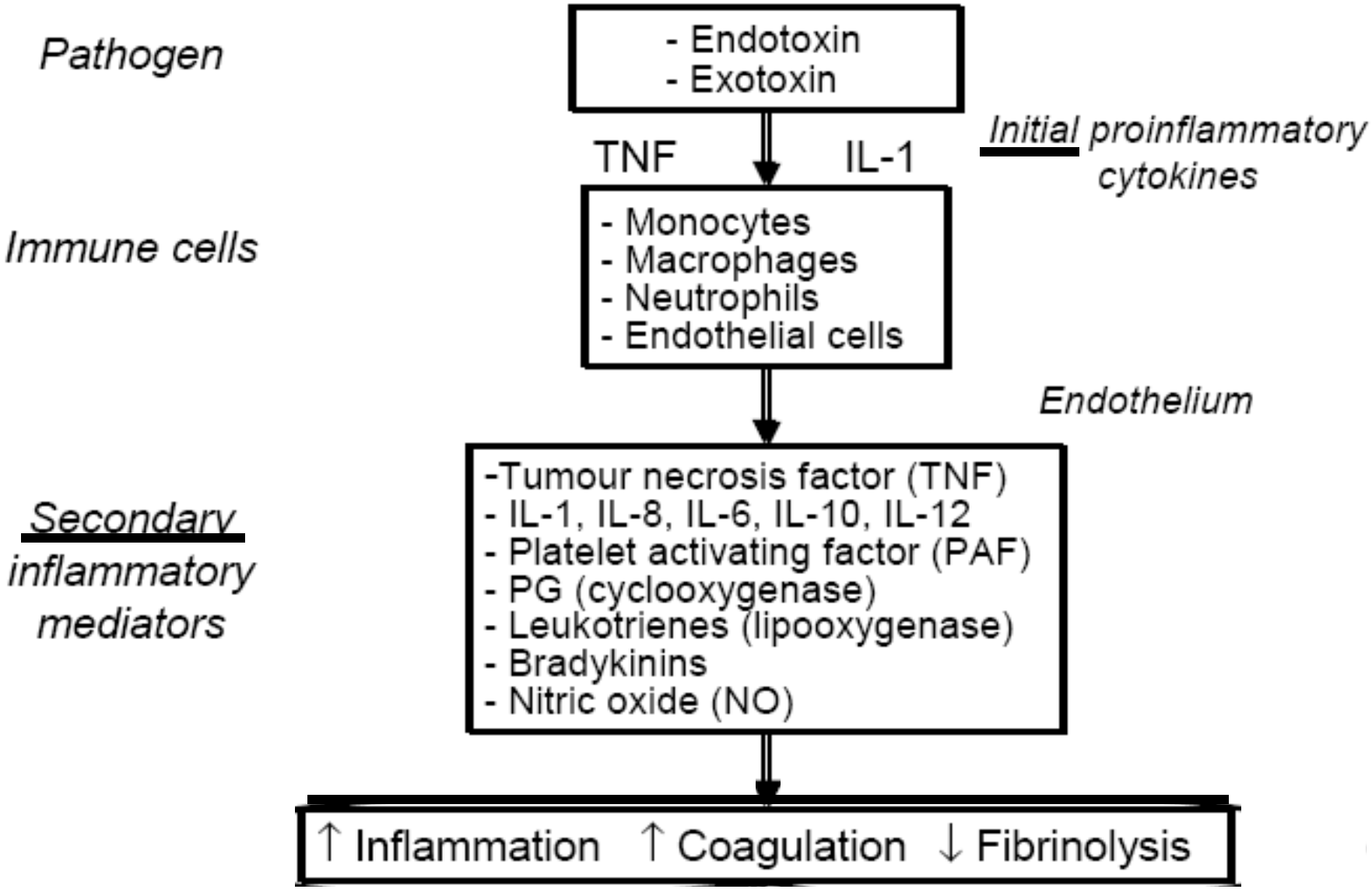
TOLL 4



Annane, Lancet 2005



NEJM 355;16 October 19, 2006



NEJM *1999;340:207-214*

Citoquinas Proinflamatoiras Iniciales

Citoquinas Proinflamatorias Secundarias

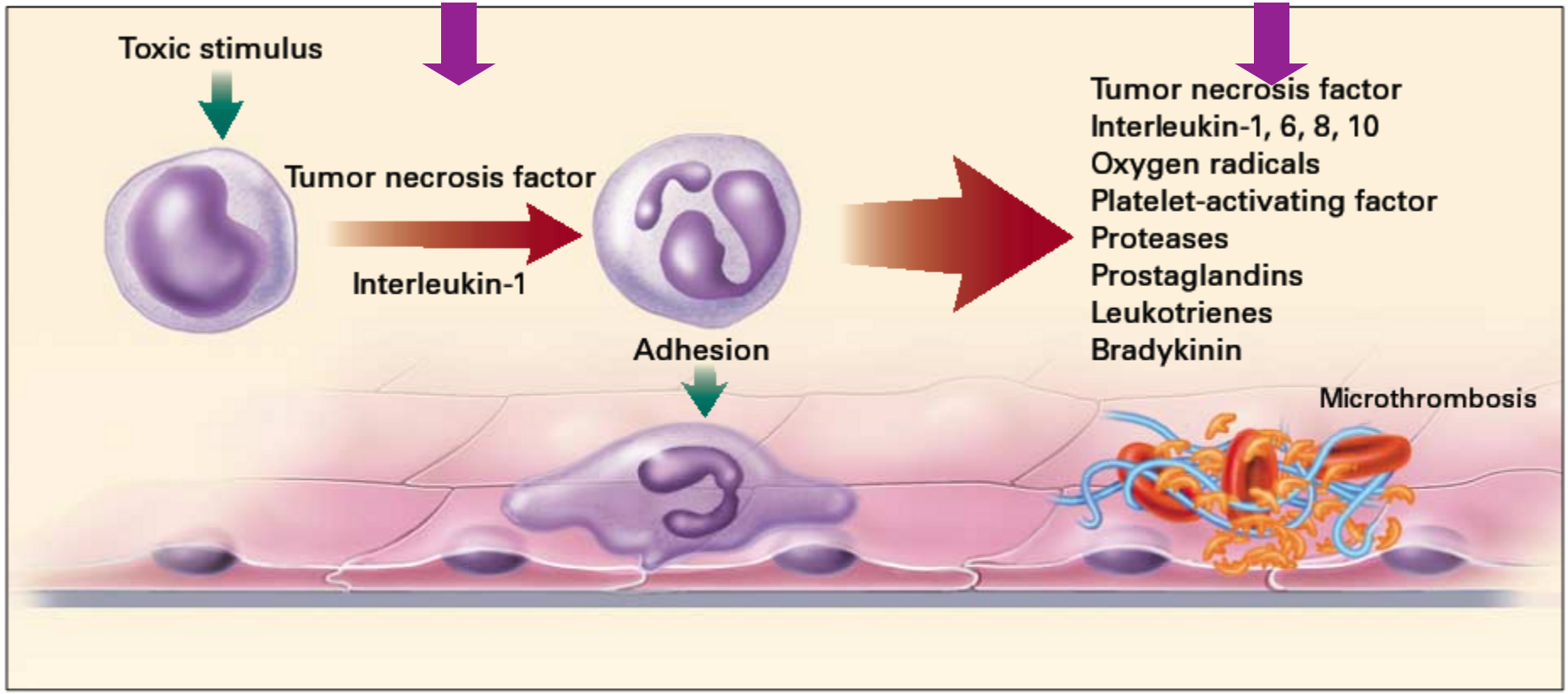
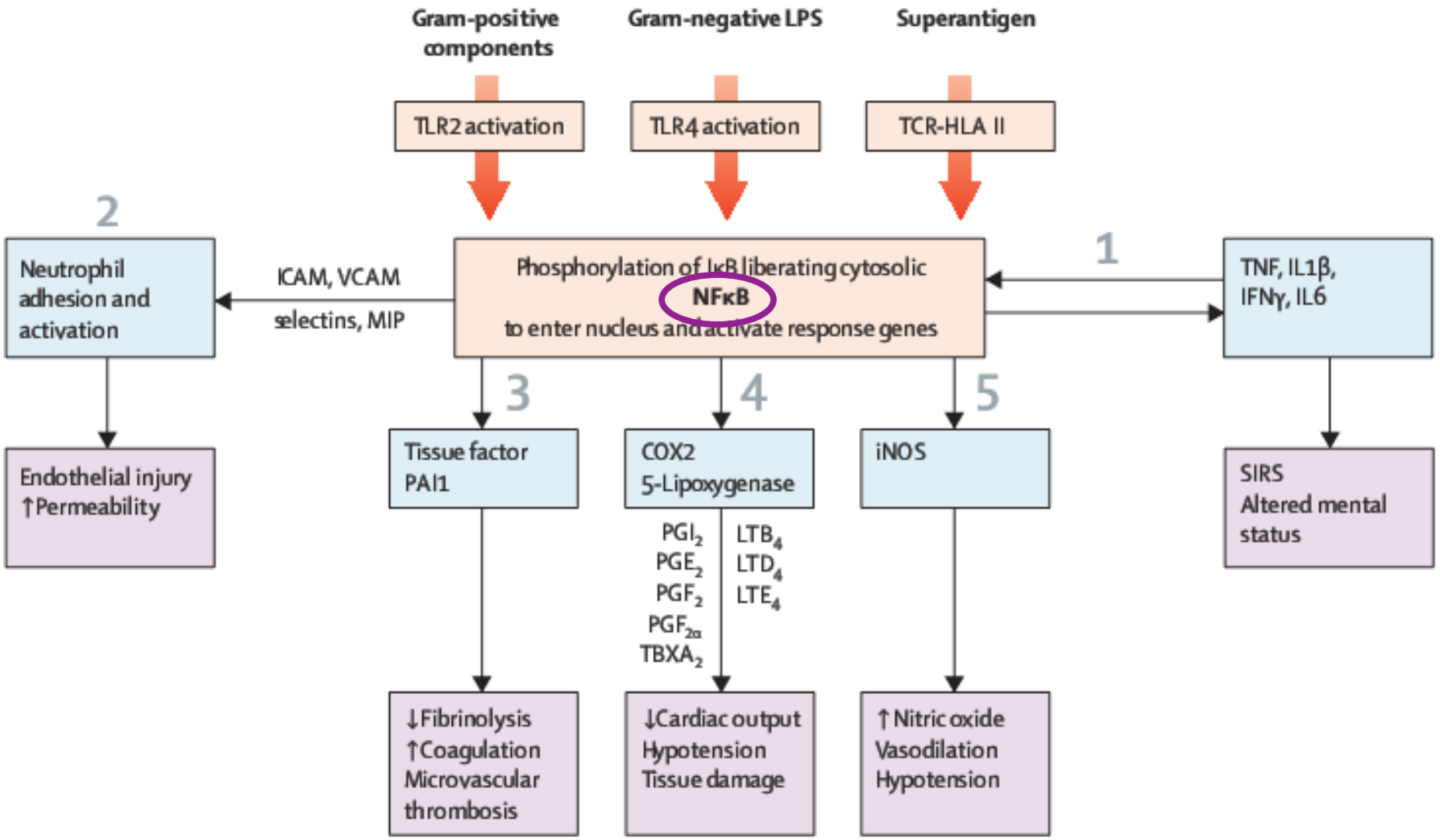


Figure 2. Early Biochemical Events in Sepsis.

An initial toxic stimulus (e.g., endotoxin) triggers the production of proinflammatory monokines (e.g., tumor necrosis factor and interleukin-1). These cytokines, in turn, result in neutrophil–endothelial-cell adhesion, activation of clotting, and generation of numerous secondary inflammatory mediators, including other cytokines, prostaglandins, leukotrienes, and proteases. Antiinflammatory compounds, such as interleukin-6 and interleukin-10, that may serve as negative feedback to the inflammatory process, are also released.

NEJM *1999;340:207-214*


Gram-positive components
Gram-negative LPS
Superantigen
TLR2 activation
TLR4 activation
TCR-HLA II
2
Neutrophil adhesion and activation
ICAM, VCAM
selectins, MIP
Phosphorylation of IκB liberating cytosolic
NFκB
to enter nucleus and activate response genes
1
TNF, IL1β, IFNγ, IL6
Endothelial injury
↑Permeability
3
Tissue factor
PAI1
4
COX2
5-Lipoxygenase
5
iNOS
SIRS
Altered mental status
PGI2
PGE2
PGF2
PGF2α
TBXA2
LTB4
LTD4
LTE4
↓Fibrinolysis
↑Coagulation
Microvascular thrombosis
↓Cardiac output
Hypotension
Tissue damage
↑Nitric oxide
Vasodilation
Hypotension

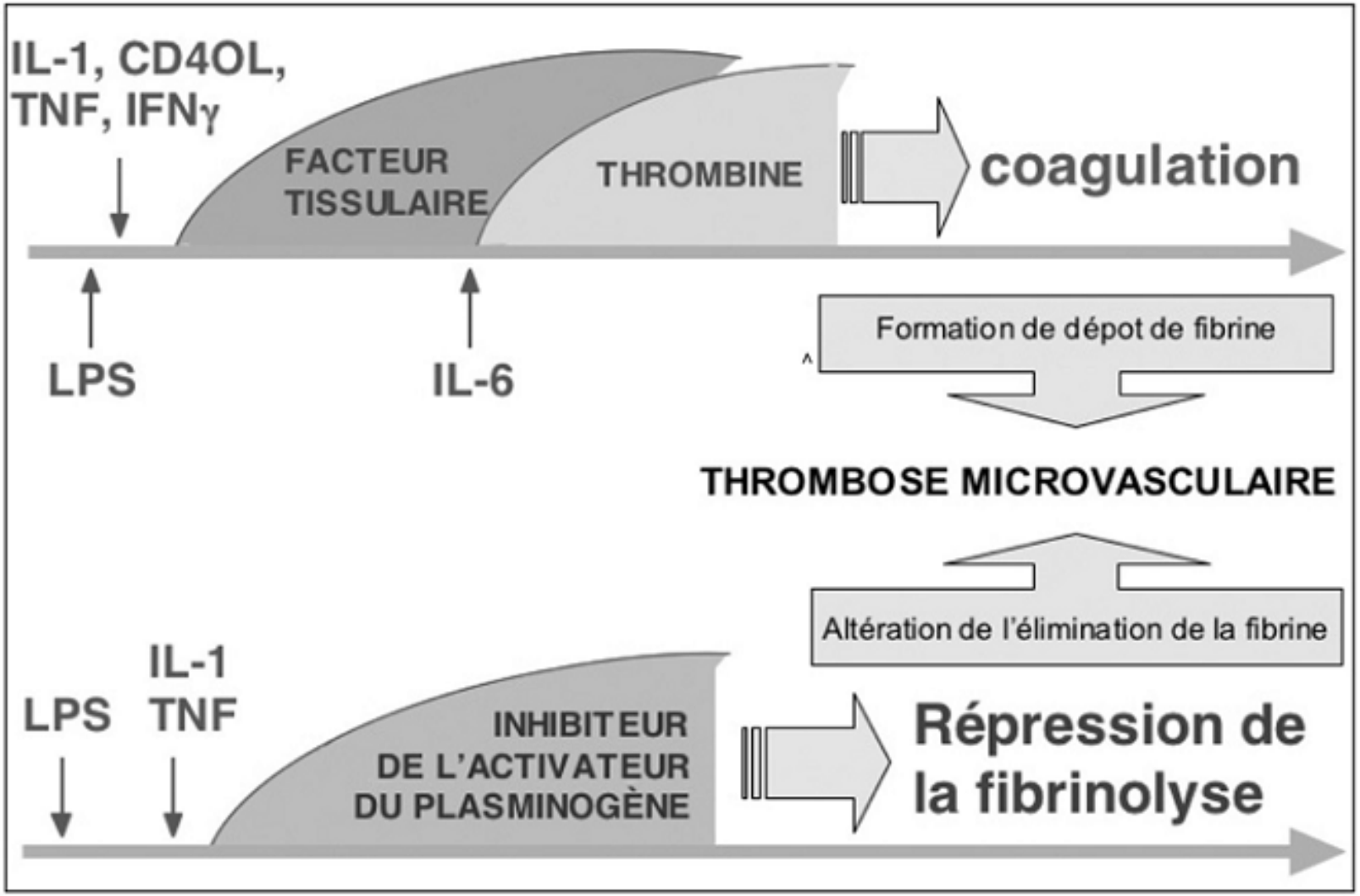
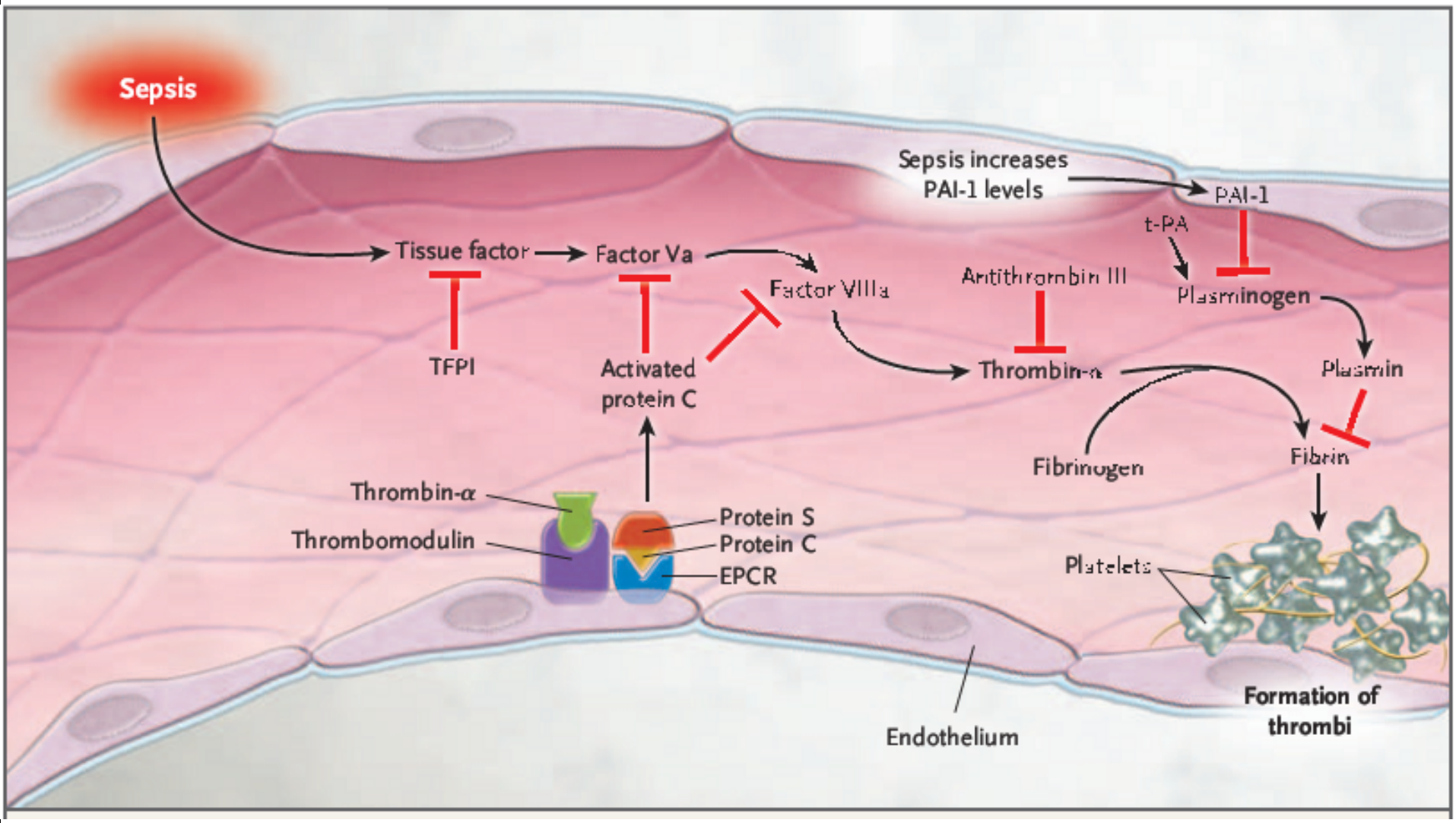


Fig. 3 – Relation entre inflammation et coagulation. L'endotoxine (LPS) et certaines cytokines inflammatoires favorisent l'initiation du processus de la coagulation et limite la fibrinolyse.



NEJM 355;16 October 19, 2006

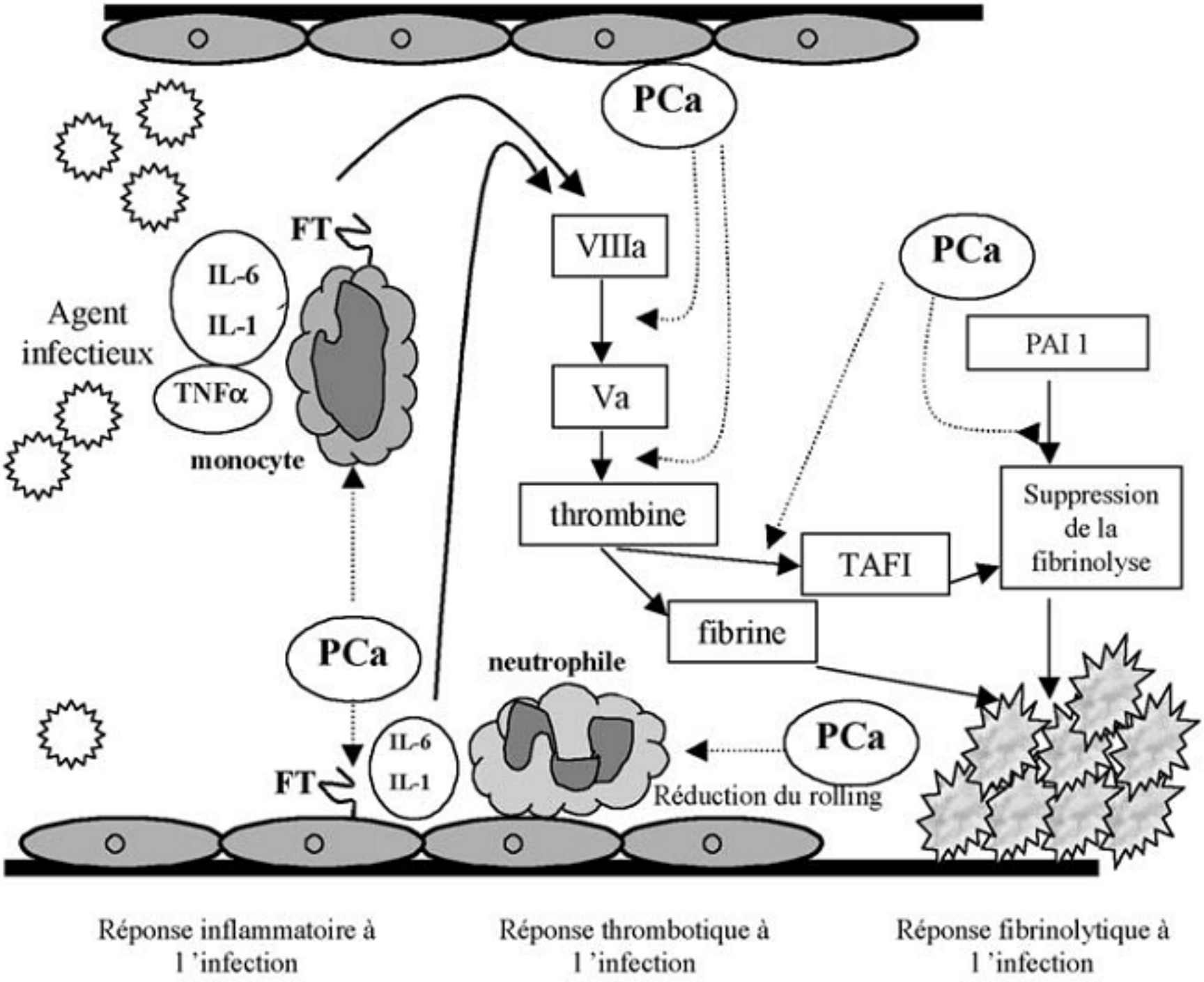

PCa
FT
IL-6
IL-1
TNFα
Agent infectieux
monocyte
VIIIa
Va
thrombine
fibrine
PCa
PAI 1
TAFI
Suppression de la fibrinolyse
PCa
neutrophile
IL-6
IL-1
FT
PCa
Réduction du rolling
Réponse inflammatoire à l 'infection
Réponse thrombotique à l 'infection
Réponse fibrinolytique à l 'infection

TABLE 29-3 Acquired Bleeding Disorders

Underlying Bleeding Disorder	Hemostatic Defect	Cause
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ASD, Atrial septal defect; *CPB*, cardiopulmonary bypass; *ECMO*, extracorporeal membrane oxygenation; *PDA*, patent ductus arteriosus; *tPA*, tissue plasminogen activator; *VWF*, von Willebrand factor.

Enfermedad Hepática

Decreased hepatic synthesis

Decreased production of natural anticoagulants

Thrombocytopenia

Hypersplenism

Compromiso Hepático

- Deficiencia de factores
- Disfunción de factores
- Anomalías plaquetarias por compromiso hepático

Rodak; Hematología Fundamentos y Aplicaciones Clínicas, 2da Ed pág 618

Deficiencia de Factores

- Disminuye la concentración de los factores y proteínas reguladores del sistema de coagulación; sobre todo los Vitamino K dependientes.
- El factor VII (vida media plasmática 5 a 8 horas) es el primero en disminuir. El TP es el más sensible incluso con compromiso hepático leve
- Factor V también disminuye
- Von Willebrand, FVIII y FXIII, no se afectan mucho porque se sintetizan también de manera extrahepática y porque son React Fase Aguda.

Disfunción de Factores

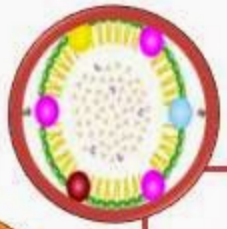
- El fibrinógeno se eleva con el compromiso hepático, incluso si es leve; sin embargo, es una proteína anómala: ***disfibrinogenemia***.
- Se producen ***formas carboxiladas*** de las proteínas de la coagulación de los factores vitamino K dependientes, sobre todo del **VII**; estas formas carboxiladas son disfuncionales

Anomalías Plaquetarias

- Adhesión de plaquetas al colágeno por FvW y gp Ib
- Activación cambio de forma
- Secreción de sustancias de gránulos alfa y densos
- Agregación por liberación de ADP, gp IIb-IIIa

Con el compromiso hepático habrá:

- Disminución del número de plaquetas.
- Alteración en la secreción del contenido de los gránulos plaquetarios.
- Alteración en la agregación plaquetaria



- Albúmina
- Lipoproteínas

Síntesis de colesterol

- Producción de triglicéridos

- Gluconeogénesis
- Glucogenólisis
- Glucogenogénesis

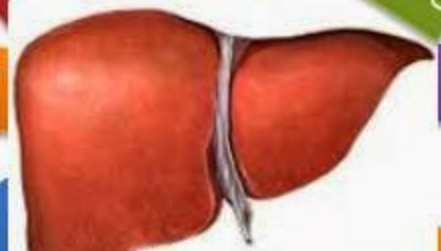
Sintetiza proteínas

Metaboliza lípidos

Metaboliza carbohidratos

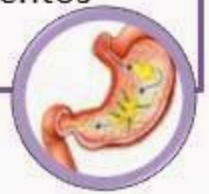
- Fibrinógeno
- Protombina
- Globulina
- Proconvertina
- Factor antihemofílico
- Factor Stuart-Prower

Sintetiza factores de coagulación



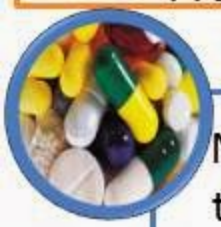
Produce bilis

Necesaria para digestión de alimentos



HÍGADO

Desintoxica sangre



Neutraliza toxinas de fármacos y hemoglobina

Transforma

Amonio en urea

Depósito de sustancias

Glucógeno, vitamina B12, hierro, cobre, etc.

Algunas consideraciones mas…

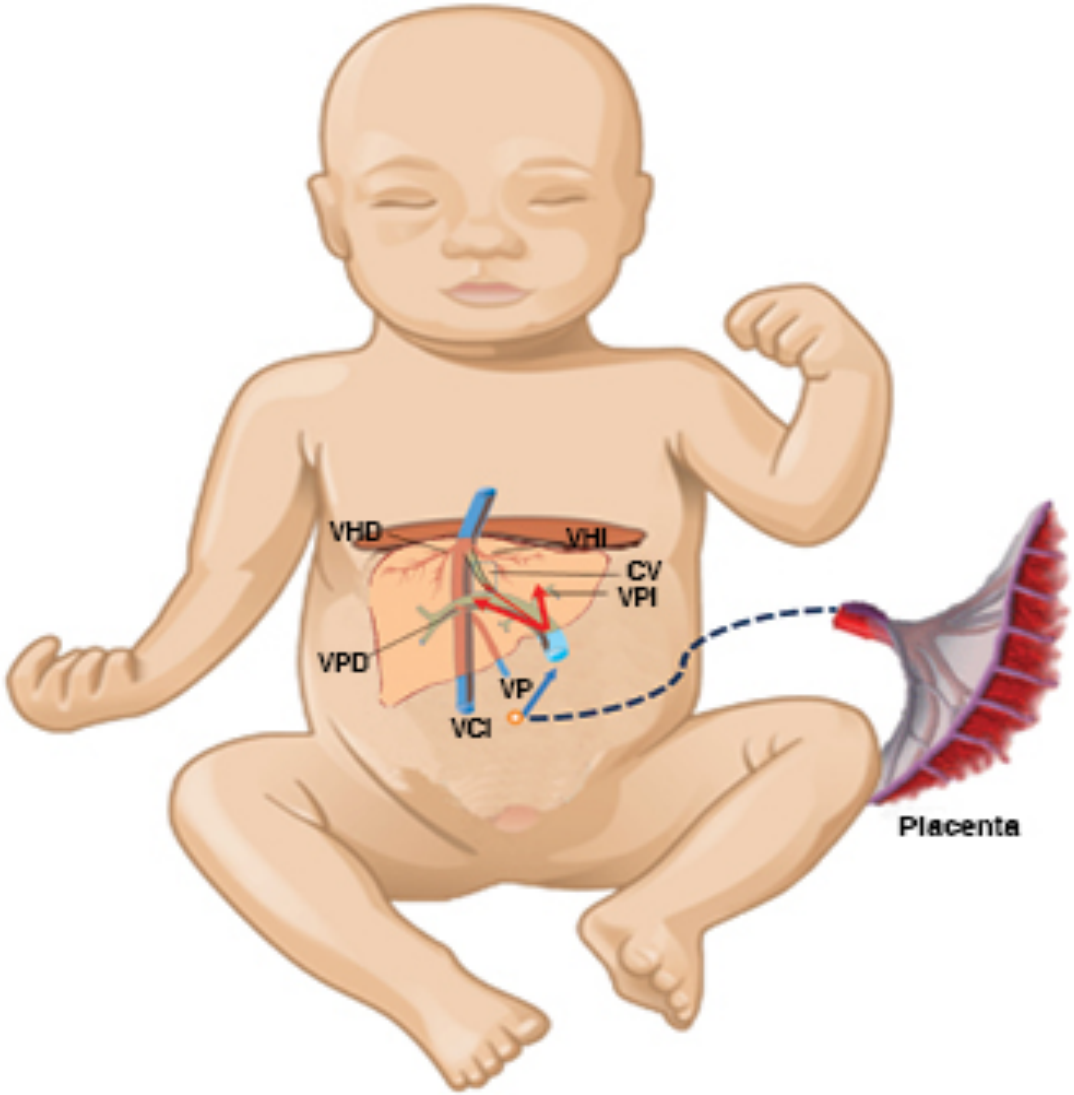


Figura 2. Principio de la circulación venosa en el hígado fetal. La dirección de flujo de sangre en el hígado se muestra mediante flechas. CV: conducto venoso; VCI: vena cava inferior; VHI: vena hepática izquierda; VPI: rama izquierda intrahepática de la vena porta; VP: vena porta; VHD: vena hepática derecha; VPD: rama derecha intrahepática de la vena porta; VU: vena umbilical.

Recién Nacidos:

1) Infecciones:
   TORCH
2) Plaquetopenia
   intrínseca
3) Colestasis
   Neonatal y NPT

1) Infecciones: TORCH

Thrombocytopenia Secondary to Congenital Infections

Severe thrombocytopenia that occurs within 72 hours in a sick neonate is likely to be due to a perinatal infection, such as toxoplasmosis, rubella, cytomegalovirus, or herpes simplex (TORCH) infections; group B streptococcus; *Listeria monocytogenes*; *Escherichia coli*; or HIV. Of the TORCH infections, cytomegalovirus (CMV) infection most commonly causes severe thrombocytopenia. Infants with congenital infections have jaundice, pallor, hepatosplenomegaly and may have a classic "blueberry muffin" rash, which is not actually petechial or purpuric in nature, but rather represents sites of extramedullary hematopoiesis in the skin. These skin lesions may also be seen in congenital leukemia. Early-onset sepsis in a neonate causes thrombocytopenia because of:

- Platelet consumption associated with disseminated intravascular coagulation
- Impaired thrombopoiesis. Often there is insufficient compensation for platelet destruction or increased platelet clearance. In these infants, thrombocytopenia resolves with treatment and resolution of the underlying infection.

2) Plaquetopenia Intrínseca

Early Human Development (2008) 84, 499–506

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BEST PRACTICE GUIDELINE ARTICLE

Neonatal thrombocytopenia: What we do and don't know ☆

Martha Sola-Visner [a,*], Matthew A. Saxonhouse [b,1], Rachel E. Brown [c,1]

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[b] *Division of Neonatology, University of Florida, PO Box 100296, 1600 SW Archer Road, Gainesville, FL 32610, United States*
[c] *Department of Pediatrics, University of Florida, PO Box 100296, 1600 SW Archer Road, Gainesville, FL 32610, United States*

Aspectos Básicos

- Incidencia de plaquetopenia en RN que ingresan a UCI Neonatal es de 22%-35%.
- 25% de estos pacientes tienen menos de 50000 plaquetas.

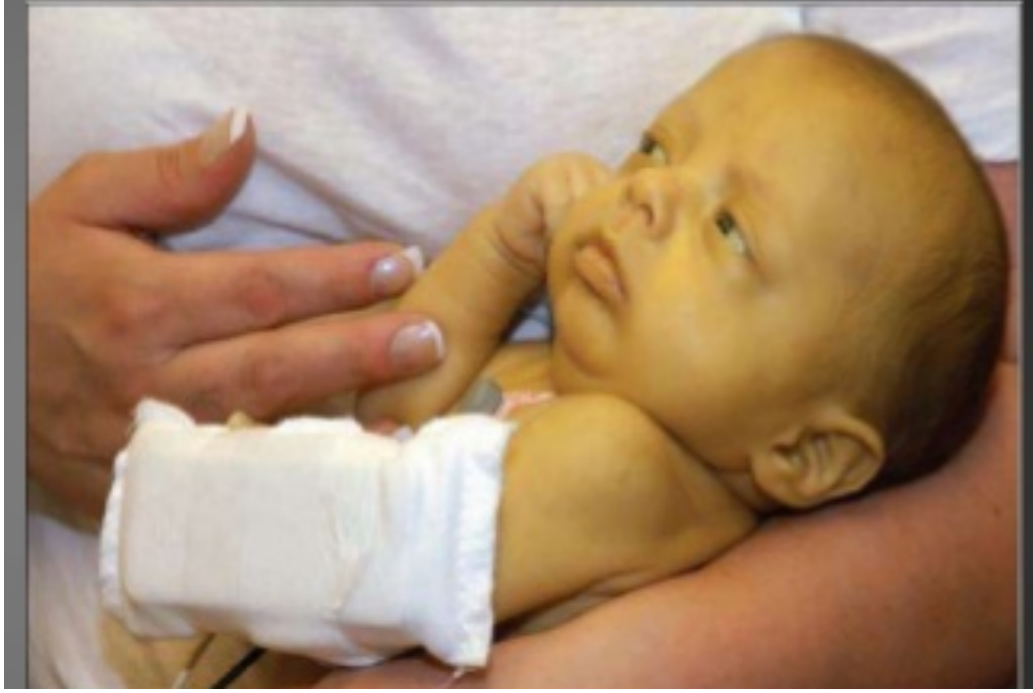
Factores Hematopoyéticos

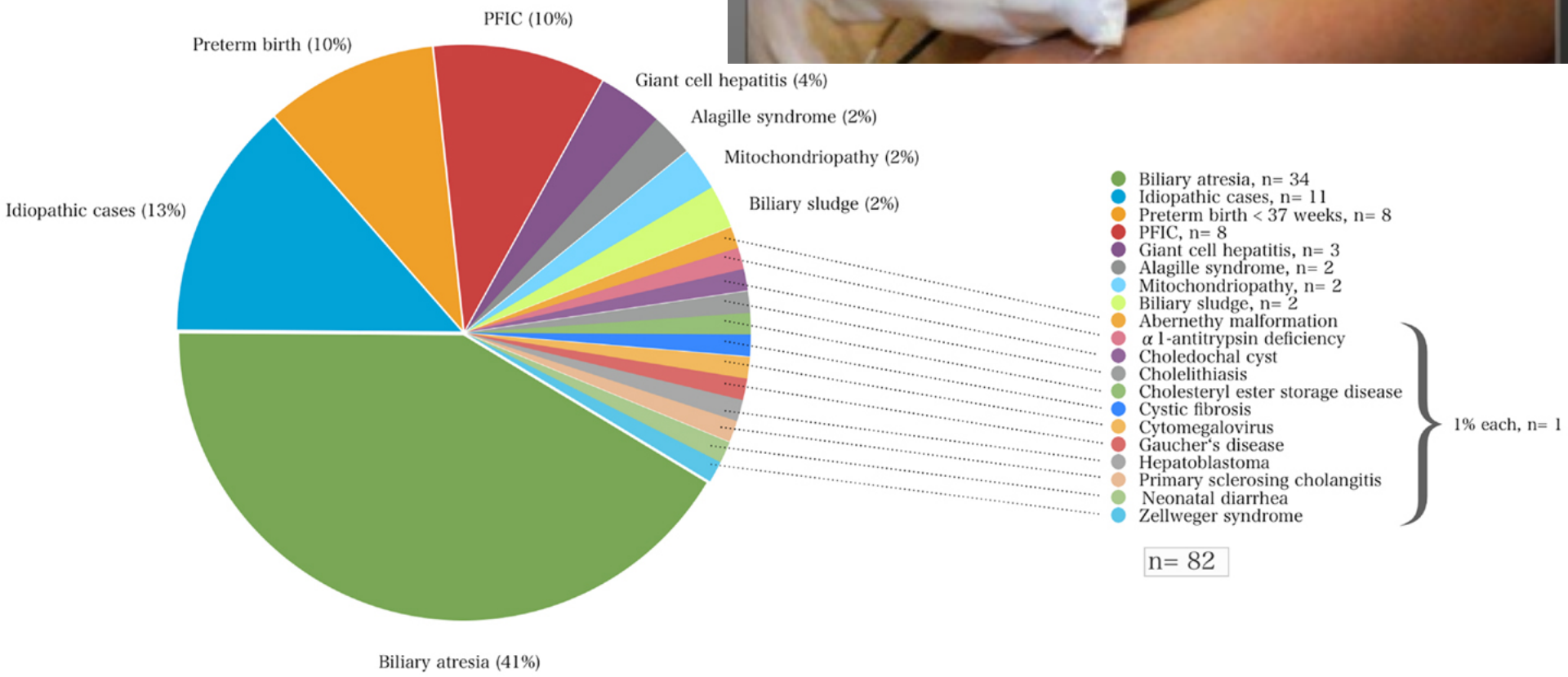
- Trombopoyetina
- Proliferación de Megacariocitos

Múltiples Factores ExtraHematopoyéticos, pero predominan:

- Sepsis, Enterocolitis Necrotizante
- Insuficiencia Placentaria

3) Colestasis Neonatal





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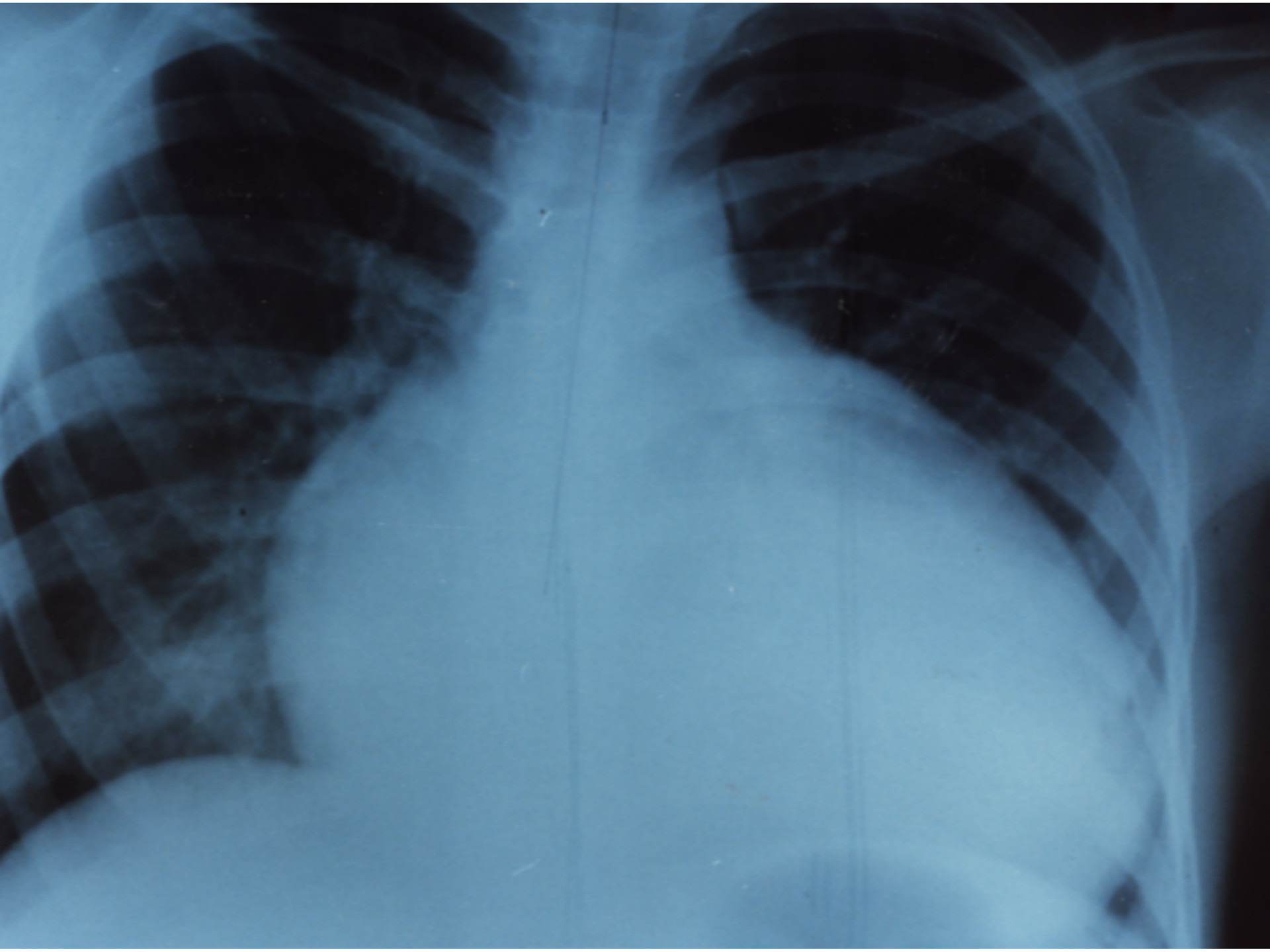
ASD, Atrial septal defect; *CPB*, cardiopulmonary bypass; *ECMO*, extracorporeal membrane oxygenation; *PDA*, patent ductus arteriosus; *tPA*, tissue plasminogen activator; *VWF*, von Willebrand factor.

Cardiopatías Congénitas

- Acianóticas: Insuficiencia Cardiaca
  - CIV CIA Ductus
  - Coartación de Aorta EA IA congénitas
  - EM IM congénitas
- Cianóticas: Crisis Hipóxica
  - T Fallot, TGV
  - Estenosis Pulm Atresia Pulm, Atresia Tricuspídea
  - Ventrículo Único
  - Doble Salida de Ventrículo Derecho
  - Drenaje Venoso Anómalo Pulmonar

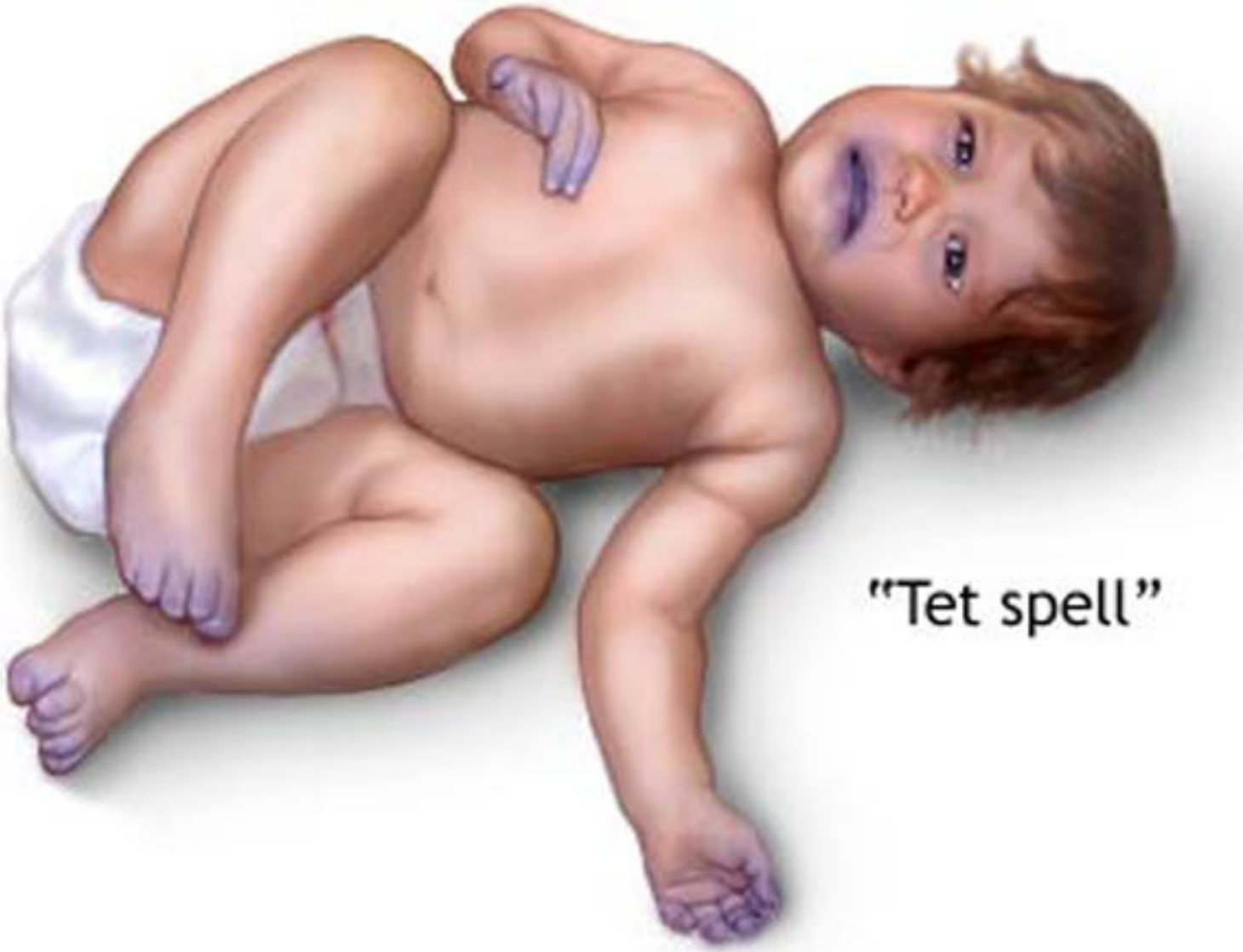


INSUFICIENCIA CARDÍACA

- Cardiomegalia clínica.
- Taquicardia – galope (R3-R4).
- Hipersudoración en reposo o sudoración a la lactancia
- Grado variable de desnutrición.
- Alteraciones del llenado capilar. Extremidades frías.
- **Signología respiratoria**:
  - Taquipnea, sibilancias, estertores, cianosis, disnea, tos, etc.
- **Signos de congestión venosa sistémica:**
  - **Hepatomegalia**, distensión venosa, edemas (raro).

- ***Disfunción Hepática → Coagulopatía***

Children with Tetralogy of Fallot exhibit bluish skin during episodes of crying or feeding.



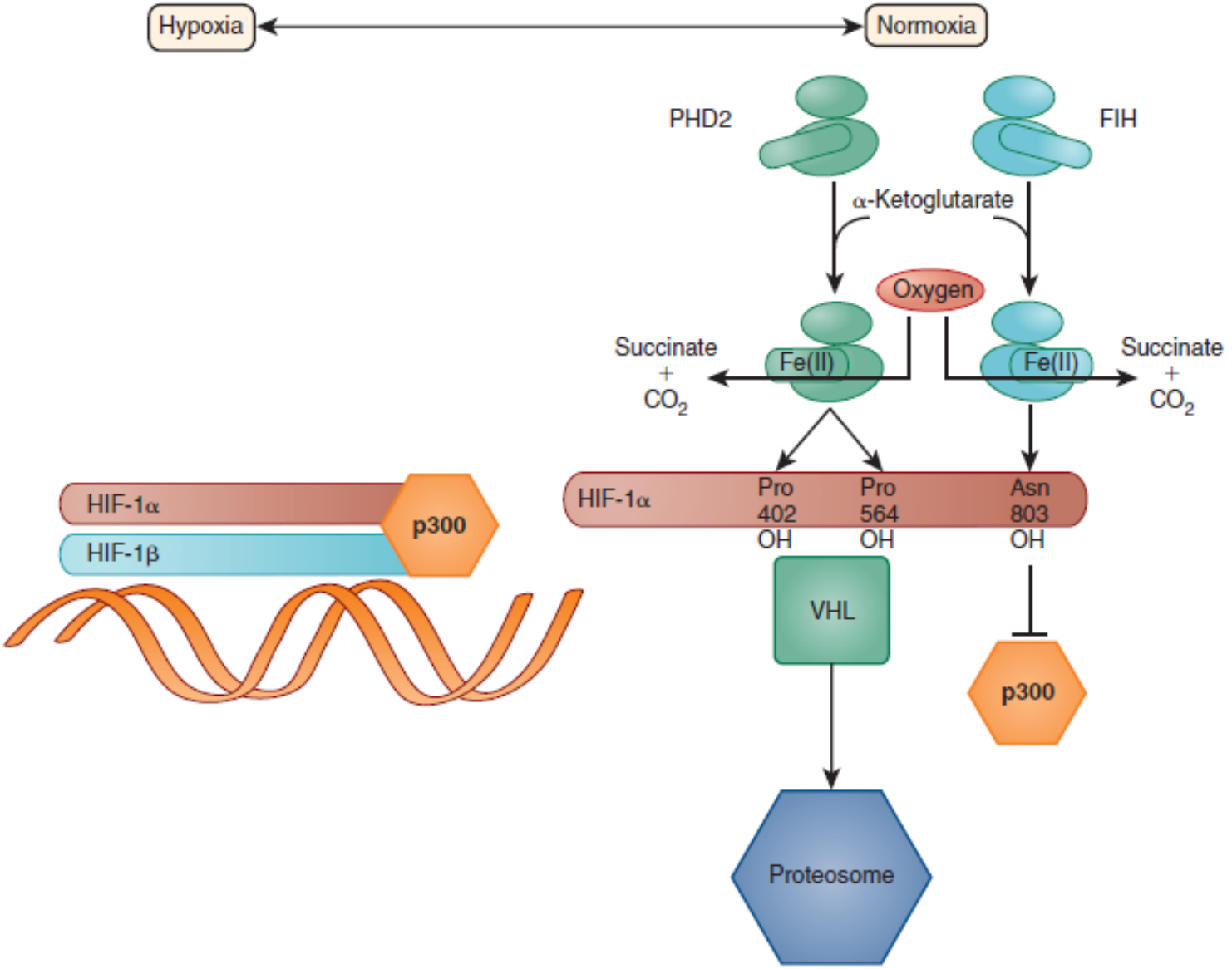
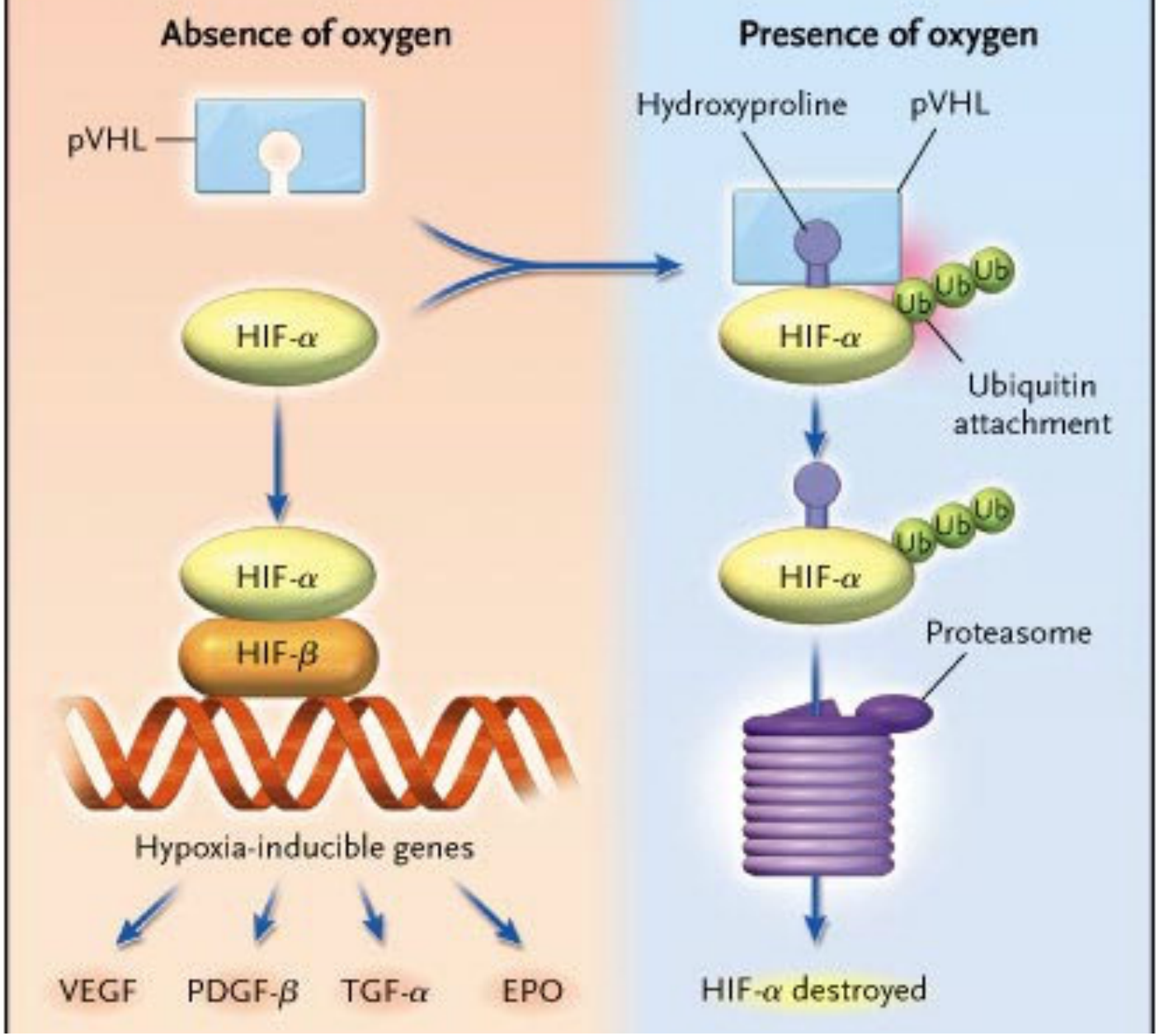


Figure 1-14 Hypoxia-inducible regulation of Epo production. Under normoxic conditions hypoxia-inducible factor 1α *(HIF-1α)* undergoes prolyl hydroxylation at Pro402 and Pro564 that leads to binding of HIF-1α to the von Hippel–Lindau *(VHL)* protein and subsequent ubiquitin-mediated destruction. This dioxygenase enzymatic reaction is catalyzed by a prolyl hydroxylase termed prolyl hydroxylase domain 2 *(PHD2)*. A second hydroxylation at asparagine 803 prevents binding of HIF-1α to its transcriptional coactivator p300, and is catalyzed by a hypoxia-inducible factor asparaginyl hydroxylase called *factor-inhibiting hypoxia-inducible factor (FIH)*. Both these reactions are dependent on oxygen, Fe(II), and α-ketoglutarate, which is oxidized to succinate with the release of CO_2. Under hypoxic conditions both hydroxylases are inhibited, leading to an increase in HIF-1α and recruitment of the p300 coactivator, which together with the ubiquitously expressed HIF-1β, activates transcription.



Daniel J. George, M.D., and William G. Kaelin, Jr., M.D.
The von Hippel–Lindau Protein, Vascular Endothelial Growth Factor, and Kidney Cancer
N Engl J Med 2003; 349:419-421July 31, 2003

Shock – Trauma

Triada:

Hipotermia Acidosis Coagulopatía


Sangrado
MUERTE
Coagulopatía
Acidosis e
hipotermia

Sangrado → Hipotermia - Hipoperfusión → Acidosis

Efectos de la Hipotermia: Reducción severa de la fx **plaquetaria**, sobretodo en la interacción con vW.

Hipoperfusión: origina Acidosis debido al metabolismo anaeróbico (lactato)

Efectos deletéreos de la Acidosis:

- Actividad disminuida de los **factores de la coagulación** sobretodo del factor VII y Factor X.
- Corazón: depresión de la contractilidad miocárdica, disminución de la respuesta inotrópica a las catecolaminas, arritmias ventriculares y **disfunción endotelial**.

Efectos del tratamiento

- **<u>Cristaloides-Coloides</u>** → Coagulopatía dilucional: la reanimación de fluídos origina una hemodilución que es muy deletérea en la función de los **factores de coagulación**.
- **<u>Componentes Sanguíneos</u>**: el almacenamiento prolongado de los componentes sanguíneos (PG) origina ↑ 2,3DPG que empeora la **acidosis**.

Hemofilia: Hemartrosis

TIPO DE HEMORRAGIA	HEMOFILIA A		HEMOFILIA B	
	NIVEL DESEADO (UI/DL)	DURACIÓN (DÍAS)	NIVEL DESEADO (UI/DL)	DURACIÓN (DÍAS)
Articular	40–60	1–2, puede ser más si la respuesta es inadecuada	40–60	1–2, puede ser más si la respuesta es inadecuada
Muscular superficial/ sin compromiso NV (excepto iliopsoas)	40–60	2–3, a veces más si la respuesta es inadecuada	40–60	2–3, a veces más si la respuesta es inadecuada

CUADRO 5-1 – DEFINICIÓN DE LAS RESPUESTAS AL TRATAMIENTO DE HEMARTROSIS AGUDA [1]

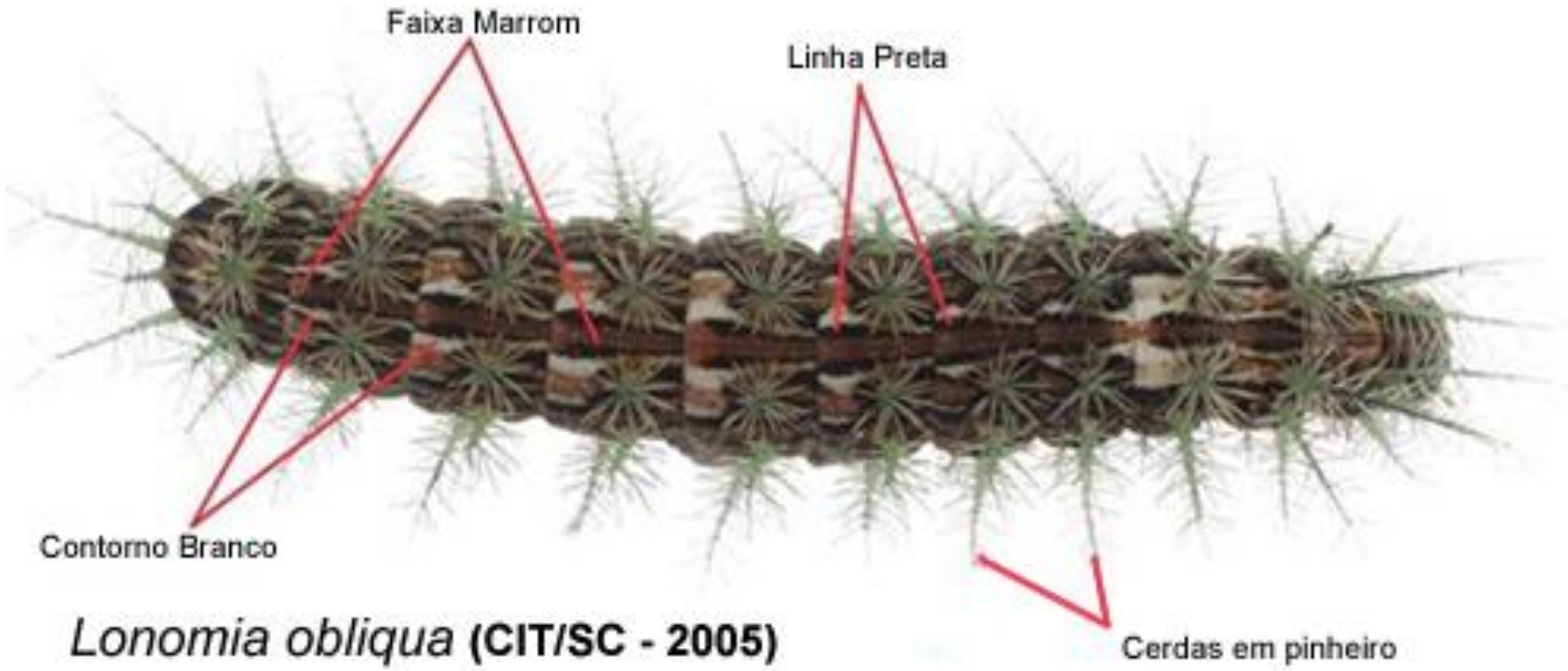
Excelente	Total alivio del dolor dentro de las 8 horas y/o desaparición de los síntomas de la hemorragia después de la inyección inicial, sin que sea necesario otra terapia de reemplazo dentro de las 72 horas.
Buena	Significativo alivio del dolor y/o mejoría de los síntomas de la hemorragia dentro de las 8 horas aproximadamente de haber aplicado una sola inyección, pero requiriendo más de una dosis de terapia de reemplazo dentro de las 72 horas para lograr una resolución completa.
Moderada	Moderado alivio del dolor y/o mejoría de los síntomas de la hemorragia dentro de las 8 horas aproximadamente de haber aplicado una sola inyección inicial y requiriendo más de una inyección dentro de las 72 horas, pero sin resolución completa.
Ninguna	Sin mejoría o con mejoría mínima, o empeoramiento de la condición, dentro de las 8 horas aproximadamente después de haber aplicado la inyección inicial.

Nota: Estas definiciones de respuesta al tratamiento de una hemartrosis aguda corresponden a personas con hemofilia que no presentan inhibidores. Es posible que tales definiciones deban modificarse en el caso de pacientes con inhibidores que reciben agentes de puenteo como cobertura hemostática o pacientes que reciben concentrados de factor con una mayor vida media.

Hemofilia: Otras Hemorragias

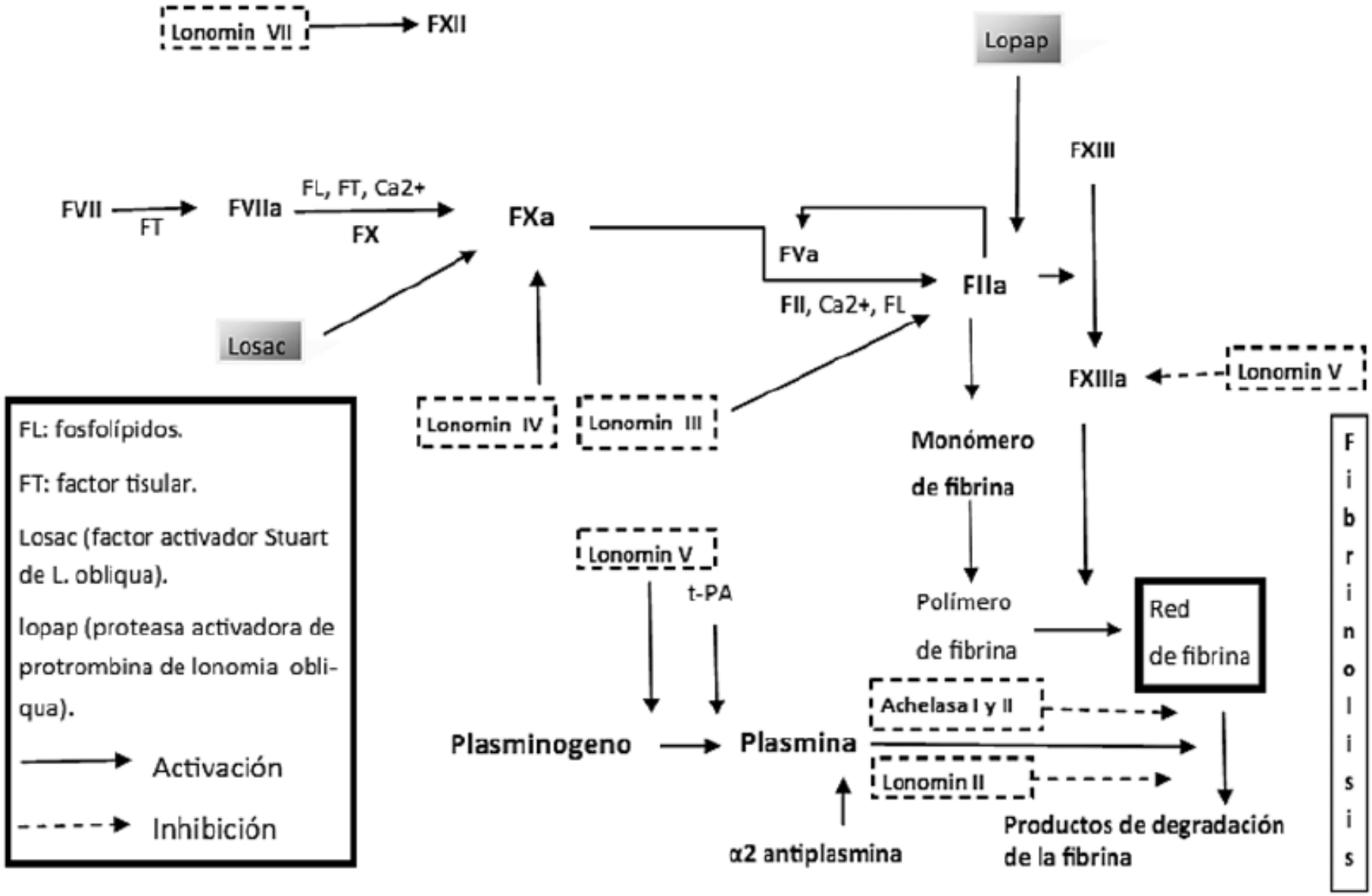
TIPO DE HEMORRAGIA	HEMOFILIA A		HEMOFILIA B	
	NIVEL DESEADO (UI/DL)	DURACIÓN (DÍAS)	NIVEL DESEADO (UI/DL)	DURACIÓN (DÍAS)
SNC/Cabeza				
▪ inicial	80–100	1–7	60–80	1–7
▪ mantenimiento	50	8–21	30	8–21
Cuello y garganta				
▪ inicial	80–100	1–7	60–80	1–7
▪ mantenimiento	50	8–14	30	8–14
Gastrointestinal				
▪ inicial	80–100	7–14	60–80	7–14
▪ mantenimiento	50		30	
Renal	50	3–5	40	3–5
Laceración profunda	50	5–7	40	5–7
Cirugía (mayor)				
▪ Preoperatorio	80–100		60–80	
▪ Post-operatorio	60–80 40–60 30–50	1–3 4–6 7–14	40–60 30–50 20–40	1–3 4–6 7–14
Cirugía (menor)				
▪ Preoperatorio	50–80		50–80	
▪ Post-operatorio	30–80	1-5, según el tipo de procedimiento	30–80	1-5, según el tipo de procedimiento

Lonomiasis



Lonomia obliqua **(CIT/SC - 2005)**

Mecanismo de acción de los componentes del veneno de Lonomia



Sospecha:

TP: 70

TPTa: 100

Fibrinógeno: <50

Coagulopatía de Consumo

Clínica de **Sangrado** y **Shock**

- PERO:
  - Procedencia: SELVA
  - No historia de Fiebre, PCR es “0”
  - Persistencia del Sangrado o muy poca mejoría a pesar de los componentes sanguíneos: PFC
- Tratamiento: antídoto y soporte con PG; evitar PFC y Crioprecipitado

Gracias…