UAI
HOSPITAL UNIVERSITARIO

Fisiopatología y farmacología de la Agregacion plaquetaria

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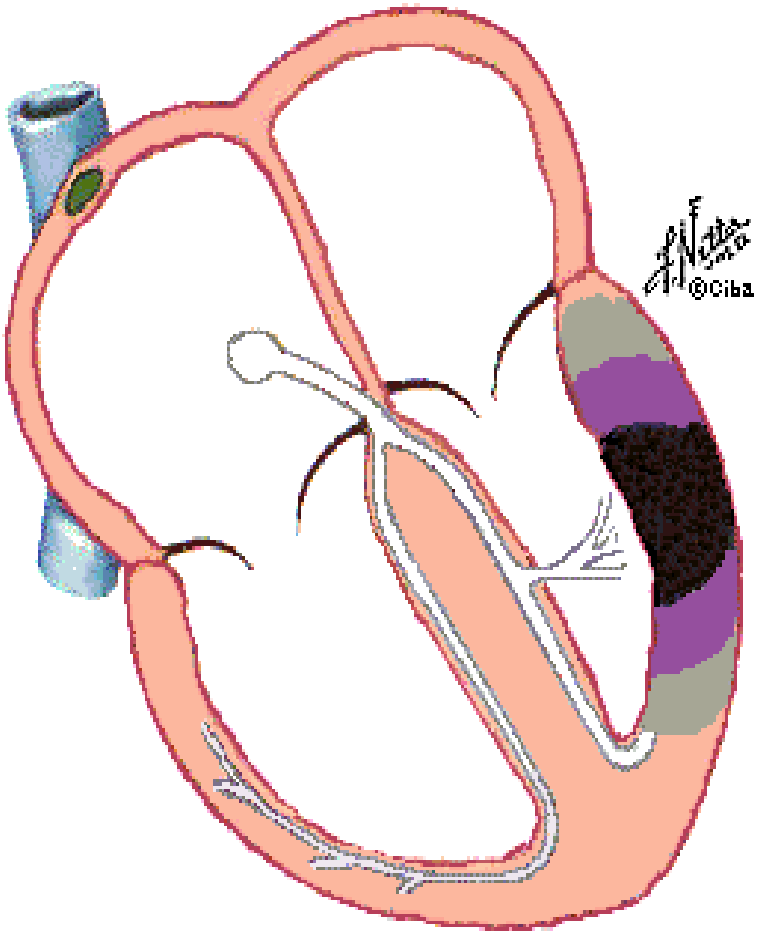
DEPARTAMENTO DE CARDIOLOGIA

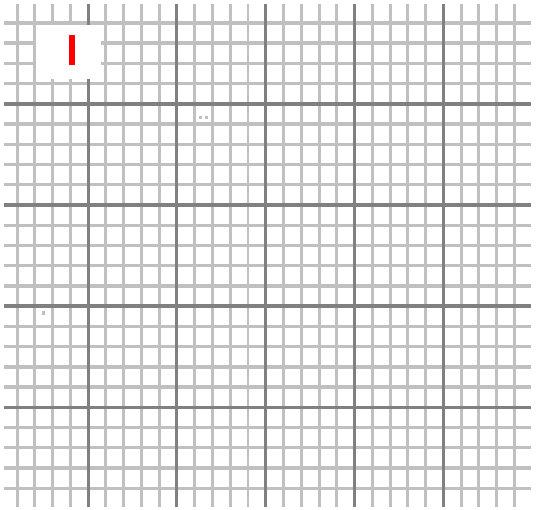
CÁTEDRA DE FISIOLOGïA

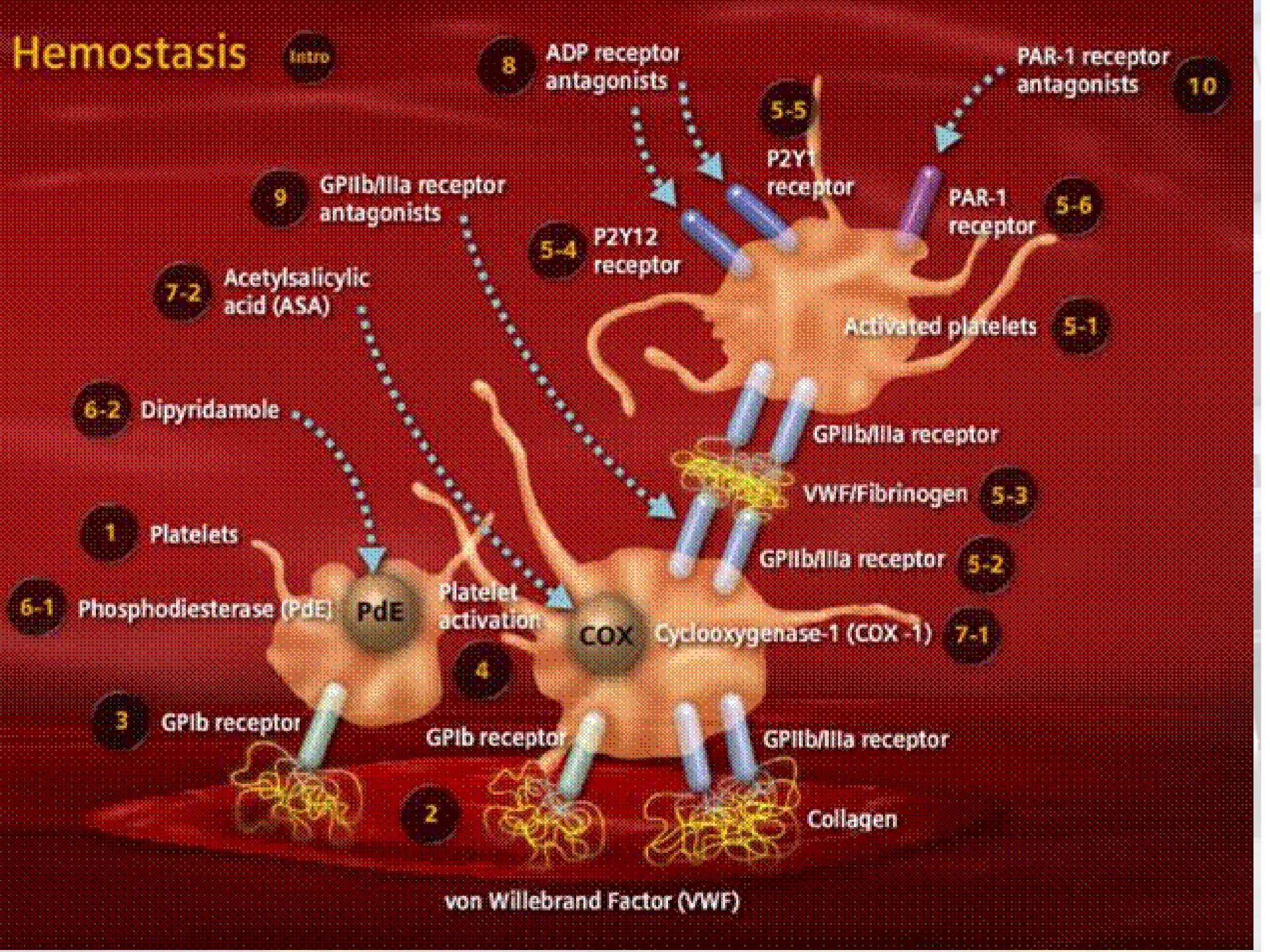
Universidad Abierta Interamericana

Differential Diagnosis of Q Waves

Presence of significant Q wave



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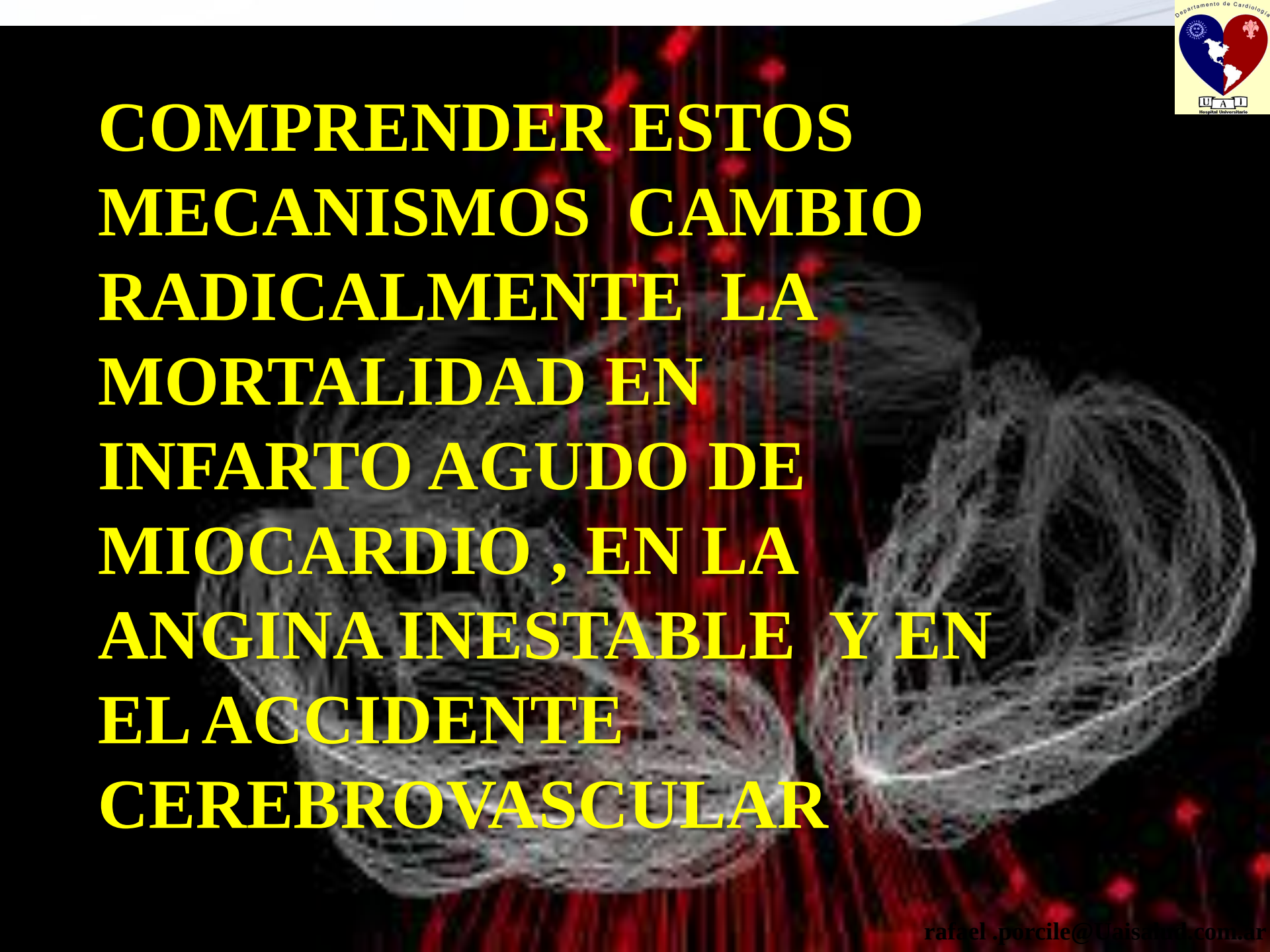
7-1
4
3
GPIb receptor
GPIb receptor
GPIIb/IIIa receptor
2
Collagen
von Willebrand Factor (VWF)

COMPRENDER ESTOS MECANISMOS CAMBIO RADICALMENTE LA MORTALIDAD EN INFARTO AGUDO DE MIOCARDIO , EN LA ANGINA INESTABLE Y EN EL ACCIDENTE CEREBROVASCULAR



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MECANISMO DE LA HEMOSTASIA

Se divide en:

Hemostasia Primaria:
Vasoconstricción
Formación del tapón plaquetario

Hemostasia Secundaria:
Mecanismo de coagulación
Reparación del tejido dañado

Primaria → secundaria

Cuatro mecanismos

1. Espasmo vascular (**vasoconstricción**)

2. Formación del tapón plaquetario (**Adherencia y agregación**)

3. Coagulación

4. Organización y/o disolución del coagulo (Fibrinólisis)

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El endotelio como protagonista

PROPIEDADES DEL ENDOTELIO

HEMOSTÁTICAS/PROTROMBÓTICAS

- Propiedades activadoras de las plaquetas

-producción de endotelina

-produccion de factor de vW.

- Propiedades procoagulantes

-producción de factor tisular

-fijación de factores de coagulación

- Inhibición de fibrinólisis

-producción de la-TP-1

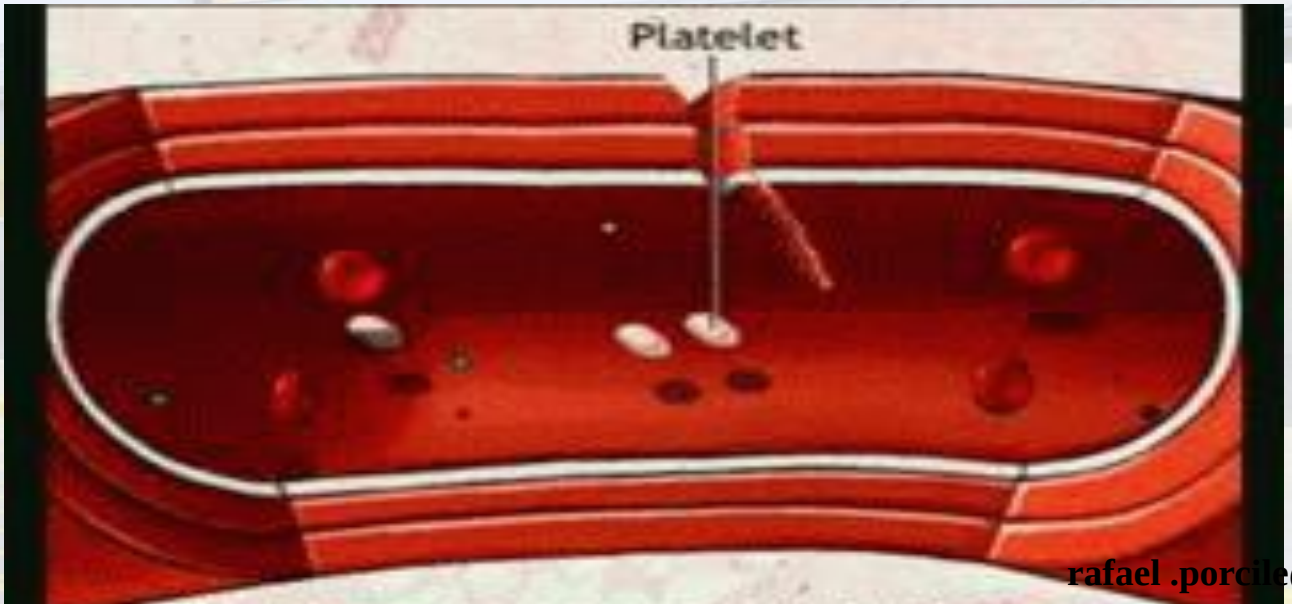
- Vasoconstricción mediada por endotelina
- Función de barrera endotelial

LESIÓN VASCULAR

VASOCONSTRICCIÓN

COAGULACIÓN

EXPOSICIÓN DEL SUBENDOTELIO (COLÁGENO)



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ADHESIÓN PLAQUETARIA

CAMBIO DE FORMA

AGREGACION PRIMARIA (LAXO)

REACCIÓN DE LIBERACIÓN

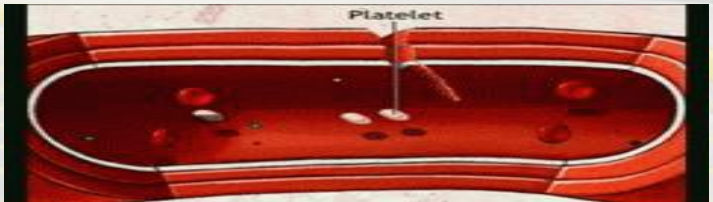
TROMBINA

FIBRINA

ADP ENDOPERÓXIDOS
TROMBOXANO A2
SEROTONINA, ETC

AGREGACION 2DARIA.
TAPÓN DEFINITIVO

REACCIONES LIMITANTES



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EXISTEN TRES PASOS IMPORTANTES

1.- contracción del <u>músculo liso</u> de la pared del vaso lesionado.

2.- adherencia de las <u>plaquetas circulantes</u> y posterior agregación. originando el tapón plaquetario.

3.- <u>coagulación</u> de la sangre.

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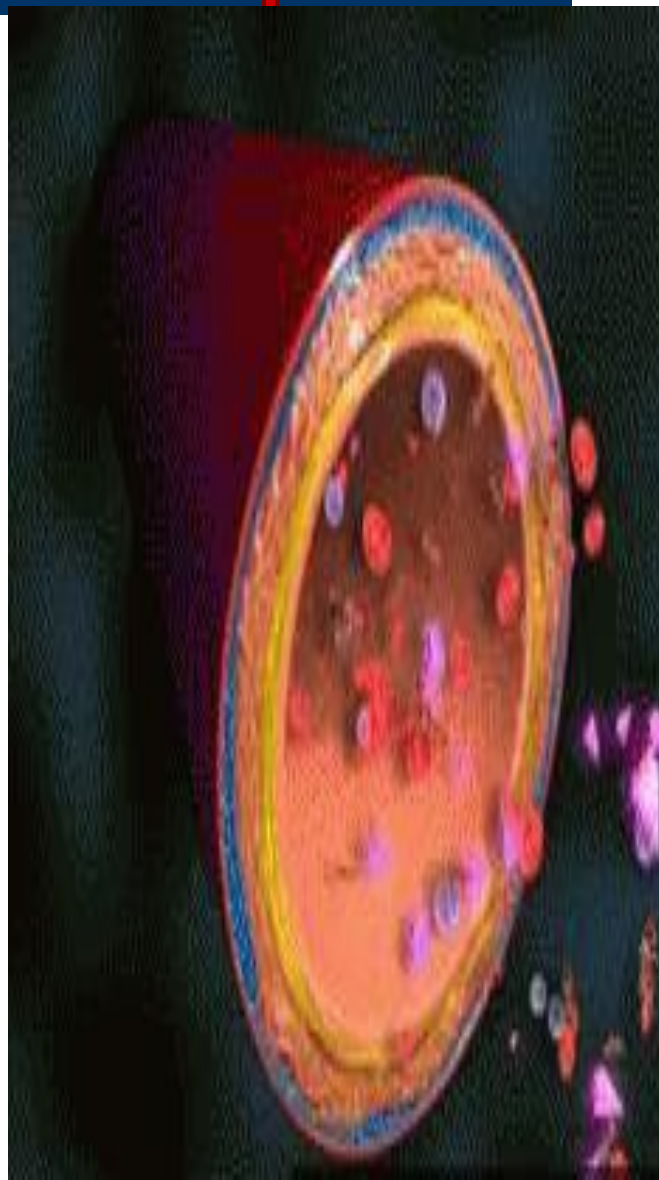
Hemostasia

Hemostasia primaria

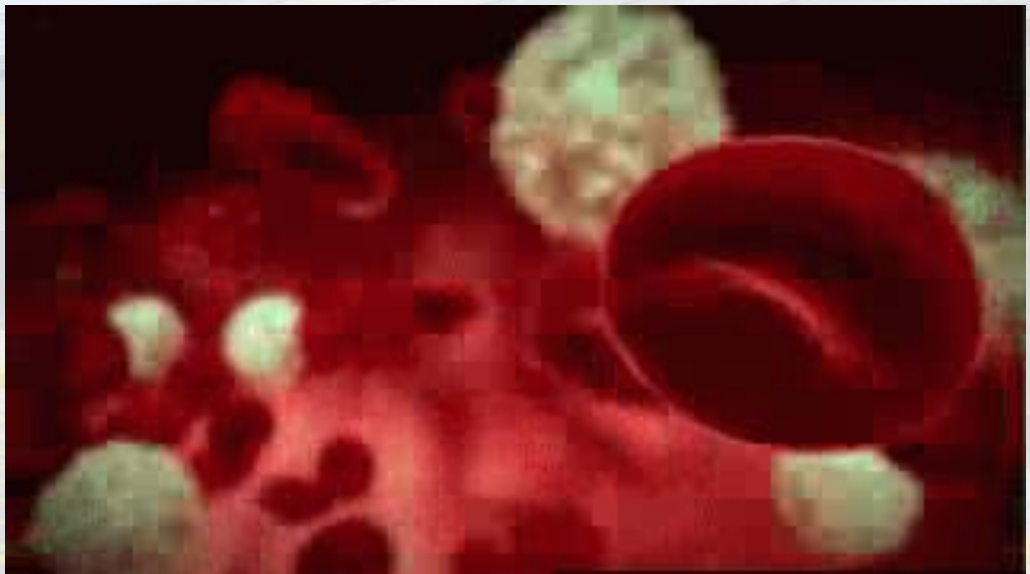
- **Espasmo vascular**
  1) Vasoconstricción nerviosa
     - SNS → noradrenalina
  2) Vasoconstricción química
     - Plaquetas → serotonina, ADP, TXA_2
- **Formación del tapón plaquetario**
  1) Adhesión plaquetaria
  2) Reacción de liberación plaquetaria
  3) Agregación plaquetaria



HEMOSTASIA SECUNDARIA:

PERMITE EL MANTENIMIENTO DEL TAPÓN HASTA LA CICATRIZACIÓN COMPLETA.

EL TAPÓN SE REABSORBE POR "FIBRINOLOSIS", REEMPLAZO POR TEJIDO ORGANIZADO.



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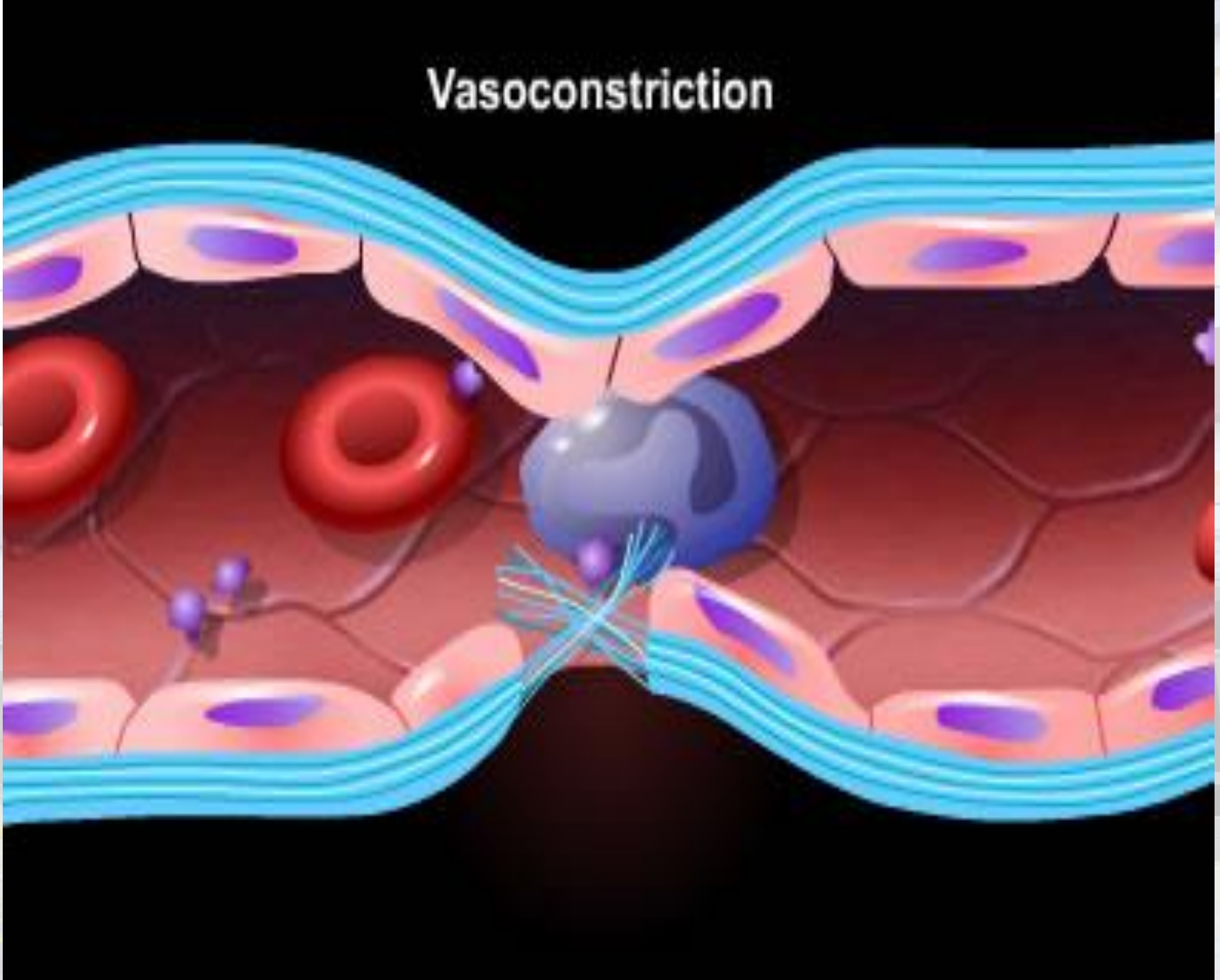
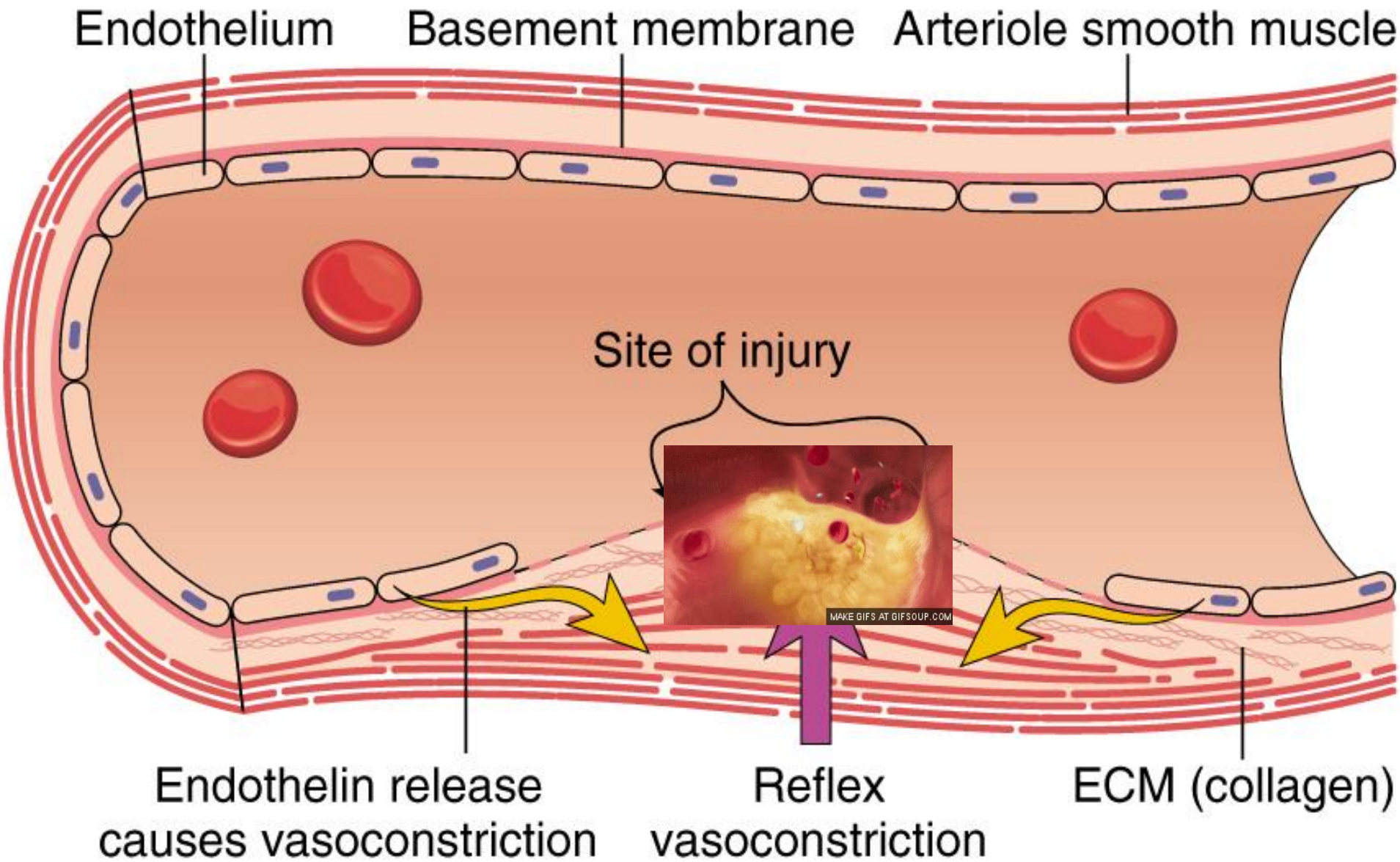

Vasoconstriction

Siempre, todo daño endotelial cursa con vasocontricción

A. VASOCONSTRICTION



VASOCONSTRICCION

- Músculo liso vascular
- Reduce flujo sanguíneo a la zona dañada
- Facilita fases hemostáticas siguientes
- Serotoninas plaquetarias y TxA2
- Endotelina
- Bradicinina: ↑ permeabilidad vascular

Espasmo vascular

Traumatismo en la pared del vaso => el musculo liso se contraiga => disminuye el flujo sanguíneo.

Reflejos nerviosos.

Factores de contracción:

factores autacoides locales de plaquetas y tejidos (tromboxano A2).

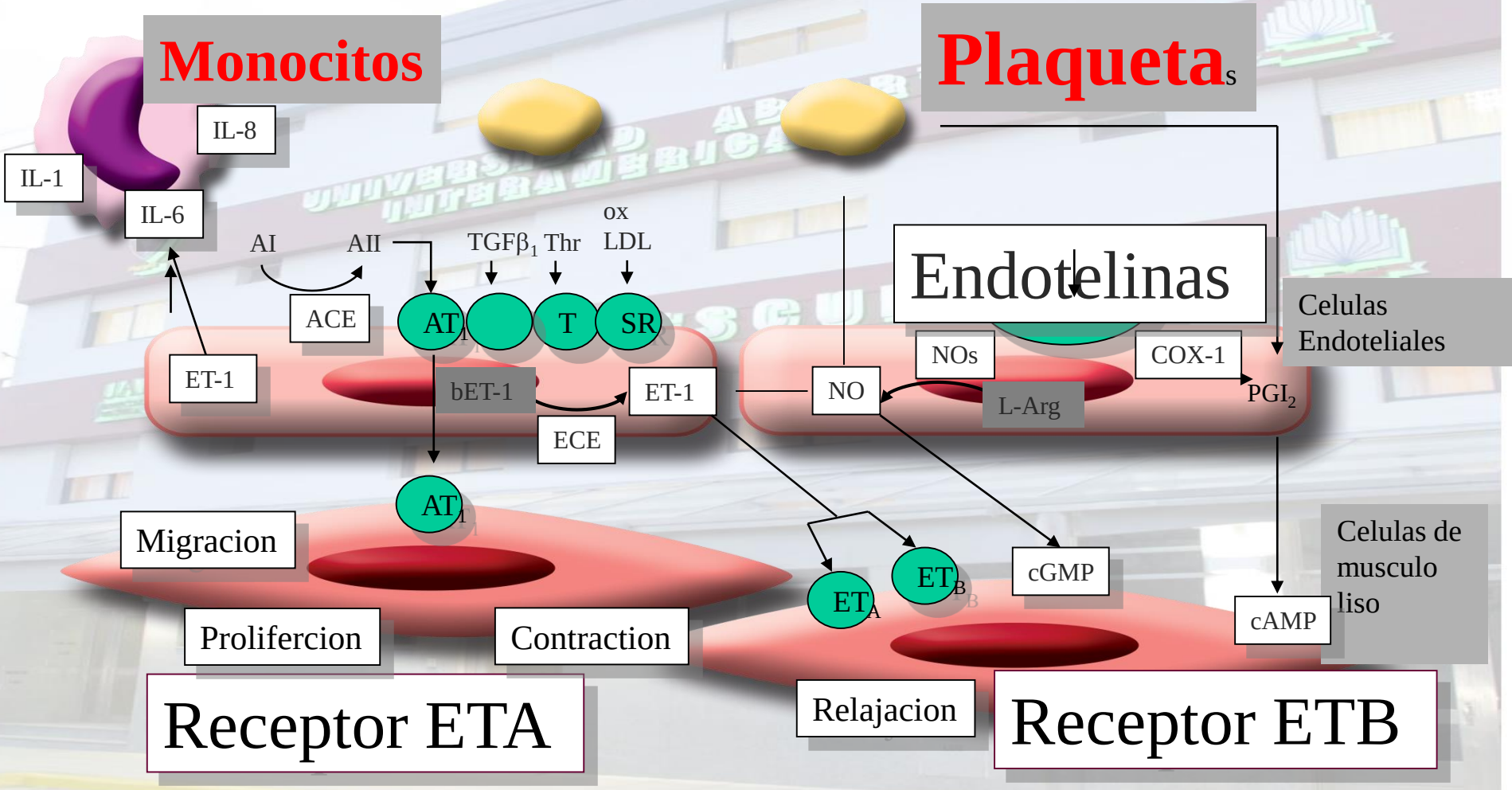
Espasmo miógeno local.

SUSTANCIAS VASOCONSTRICTORAS DEL ENDOTELIO.

- ENDOTELINA
- TROMBOXANO A2
- ANGIOTENSINA II

ENDOTELINA

desempeña un papel importante en el daño endotelial



Vasoconstriccion

SMC migracion + proliferacion

ET-1 clearance

Vasodilacion/antiproliferativo

Spieker LE *et al J Am Coll Cardiol* 2001; 37: 1493–1505

Primaria → secundaria

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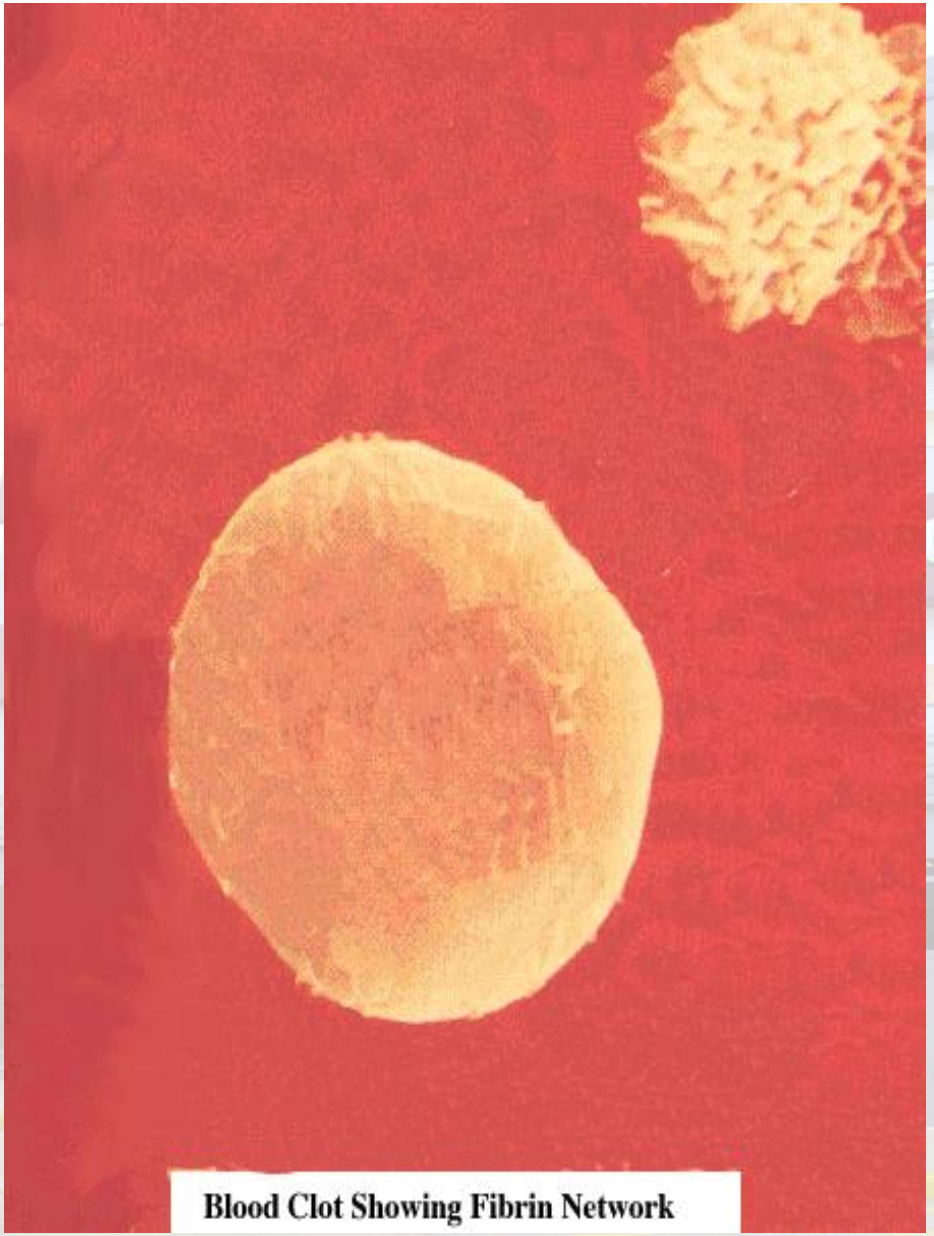


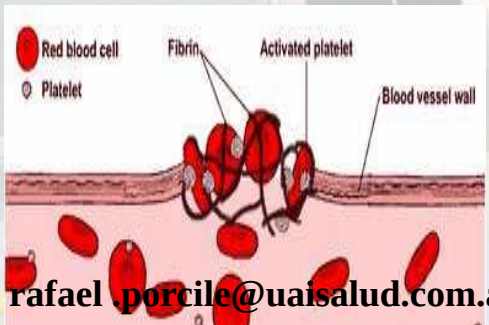
Adhesion paquetaria

+

Agregación plaquetaria

=

Tapón plaquetario



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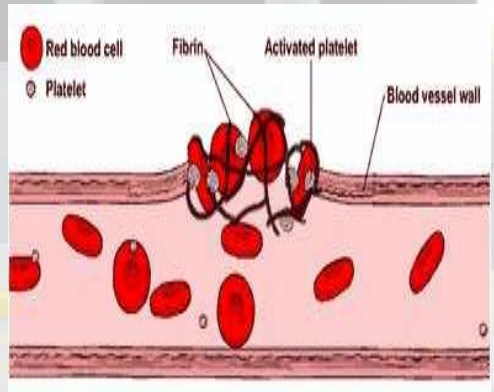
(a few seconds later)

De tapon plaquetario primario
a
plaquetario estable
a
tapon hemostatico



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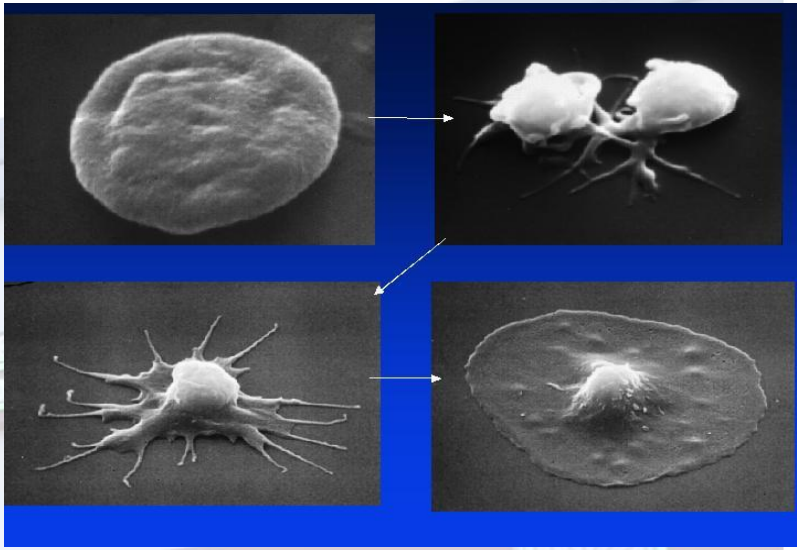
Coagulación



Fibrinogeno → **Fibrina**

plaquetario estable
a
tapon hemostatico

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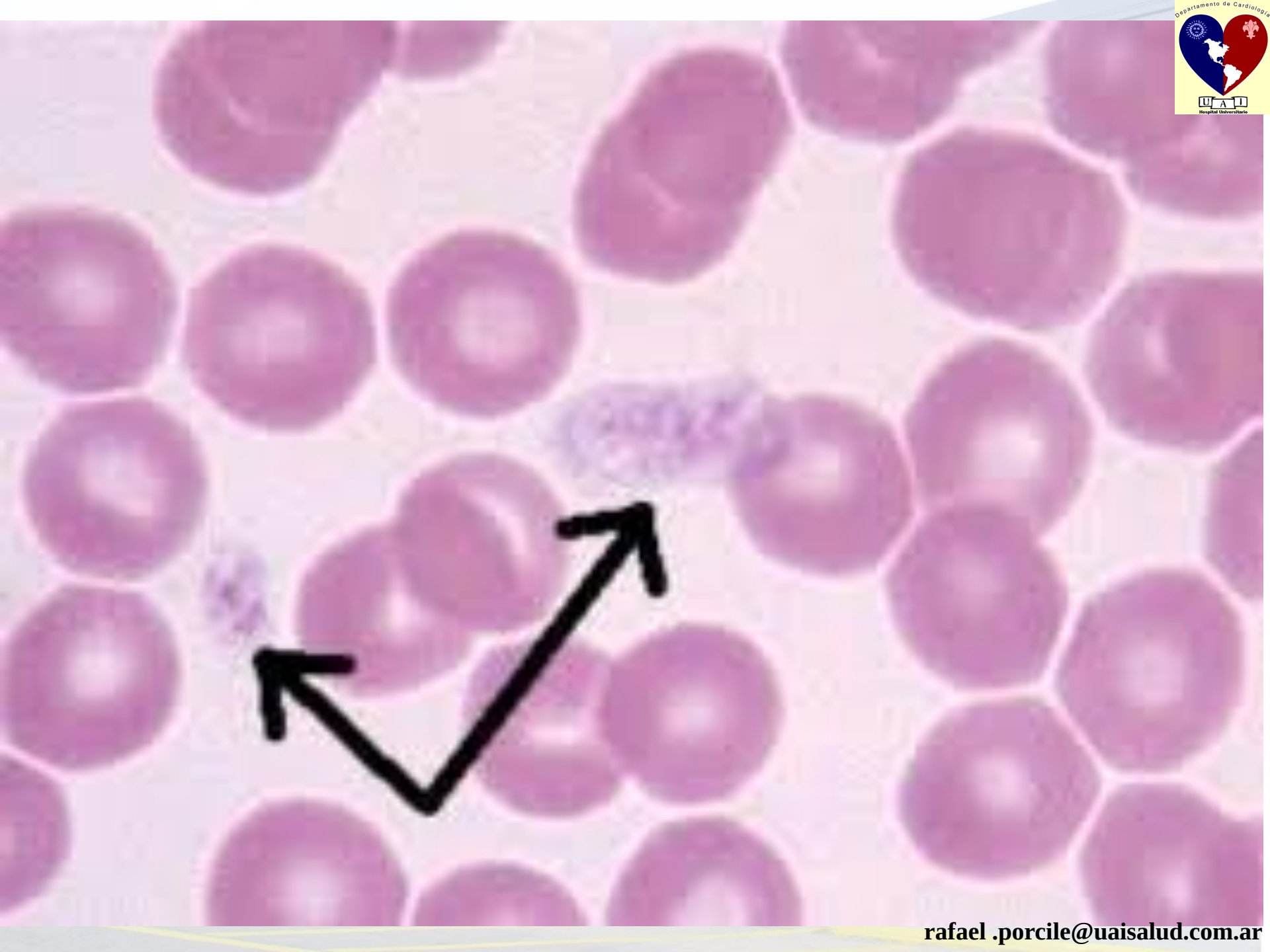

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Dialogo químico entre plaquetas y endotelio

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ACTIVACIÓN Y RESPUESTA PLAQUETARIA

1.- ACTIVACIÓN POR DIFERENTES "INDUCTORES" (TROMBINA, COLÁGENO, ADP).

PARCIALMENTE ACTIVADAS: POR SUST.EXTRAÑAS (VIDRIO) U OTRAS PLAQUETAS.

2.-RESPUESTA PLAQUETARIA: SIMILAR PARA TODOS LOS INDUCTORES.

a) CAMBIO DE FORMA

b) AGREGACIÓN (SE ACUMULAN)

c) 3 PROCESOS SECRETORIOS DIFERENTES (ADP)

d) LIBERACIÓN DE AC.ARAQUIDÓNICO (PG Y TX. A_2)

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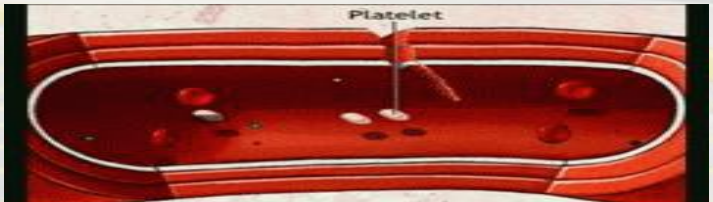

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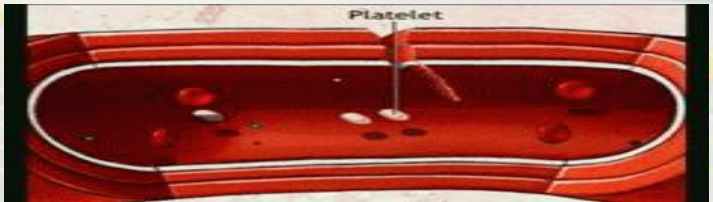

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Plaquetas

Médula osea – megacariocitos – plaquetas

- No tienen núcleo

Circulan de 150,000 – 400,000/mm.

- Vida media de 7 – 9 días

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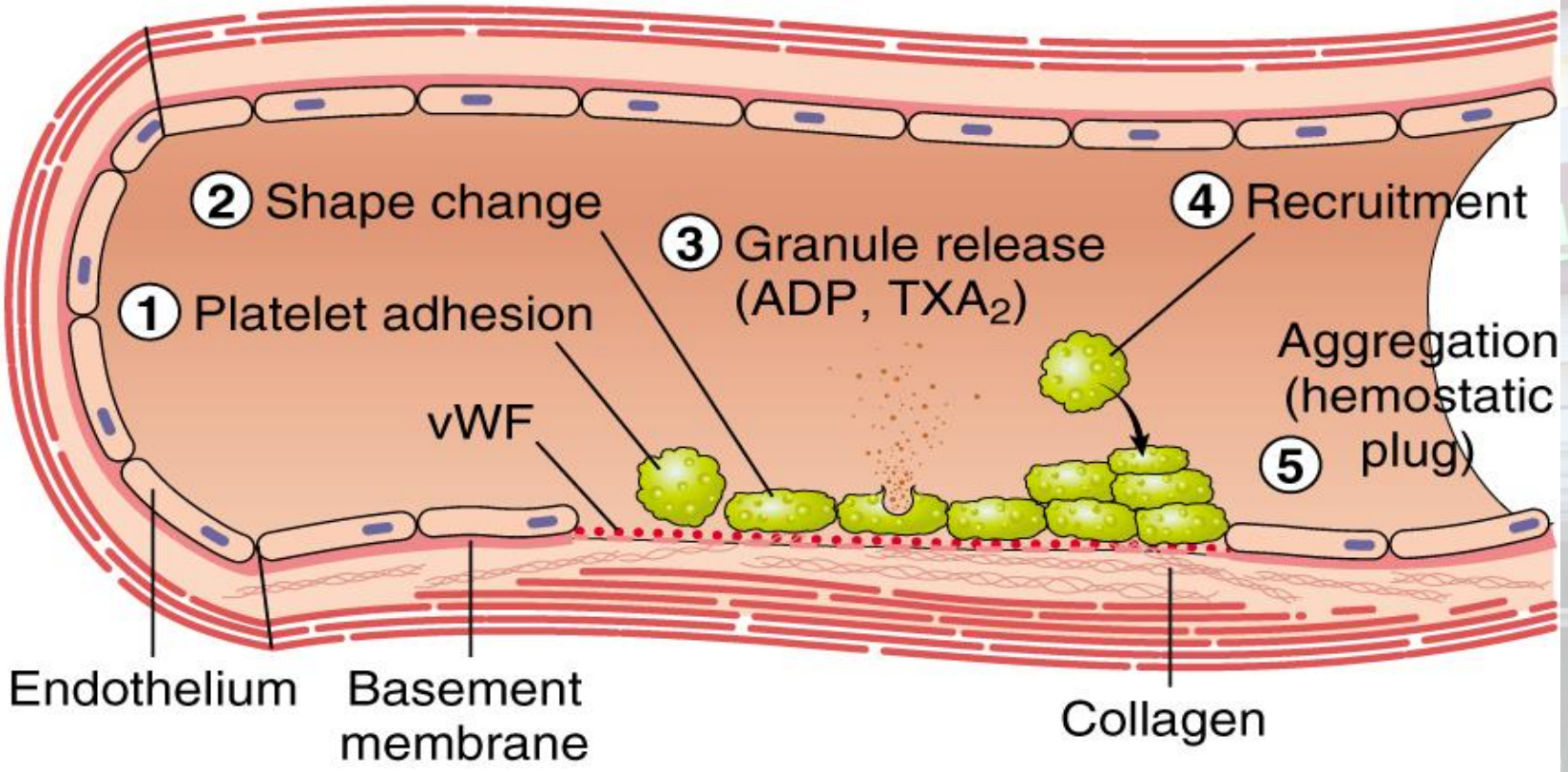
B. PRIMARY HEMOSTASIS



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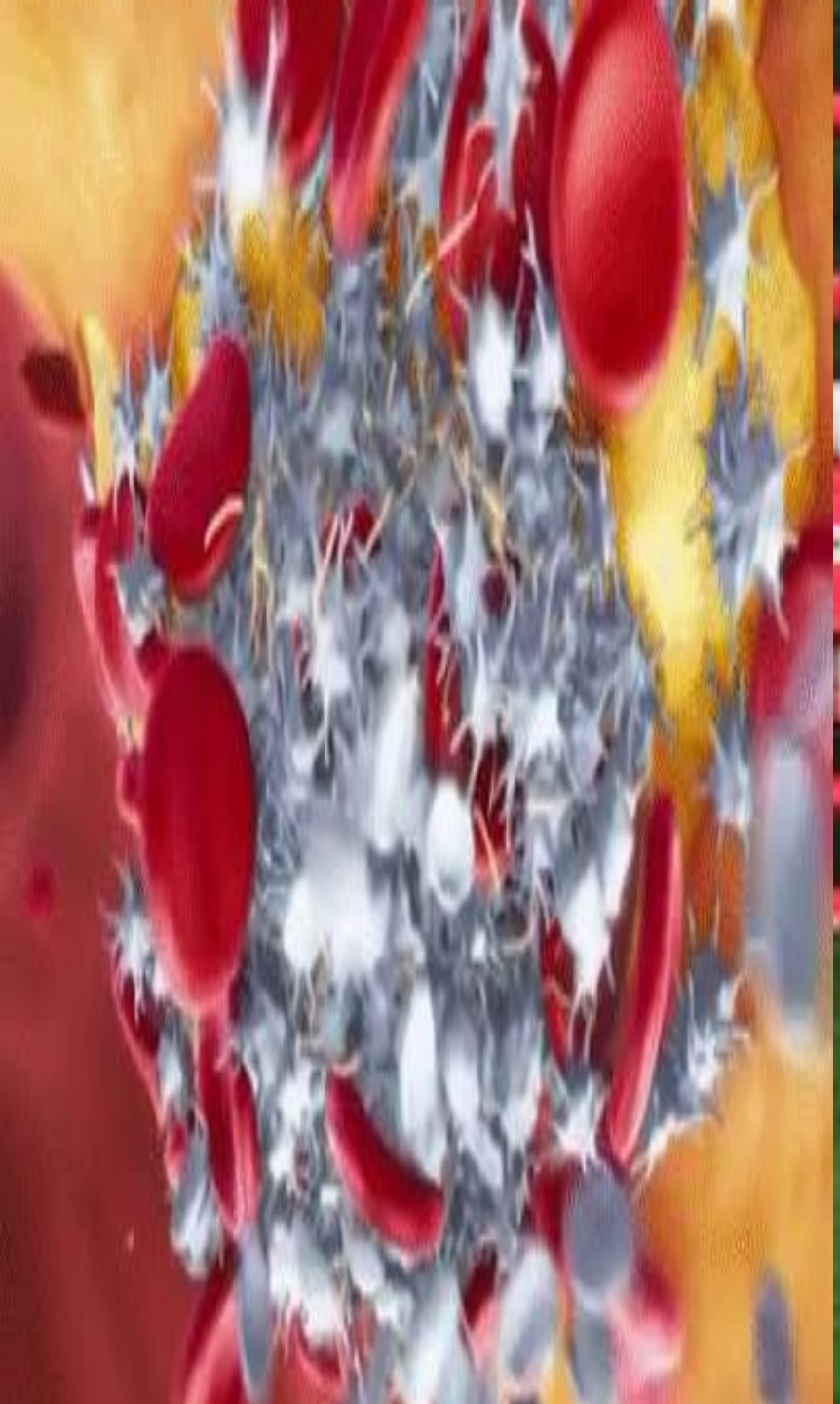


15

Primaria → secundaria

Cuatro mecanismos

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La adhesión

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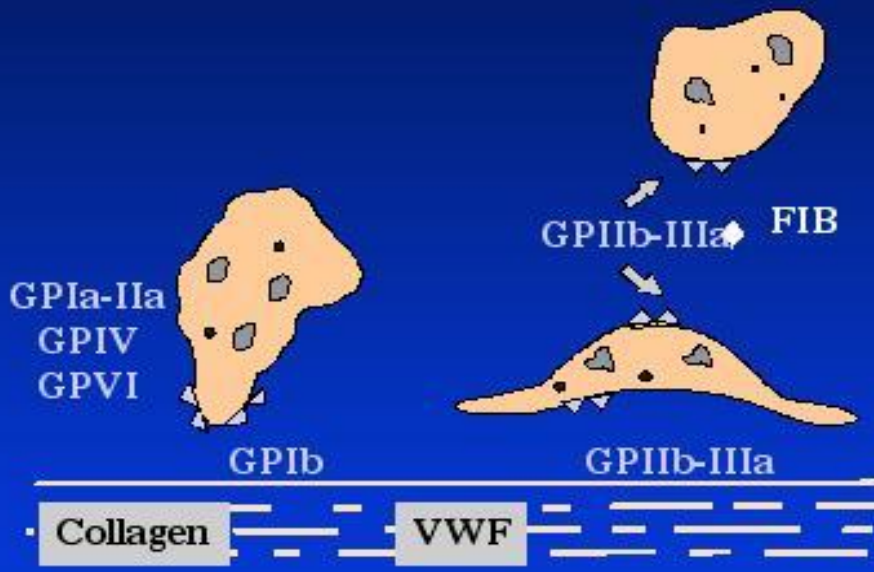
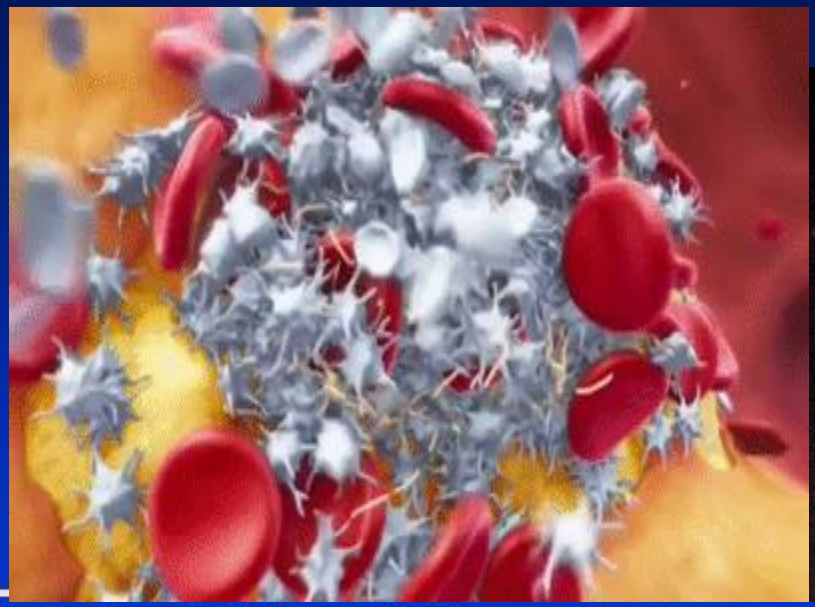
PLATELET FUNCTIONS





CONTACT ADHESION AGGREGATION AND RELEASE

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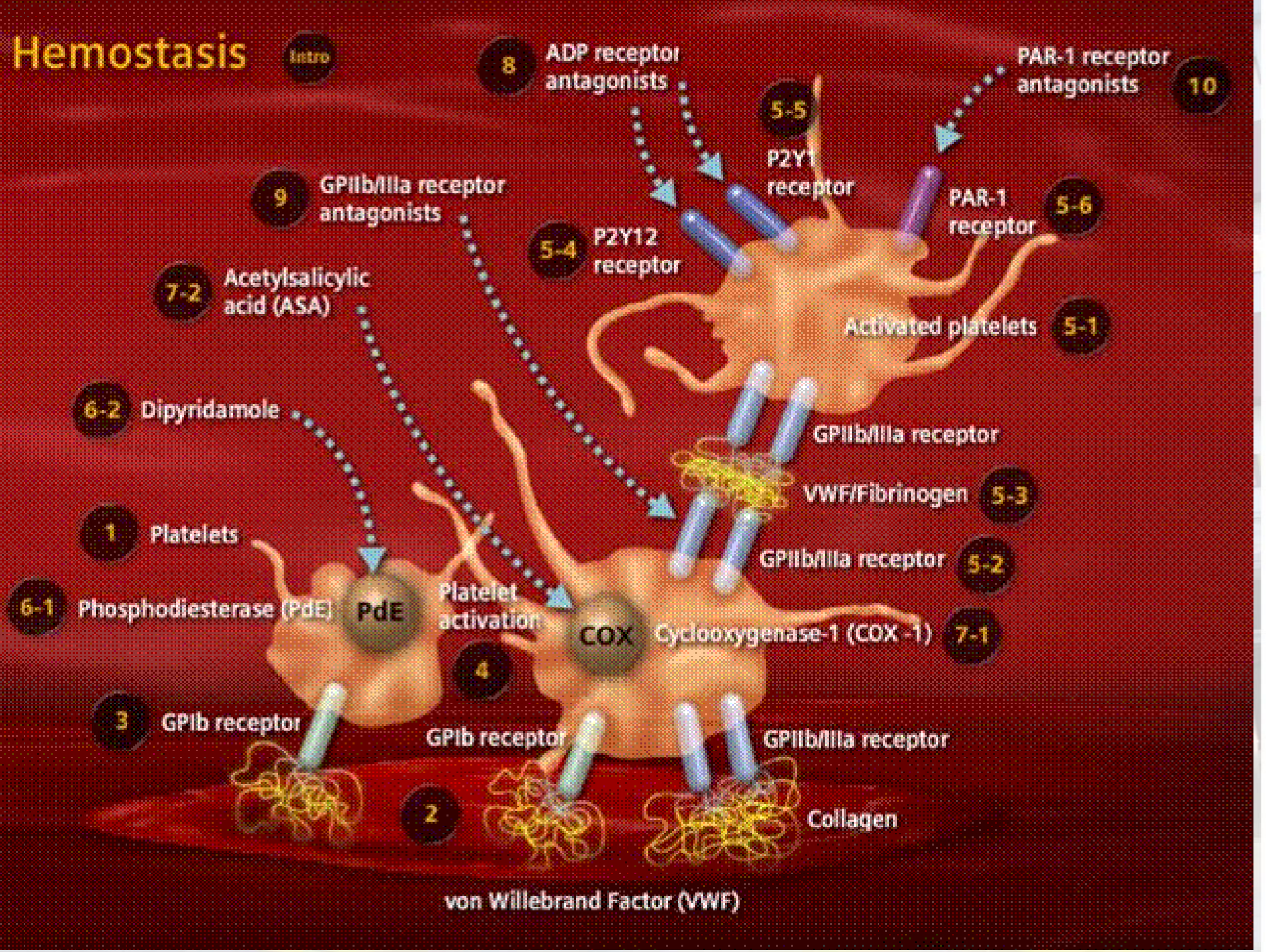
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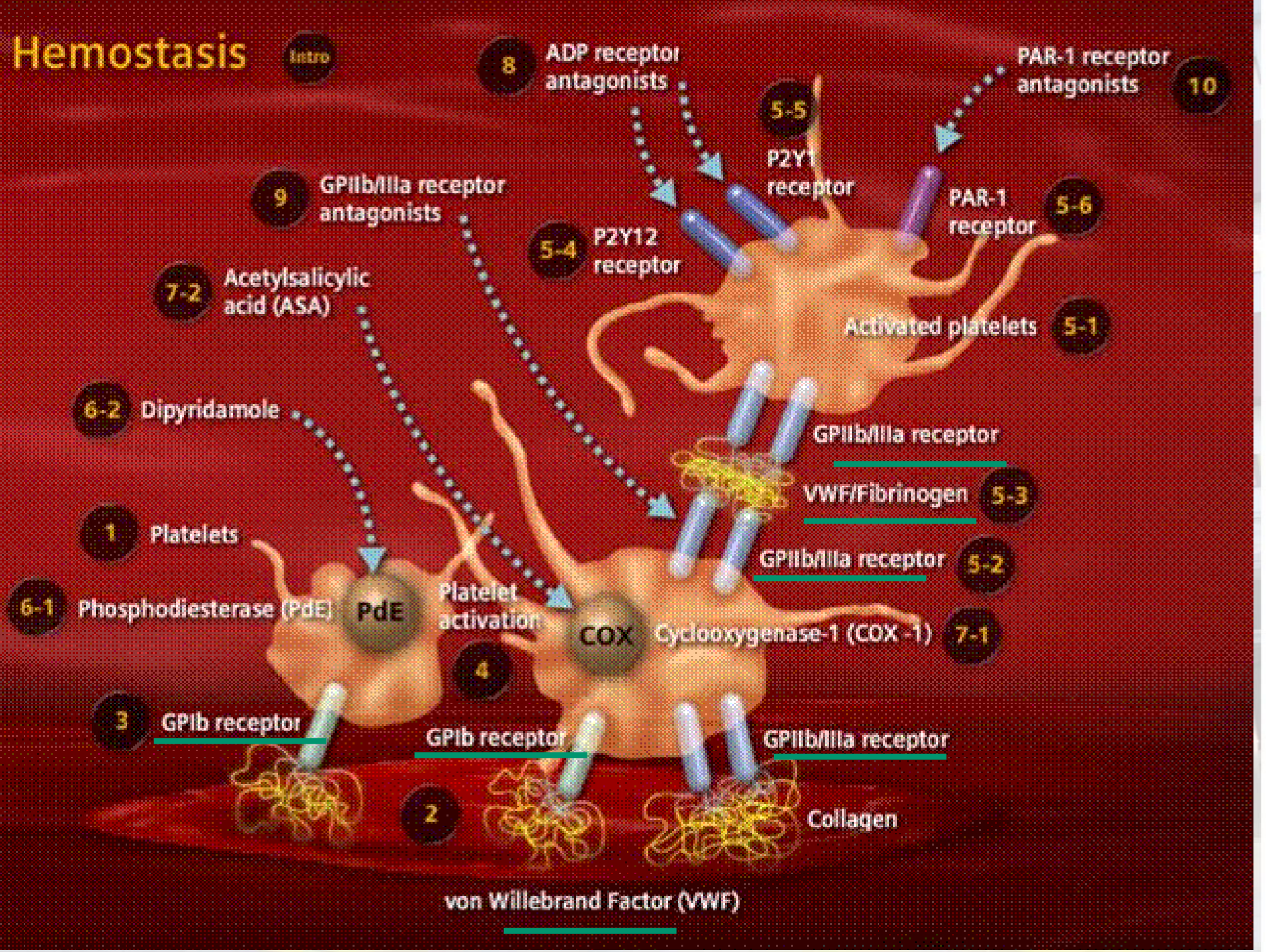
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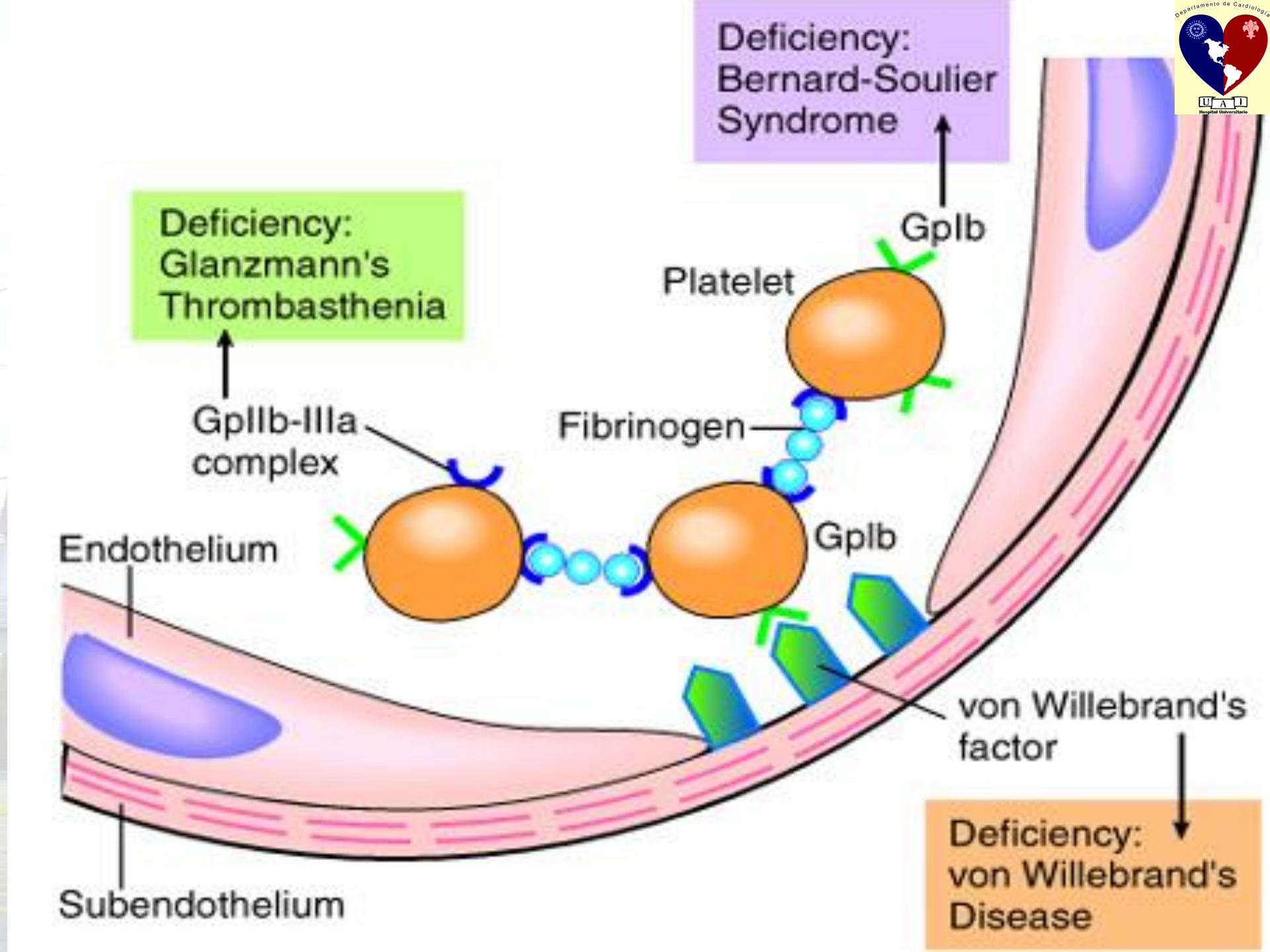
Deficiency:
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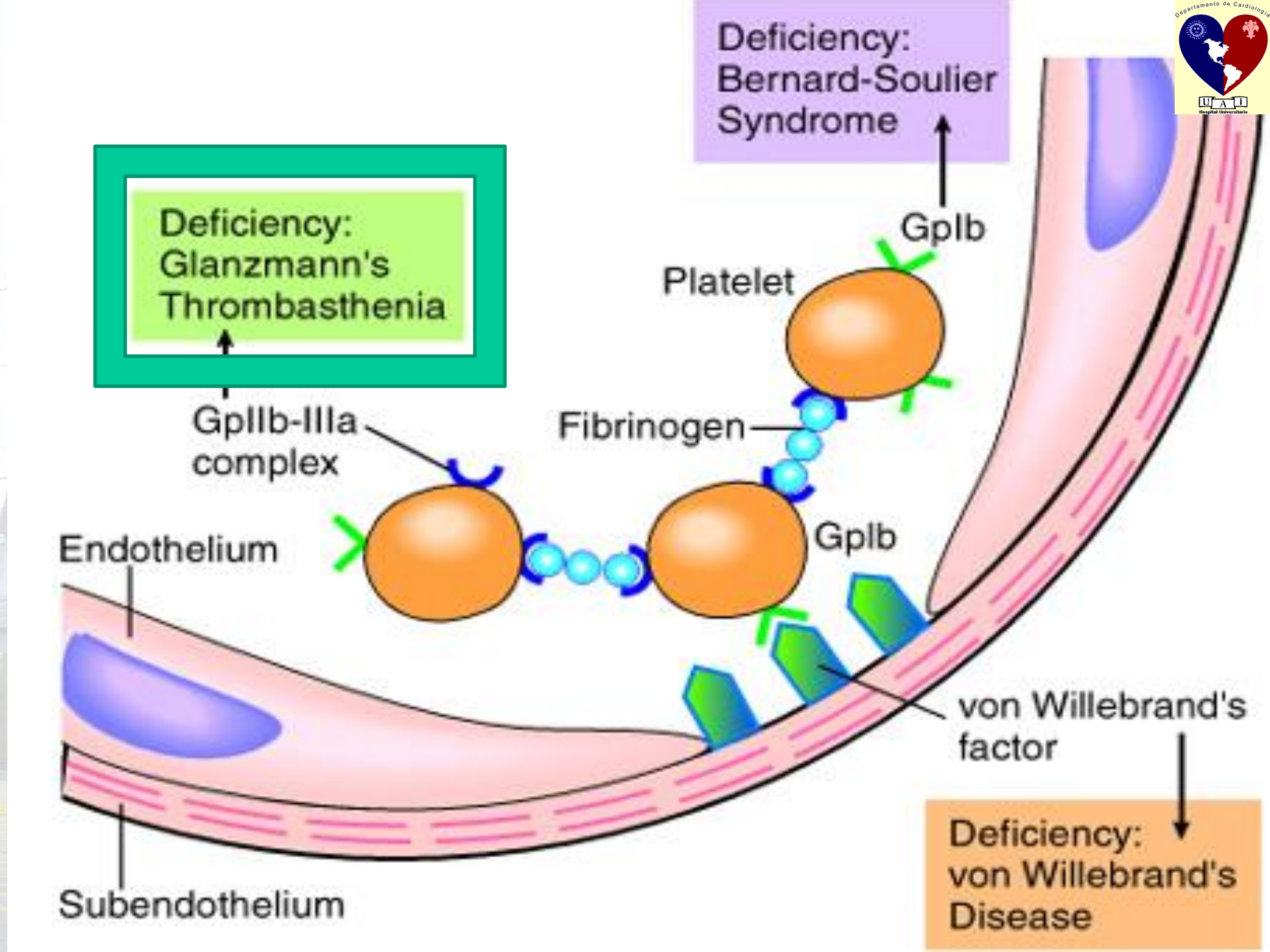
Syndrome
Deficiency:
Glanzmann's
Thrombasthenia
GpIb
Platelet
GpIIb-IIIa
complex
Fibrinogen
Endothelium
GpIb
von Willebrand's
factor
Subendothelium
Deficiency:
von Willebrand's
Disease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Disease

βetascript publishing

Glanzmann's Thrombasthenia

Autoimmune Disorder, Coagulopathy

High Quality Content by WIKIPEDIA articles!

Lambert M. Surhone, Miriam T. Timpledon, Susan F. Henssonow (Ed.)

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La enfermedad de Glanzmann o trombastenia es una enfermedad hereditaria con un patrón de herencia de tipo autosómico recesivo en la que el recuento de plaquetas es normal, pero aparecen aisladas sobre el frotis de sangre. El tiempo de sangrado es prolongado, la retracción del coágulo está ausente o disminuida y las plaquetas no se aglutinan al agregar ADP. La cifra de fibrinógeno plaquetario es baja. Se presenta una alteración de la disponibilidad del factor plaquetario 3

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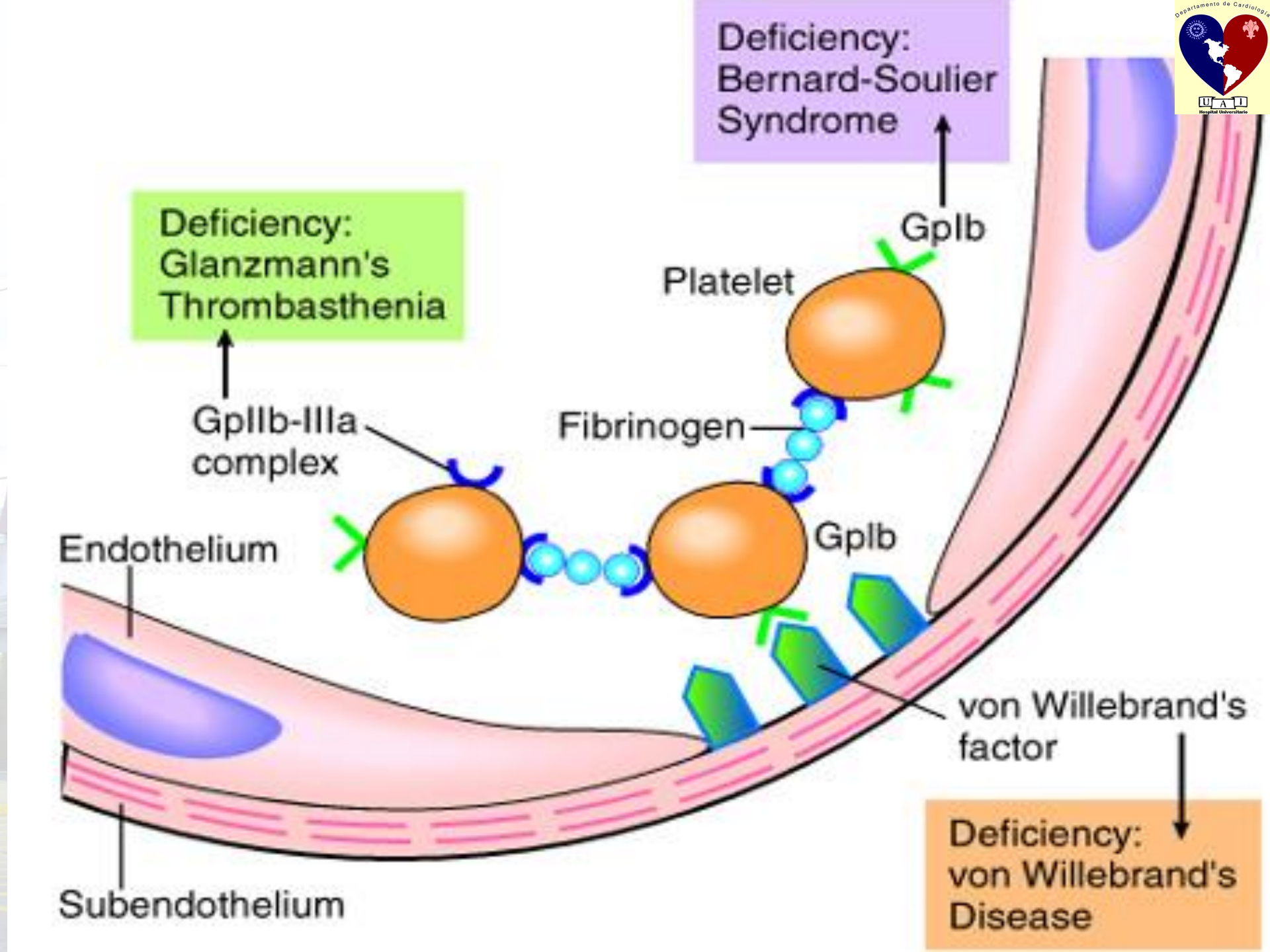
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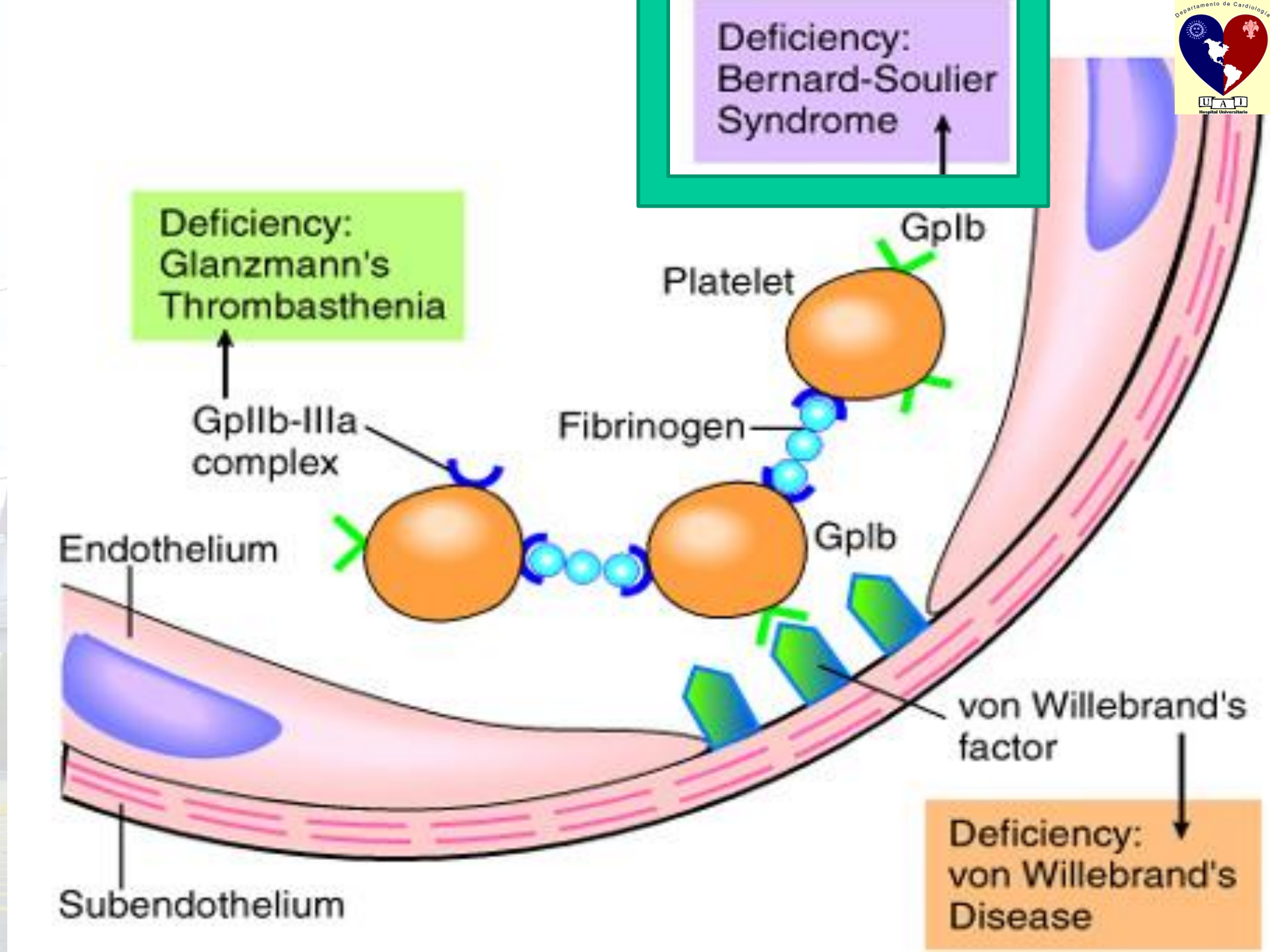
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Subendothelium

El Síndrome de Bernard-Soulier también llamado distrofia trombocítica hemorrágica es una enfermedad rara genética de herencia autosómica recesiva que afecta la correcta coagulación debido a la deficiencia de la glicoproteína Ib, receptor para el factor de von Willebrand, alterando de esta forma la hemostasia primaria

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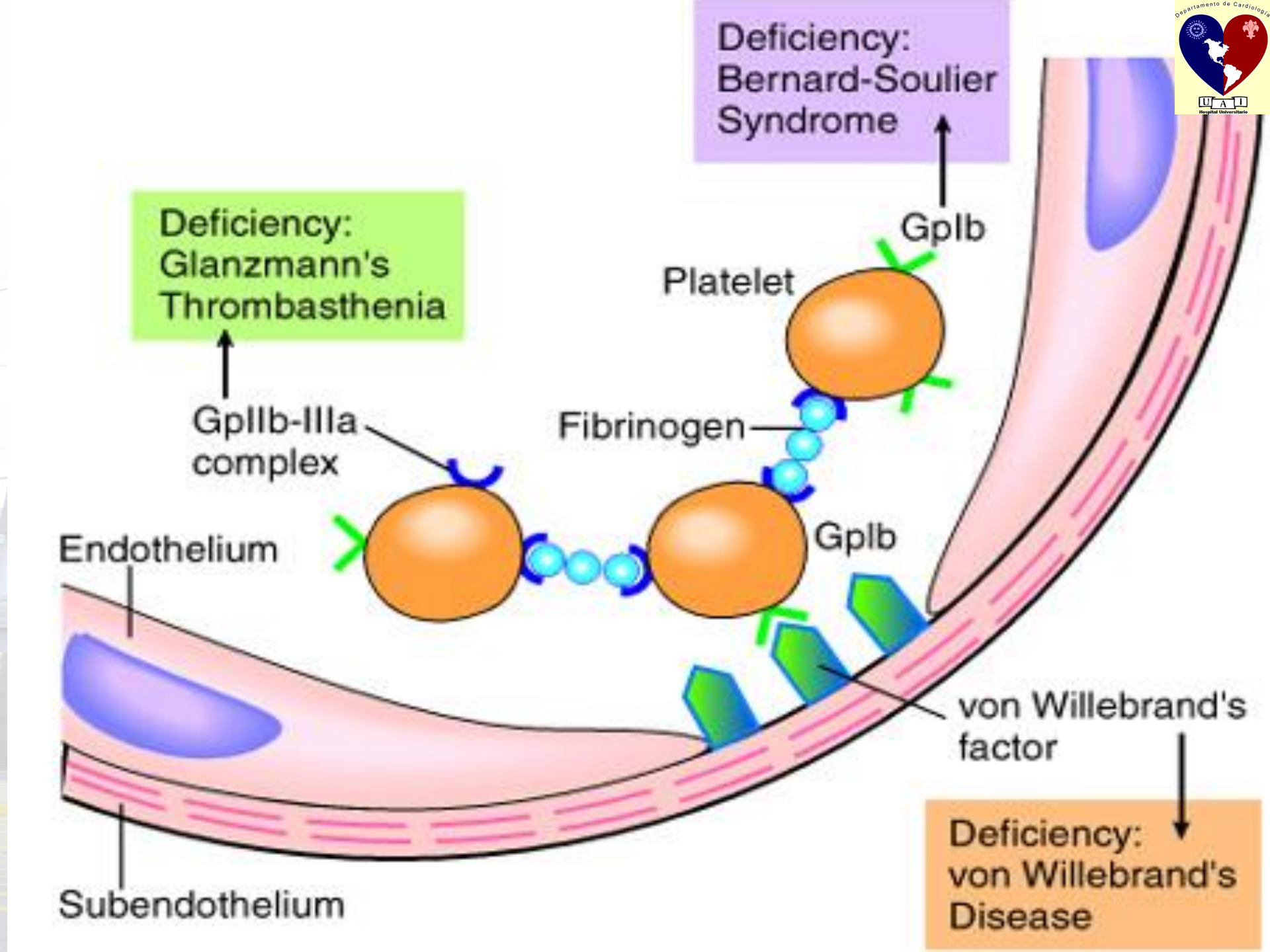
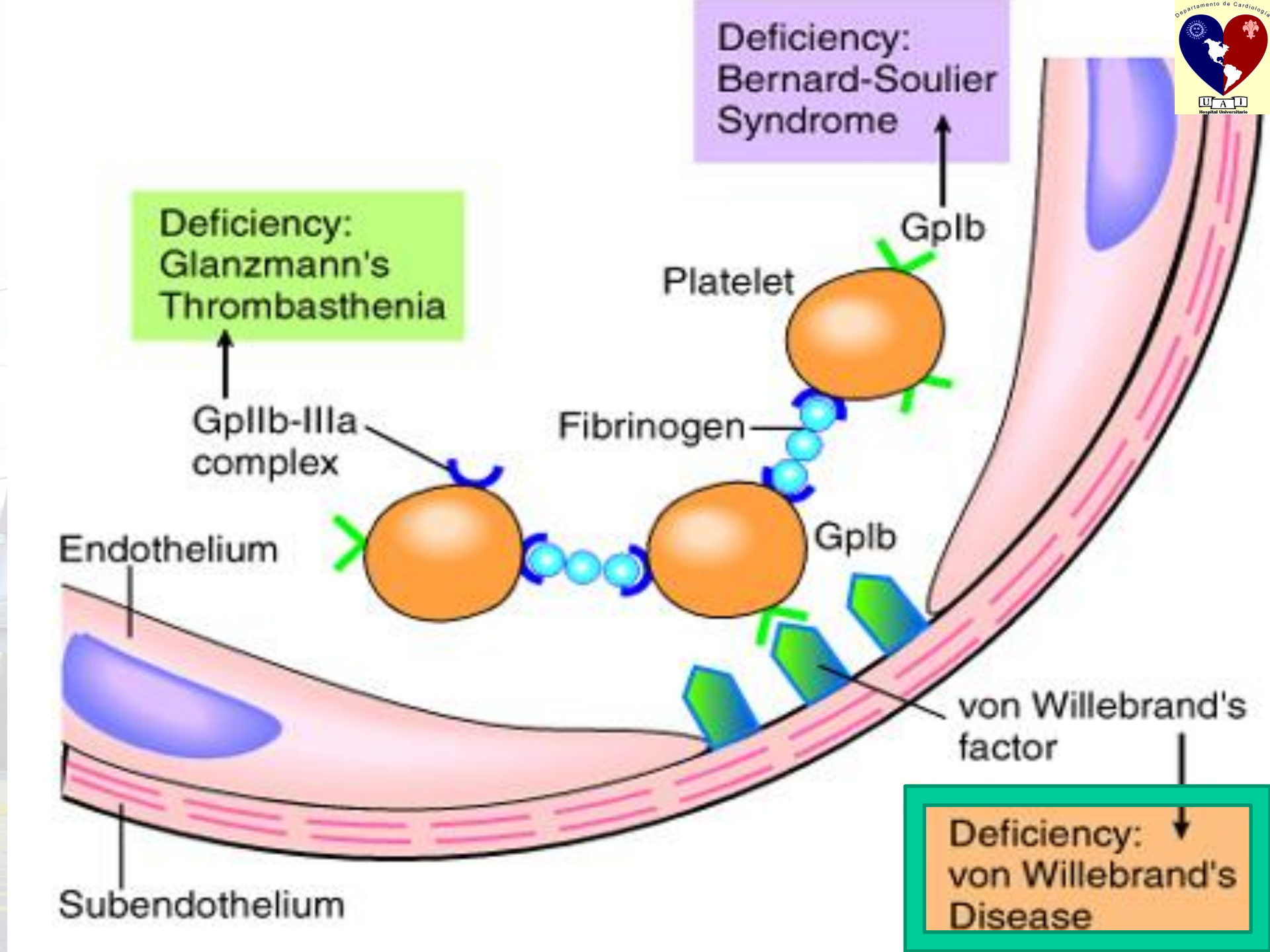

Deficiency:
Bernard-Soulier
Syndrome
Deficiency:
Glanzmann's
Thrombasthenia
GpIb
Platelet
GpIIb-IIIa
complex
Fibrinogen
Endothelium
GpIb
von Willebrand's
factor
Subendothelium
Deficiency:
von Willebrand's
Disease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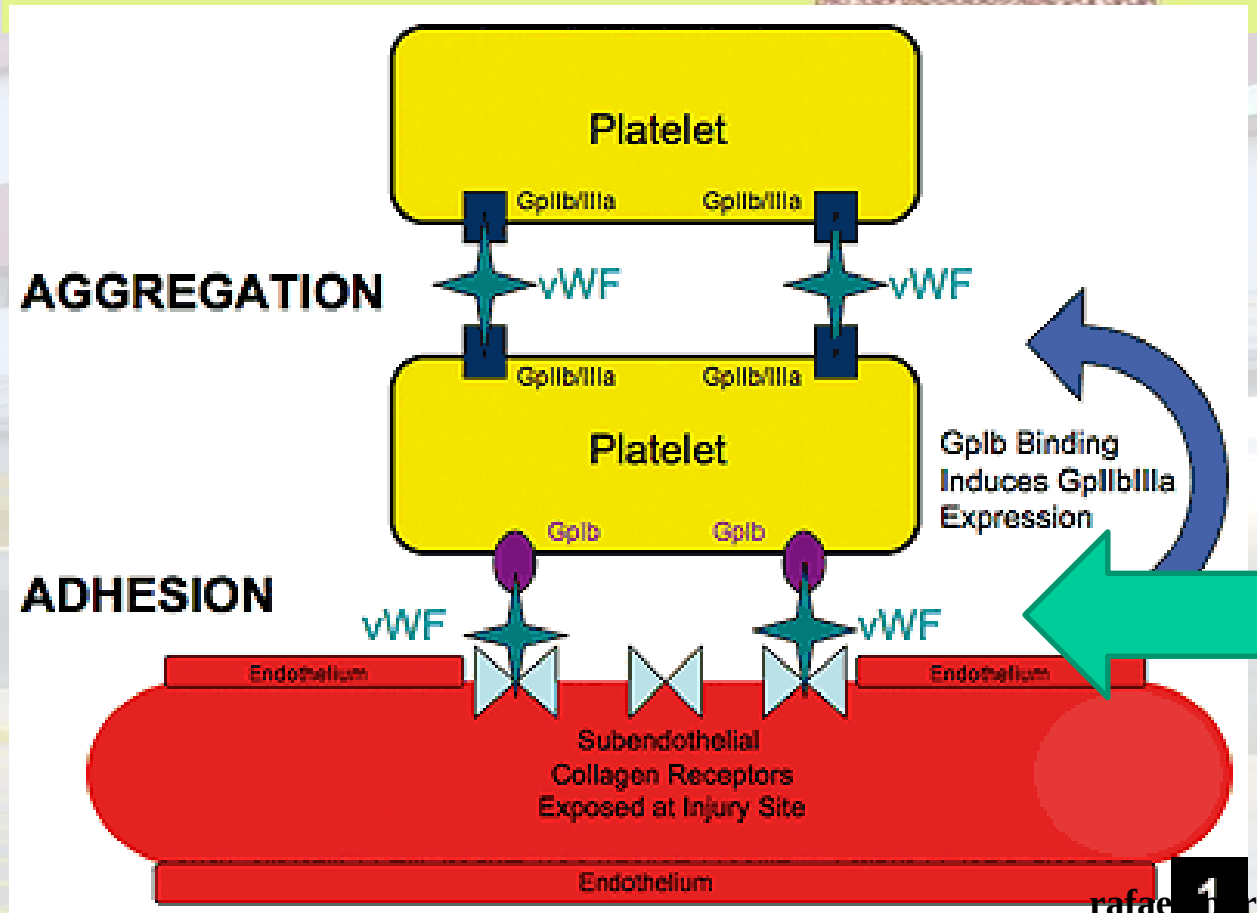
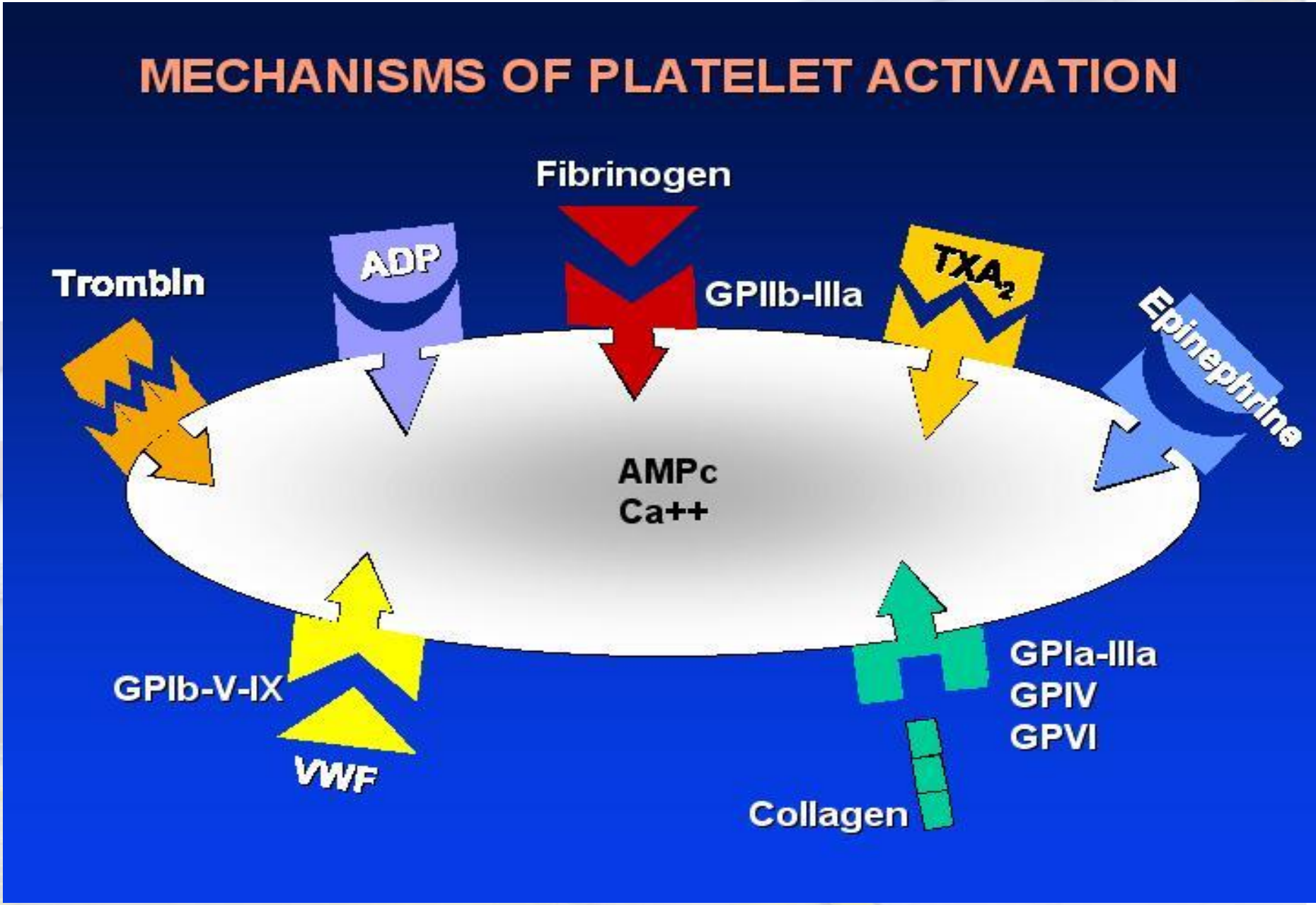
von Willebrand Disease



rafael[illegible]rcile@uaisalud.com.ar



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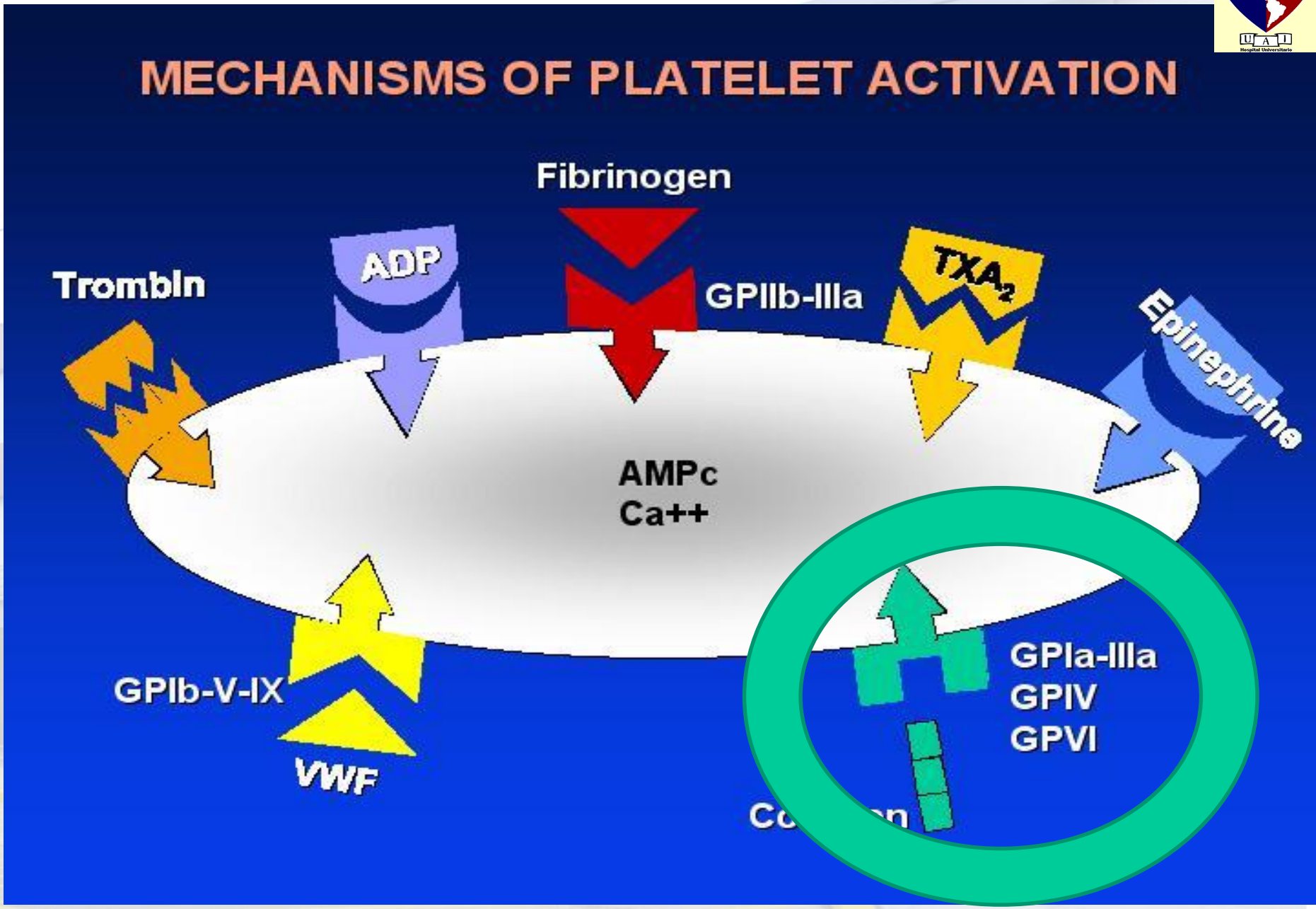

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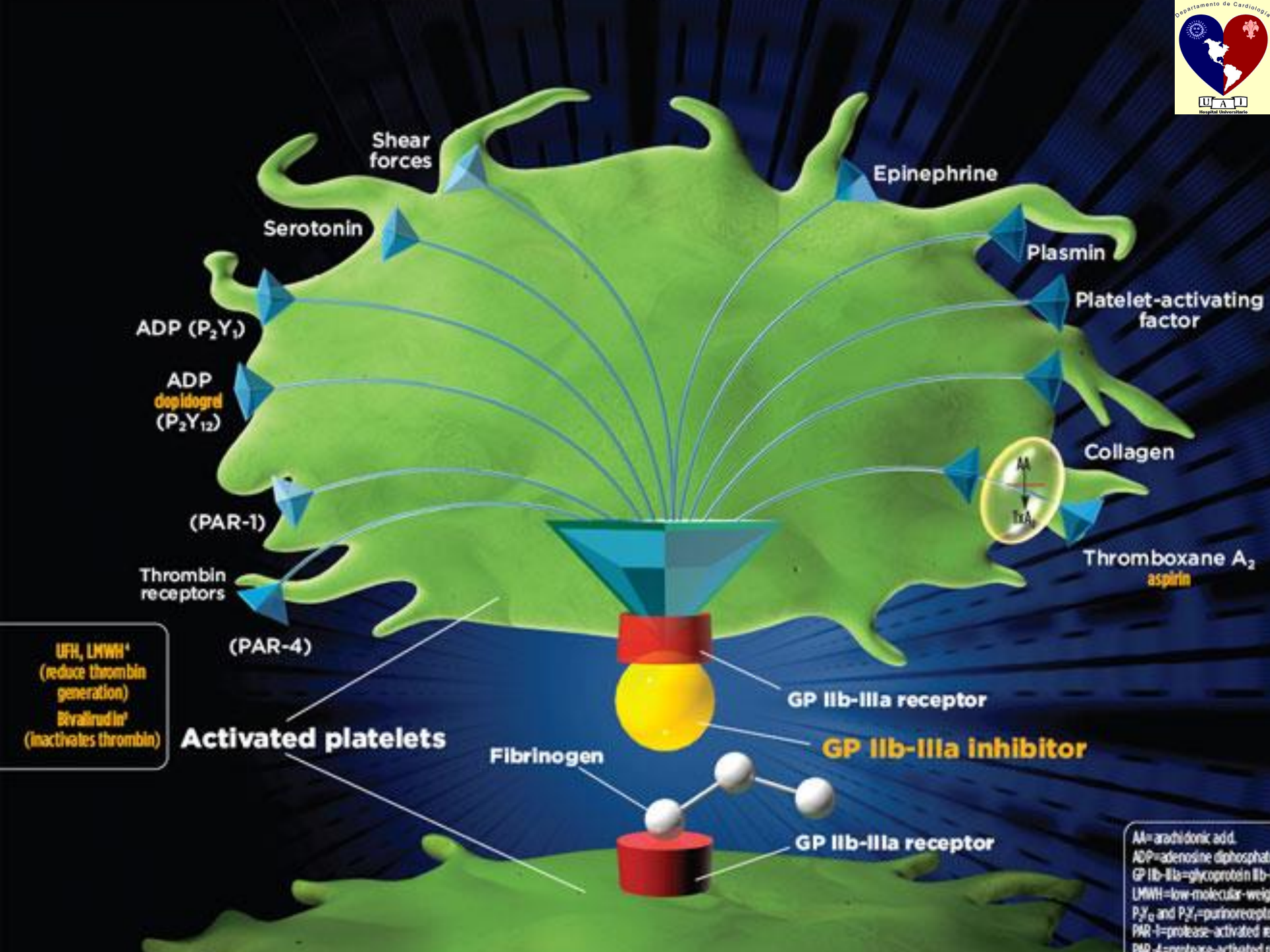
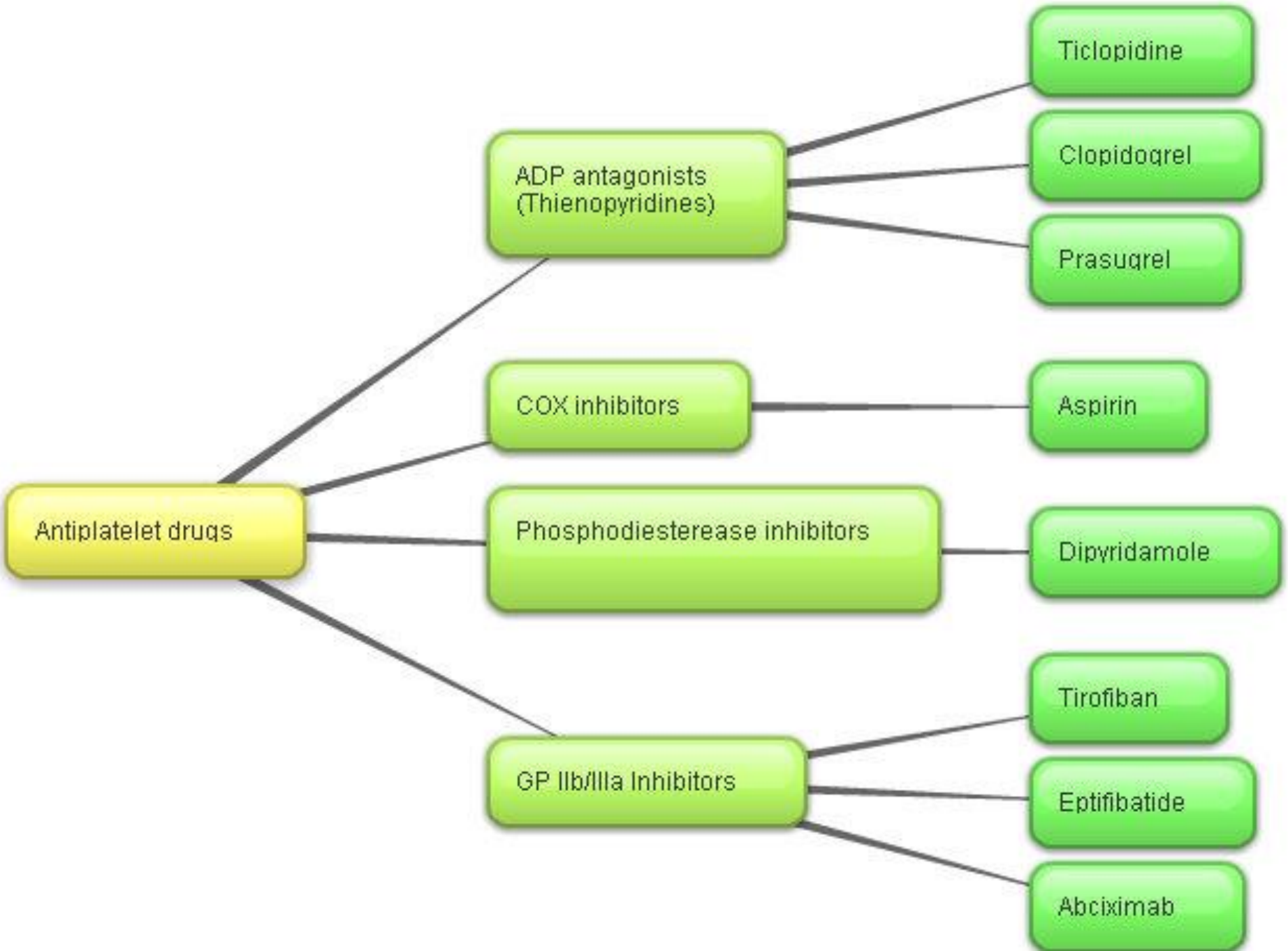

Shear forces
Epinephrine
Serotonin
Plasmin
Platelet-activating factor
ADP (P_2Y_1)
ADP
clopidogrel
(P_2Y_{12})
Collagen
AA
TxA_2
(PAR-1)
Thrombin receptors
Thromboxane A_2
aspirin
(PAR-4)
UFH, LMWH*
(reduce thrombin generation)
Bivalirudin†
(inactivates thrombin)
Activated platelets
GP IIb-IIIa receptor
GP IIb-IIIa inhibitor
Fibrinogen
GP IIb-IIIa receptor
AA=arachidonic acid.
ADP=adenosine diphosphat
GP IIb-IIIa=glycoprotein IIb-
LMWH=low-molecular-weig
PAR-1=protease-activated


Antiplatelet drugs
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Clopidogrel
Prasugrel
COX inhibitors
Aspirin
Phosphodiesterease inhibitors
Dipyridamole
GP IIb/IIIa Inhibitors
Tirofiban
Eptifibatide
Abciximab

Inhibidores de los receptores GpIIb-IIIa.

Abciximab(ReoPro)

En el estudio **EPIC** 2099 pacientes de alto riesgo en angina inestable fueron randomizados a una de tres ramas:

1.bolo e infusión de placebo,

2.bolo de 0.25 mg/kg de abciximab seguido por infusión de placebo

3.bolo de 0.25 mg/kg de abciximab seguido de una infusión de 10 g / min.

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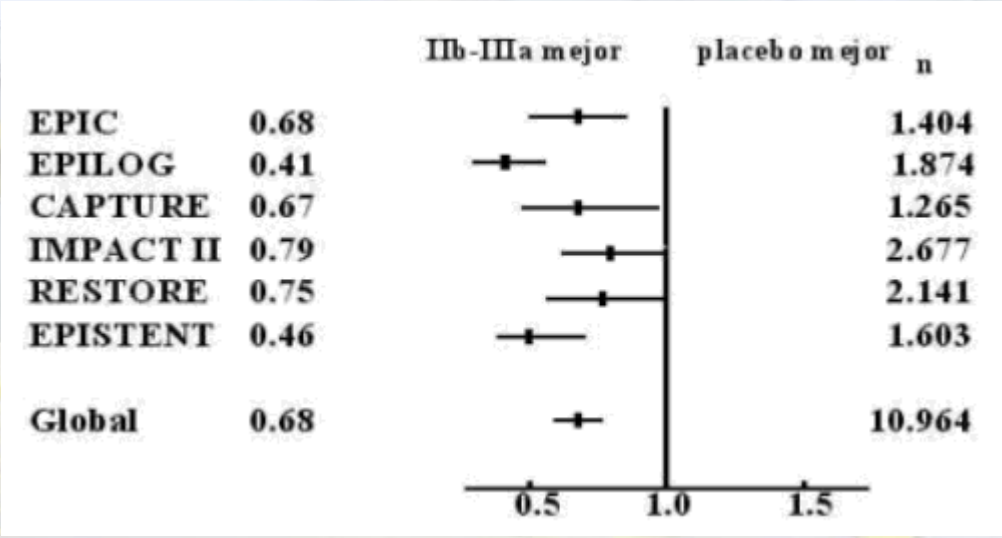
En el grupo que recibió el bolo y la infusión de **abciximab** se encontró una reducción de 35 % (13.1% vs 7.7 %, p=0.008) en la tasa de un punto final combinado de muerte, infarto no fatal y recurrencia de isquemia

Exceso de complicaciones hemorrágicas en el grupo con tratamiento activo.



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Inhibidores de los receptores GpIIb-IIIa En ANGINA INESTABLE

Tirofiban

PRISM es un ensayo multicéntrico con 3231 pacientes, destinado a probar la eficacia de una infusión de tirofiban de 48 horas, comparada con heparina IV en pacientes con angor inestable /IAM no Q tratados con aspirina

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IMPACT I
IMPACT II

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IMPACT II

El punto final primario de muerte/infarto/cirugía no planeada o necesidad de stent por cierrre súbito o repetición de angioplastía, se verificó en 11.4 % de los pacientes placebo, comparado con 9.2 % y 9.9 % en los grupos con ***eptifibatide.***

Con respecto a placebo, en la rama con dosis 135/0.5 el OR fue de 0.79 (0.61-1.01), p=0.063, y en el esquema 135/0.75 de 0.86 (0.67-1.10), p=0.22. **Ninguna de las diferencias alcanzó el nivel de significación**

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Inhibidores de los receptores GpIIb-IIIa En ANGINA INESTABLE

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Inhibidores de los receptores GpIIb-IIIa En ANGINA INESTABLE

Tirofiban ESTIDIO PRISM

Tirofiban redujo el punto final combinado de infarto/muerte/isquemia recurrente a 48 horas de 5.9 % a 3.8 % (OR 0.63 , IC 95 %=0.45-0.88, p<0.007). El tratamiento con tirofiban se asoció a una reducción de la muerte a 30 dias de 3.6 % a 2.3 % (p=0.020).

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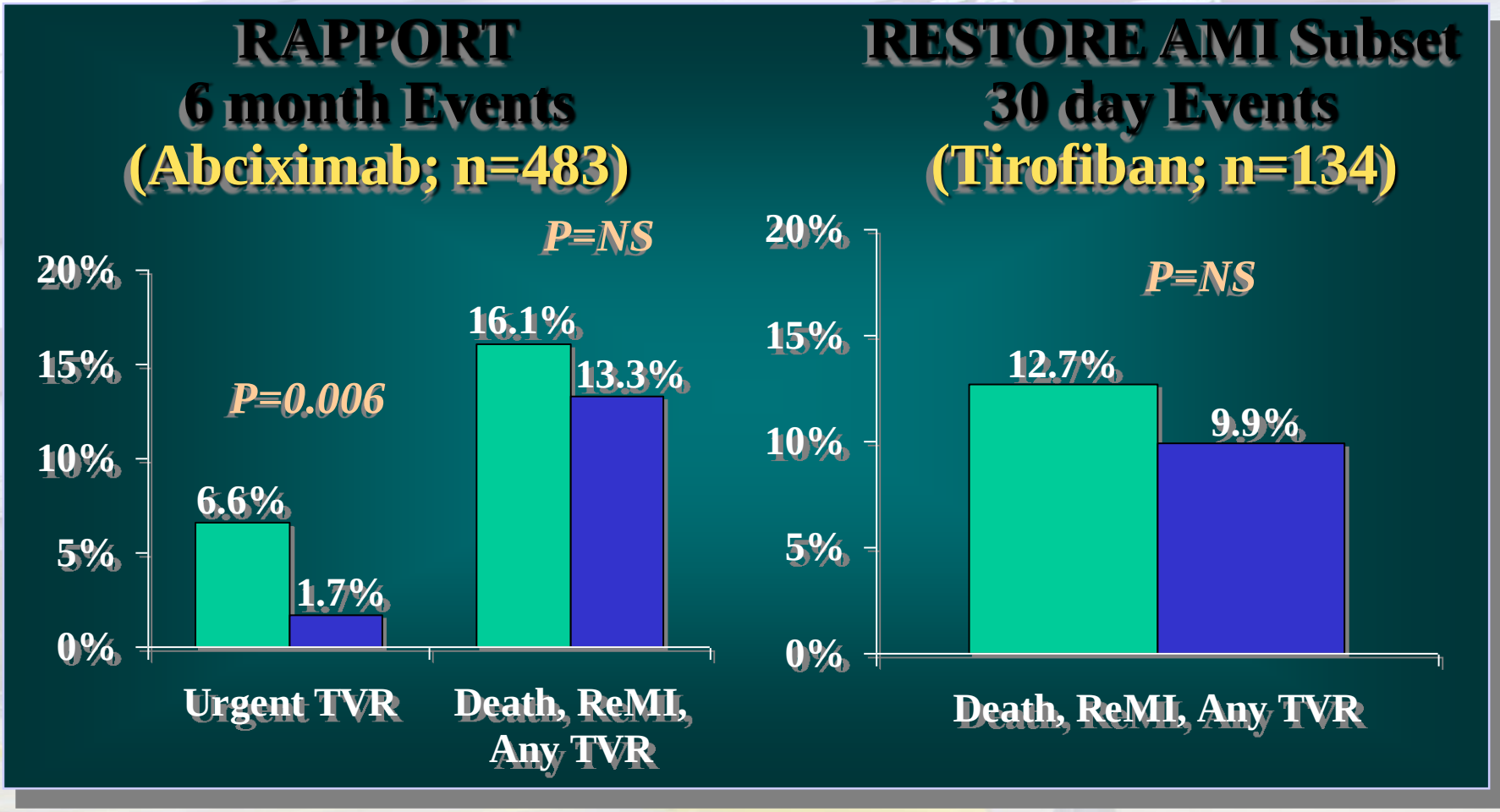
IIb/IIIa Inhibitors During Primary PTCA

Placebo **GP IIb/IIIa**



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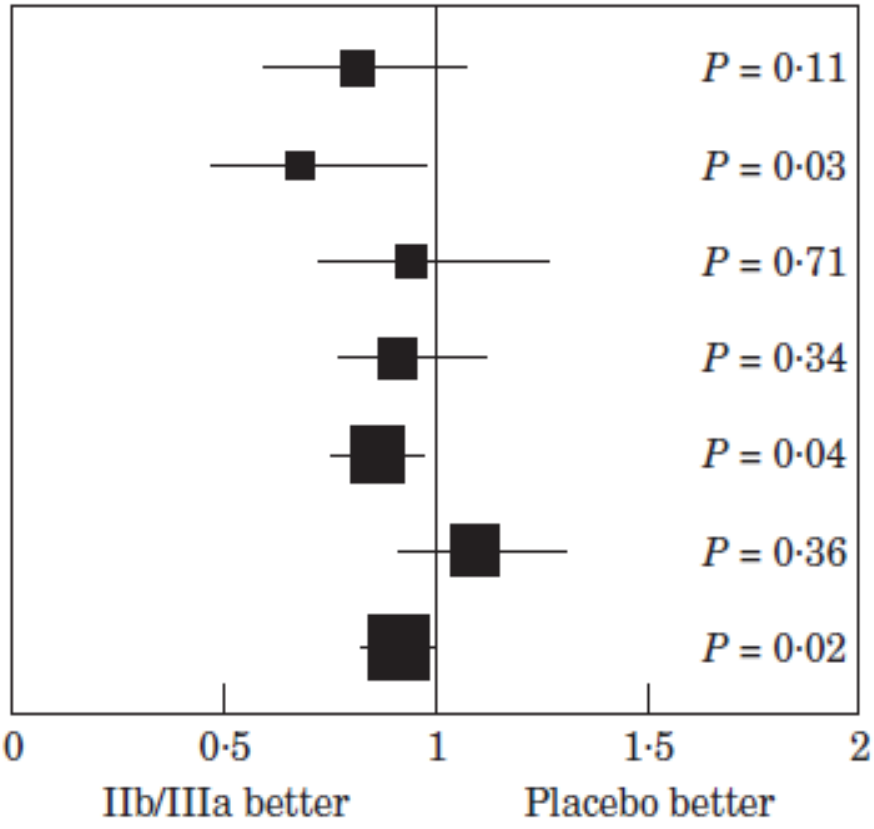
All patients
Death/MI at 30 days

Trial	n	Odds ratio and 95% CI	Placebo	IIb/IIIa
PRISM	3232	$P = 0{\cdot}11$	7·1%	5·8%
PRISM-PLUS	1570	$P = 0{\cdot}03$	11·9%	8·7%
PARAGON A	2282	$P = 0{\cdot}71$	12·0%	11·5%
PARAGON B	5225	$P = 0{\cdot}34$	11·4%	10·6%
PURSUIT	9461	$P = 0{\cdot}04$	15·7%	14·2%
GUSTO IV	7800	$P = 0{\cdot}36$	8·0%	8·7%
Pooled	29 570	$P = 0{\cdot}02$	11·5%	10·7%



Breslow-Day $P = 0{\cdot}19$

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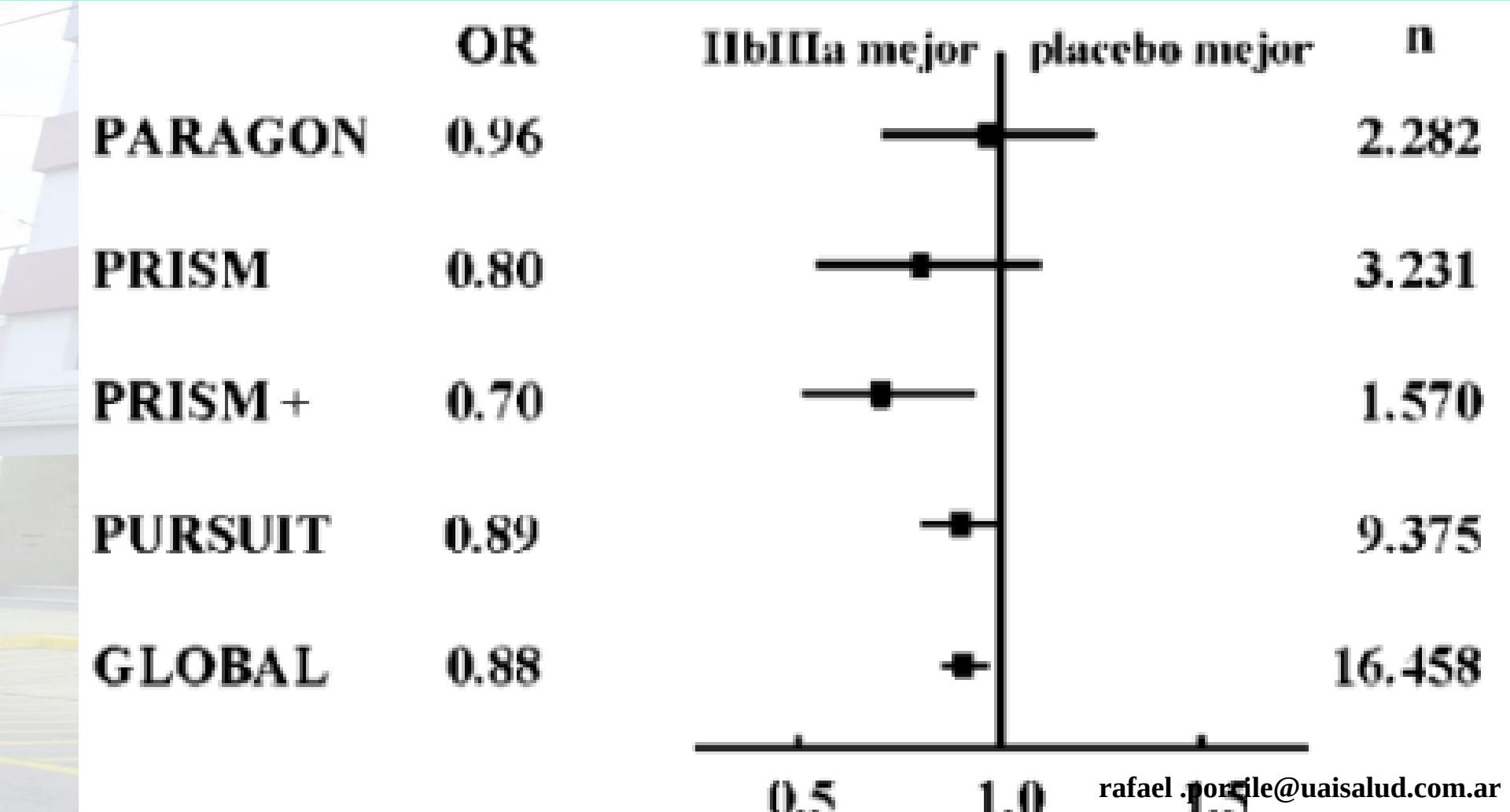
Como se observa en la figura, el efecto global consiste en un 12 % de reducción de eventos. El efecto más importante se observó en el ensayo con pacientes de mayor riesgo(PRISM PLUS). Por lo tanto, al igual que ocurre con otras terapéuticas, el beneficio producido por estos nuevos agentes probablemente tenga relación con el riesgo propio del paciente.



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Consenso 2013

Inhibidores de la Glicoproteína IIb/IIIa
Recomendaciones SAC 2013

Al momento de la intervención en pacientes seleccionados para terapéutica invasiva precoz (en la evolución aguda de la angina inestable, dolor reciente, angina recurrente, troponina elevada, trombo visible). **I A**

Angina refractaria: si es derivada a intervención. En situaciones de alto riesgo en espera de derivación a un centro de alta complejidad **I b**

Pacientes que no serán derivados a coronariografía de urgencia y que no tienen criterios de alto riesgo al ingreso ni evolutivos. **III C**

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5 minutos …

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Primaria → secundaria

Cuatro mecanismos

1. Espasmo vascular (**vasoconstricción**)

2. Formación del tapón plaquetario (**Adherencia y agregación**)

3. Coagulación

4. Organización y/o disolución del coagulo (Fibrinólisis)


Primaria
secundaria
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1. Espasmo vascular (vasoconstricción)
2. Formación del tapón plaquetario (Adherencia y agregación)
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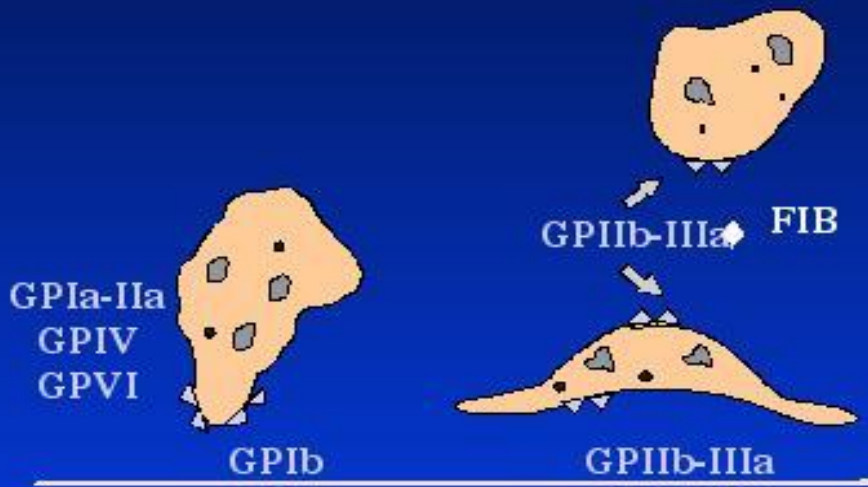
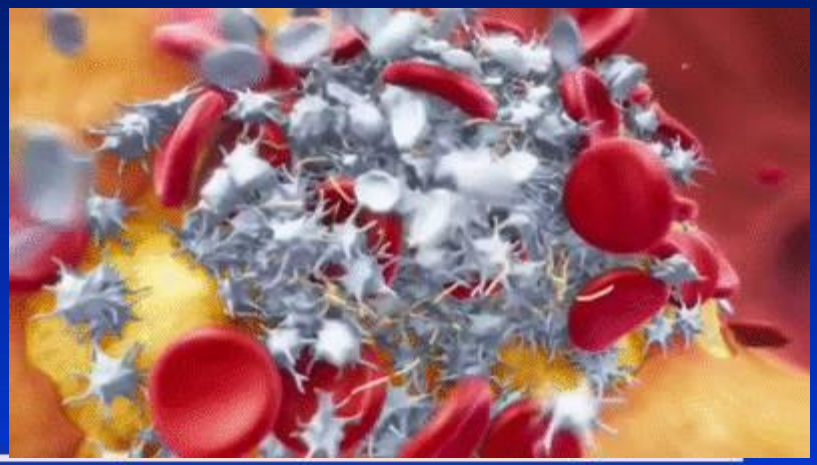
PLATELET FUNCTIONS





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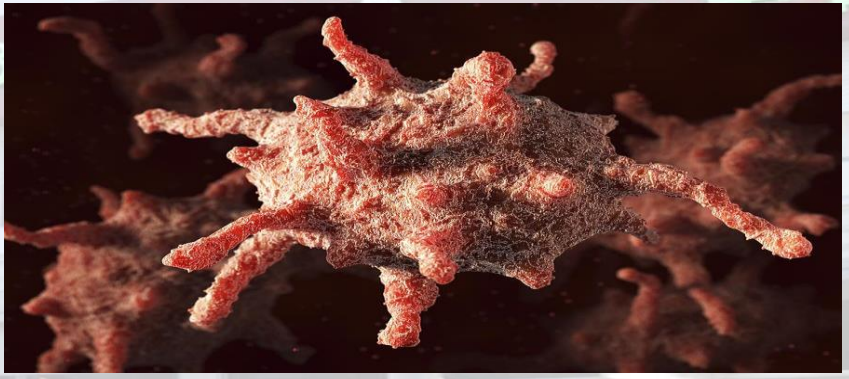
La agregación

y la

Activación



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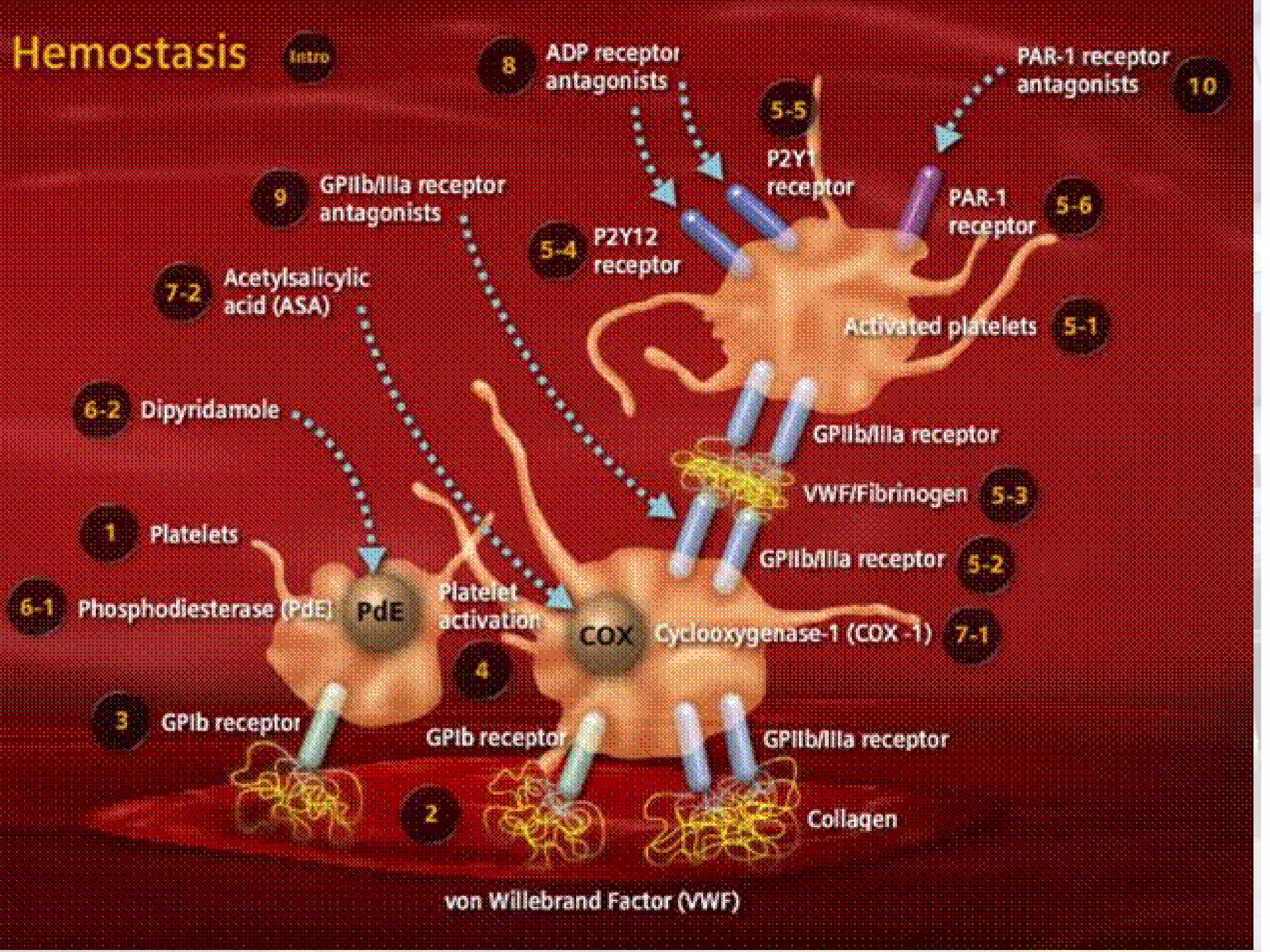
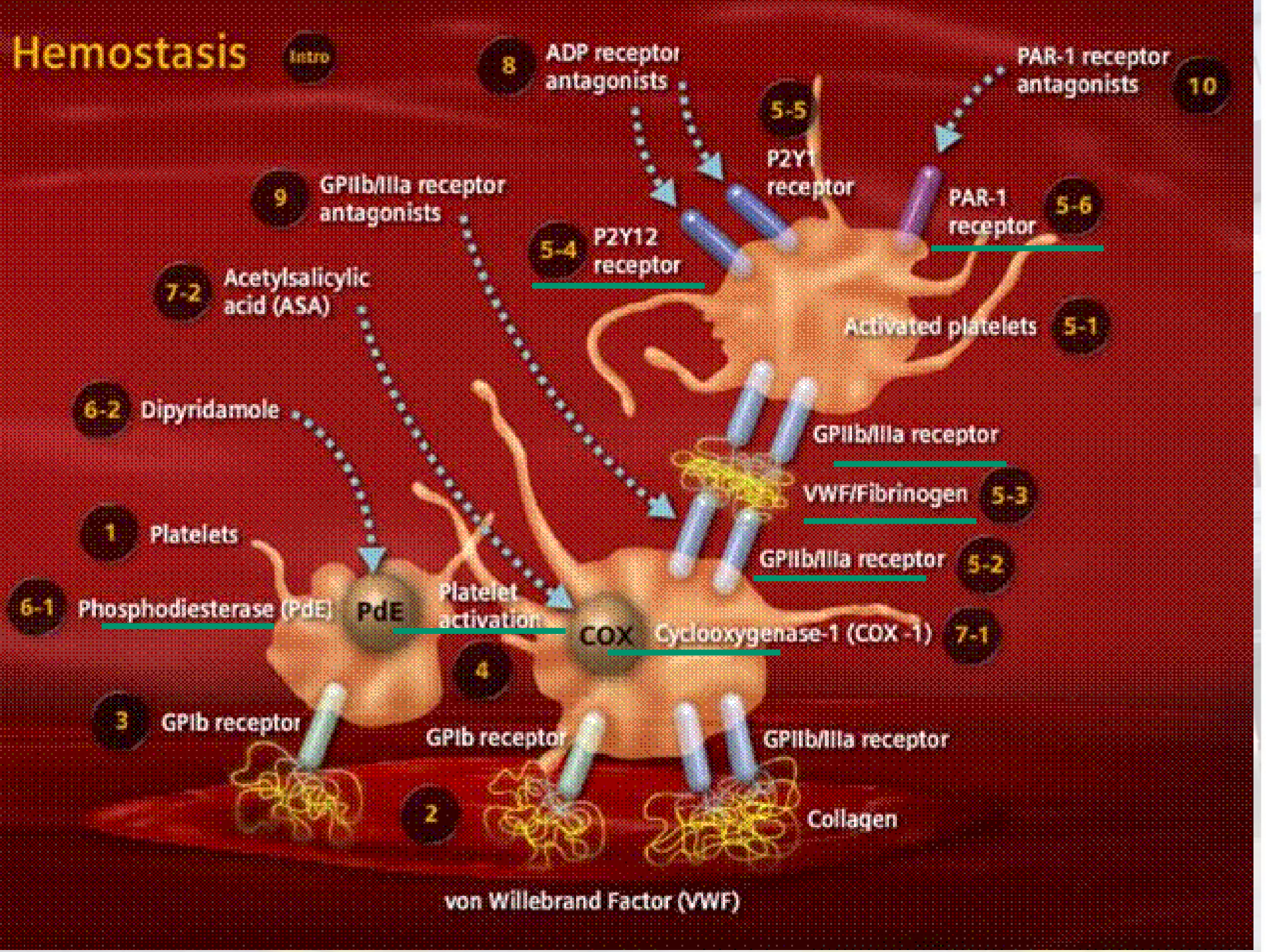

Hemostasis
Intro
8
ADP receptor antagonists
10
PAR-1 receptor antagonists
5-5
P2Y1 receptor
9
GPIIb/IIIa receptor antagonists
5-4
P2Y12 receptor
PAR-1 receptor
5-6
7-2
Acetylsalicylic acid (ASA)
Activated platelets
5-1
6-2
Dipyridamole
GPIIb/IIIa receptor
VWF/Fibrinogen
5-3
1
Platelets
GPIIb/IIIa receptor
5-2
6-1
Phosphodiesterase (PdE)
PdE
Platelet activation
COX
Cyclooxygenase-1 (COX -1)
7-1
4
3
GPIb receptor
GPIb receptor
GPIIb/IIIa receptor
2
Collagen
von Willebrand Factor (VWF)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ACTIVACIÓN Y RESPUESTA PLAQUETARIA

1.- ACTIVACIÓN POR DIFERENTES "INDUCTORES" (TROMBINA, COLÁGENO, ADP).

PARCIALMENTE ACTIVADAS: POR SUST.EXTRAÑAS (VIDRIO) U OTRAS PLAQUETAS.

2.-RESPUESTA PLAQUETARIA: SIMILAR PARA TODOS LOS INDUCTORES.

a) CAMBIO DE FORMA

b) AGREGACIÓN (SE ACUMULAN)

c) 3 PROCESOS SECRETORIOS DIFERENTES (ADP)

d) LIBERACIÓN DE AC.ARAQUIDÓNICO (PG Y TX. A_2)

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ADP DE LOS GRÁNULOS DESENCADENA LA DESCARGA DE LOS GRANÚLOS EN OTRAS PLAQUETAS

Se produce la liberación del ac. araquidónico de los fosfolípidos de membrana que se metaboliza en dos endoperóxidos cíclicos por acción de ciclooxigenasa: PGH2 Y PGG2

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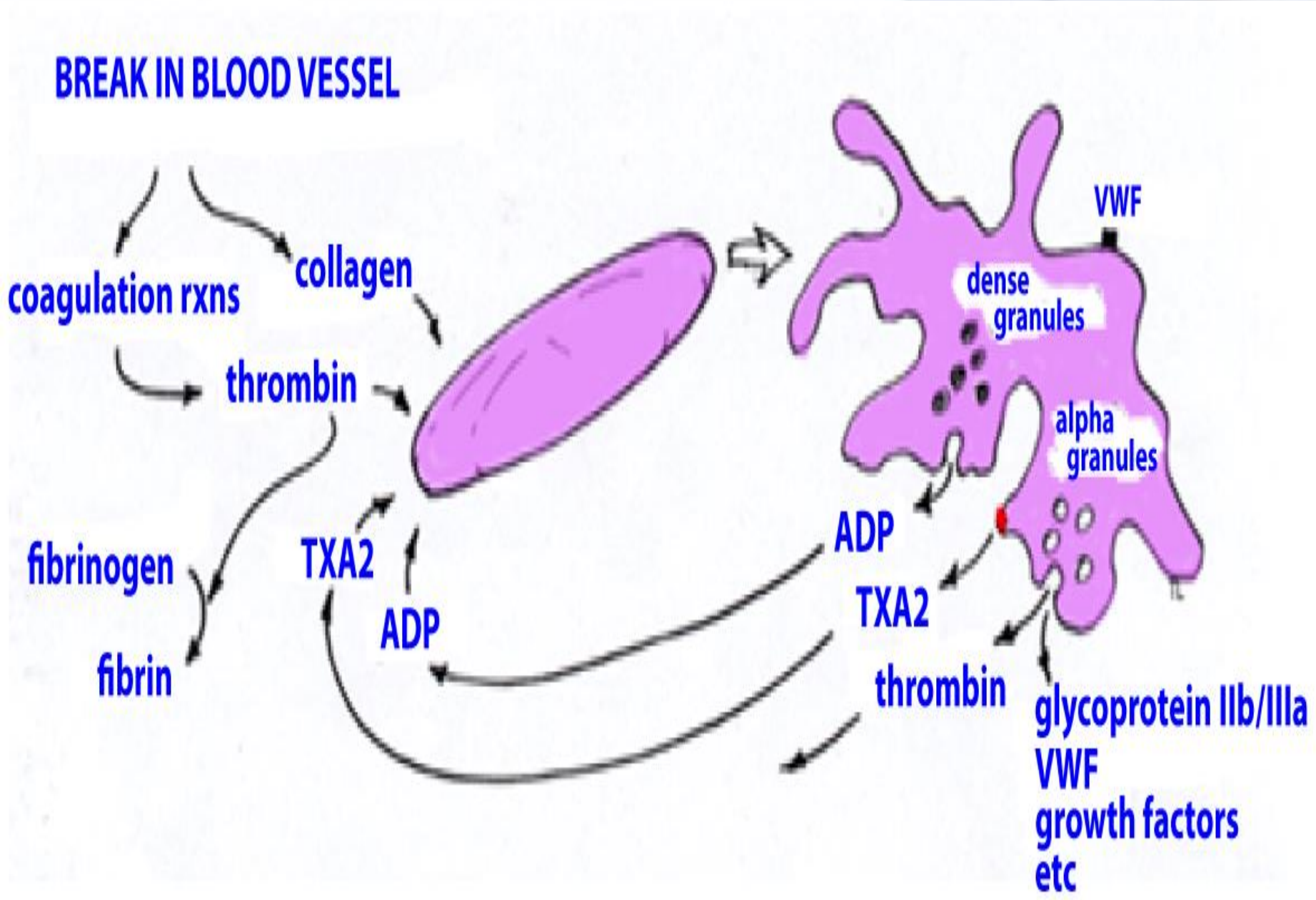
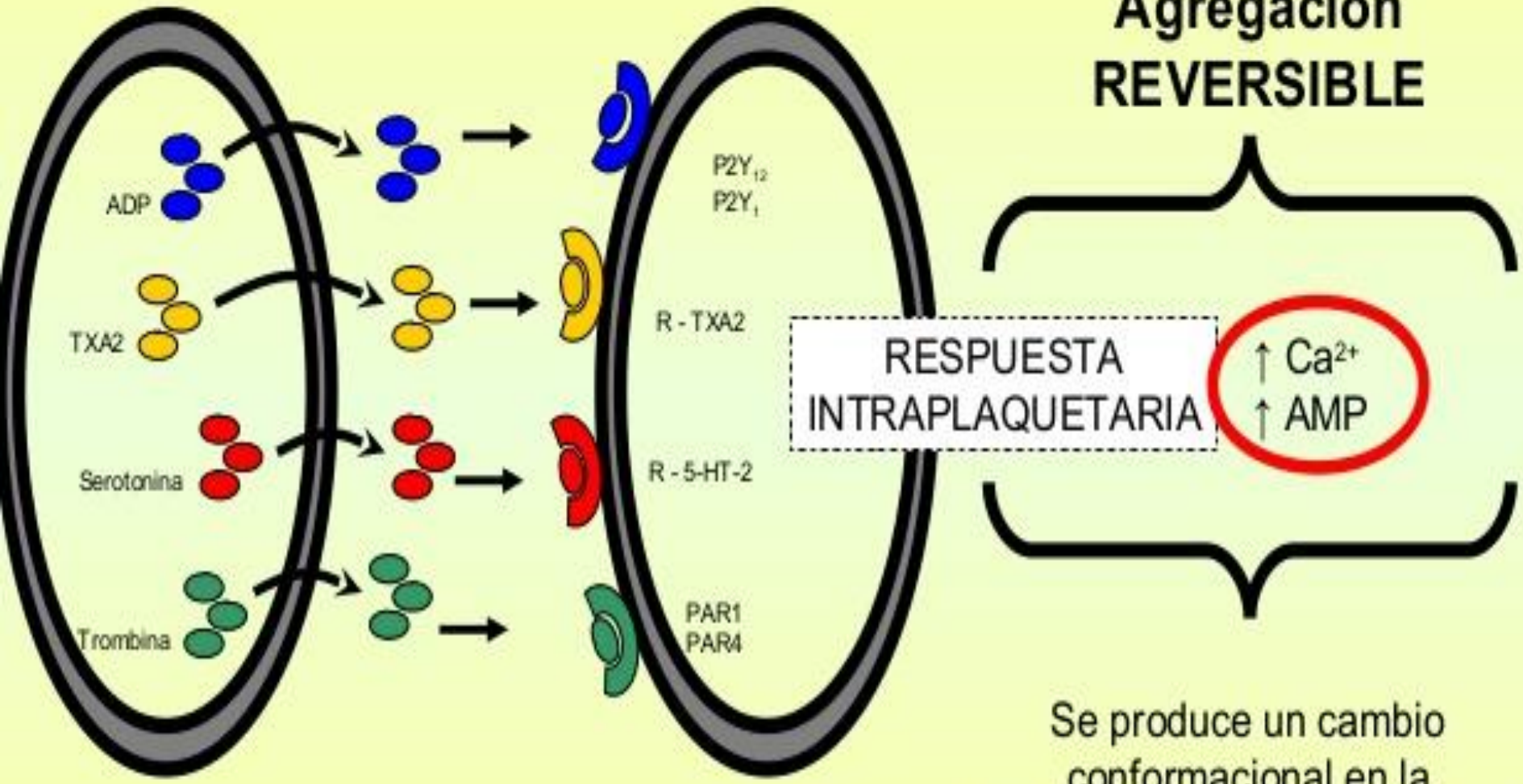
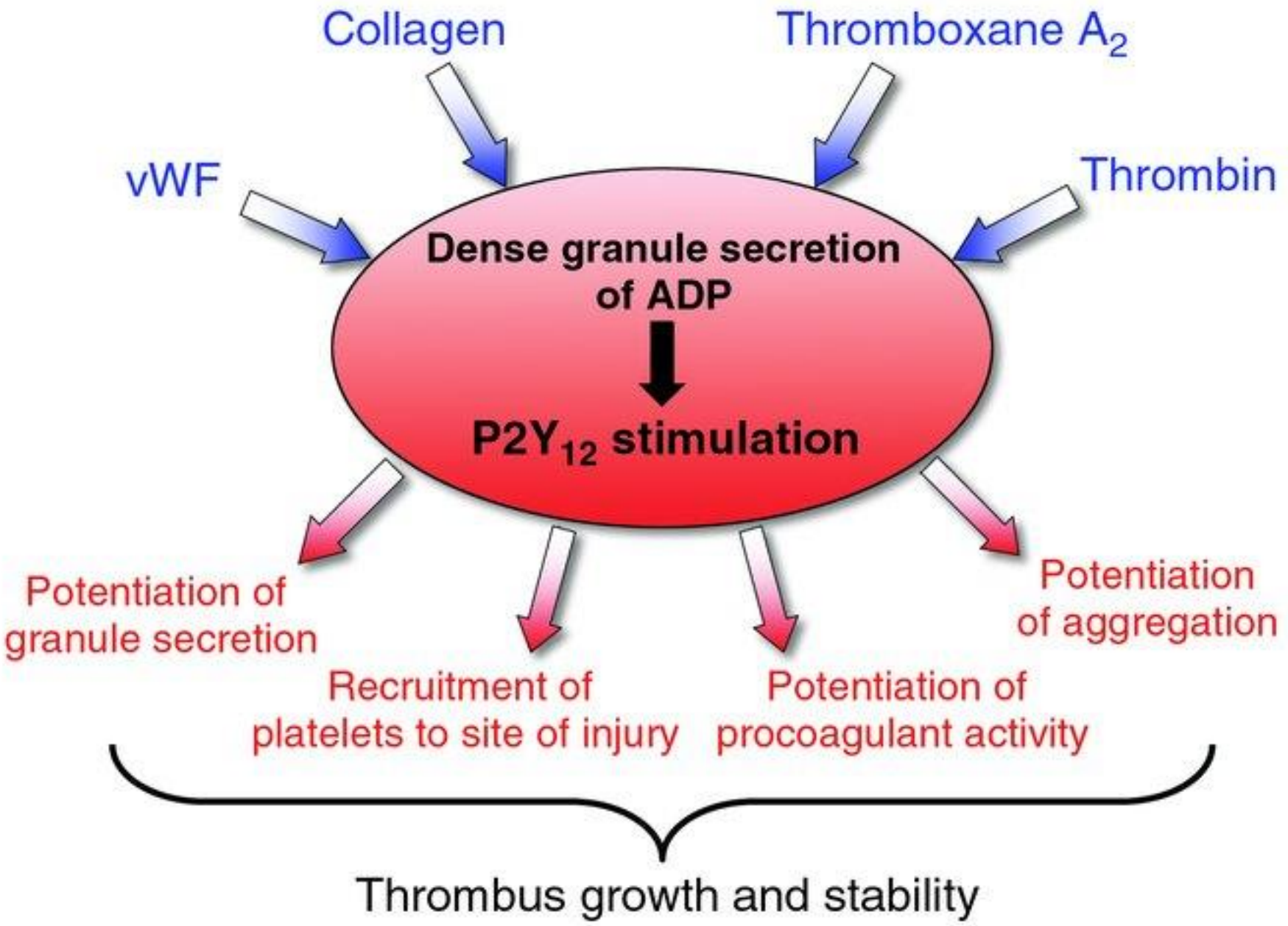

BREAK IN BLOOD VESSEL
coagulation rxns
collagen
thrombin
fibrinogen
fibrin
TXA2
ADP
VWF
dense granules
alpha granules
ADP
TXA2
thrombin
glycoprotein IIb/IIIa
VWF
growth factors
etc

LAS PLAQUETAS SE ACTIVAN UNAS A OTRAS





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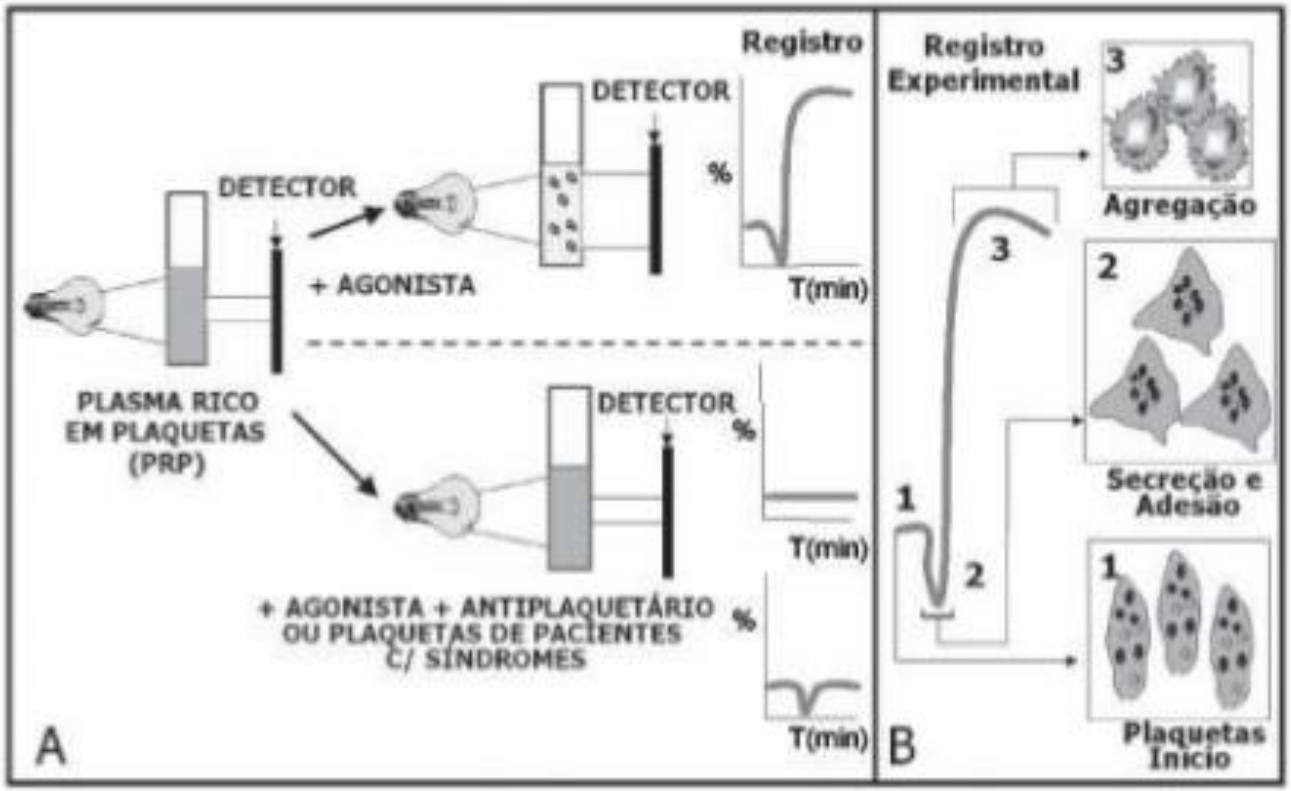
AGREGOMETRIA PLAQUETARIA

- Substancias con capacidad agregante :
  - ADP, epinefrina, colágeno y ristocetina.



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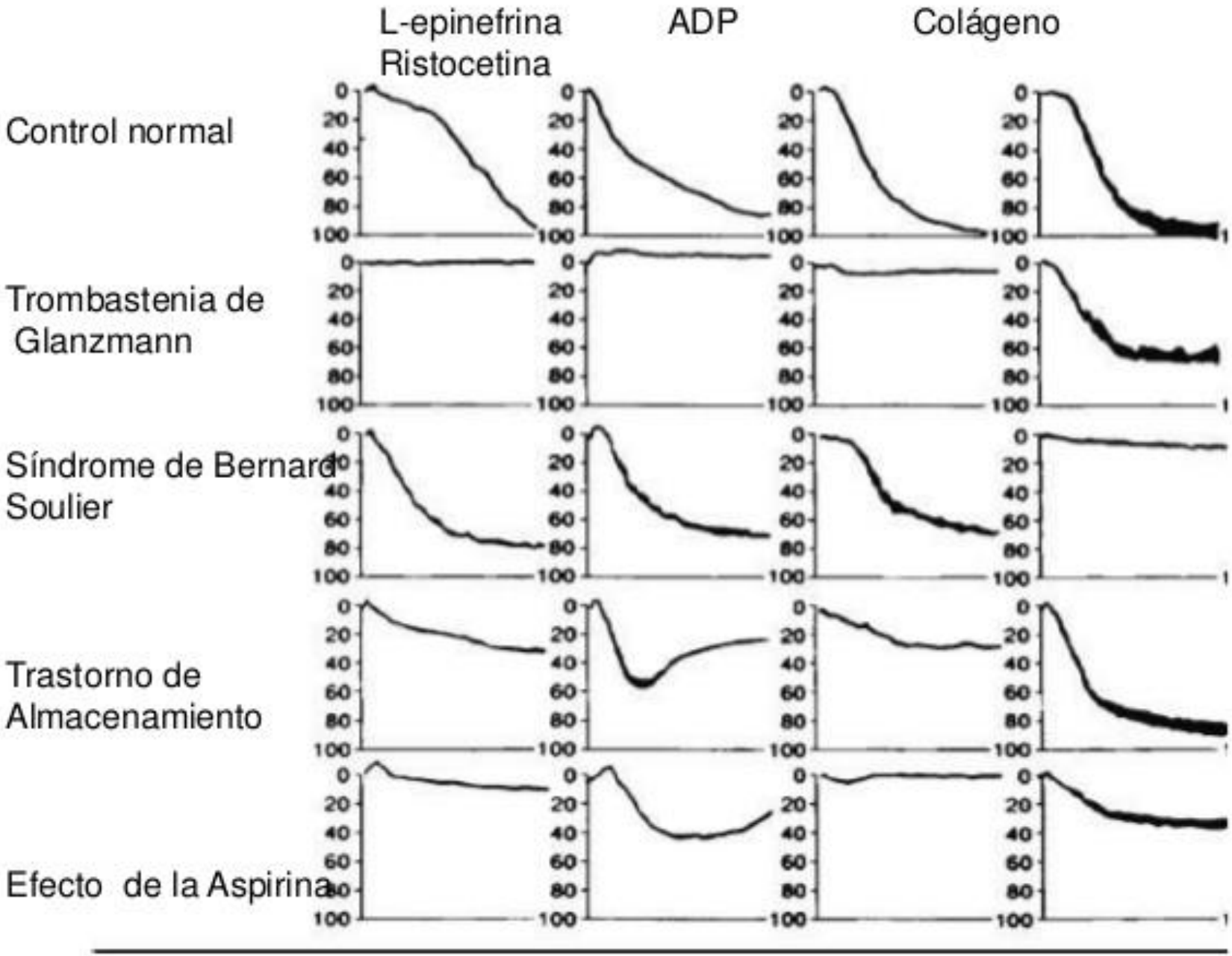

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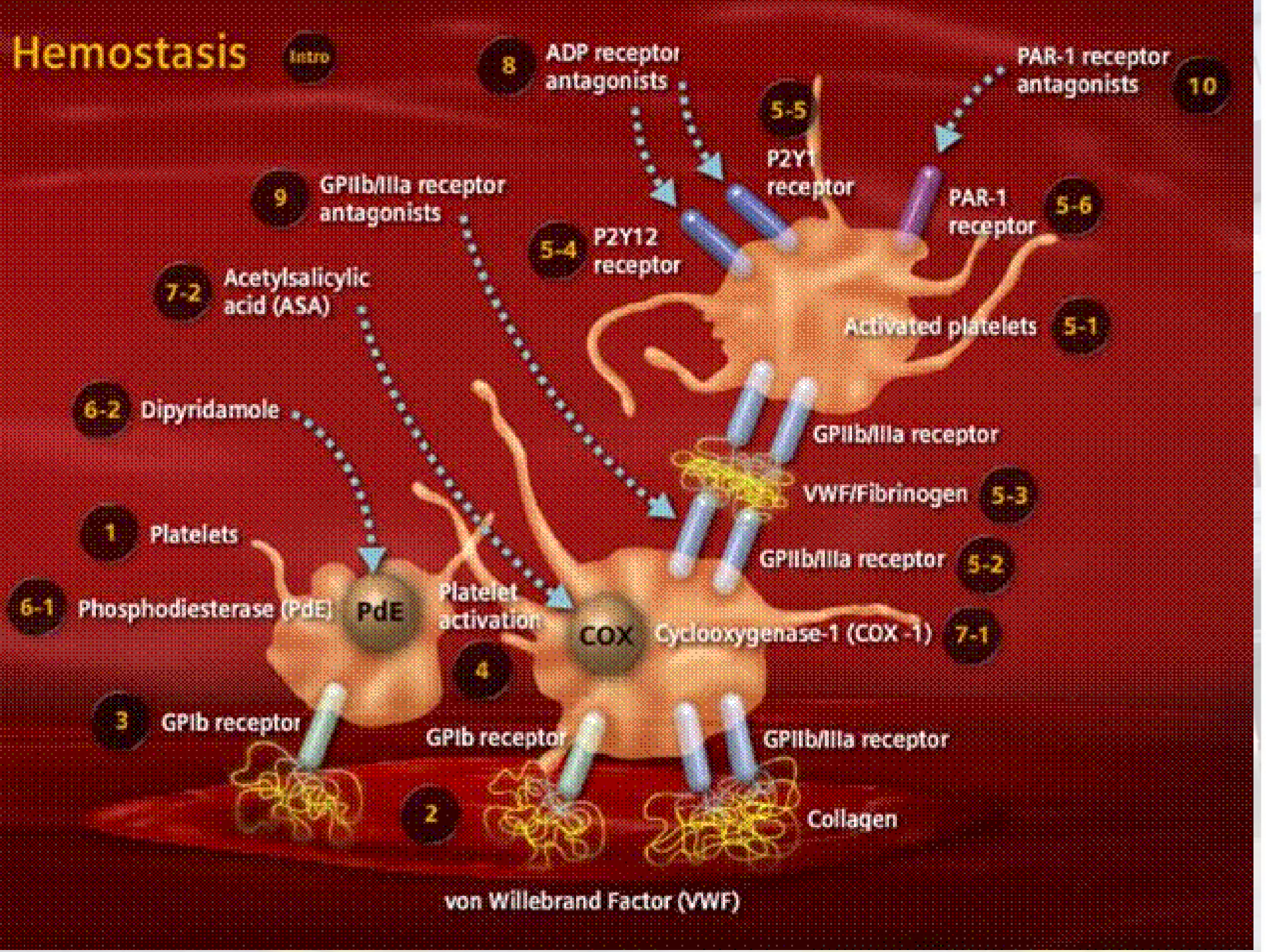
¿?
STORMWATER
Holly Ellenbogen
NEWS 9
HilariousGifs.com

¿COMO DETENER ESTE PROCESO?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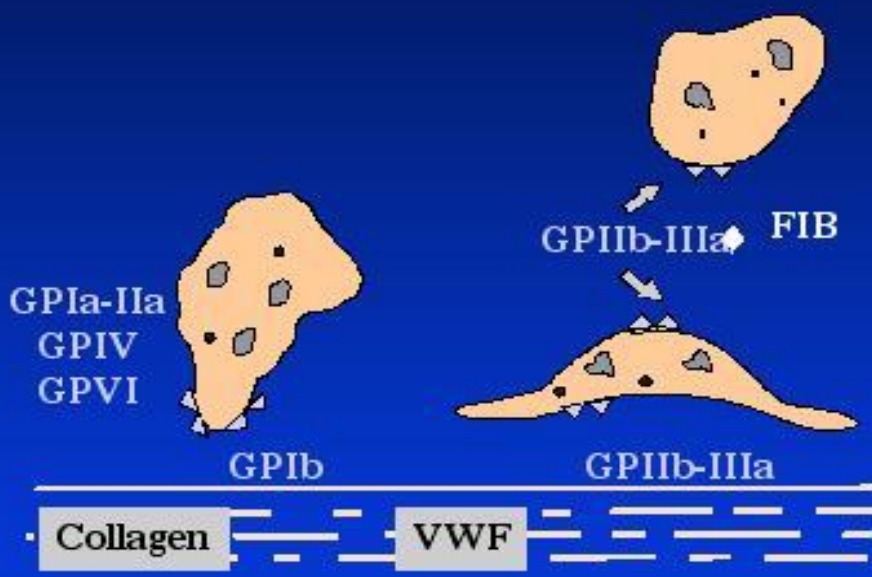
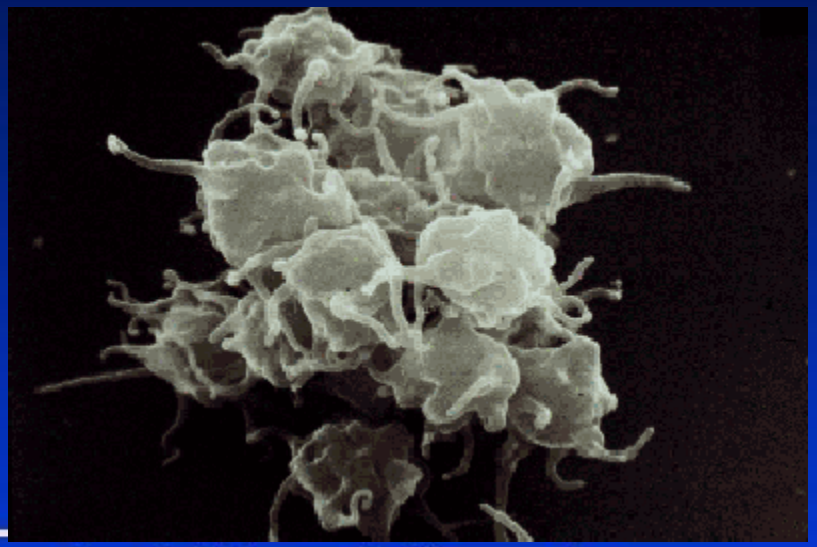
PLATELET FUNCTIONS





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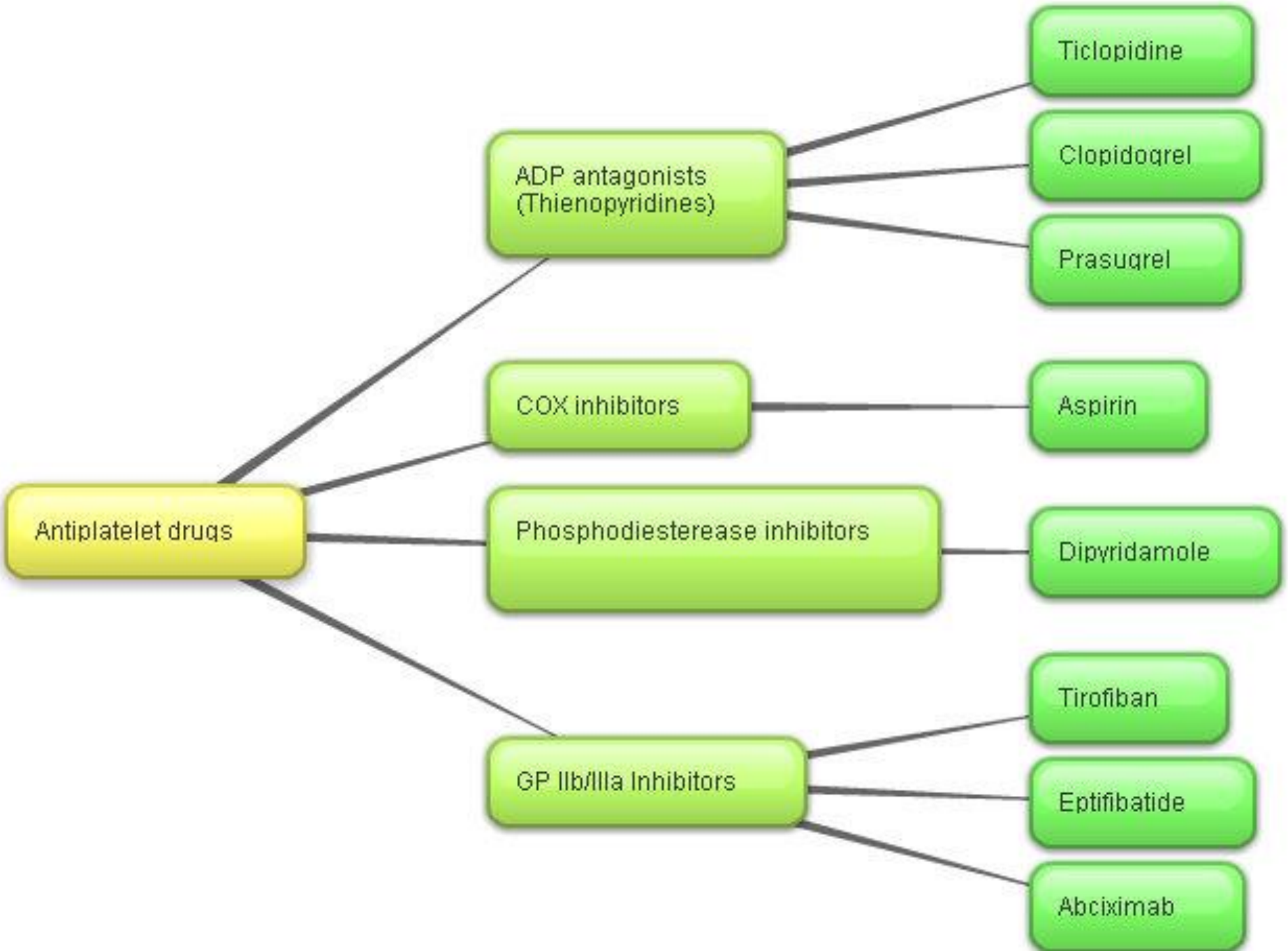
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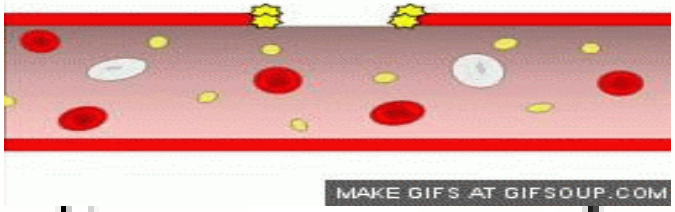
Prasugrel
COX inhibitors
Aspirin
Phosphodiesterease inhibitors
Dipyridamole
GP IIb/IIIa Inhibitors
Tirofiban
Eptifibatide
Abciximab

Diphosphoesterase inhibitor e.g.dipyridamole

Platelet ADP receptor inhibitor e.g. clopidogrel, ticlopidine



Cyclo-oxygenase inhibitor e.g. aspirin

Platelet GP IIb/IIIa receptor antagonists e.g.tirofiban, lamifiban, eptifibatide, abxicimab

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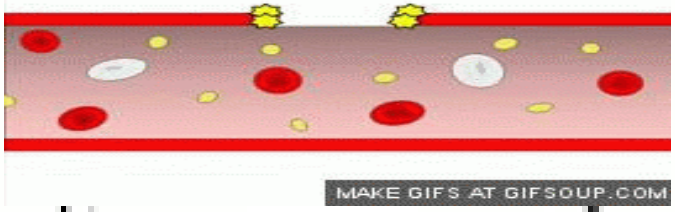
Diphosphoesterase inhibitor e.g.dipyridamole

Platelet ADP receptor inhibitor e.g. clopidogrel, ticlopidine



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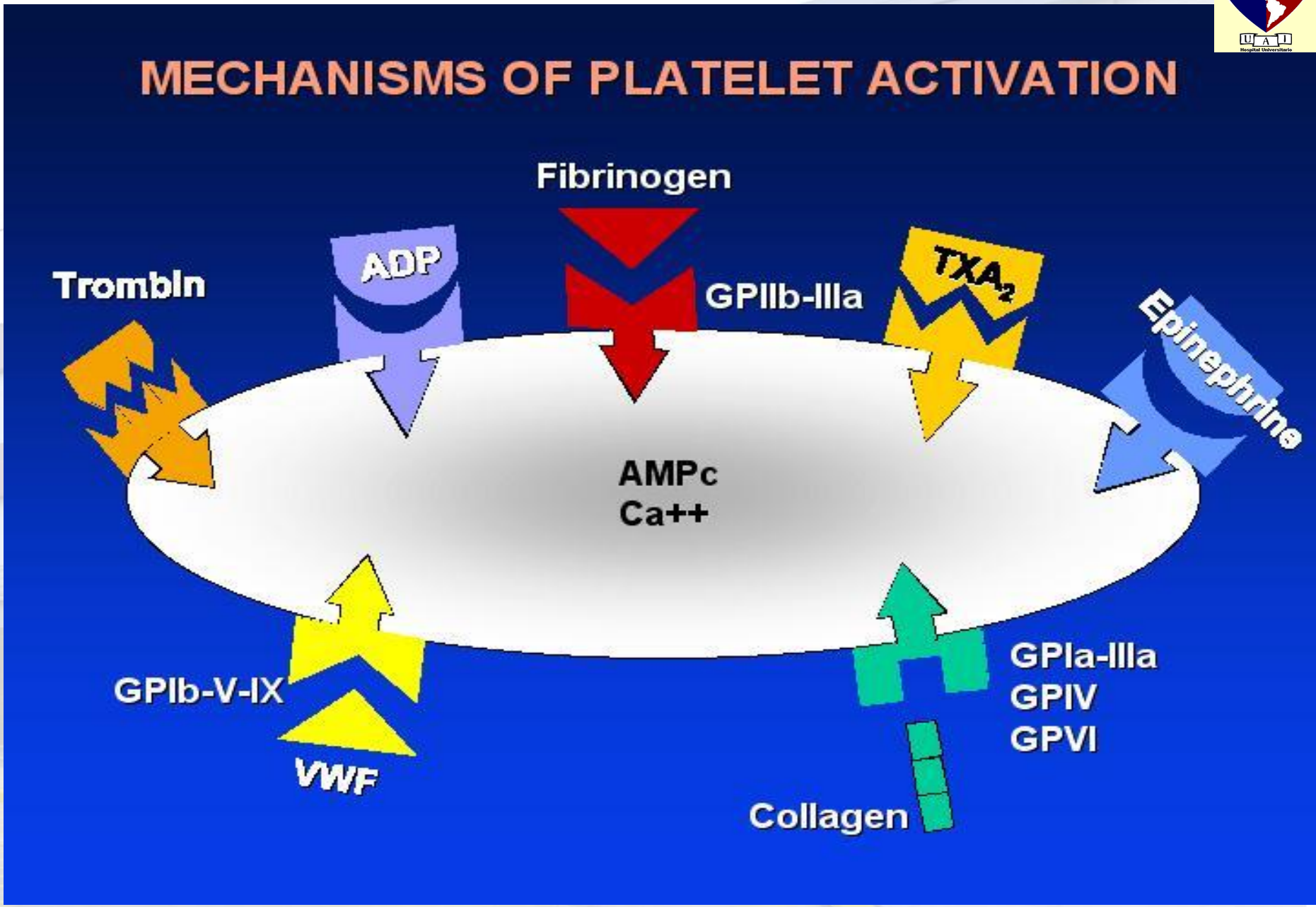
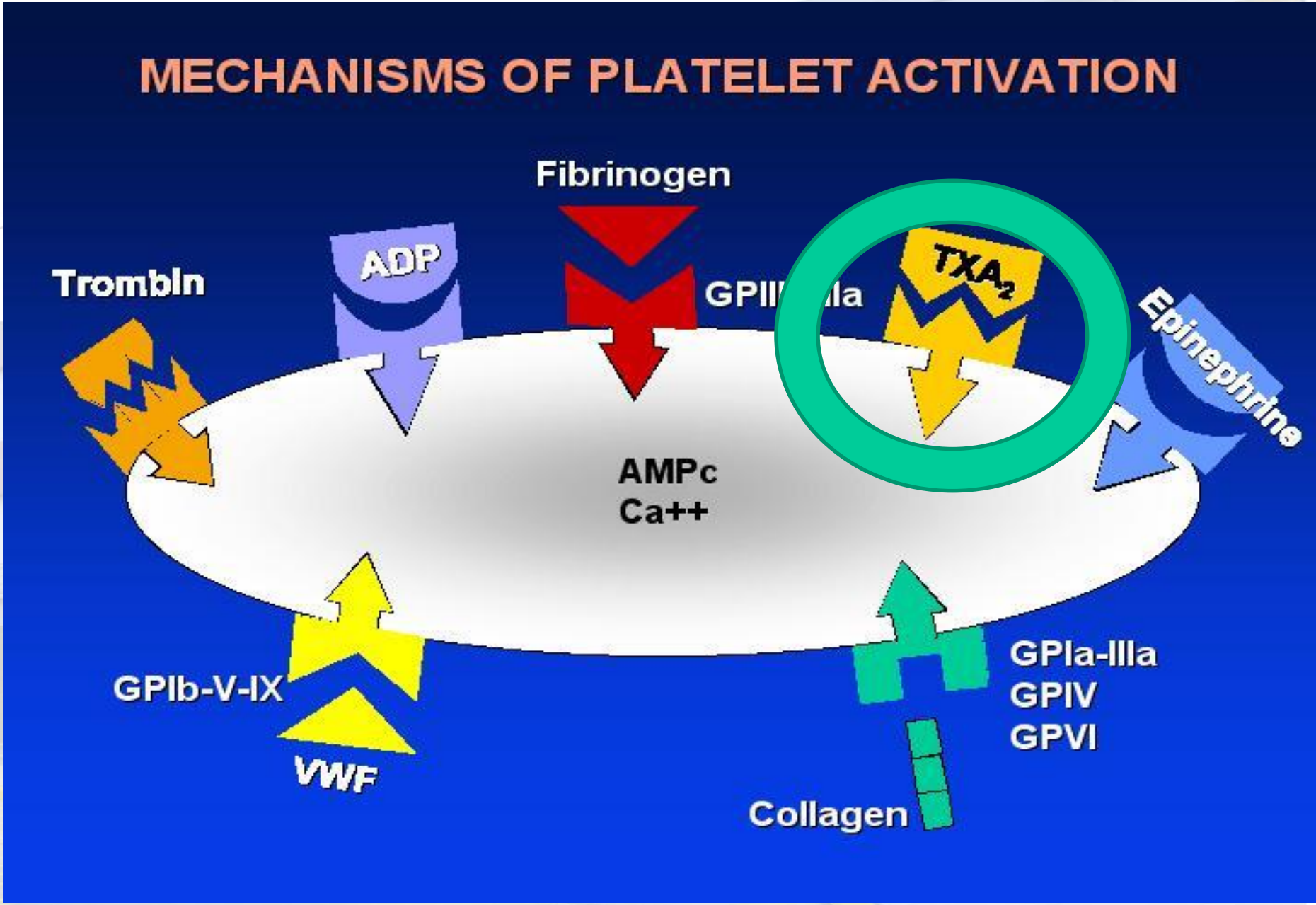

MECHANISMS OF PLATELET ACTIVATION
Fibrinogen
ADP
Trombin
GPIIb-IIIa
TXA2
Epinephrine
AMPc
Ca++
GPIb-V-IX
VWF
GPIa-IIIa
GPIV
GPVI
Collagen



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Todo comienza con el acido araquidónico

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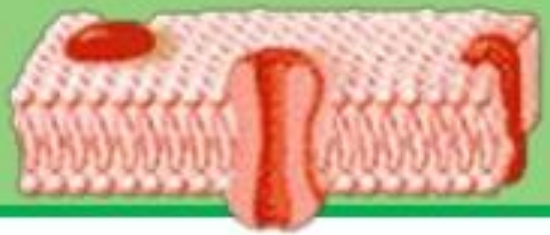
- El ácido araquidónico se libera de los fosfolípidos de la membrana por la acción de **fosfolipasas**, que son enzimas lisosomales: la Fosfolipasa A2 y/o la Fosfolipasa C.
- Existen 2 genes que codifican la enzima cicloxigenasa. La **CICLOXIGENASA-1** (COX-1), es produida en condiciones normales, de reposo; mientras que la **CICLOXIGENASA-2** (COX-2) es inducida en células endoteliales y fibroblas tos de líquido sinovialreumatoide, por agentes inflamatorios comola interleucina-1 (IL-1).



Fosfolipasa A2

Ácido Araquidónico

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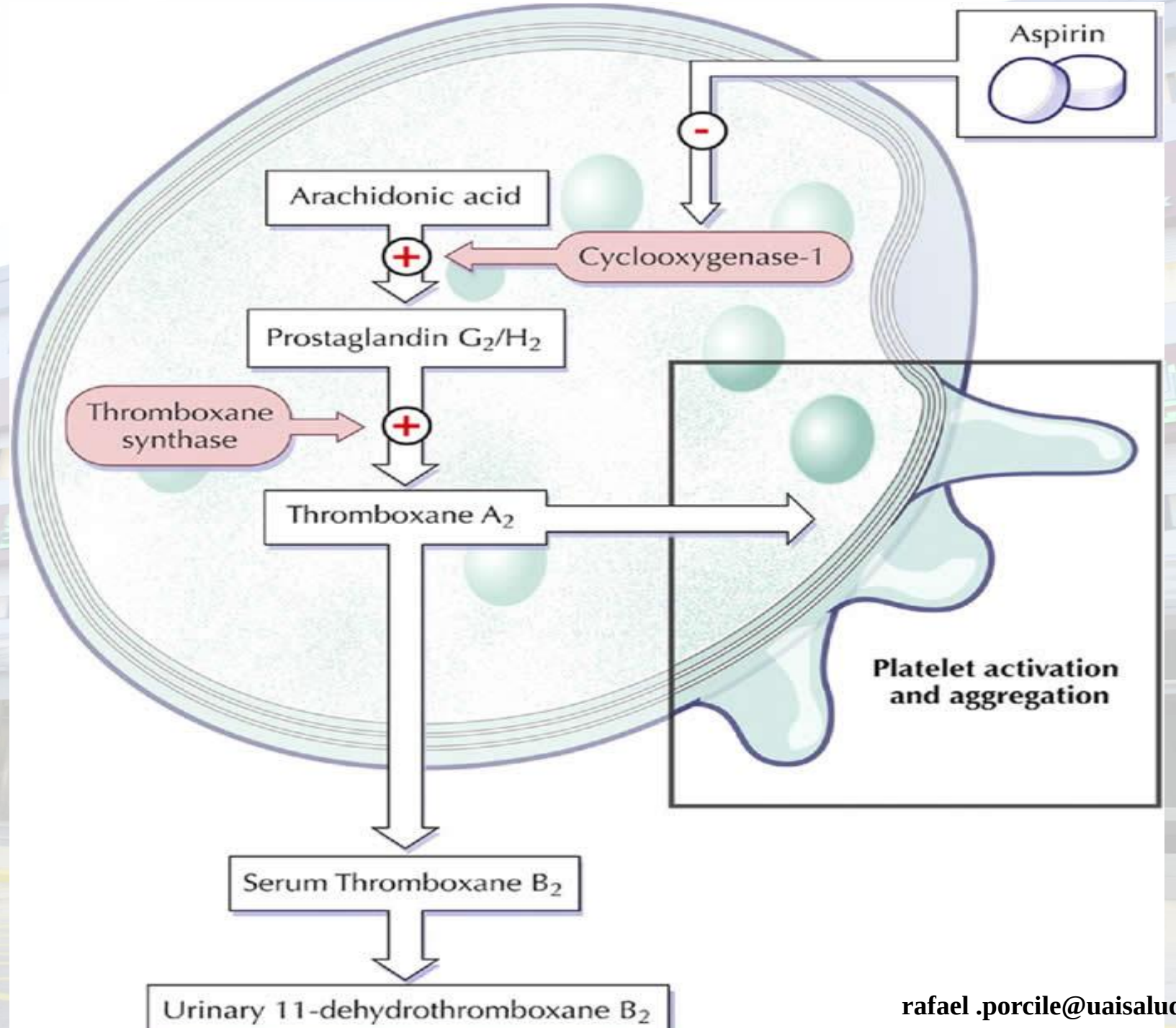

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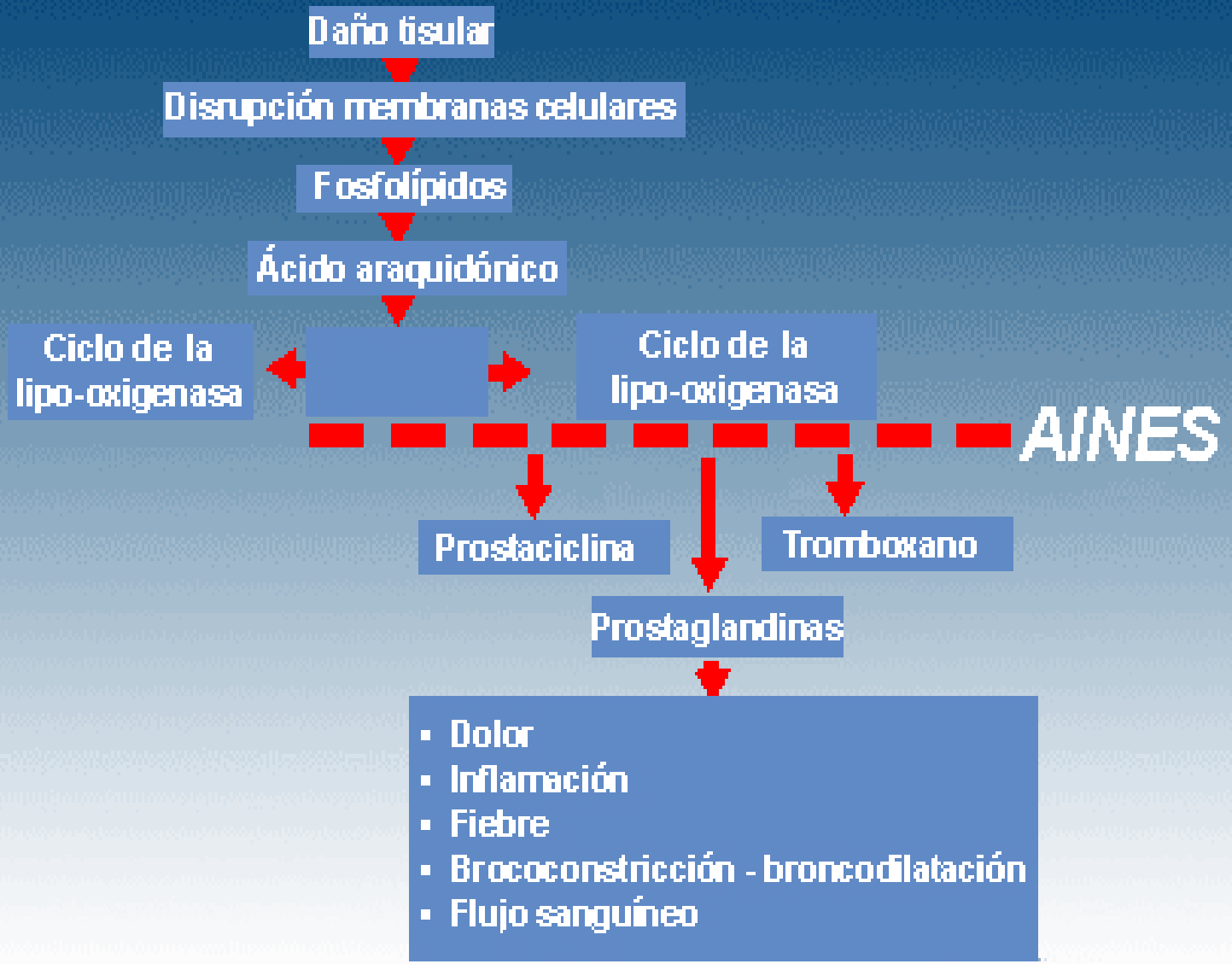
SÍNTESIS DE PROSTAGLANDINAS

Figura 1



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Antiagregantes plaquetarios

ACIDO
ACETIL
SALICILICO

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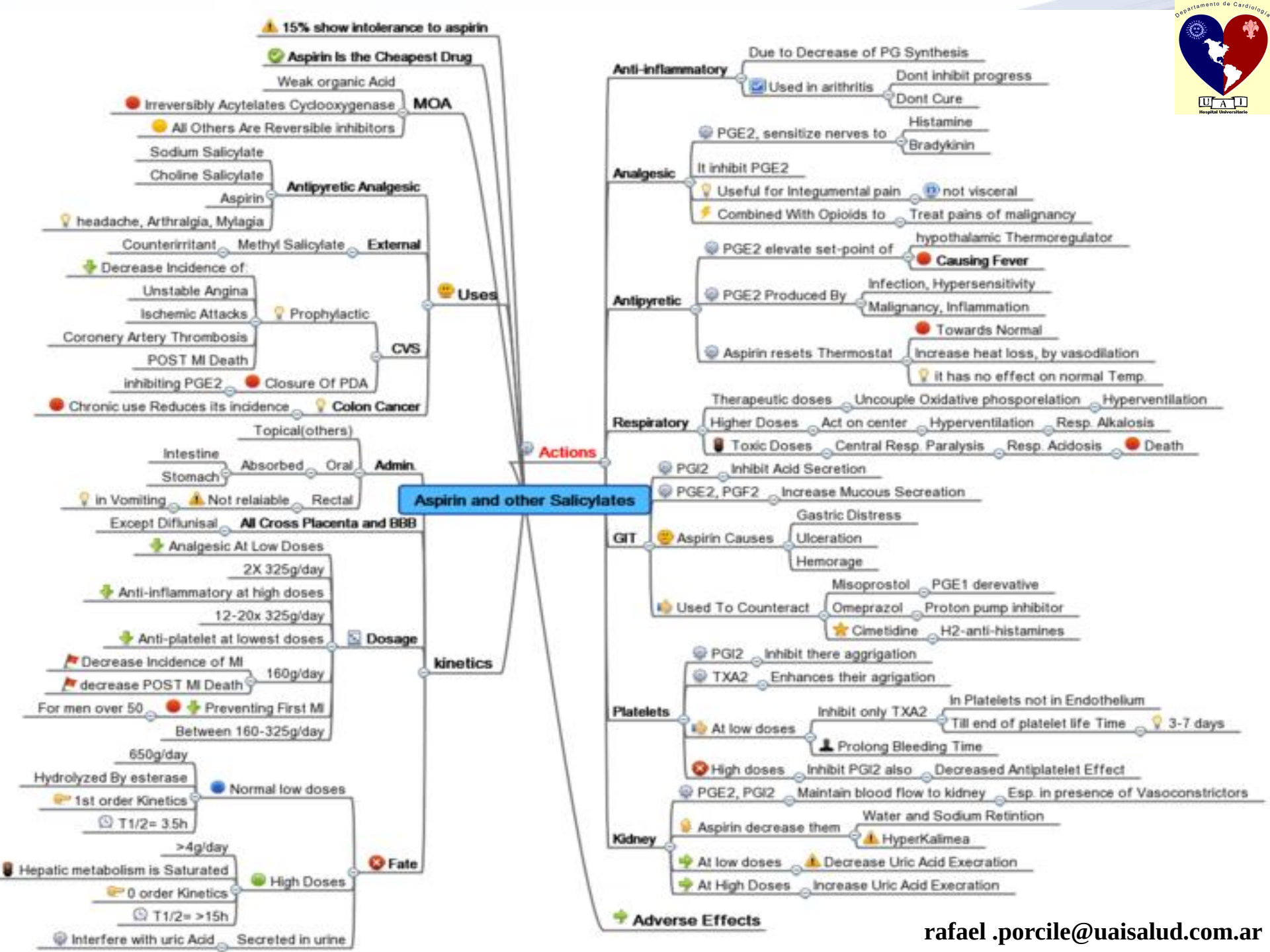

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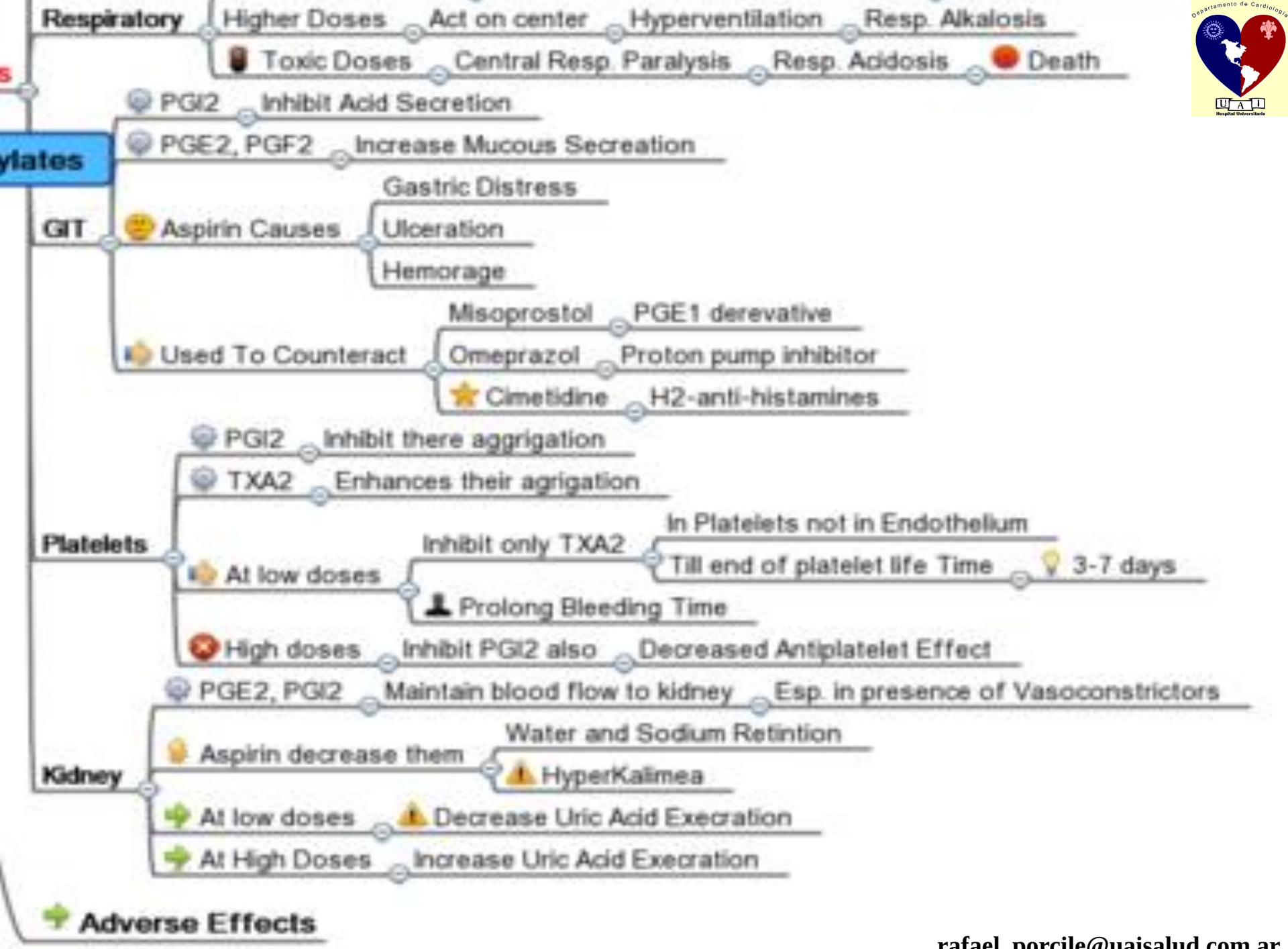

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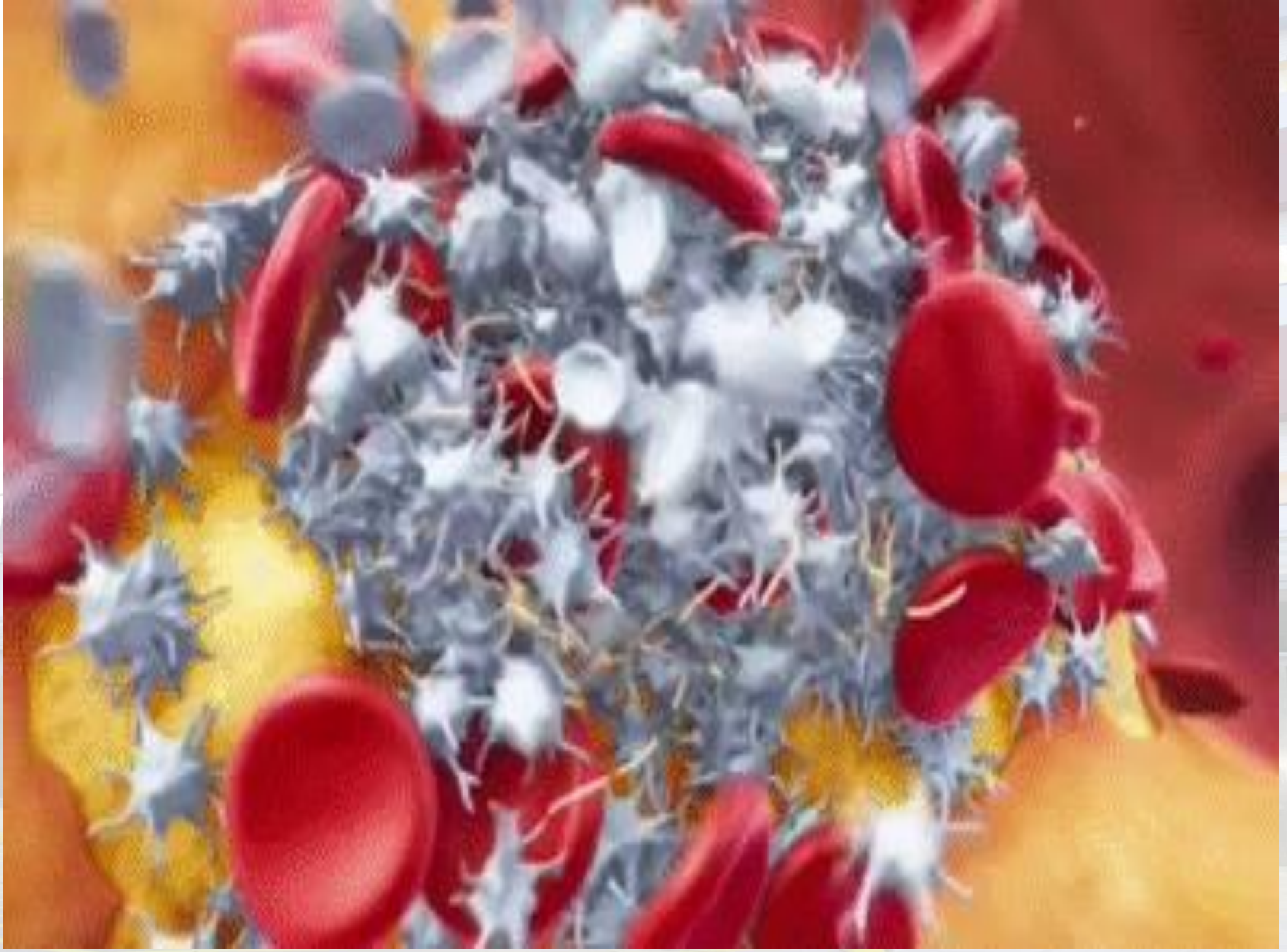

ASPIRINA PARA INFARTO AGUDO DE MIOCARDIO

Second International Study of Infarct Survival

ISIS-II (Second International Study of Infarct Survival) collaborative group. Randomized trial of intravenous streptokinase, oral aspirin, both or neither among 17187 cases suspected acute myocardial infarction:ISIS-II. Lancet1988;2: 349-60

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Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2

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En el ensayo ISIS-II, en los enfermos que recibieron estreptoquinasa y aspirina, la mortalidad fue bastante menor al compararla con el grupo placebo. Si sólo se daba aspirina o estreptoquinasa, la mortalidad también era menor al compararla con el grupo control. La aspirina en este grupo de pacientes intenta prevenir la re oclusión durante la fase aguda del infarto

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Aspirin significantly reduced non-fatal reinfarction (1·0% vs 2·0%) and non-fatal stroke (0·3% vs 0·6%), and was not associated with any significant increase in cerebral haemorrhage or in bleeds requiring transfusion

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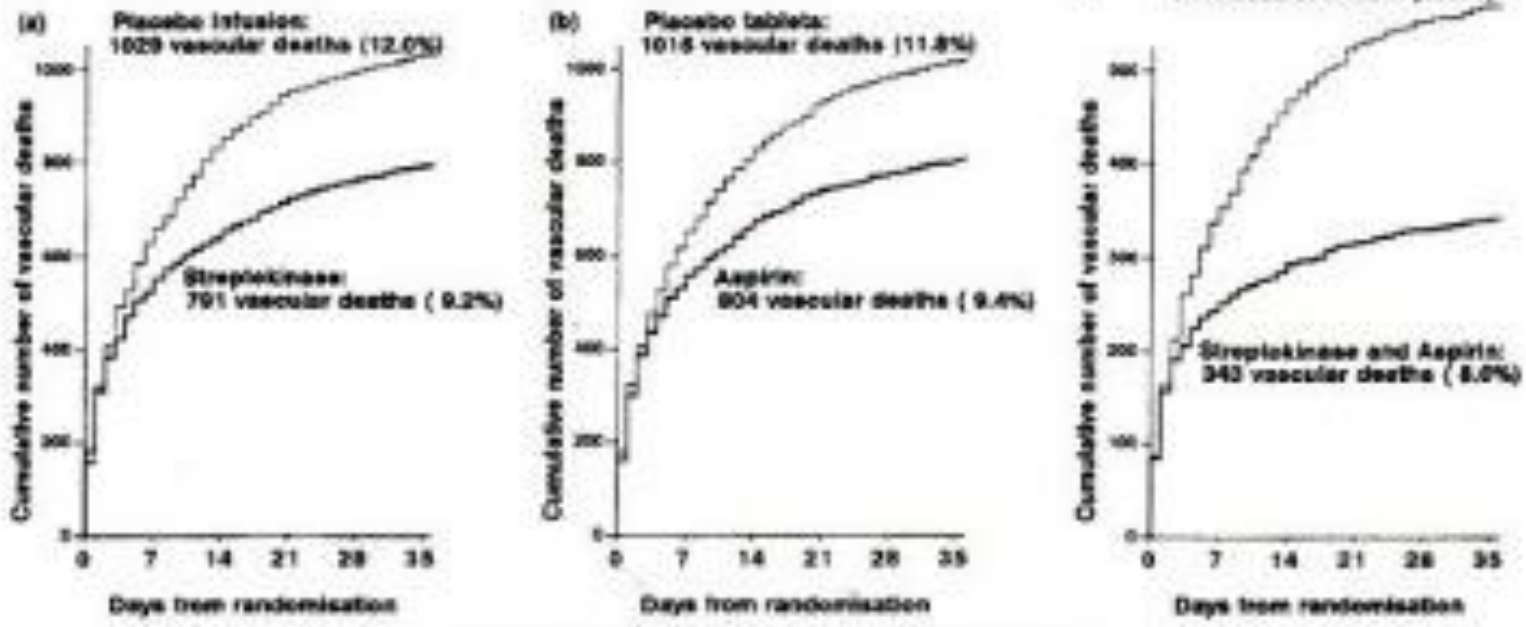

Fig 1—Cumulative vascular mortality in days 0–35.

(a) All patients allocated active streptokinase vs all allocated a placebo infusion; (b) all patients allocated active aspirin vs all allocated placebo tablets; and (c) all patients allocated both active treatments vs all allocated neither. (Statistical* tests at day 35—observed number of vascular deaths in active treatment group minus expected number, and the standard deviation of this difference: (a) −118·8 SD 20·2; (b) −105·3 SD 20·2; (c) −112·1 SD 14·3.)

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En base a estas evidencias resulta claro el valor de la aspirina en la prevención del infarto agudo de miocardio fatal y no fatal en pacientes con angina inestable o infarto no Q, y por esta razón su empleo sistemático en estos pacientes es universalmente aceptado

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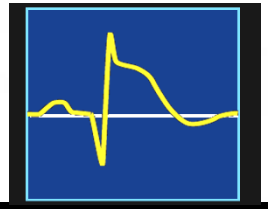

ACC/AHA STEMI Focused Update: Acute Medical Therapy

General treatment measures	• Aspirin, nitrates, oxygen, analgesics[a] (morphine)
Infarct size limitation	• β-blockers (not for acute use in patients with evidence of heart failure)
Reperfusion	• Thrombolysis (within 30 min) or primary PCI (within 90 min)
Anticoagulant and antiplatelet therapy	• UFH or enoxaparin or fondaparinux[b] • Clopidogrel 75 mg/d added to aspirin for patients undergoing fibrinolysis; 300 mg loading dose for patients <75 y who receive fibrinolytic therapy or who do not receive reperfusion therapy • If PCI: clopidogrel, GP IIb/IIIa inhibitors

[a] Patients routinely taking NSAIDs (except for aspirin), both nonselective as well as COX-2 selective agents, before STEMI should have those agents discontinued at the time of presentation with STEMI because of the increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use.

[b] Because of the risk of catheter thrombosis, fondaparinux should not be used as the sole anticoagulant to support PCI. An additional anticoagulant with anti-IIa activity should be administered.

Antman E, et al. *J Am Coll Cardiol.* doi:10.1016/j.jacc.2007.10.001.

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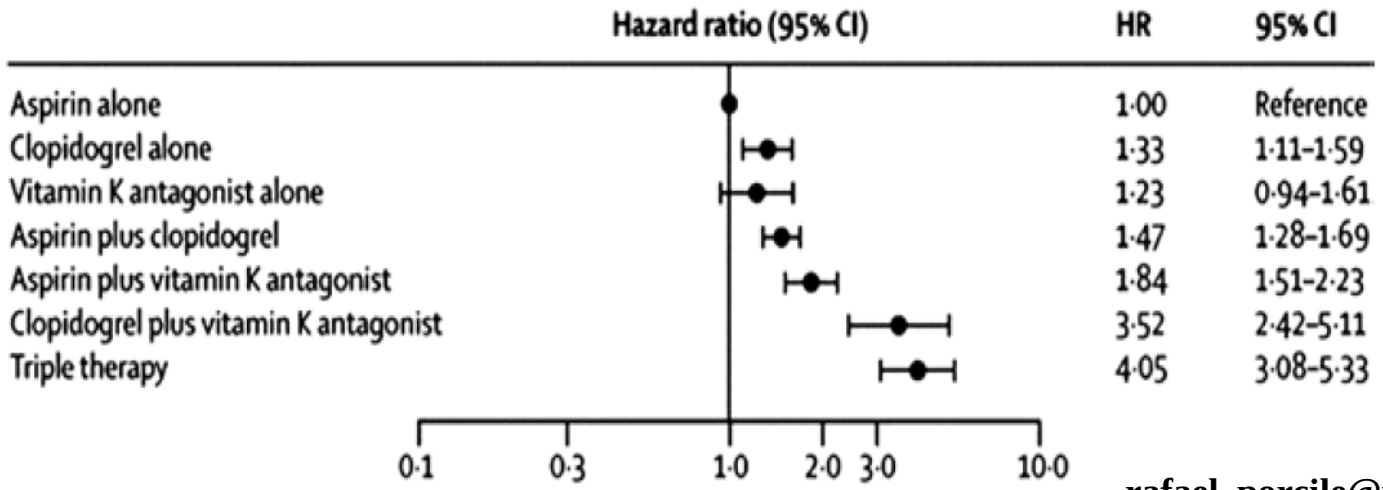
Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction :

e396 *Circulation* **January 29, 2013**



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ASPIRINA PARA PREVENCION PRIMARIA

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BENEFICIOS

- La aspirina reduce de forma estadísticamente significativa la incidencia de evento vascular grave*
  (0.51 % Vs 0.57 % por año.).

- **Esta reducción fue atribuible principalmente a la reducción significativa del riesgo de primer infarto**
  (0.18 % Vs 0.23 % por año) .

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- Históricamente, sólo se tenían en cuenta los potenciales beneficios cardiovasculares de la antiagregación de larga duración con aspirina .

BALANCE BENEFICIO AAS

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LA AMENAZA PUEDE VENIR DE OTRO LADO

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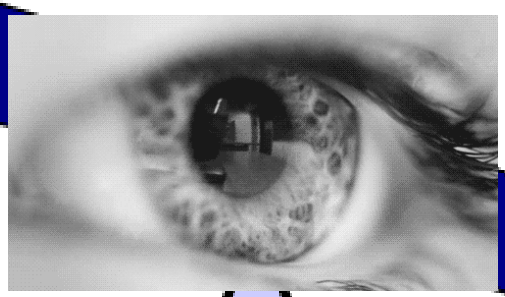
Aspirin for primary prevention

Fewer heart attacks



More bleeding events

Annual coronary event risk

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RIESGOS

- **Sangrado GI *** : Aumento estadísticamente significativo del riesgo de sangrado en aquellos que tomaban aspirina respecto a los que tomaron placebo. (OR 1.68 / IC 95 % 1.51-1.88)

- **Hemorragia intracraneal **:** Aumento relativo del riesgo de infarto hemorrágico (resultado no estadísticamente significativo (RR 1.32 /IC 95% 1.00-1.75)

- **Sangrado mayor **:** Asociación estadísticamente significativa de toma de AAS con aumento del riesgo de sangrado mayor (RR 1.53 / IC 95 % 1.30-1.82)

*Metanalisis de 24 RCT de aproximadamente 66.000 personas tomado AAS durante más de un año.
** Metaanalisis de datos individuales por pacientes recogidos en 6 ensayos de prevención primaria.

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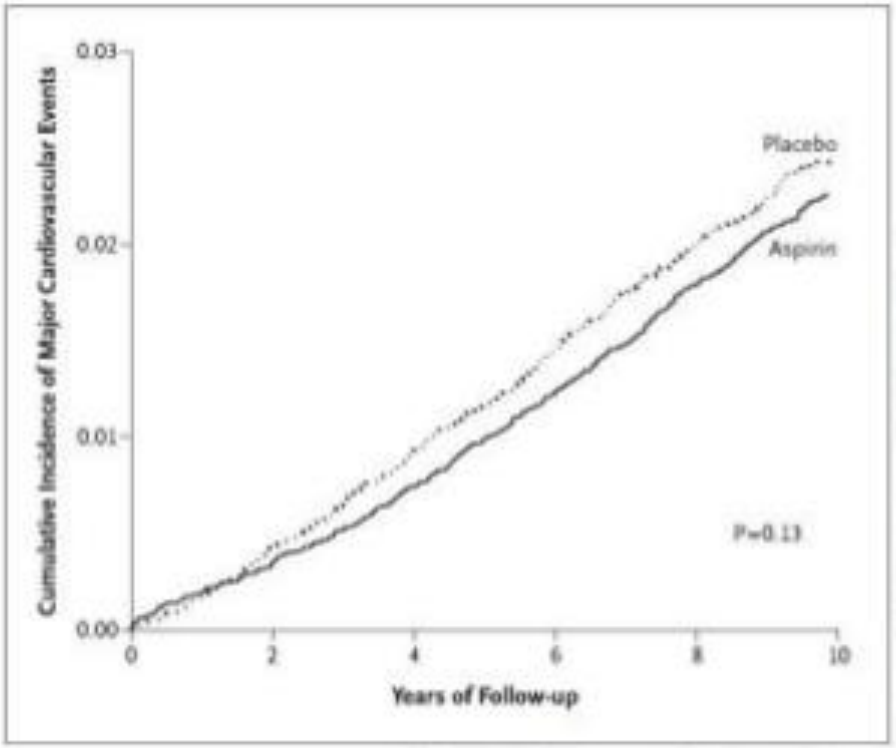
Aspirin Evidence: Primary Prevention

Womens' Health Study (WHS)

39,876 women randomized to aspirin (100 mg every other day) or placebo for an average of 10 years



Aspirin does not reduce cardiovascular events among women

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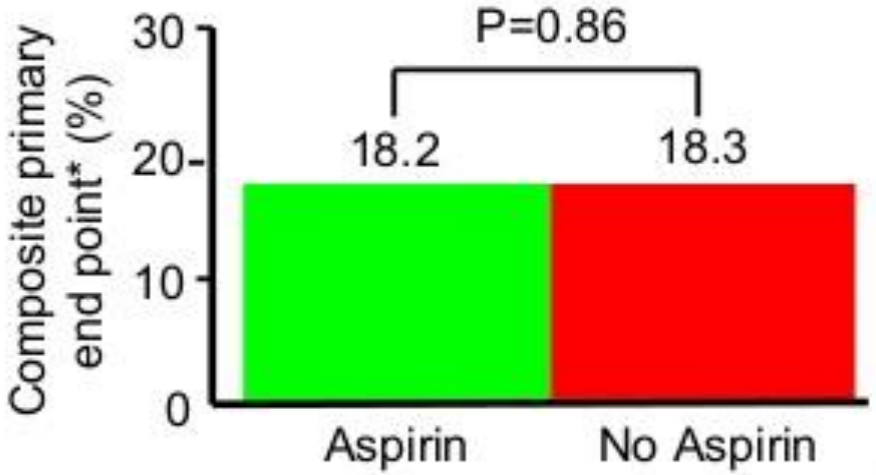
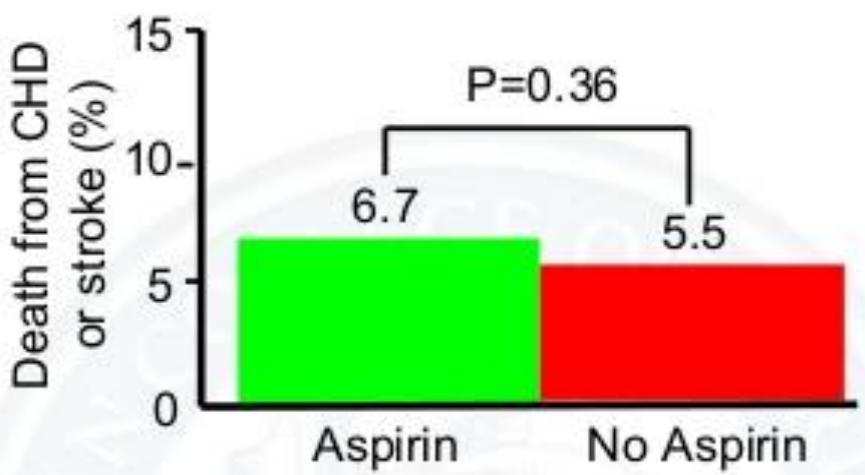
Source: Ridker P et al. *NEJM* 2005;352:1293-1304

Aspirin Evidence: Primary Prevention

Prevention of Progression of Arterial Disease and Diabetes (POPADAD) Study

1,276 asymptomatic patients with DM and an ABI <0.99 randomized in a 2 x 2 design to aspirin (100 mg), antioxidants, aspirin plus antioxidants, or placebo





Aspirin does not reduce the risk of adverse CV events in diabetics

*Includes fatal CHD or stroke, non-fatal MI or stroke, or amputation above the ankle for critical limb ischemia

ABI=Ankle brachial index, CHD=Coronary heart disease, CV=Cardiovascular, DM=Diabetes mellitus, MI=Myocardial infarction

Source: Belch J et al. *BMJ*. 2008;337:a1840

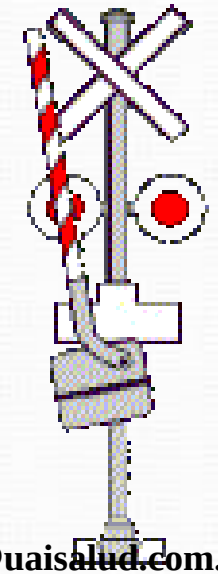
European Heart Journal (2012) 33, 1635–1701
doi:10.1093/eurheartj/ehs092

JOINT ESC GUIDELINES

European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)

- AAS no puede ser recomendado en individuos sin ECV debido al riesgo incrementado de hemorragia grave.

(Grado de Recomendación III, nivel de evidencia B)



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CHEST Supplement

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Primary and Secondary Prevention of Cardiovascular Disease

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

- Recomiendan la utilización de AAS (75-100 mg / día) frente a no utilizar AAS en personas mayores de 50 años sin ECV sintomática. **

(Grado de Recomendación 2B)

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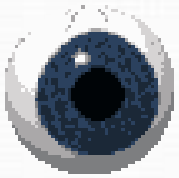
Propuesta de toma de decisiones (USPSTF)



1. Calcular Riesgo Cardiovascular del paciente.
    1. - FRAMINGHAM/SCORE.
2. La magnitud del riesgo y del beneficio puede estimarse con tablas que propone la USPSTF.
3. **AAS debe ser prescrito basándonos en un juicio clínico individualizado cuando el beneficio absoluto es mayor que el riesgo absoluto.**
4. Cuando la magnitud del riesgo es similar a la del beneficio, la preferencia del paciente debe ser tenida en cuenta.
5. **Este aproximación general puede que no se a útil en paciente que tienen factores de riesgo de sangrado de base.**

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Escores de Framingham

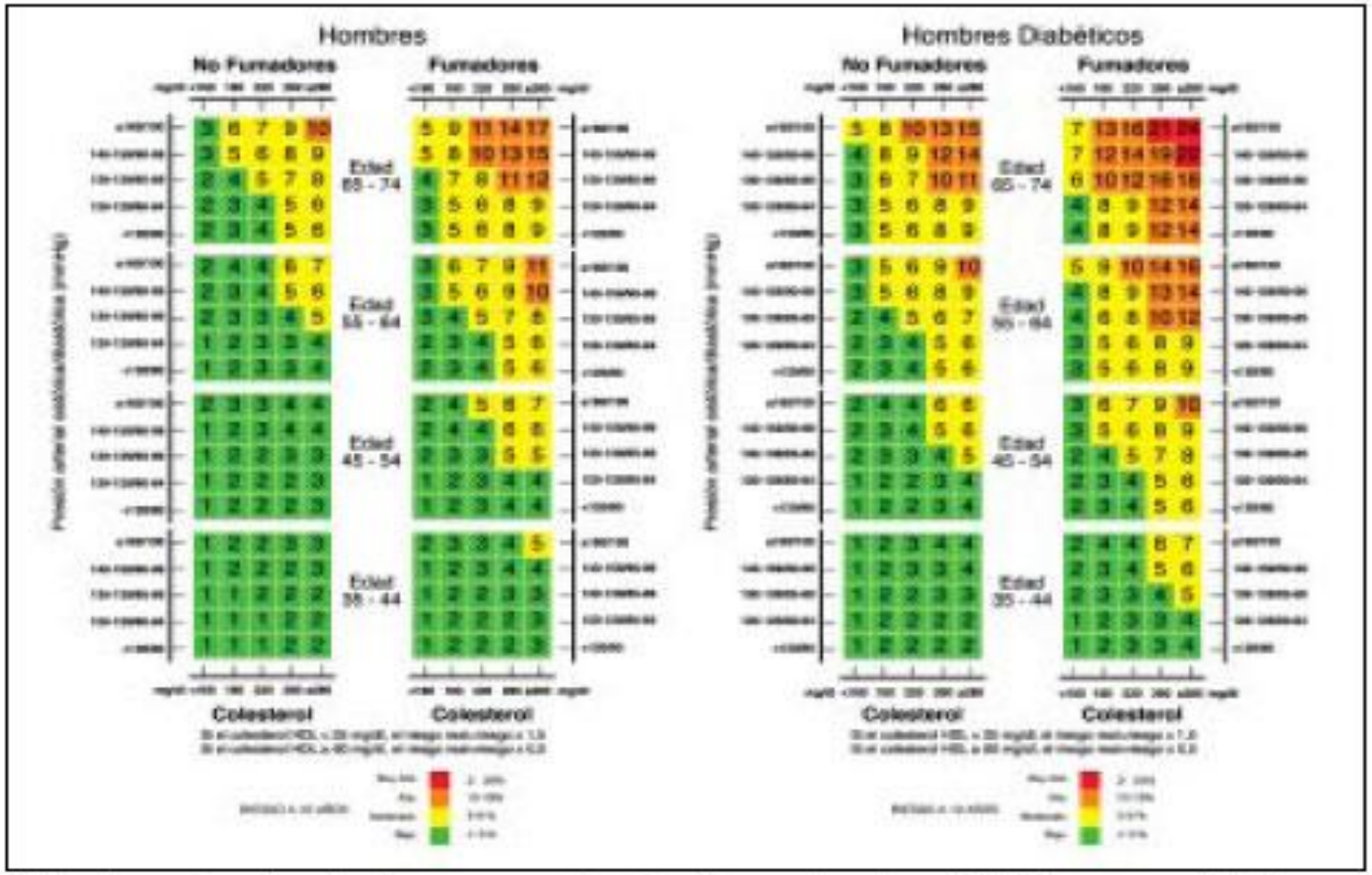

Figura 2. Tabla de estimación de riesgo coronario a 10 años en hombres diabéticos y no diabéticos de 35 a 74 años para población chilena.

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Dosis

- En general todas las guías establecen el mejor ratio beneficio/riesgo entre 75-325 mg /día.
  - FDA 75-325 mg/día.
  - ACC/AHA 75-160 mg/día.
  - ACCP 75-100.
- **Antitrombotic Trialist Collaboration meta-analyses:**
  - **Son igual de efectivas dosis comprendidas entre 75 y 325 mg/diarios en la prevención de evento vascular.**

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Aspirin Recommendations

Primary Prevention

Aspirin (81 mg daily or 100 mg every other day) in at risk women ≥65 years of age

Aspirin in at risk women <65 years of age for ischemic stroke prevention

Aspirin in optimal risk women <65 years of age

Source: Mosca L et al. *Circulation* 2007;115:1481-1501

Prevención secundaria

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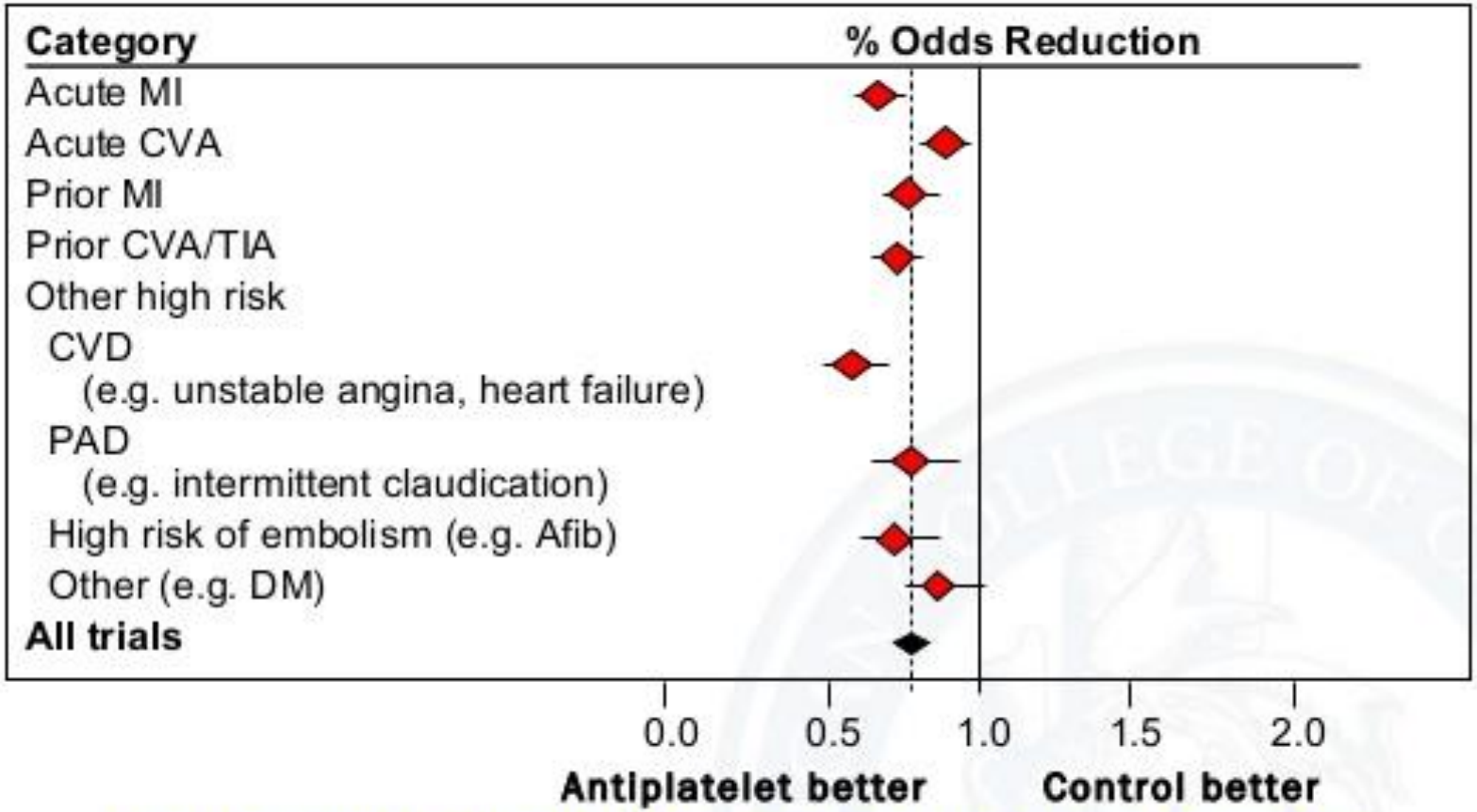
Aspirin Evidence: Secondary Prevention

Effect of antiplatelet treatment* on vascular events**



Aspirin reduces the risk of adverse cardiovascular events

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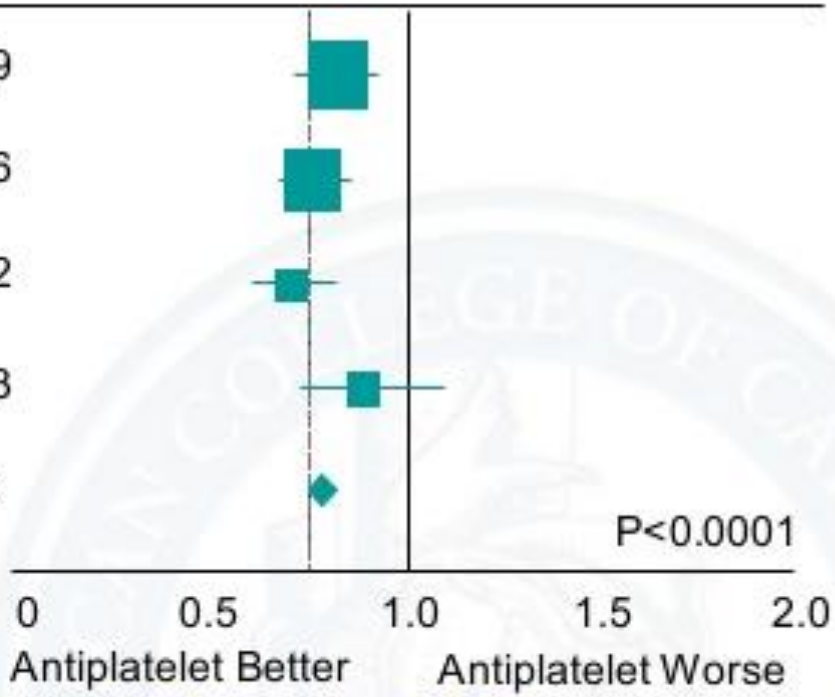
*Aspirin was the predominant antiplatelet agent studied
**Include MI, stroke, or death

Source: Antithrombotic Trialists' Collaboration. *BMJ* 2002;324:71–86

Aspirin Evidence: Dose and Efficacy

Effect of aspirin doses on vascular events in high-risk patients (excluding those with acute stroke)

Aspirin Dose	No. of Trials	% Odds Reduction
500-1500 mg	34	19
160-325 mg	19	26
75-150 mg	12	32
<75 mg	3	13
Any aspirin	65	23



High dose aspirin does not provide improved efficacy

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Source: Antithrombotic Trialists' Collaboration. *BMJ* 2002;324:71-86

Aspirin Recommendations (Continued)

Secondary Prevention

I IIa IIb III

Aspirin (75-162 mg daily) if known CAD† or NSTE-ACS‡

I IIa IIb III

Aspirin (81-325 mg daily) following PCI or fibrinolytic therapy for a STEMI*

I IIa IIb III

Aspirin (preferentially at 81 mg daily) following PCI for a NSTE-ACS# or a STEMI*, or fibrinolytic therapy for a STEMI*

ASA=Acetylsalicylic acid, CAD=Coronary artery disease, NSTE-ACS=Non-ST segment elevation acute coronary syndrome, PCI=Percutaneous coronary intervention, STEMI=ST-segment elevation myocardial infarction

Sources:

†Smith SC Jr. et al. *JACC* 2011;58:2432-2446

‡Wright RS et al. JACC 2011;57:e215-367

*O'Gara PT et al. *JACC* 2013;61:e78-e140

#Jneid H et al. *JACC* 2012;60:645-681

5 minutos …

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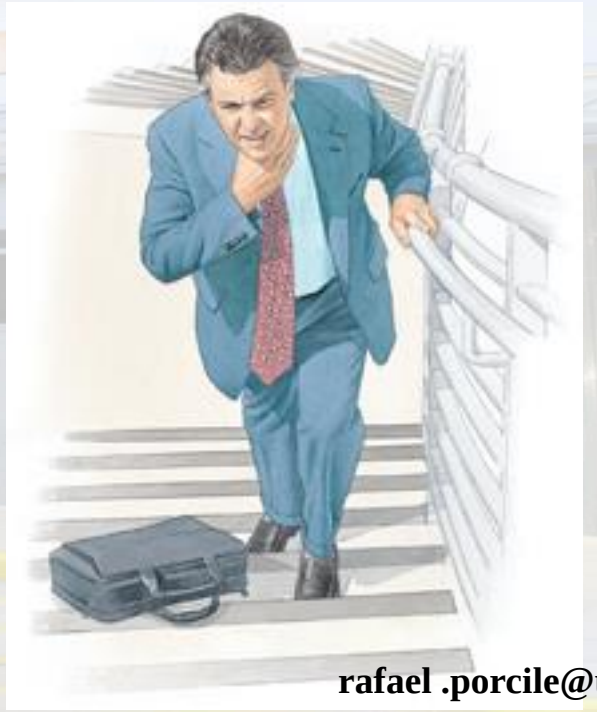
Angina Inestable y aspirina



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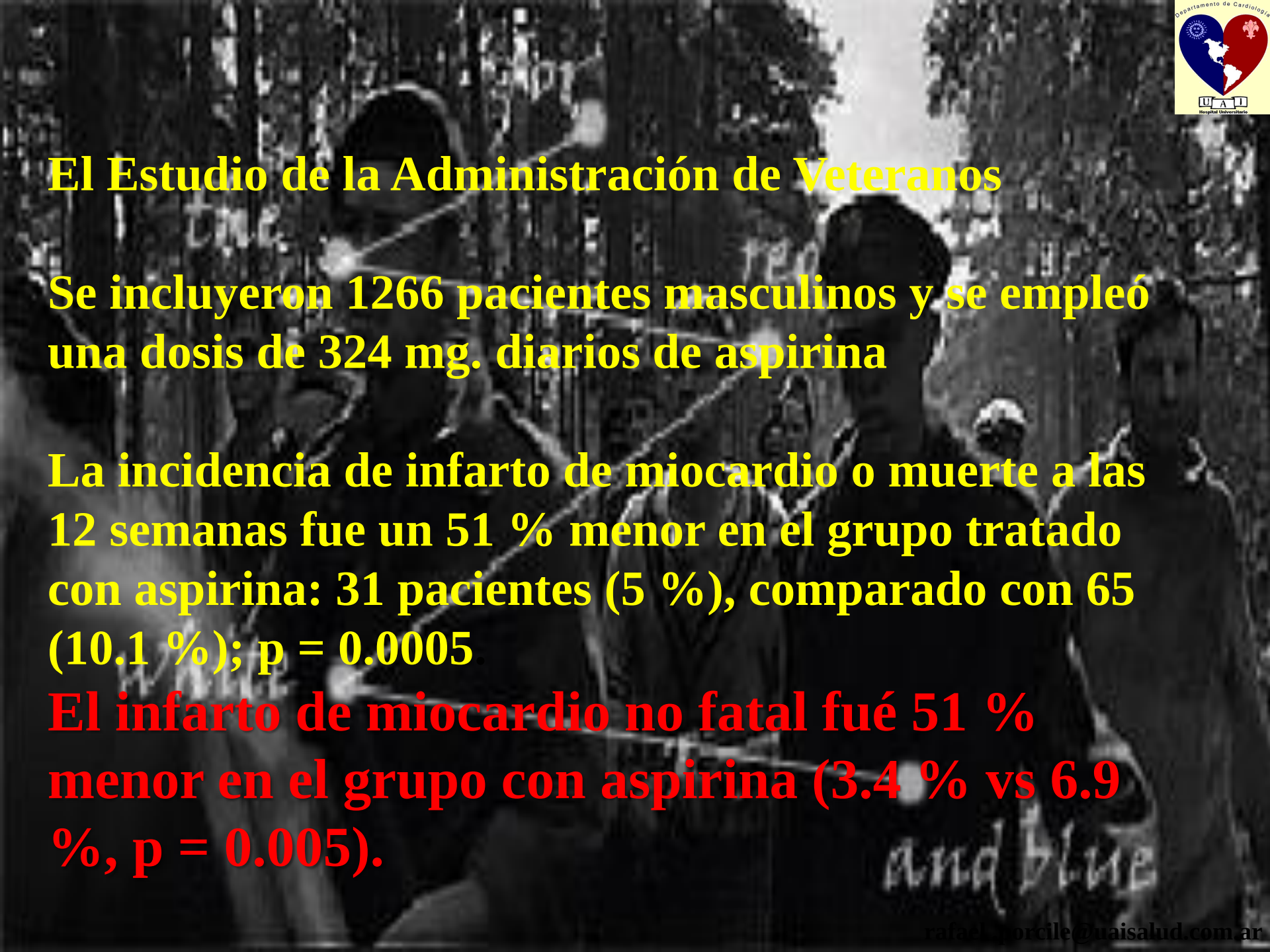
red
white
and blue



El Estudio de la Administración de Veteranos

Se incluyeron 1266 pacientes masculinos y se empleó una dosis de 324 mg. diarios de aspirina

La incidencia de infarto de miocardio o muerte a las 12 semanas fue un 51 % menor en el grupo tratado con aspirina: 31 pacientes (5 %), comparado con 65 (10.1 %); p = 0.0005

El infarto de miocardio no fatal fué 51 % menor en el grupo con aspirina (3.4 % vs 6.9 %, p = 0.005).

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Grupo de Investigación de Inestabilidad en la Arteriopatía Coronaria (RISC)

911 pacientes masculinos con angina inestable o infarto de miocardio no Q, fueron randomizados a placebo o baja dosis de aspirina (75 mg. por día). **El análisis de los 796 pacientes mostró una reducción de muerte e infarto a los 5 días del 5,7 % a 2,5 %,** (riesgo relativo = 0.43; intervalo de confianza = 0.21-0.91), a los 30 días de 13,3 % al 4,2 %, (riesgo relativo = 0.31, intervalo de confianza = 0.18-0.43) y a los 90 días del 17 % al 6,5 % (riesgo relativo 0.36, intervalo de confianza = 0.23- 0.57

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Review

Adding Heparin to Aspirin Reduces the Incidence of Myocardial Infarction and Death in Patients With Unstable Angina

A Meta-analysis

Allison Oler, MD; Mary A. Whooley, MD; Jacqueline Oler, PhD; Deborah Grady, MD, MPH

Objective.—To estimate the risk of myocardial infarction (MI) and death in patients with unstable angina who are treated with aspirin plus heparin compared with patients treated with aspirin alone.

Data Sources.—Studies were retrieved using MEDLINE, bibliographies, and consultation with experts.

Study Selection.—Only published trials that enrolled patients with unstable angina, randomized participants to aspirin plus heparin vs aspirin alone, and reported incidence of myocardial infarction or death were included in the meta-analysis.

Data Extraction.—Patient outcomes including MI or death, recurrent ischemic pain, and major bleeding during randomized treatment; revascularization procedures after randomization; and MI or death during the 2 to 12 weeks following randomization were extracted by 2 authors, 1 of whom was blinded to the journal, institution, and author of each study.

Data Synthesis.—Six randomized trials were included. The overall summary relative risk (RR) of MI or death during randomized treatment was 0.67 (95% confidence interval [CI], 0.44-1.02) in patients with unstable angina treated with aspirin plus heparin compared with those treated with aspirin alone. The summary RRs for secondary endpoints in patients treated with aspirin plus heparin compared with those treated with aspirin alone were 0.68 (95% CI, 0.40-1.17) for recurrent ischemic pain; 0.82 (95% CI, 0.56-1.20) for MI or death 2 to 12 weeks following randomization; 1.03 (95% CI, 0.74-1.43) for revascularization; and 1.99 (95% CI, 0.52-7.65) for major bleeding. We found no statistically significant heterogeneity among individual study findings.

Conclusions.—Our findings are consistent with a 33% reduction in risk of MI or death in patients with unstable angina treated with aspirin plus heparin compared with those treated with aspirin alone. The bulk of evidence suggests that most patients with unstable angina should be treated with both heparin and aspirin.

JAMA. 1996;276:811-815

UNSTABLE ANGINA, ranging from progressive angina to angina at rest, results from intracoronary plaque disruption causing increased stenosis and, in some cases, intermittent thrombosis.[1] Prospective studies have found that 12% of patients admitted to the hospital with unstable angina progress to myocardial infarction (MI) within 2 weeks of diagnosis.[2,3] One-year mortality of patients with unstable angina ranges from 5% to 14% with approximately half of these deaths occurring within 4 weeks of diagnosis.[4] In patients with unstable angina, aspirin reduces the risk of thrombosis by inhibiting platelet aggregation and decreases the risk of cardiac death or nonfatal MI by 30% to 51%.[5-7]

Heparin binds to antithrombin III and induces a conformational change that results in rapid inhibition of thrombin.[8] This inhibition of thrombin prevents propagation of an established thrombus and allows time for endogenous fibrinolysis to occur. In theory, adding heparin to aspirin should reduce intracoronary obstruction, improve coronary blood flow, reduce myocardial ischemia, and ultimately decrease cardiac morbidity and mortality in patients with unstable angina.[9] Several randomized clinical trials have demonstrated a trend toward reduced risk of death or nonfatal myocardial infarction in patients with unstable angina treated with aspirin plus intravenous heparin compared with patients treated with aspirin alone.[7,10-14] However, it has not been established definitively that the combination of aspirin plus heparin is superior to aspirin alone. We performed a meta-analysis of published randomized trials to determine whether treatment with intravenous heparin and aspirin is more effective than treatment with aspirin alone in preventing MI or death in patients with unstable angina.

METHODS

Literature Review

We performed a literature search using the MEDLINE database (January 1966 to September 1995) with the keywords "aspirin," "heparin," and "unstable angina." The search was not restricted to citations in the English-language literature. In addition, a manual search was done using reference lists from identified articles and consultation with experts.

Studies included in the meta-analysis met the following criteria: (1) a randomized clinical trial; (2) eligible participants were admitted to the hospital with the diagnosis of unstable angina or non–Q-wave myocardial infarction; (3) participants were assigned either to intravenous heparin and aspirin or to aspirin alone; and (4) the incidence of myocardial infarction (prolonged chest pain associated with Q waves or persistent ST changes on electrocardiogram and/or a 2-fold increase over baseline creatine

From the Departments of Medicine (Drs A. Oler, Whooley, and Grady) and Epidemiology and Biostatistics (Dr Grady), University of California, San Francisco, School of Medicine; the General Internal Medicine Section, San Francisco Veterans Affairs Medical Center (Drs Whooley and Grady); and the Department of Quantitative Methods, Drexel University, Philadelphia, Pa (Dr J. Oler).

Reprints: Deborah Grady, MD, MPH, General Internal Medicine Section, San Francisco Veterans Affairs Medical Center, 111A1, 4150 Clement St, San Francisco, CA 94121.

yielded a summary RR of MI or death during randomized treatment of 0.56 (95% CI, 0.40-0.80; for test of heterogeneity, $P=.52$) in patients with unstable angina treated with aspirin plus heparin compared with those treated with aspirin alone. We believe the possibility that low-molecular-weight heparin is superior to unfractionated heparin in patients with unstable angina should be explored in a randomized controlled trial.

CONCLUSION

This meta-analysis of 6 randomized controlled trials demonstrated a strong trend toward reduction in risk of MI or death during randomized therapy in patients with unstable angina treated with aspirin plus heparin compared with those treated with aspirin alone. Current evi-

Comparison of the effect of heparin and as[illegible] versus aspirin alone on transient myocardial is[illegible]mia and in-hospital prognosis in patients with stable angina. *J Am Coll Cardiol.* 1994;24:39-

14. Gurfinkel EP, Manos EJ, Mejail RI, et al. [illegible] molecular weight heparin versus regular heparin or aspirin in the treatment of unstable angina and silent ischemia. *J Am Coll Cardiol.* 1995;26:313-318.
15. Walter S, Cook R. A comparison of several point estimators of the odds ratios in a single 2×2 contingency table. *Biometrics.* 1991;47:795-811.
16. Fleiss JL. *Statistical Methods for Rates and Proportions.* 2nd ed. New York, NY: John Wiley & Sons Inc; 1981.
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20. *BMDP Statistical Software, Inc.* PC90 ed. Los Angeles: University of California Press; 1990.

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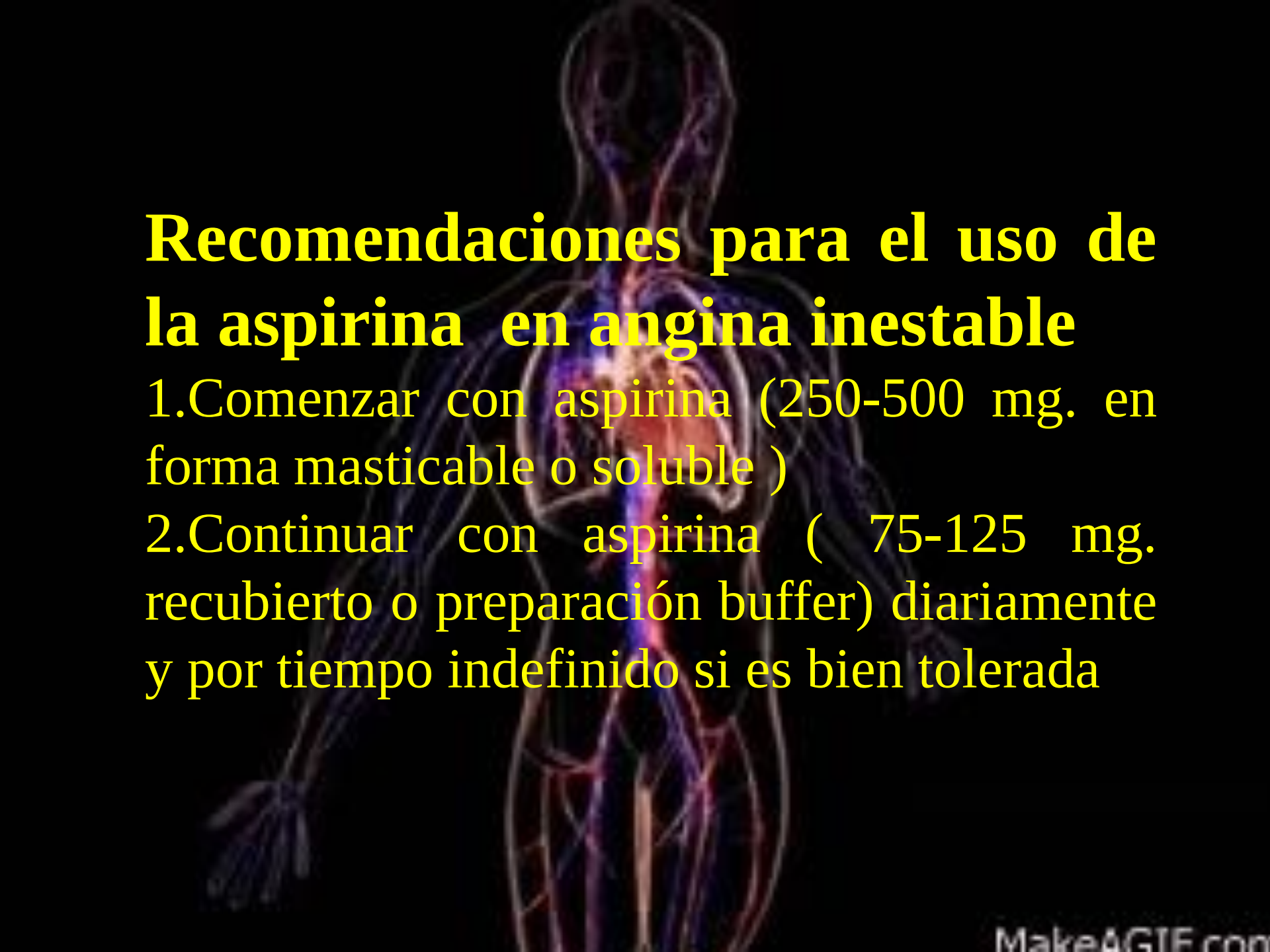
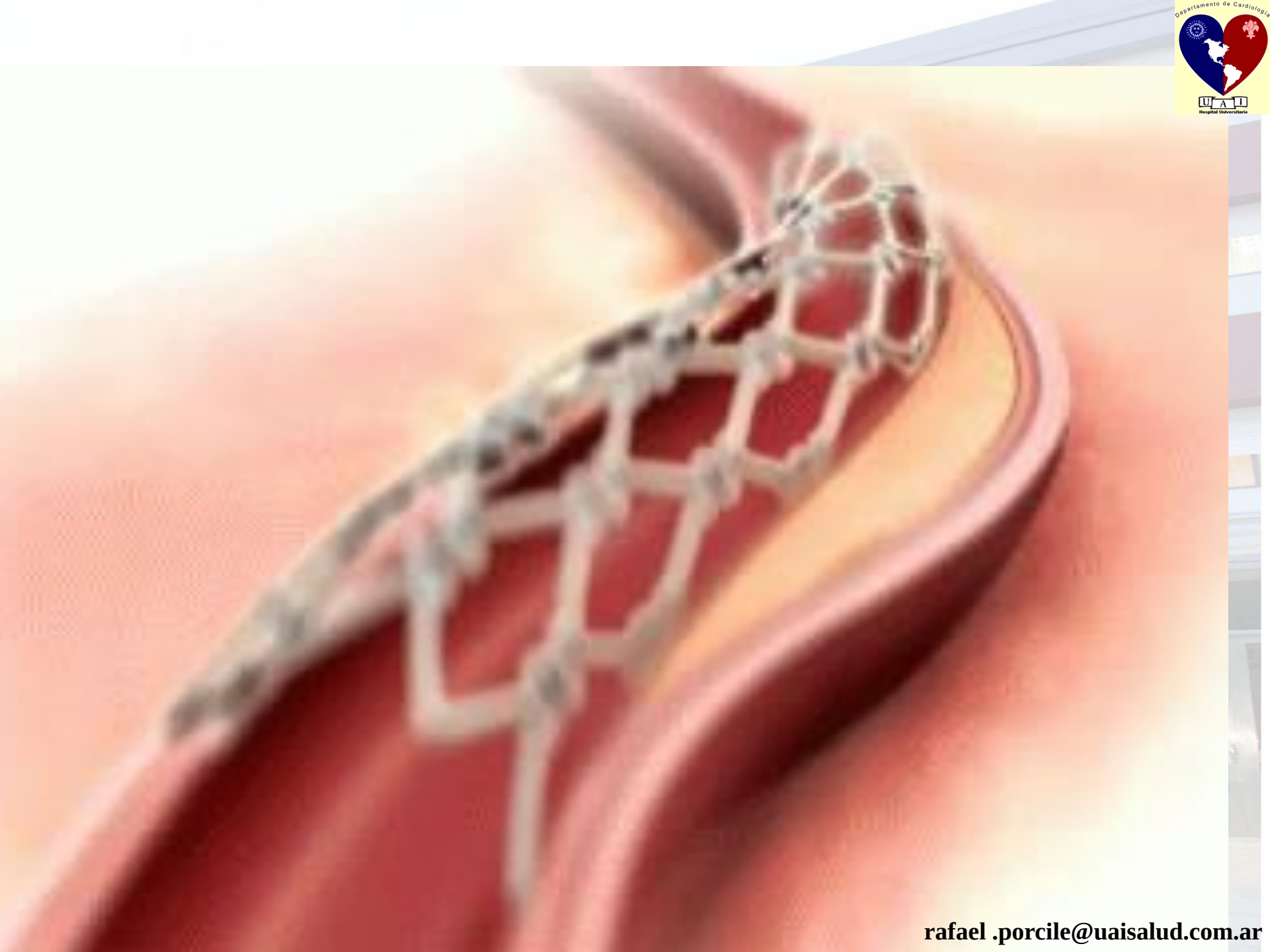
MakeAGIF.com



Recomendaciones para el uso de la aspirina en angina inestable

1.Comenzar con aspirina (250-500 mg. en forma masticable o soluble)

2.Continuar con aspirina (75-125 mg. recubierto o preparación buffer) diariamente y por tiempo indefinido si es bien tolerada



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Stent Intra Coronario

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RECONOCIMIENTO A NUESTROS MAYORES

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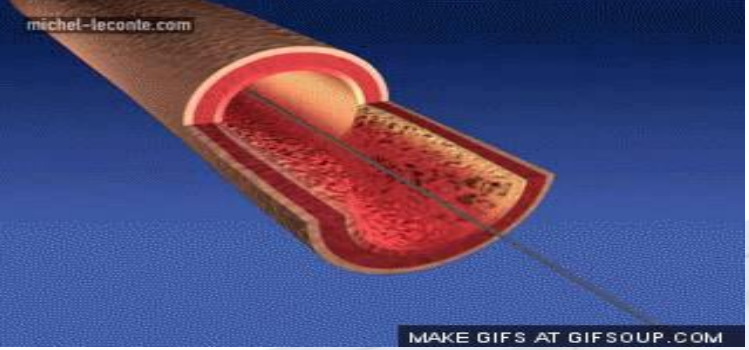

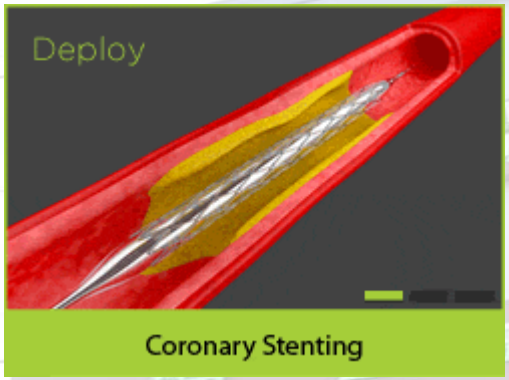

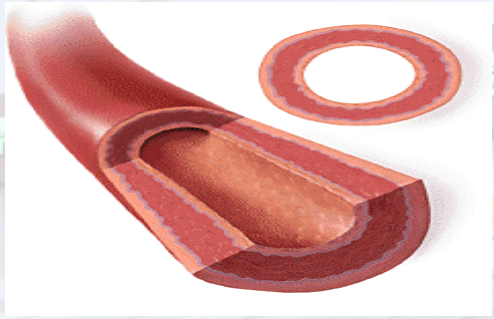

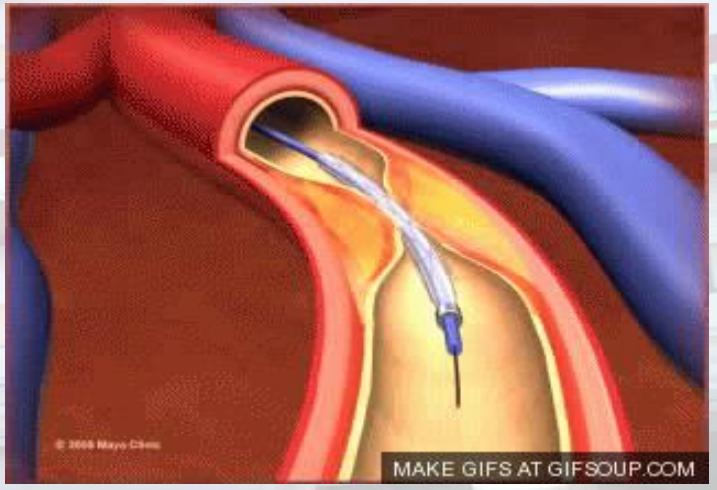

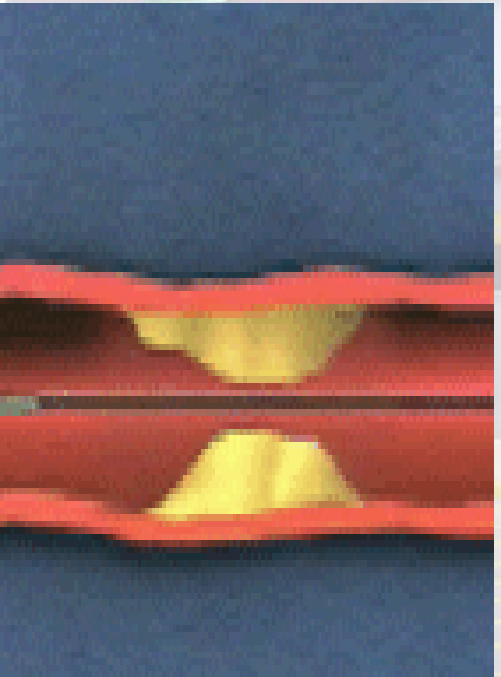

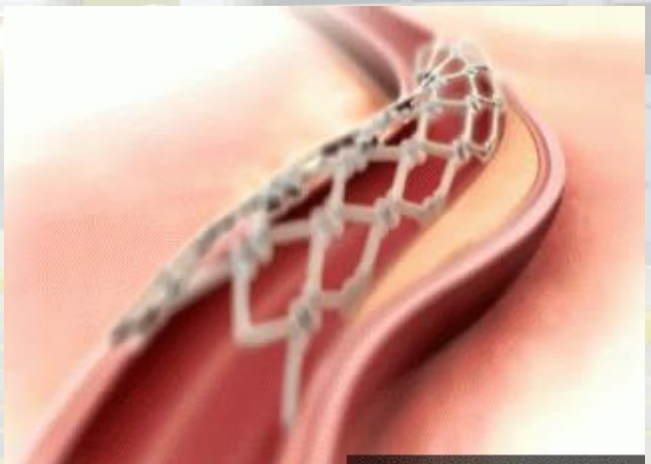

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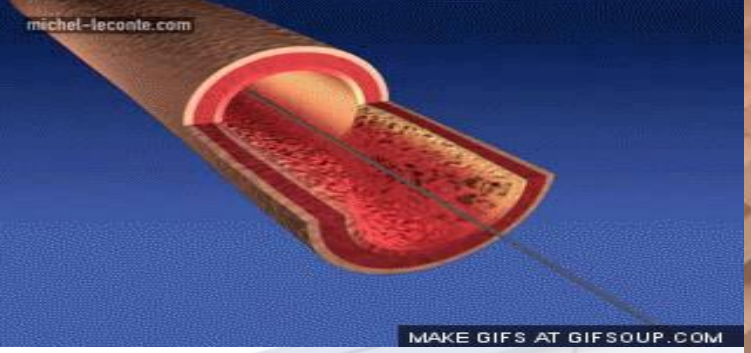
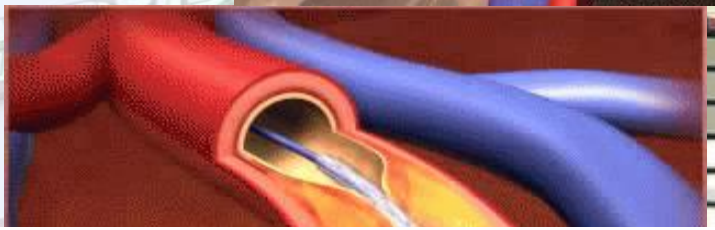
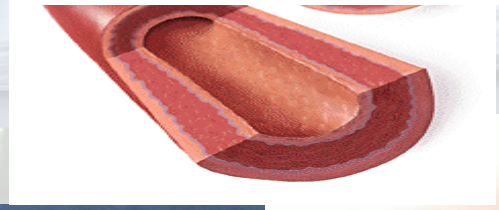
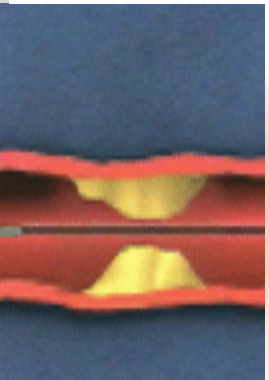
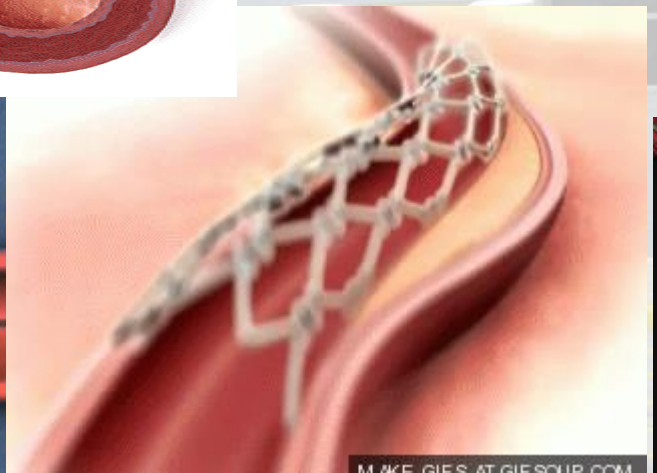




Julio César Palmaz







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Julio César Palmaz

Nacido el 13 de diciembre de 1945 en **La Plata, Argentina**

Estudió en la Universidad Nacional de La Plata, obteniendo su título de médico en 1971.
Realizó sus prácticas en la especialidad de radiología en el Hospital Interzonal General de Agudos San Martín de La Plata, antes de trasladarse a Estados Unidos.
Es conocido por inventar el *stent expandible*, por el que obtuvo una patente en 1988 En 2013 recibió la Mención Especial por Trayectoria de los Premios Konex a la Ciencia y Tecnología
El stent desarrollado por Palmaz fue aprobado para su uso en arterias periféricas en 1991 y en arterias coronarias en 1994.

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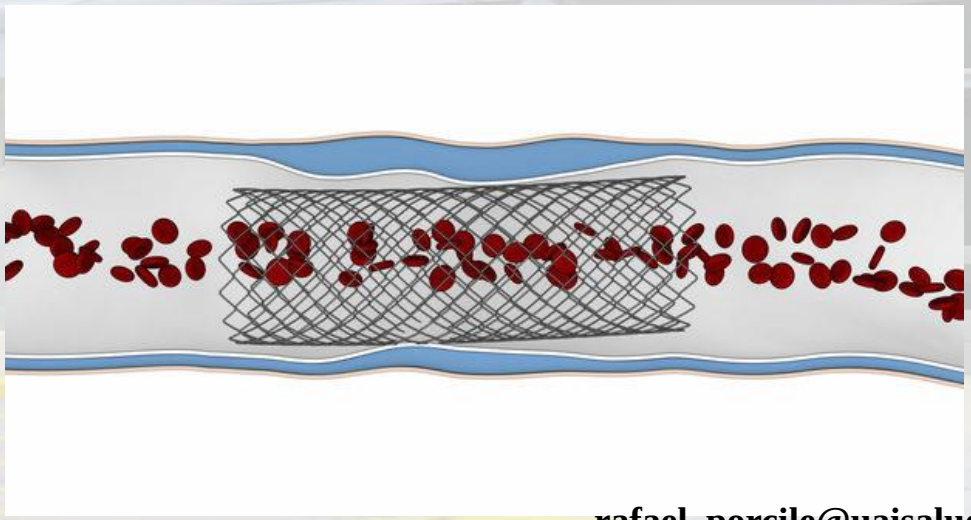
Aspirina y angioplastia

CHARISMA trial, a subgroup of 9,478 patients with prior MI, stroke, and symptomatic peripheral arterial disease did appear to benefit from dual antiplatelet therapy



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¿ASPIRINA EN FORAMEN OVAL PERMEABLE?

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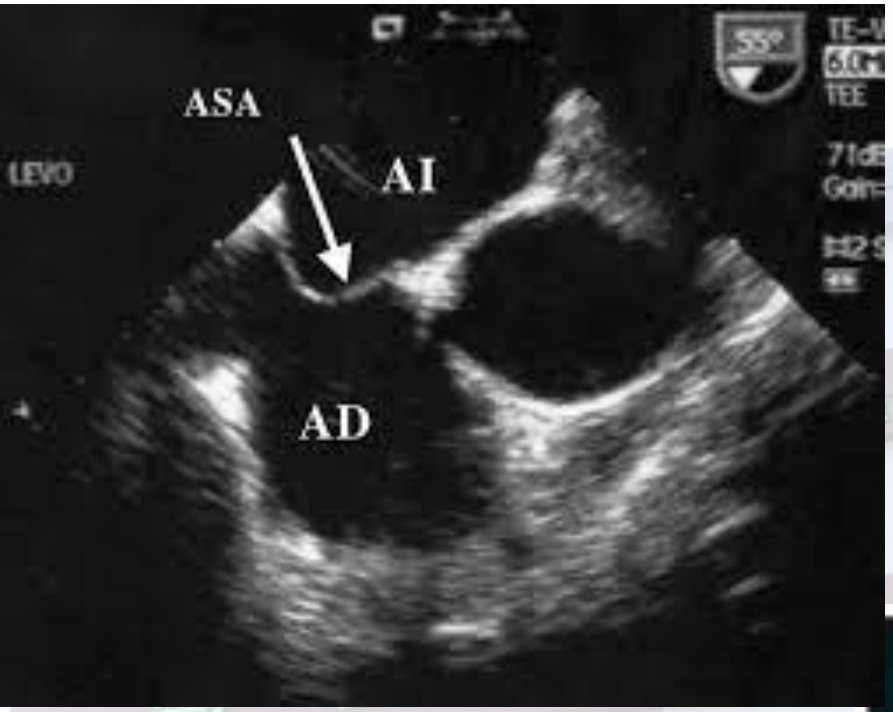

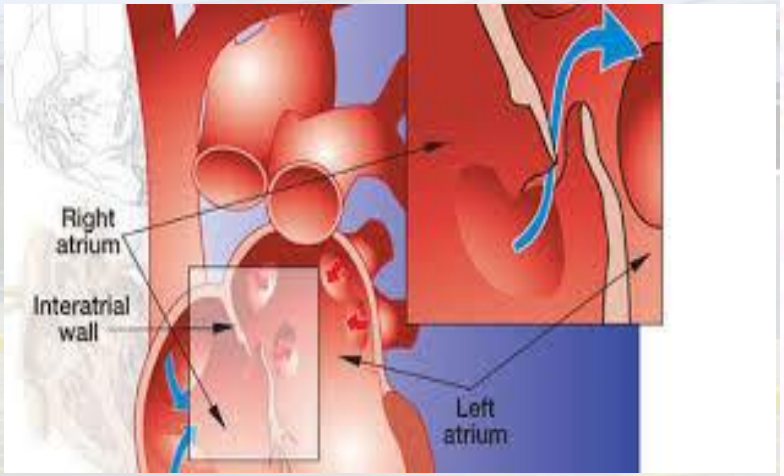

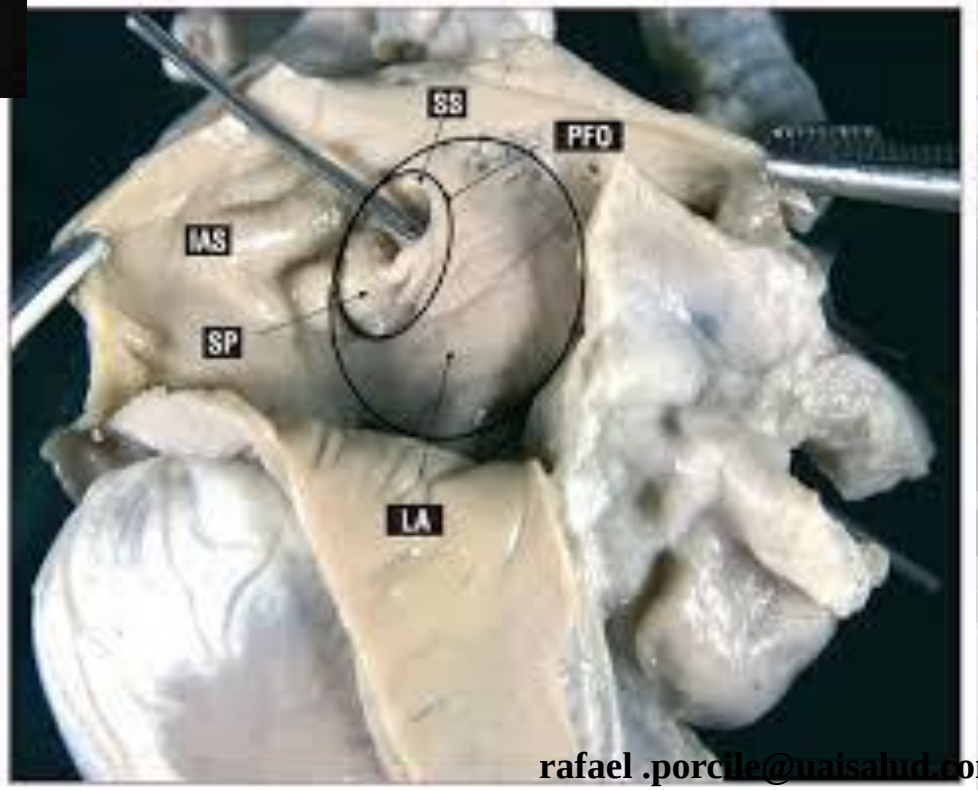

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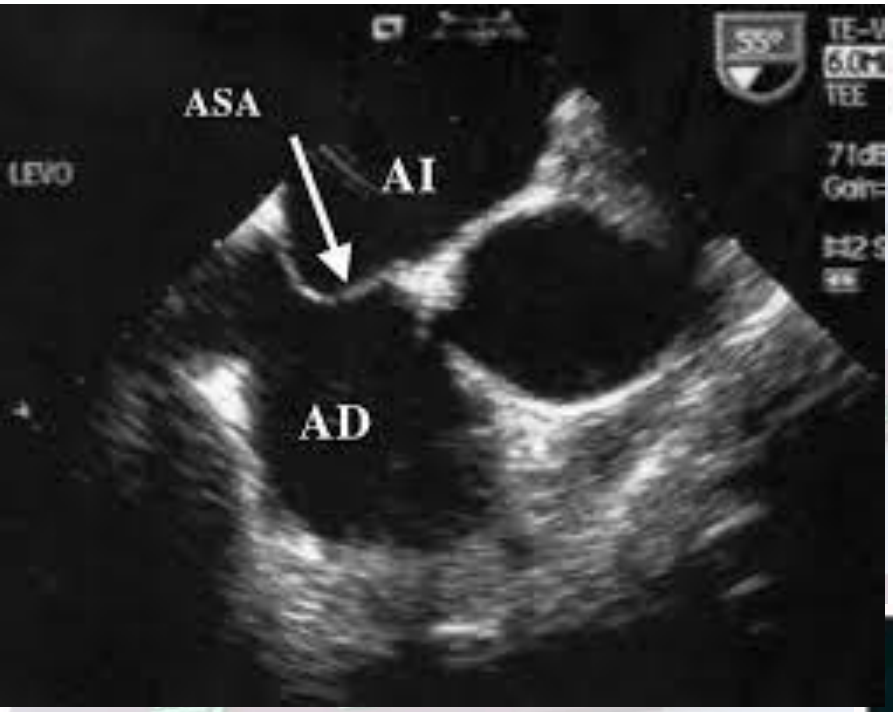

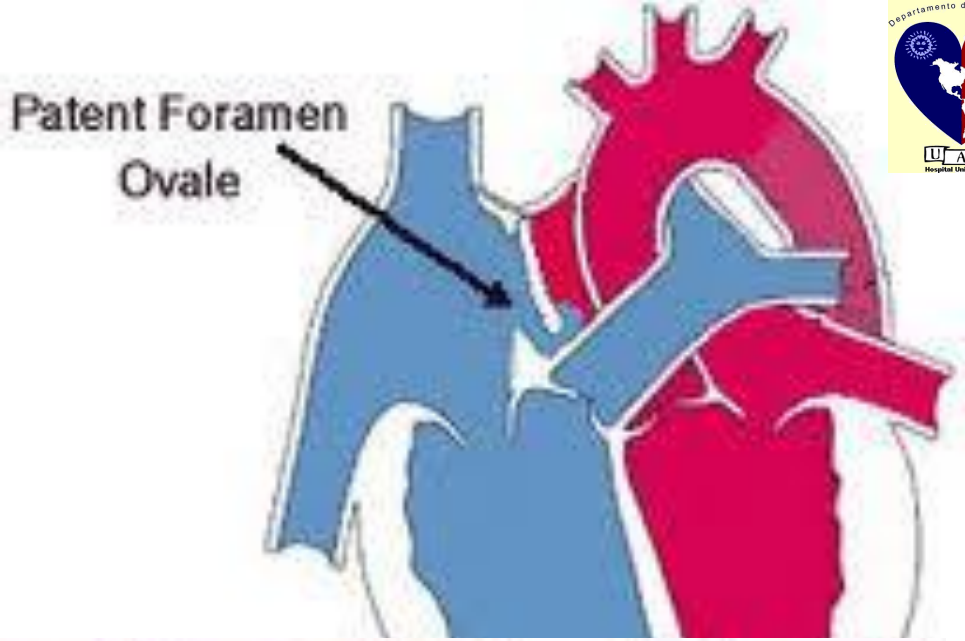

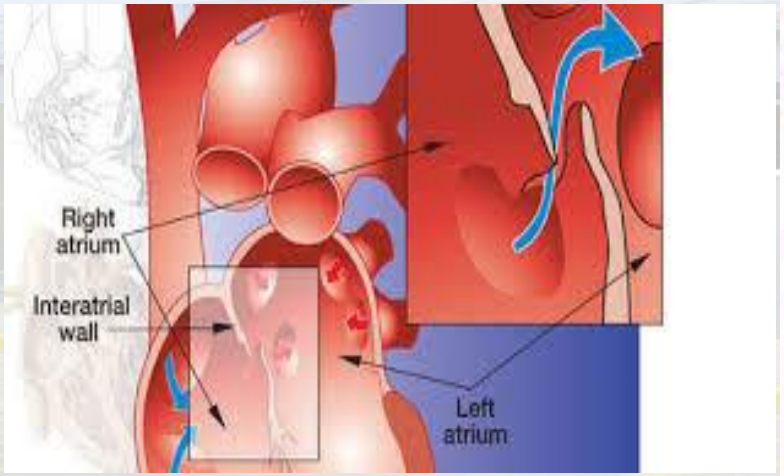

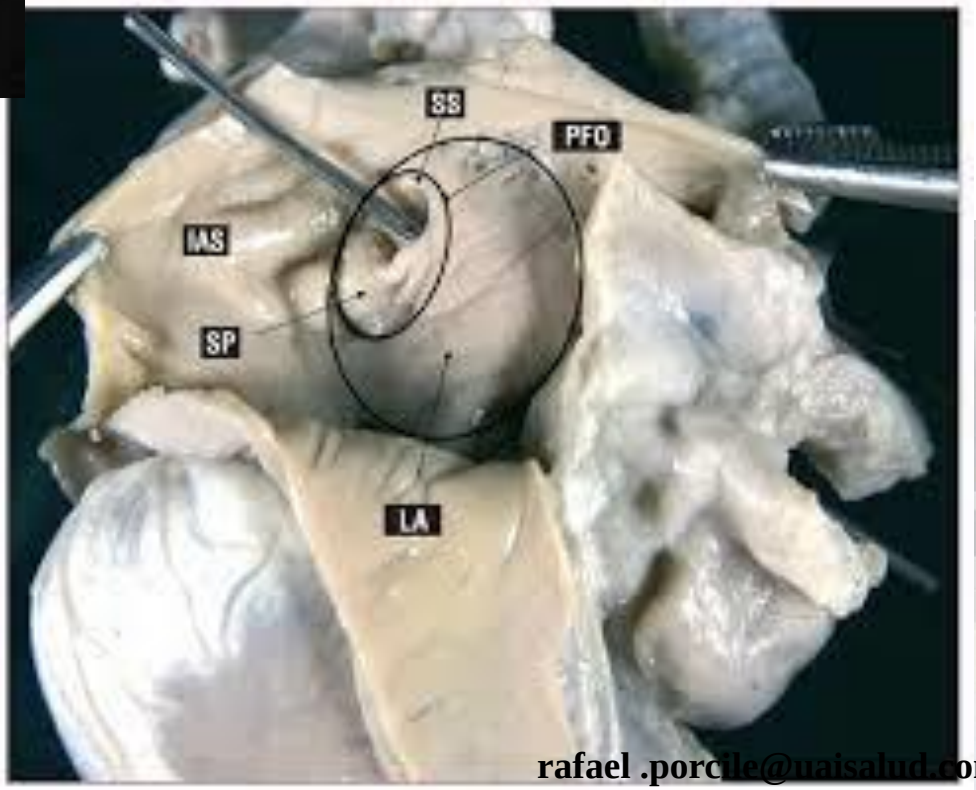

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La persistencia del foramen oval permeable (FOP) en adultos es un hallazgo común, del que se ha descrito una prevalencia del 25% en la población general.

Es un hallazgo casual sin repercusiones clínicas.

Sin embargo, se ha señalado la posible relación del FOP con accidentes cerebrovasculares embólicos, el síndrome platipnea-ortodesoxia,
la embolia gaseosa de los buceadores o las migrañas.

El tratamiento de elección del FOP todavía no está definido, y muchos de los estudios publicados presentan resultados contradictorios.

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Platipnea-ortodesoxia

Disnea y desaturación arterial **sentado o parado**; mejorando cuando se adopta la posición de decúbito dorsal (DD).

Esta dado por shunt de **derecha a izquierda** a través de un foramen oval permeable

Esto es permitido por un cambio en la arquitectura cardiaca durante la posición de sentado, que hace que el jet de sangre proveniente de la vena cava inferior se dirija hacia el FOP permitiendo el shunt.

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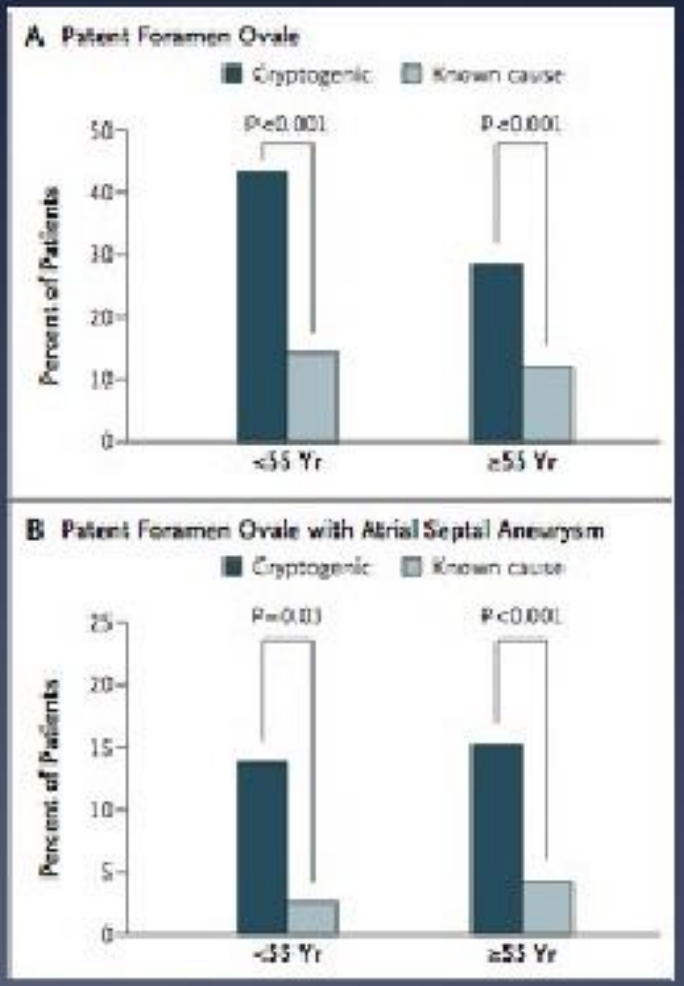
Ictus cerebral y foramen oval

* En pacientes con ictus criptogénico hay mayor prevalencia de FO comparado a sujetos normales o con ictus de causa identificable.
* La asociación FO con ictus criptogénico es mayor en menores de 55 años.



Handke M, Harloff A, Olschewski M, et al. Patent foramen ovale and cryptogenic stroke in older patients. N Engl J Med. 2007;357:2262–8

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VOLVAMOS A LO NUESTRO… ASPIRINA

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¿ASPIRINA EN FORAMEN OVAL PERMEABLE?

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Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2012;141(2 Suppl):e576S

In patients with patent foramen ovale (PFO) and stroke or transient ischemic attack, we recommend initial aspirin therapy (Grade 1B) and suggest substitution of VKA if recurrence (Grade 2C)

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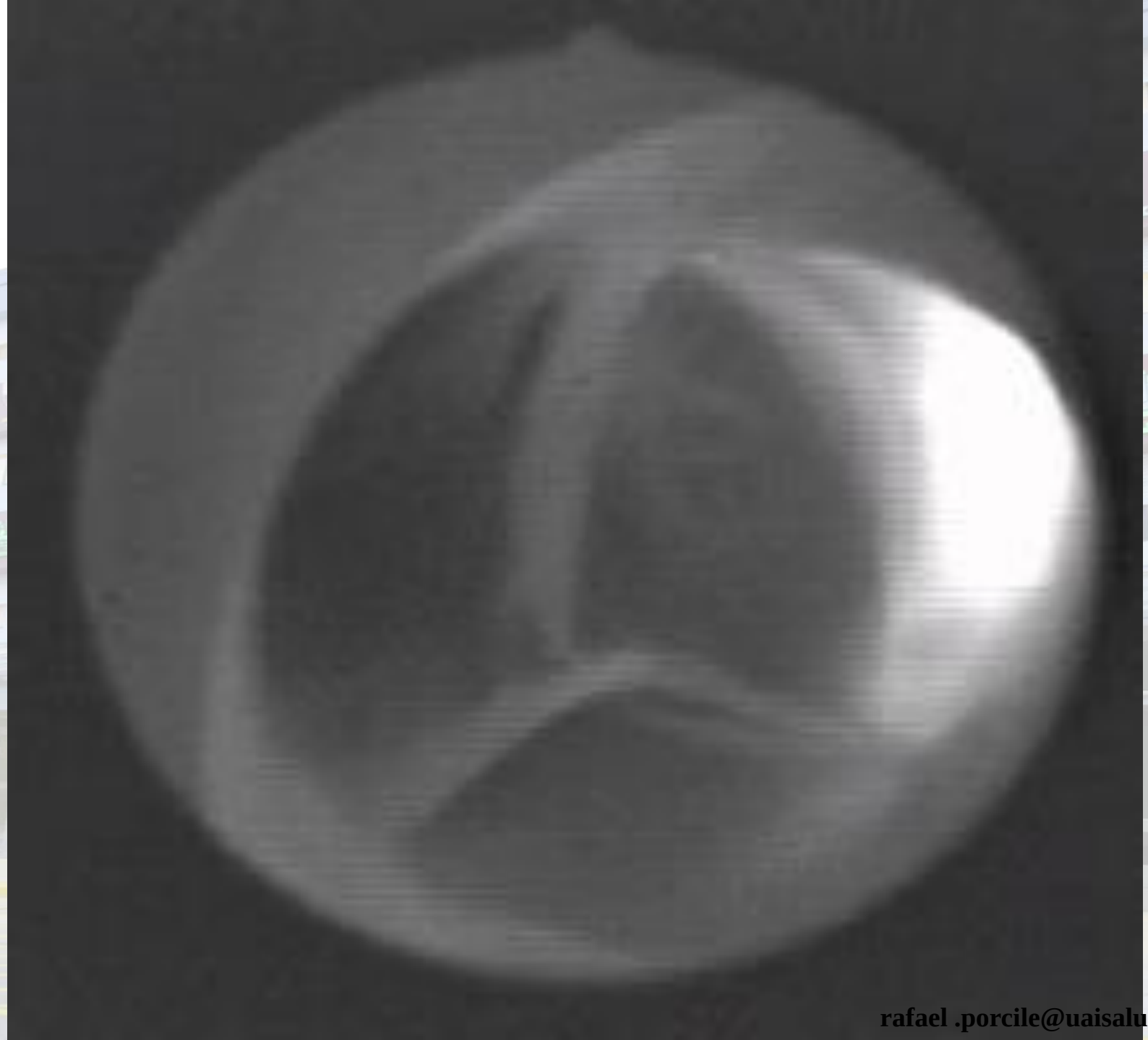

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ASPIRINA EN REEMPLAZO VALVULAR AORTICO

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Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2012;141(2 Suppl):e576S

In the first 3 months after bioprosthetic valve implantation, we recommend aspirin for aortic valves (Grade 2C)

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ASPIRINA EN PASTICAS QUIRURGICA VALVULARES

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Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2012;141(2 Suppl):e576S

In valve repair patients, we suggest aspirin therapy (Grade 2C)

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Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2012;141(2 Suppl):e576S

The addition of clopidogrel to aspirin if the aortic valve is transcatheter (Grade 2C),

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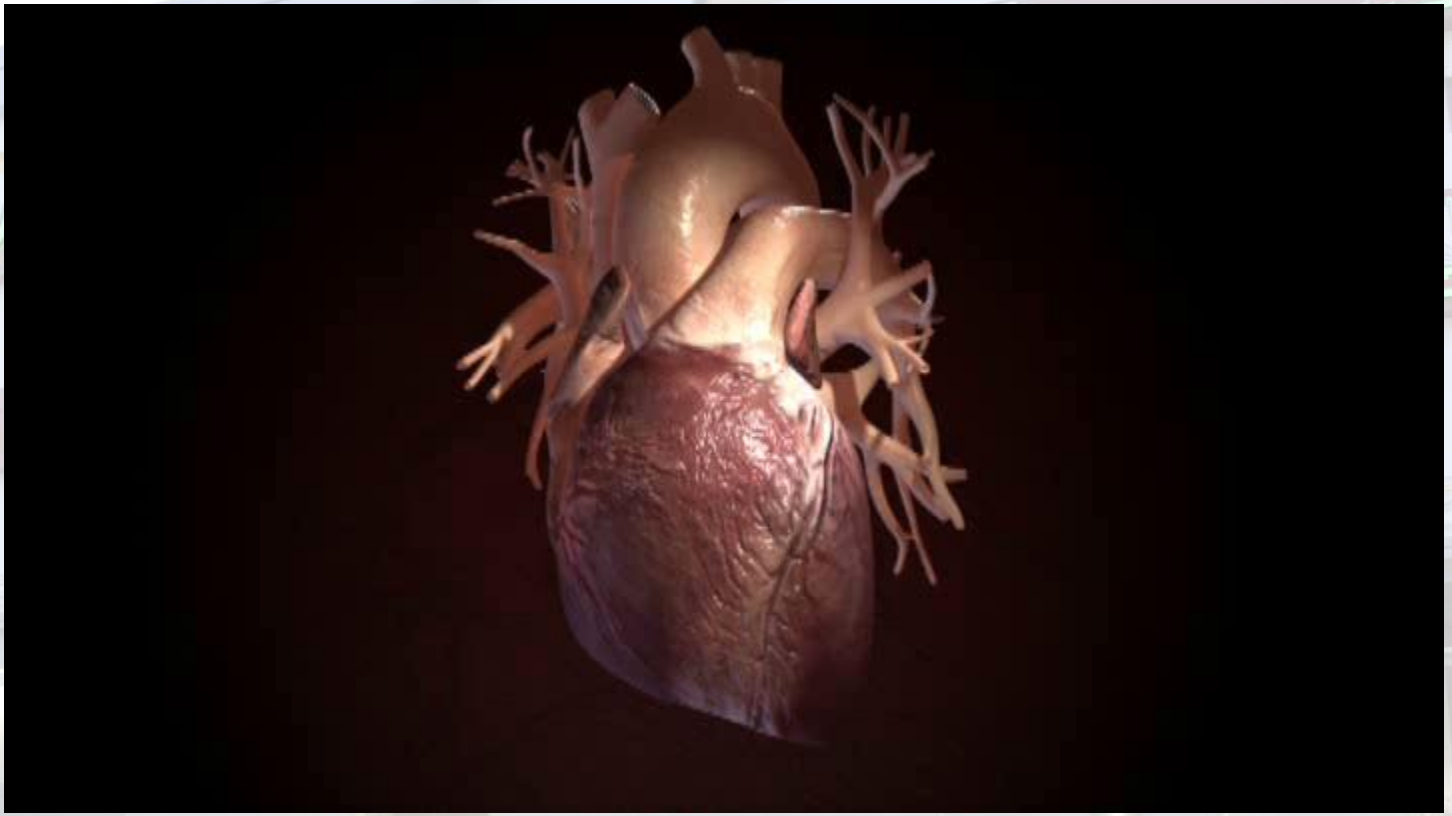

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ASPIRINA PARA PREVENIR EMBOLIAS EN LA FIBRILACION AURICULAR

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Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation.

AUHart RG, Pearce LA, Aguilar MI

SOAnn Intern Med. 2007;146(12):857.

Adjusted-dose warfarin and antiplatelet agents reduce stroke by approximately 60% and by approximately 20%, respectively, in patients who have atrial fibrillation.

Warfarin is substantially more efficacious (by approximately 40%) than antiplatelet therapy.

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ASPIRINA EN LA FA

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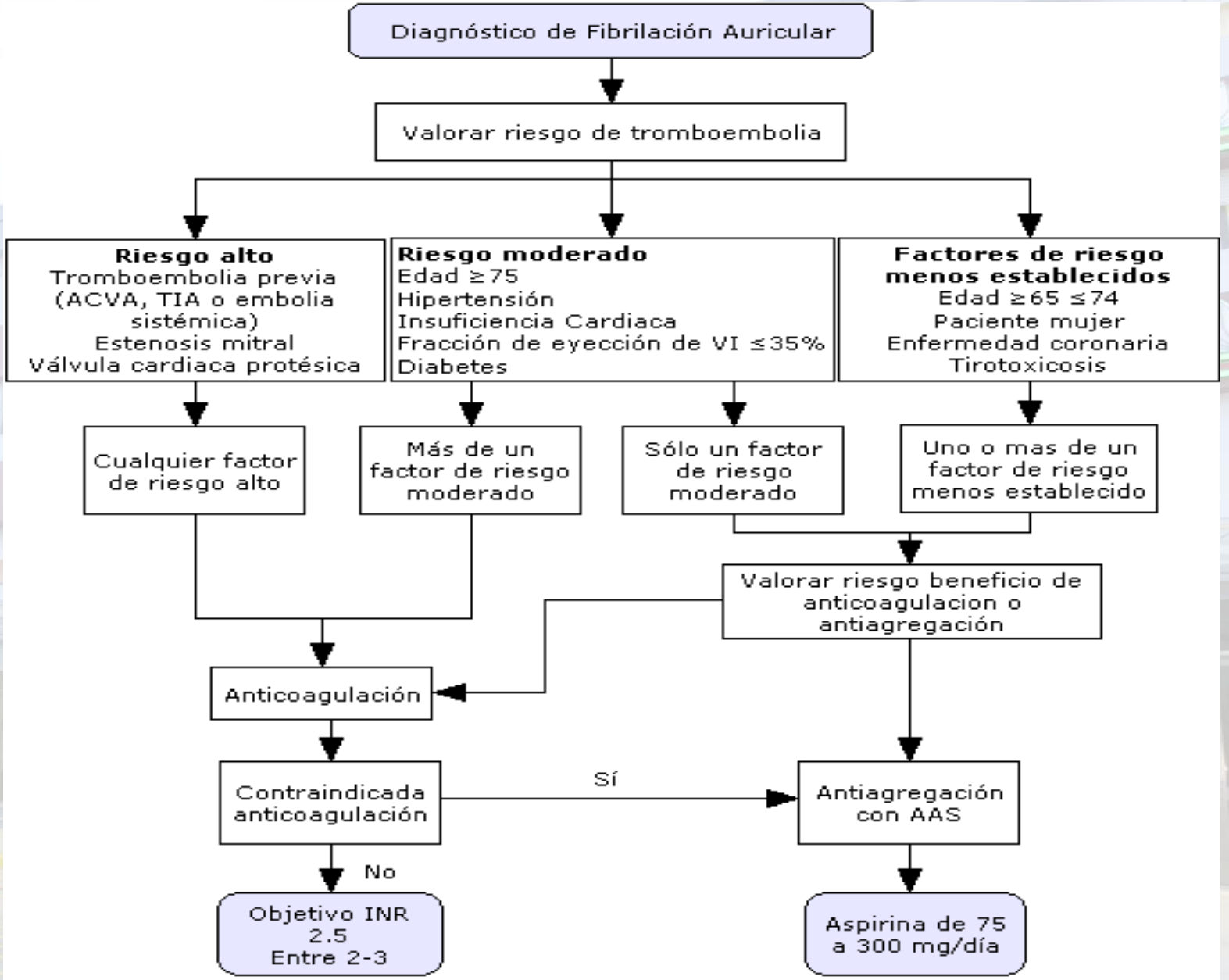

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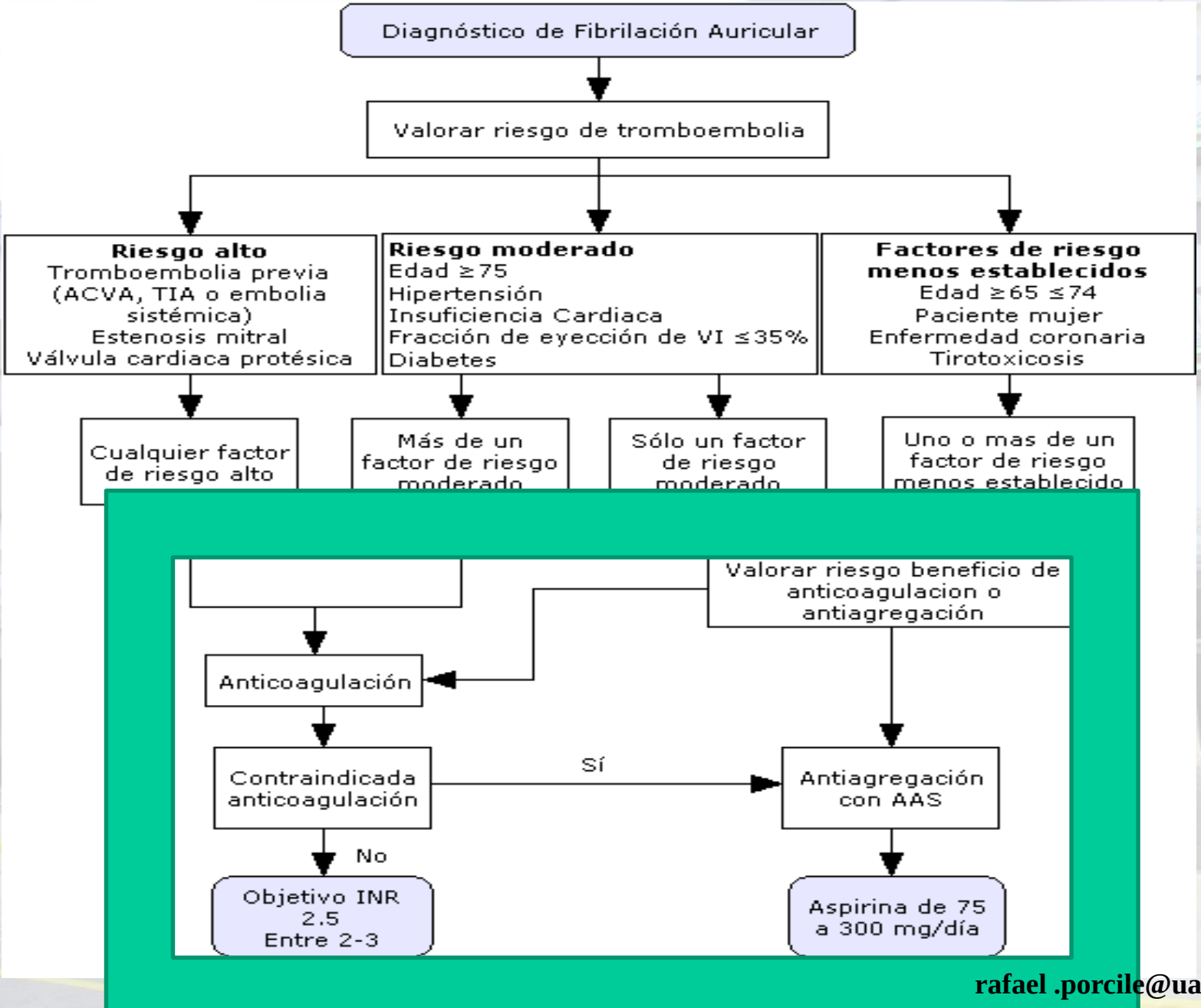

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CAFÉ Y PREGUNTAS

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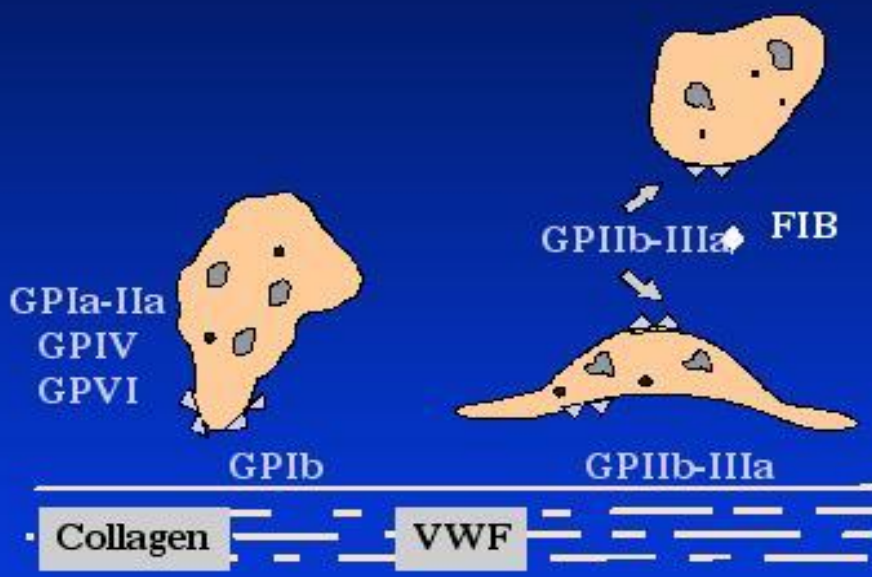
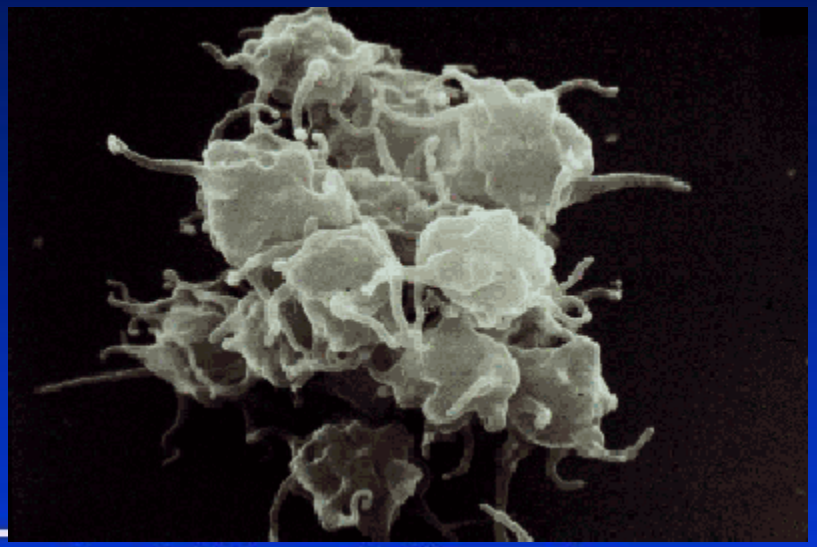
PLATELET FUNCTIONS





CONTACT ADHESION AGGREGATION AND RELEASE

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ACTIVACIÓN Y RESPUESTA PLAQUETARIA

1.- ACTIVACIÓN POR DIFERENTES "INDUCTORES" (TROMBINA, COLÁGENO, ADP).

PARCIALMENTE ACTIVADAS: POR SUST.EXTRAÑAS (VIDRIO) U OTRAS PLAQUETAS.

2.-RESPUESTA PLAQUETARIA: SIMILAR PARA TODOS LOS INDUCTORES.

a) CAMBIO DE FORMA

b) AGREGACIÓN (SE ACUMULAN)

c) 3 PROCESOS SECRETORIOS DIFERENTES (ADP)

d) LIBERACIÓN DE AC.ARAQUIDÓNICO (PG Y TX. A_2)

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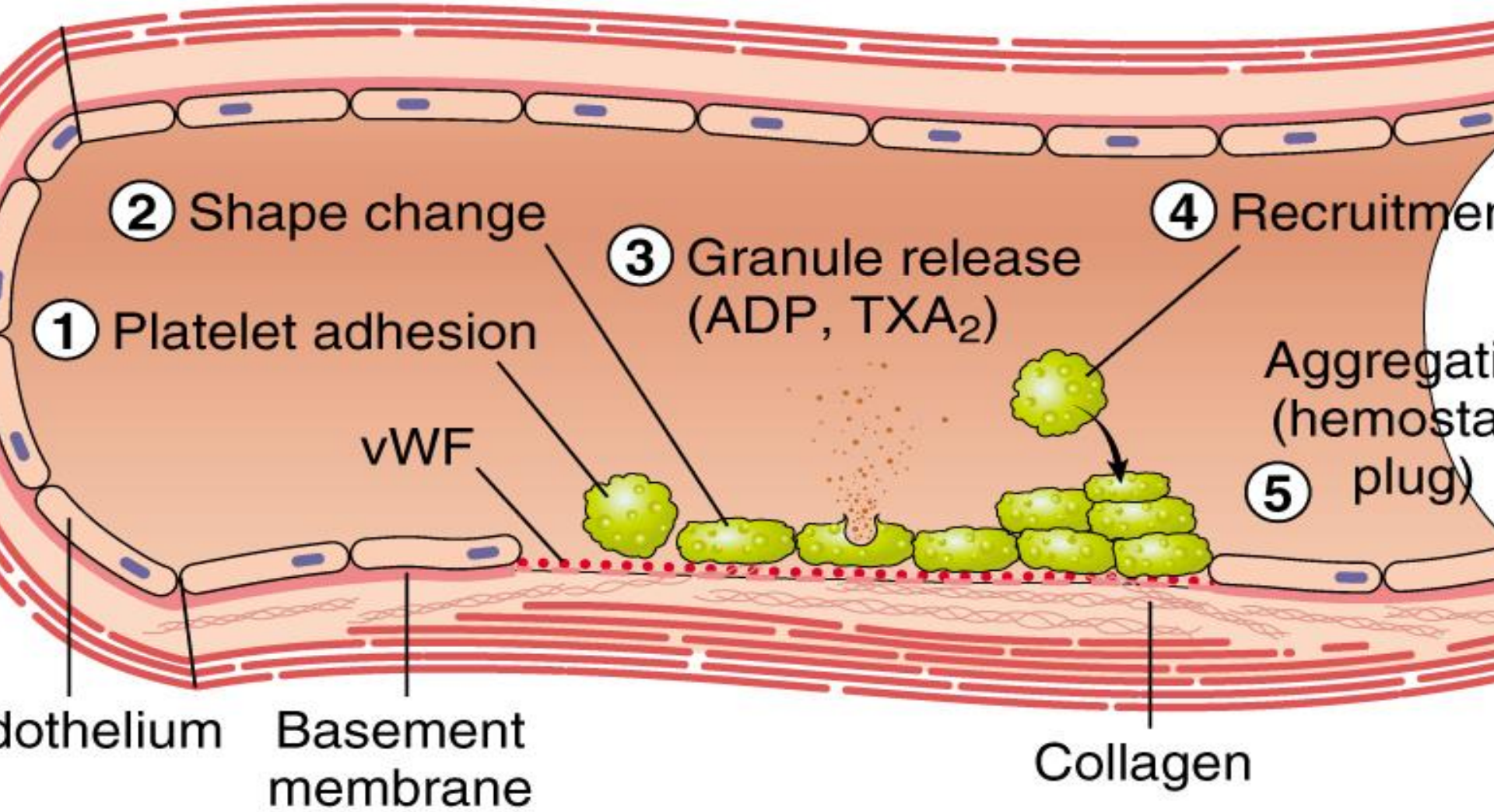
PRIMARY HEMOSTASIS



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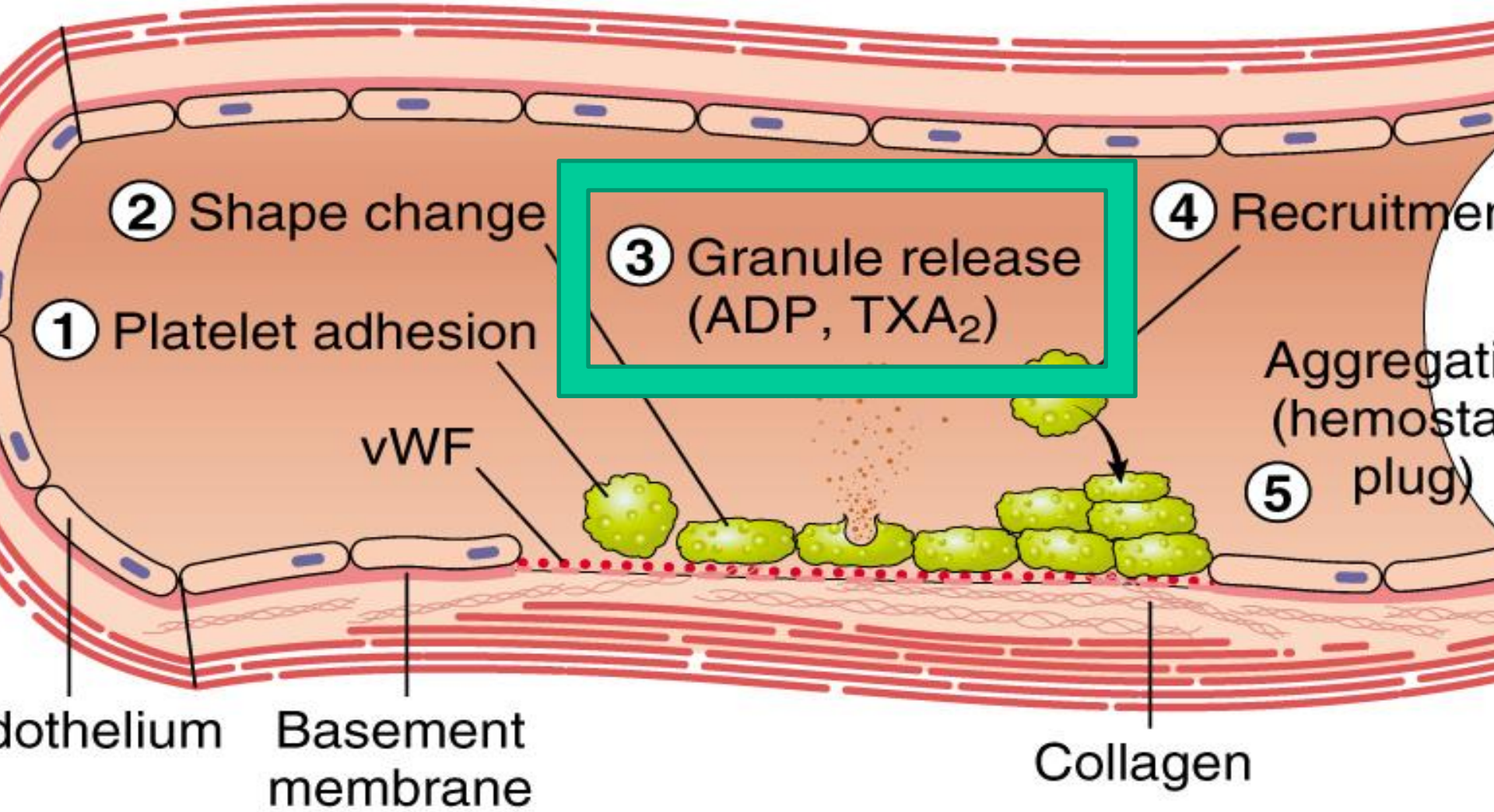
PRIMARY HEMOSTASIS



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RESISTENCIA A LA ASPIRINA

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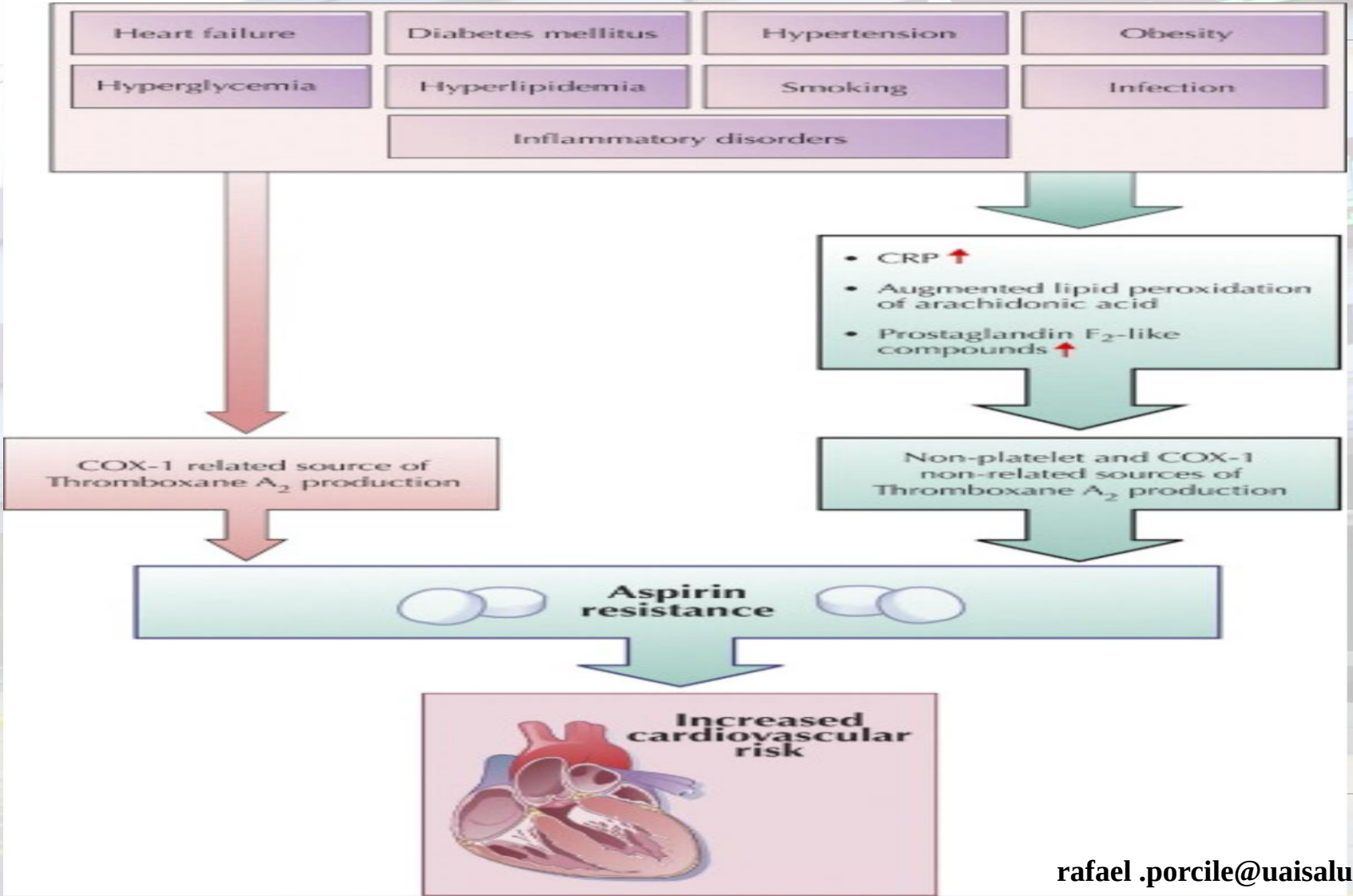
From: The Role of Aspirin in Cardiovascular Prevention: Implications of Aspirin Resistance

J Am Coll Cardiol. 2008;51(19):1829-1843. doi:10.1016/j.jacc.2007.11.080



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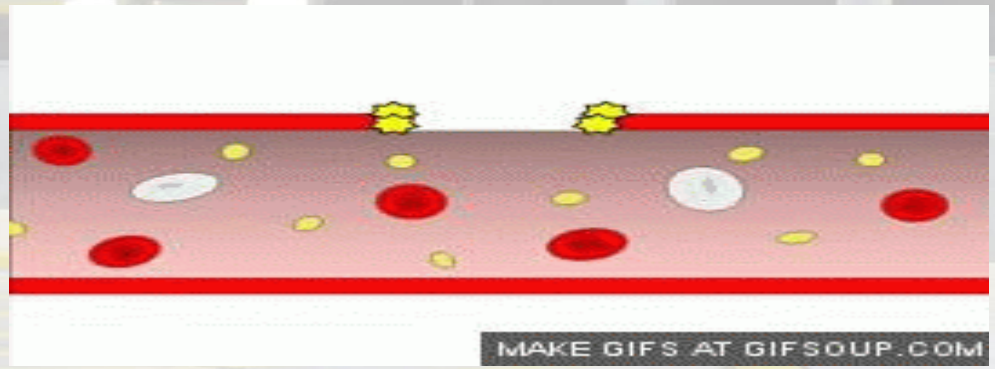
ADP DE LOS GRÁNULOS DESENCADENA LA DESCARGA DE LOS GRANÚLOS EN OTRAS PLAQUETAS



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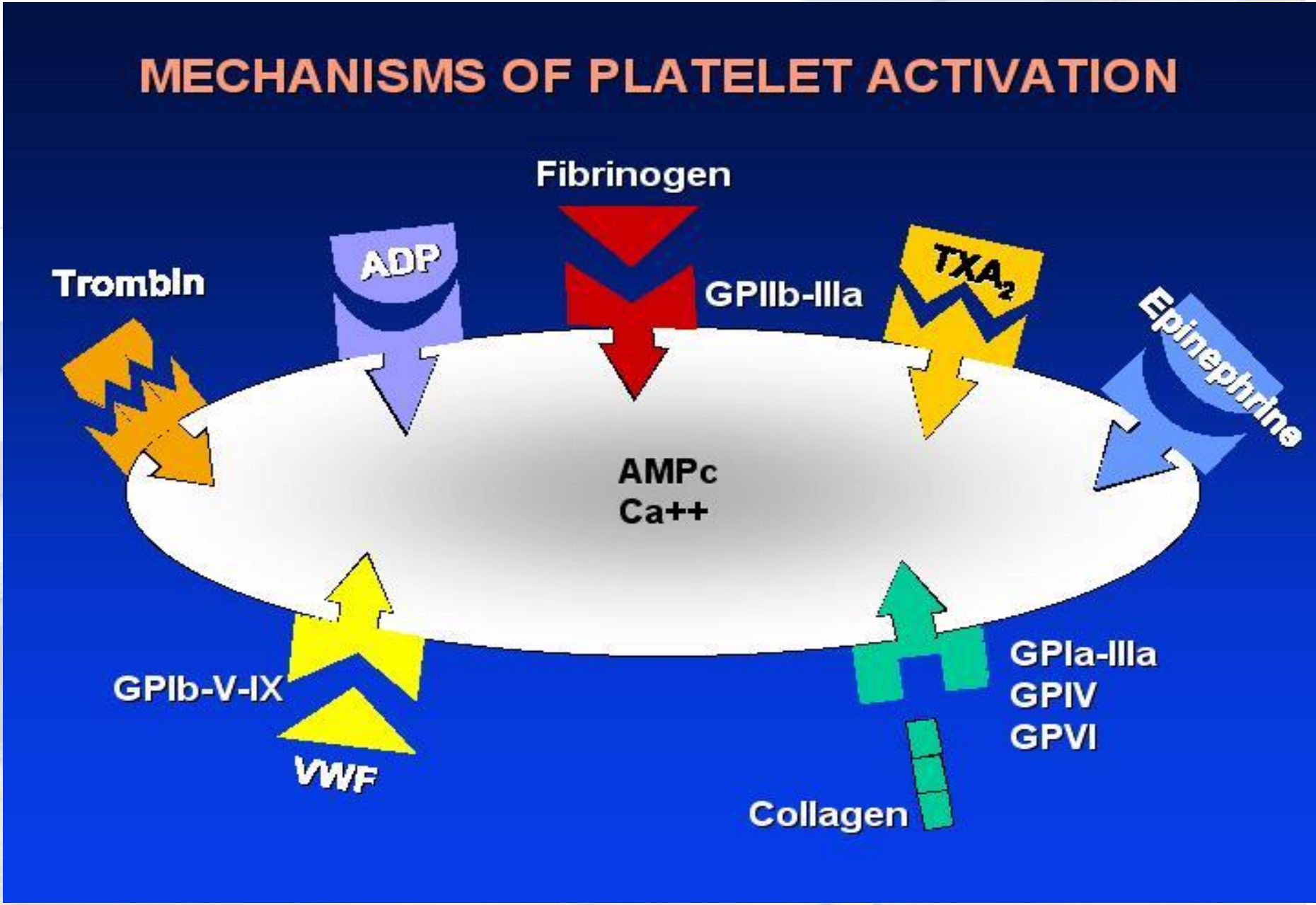

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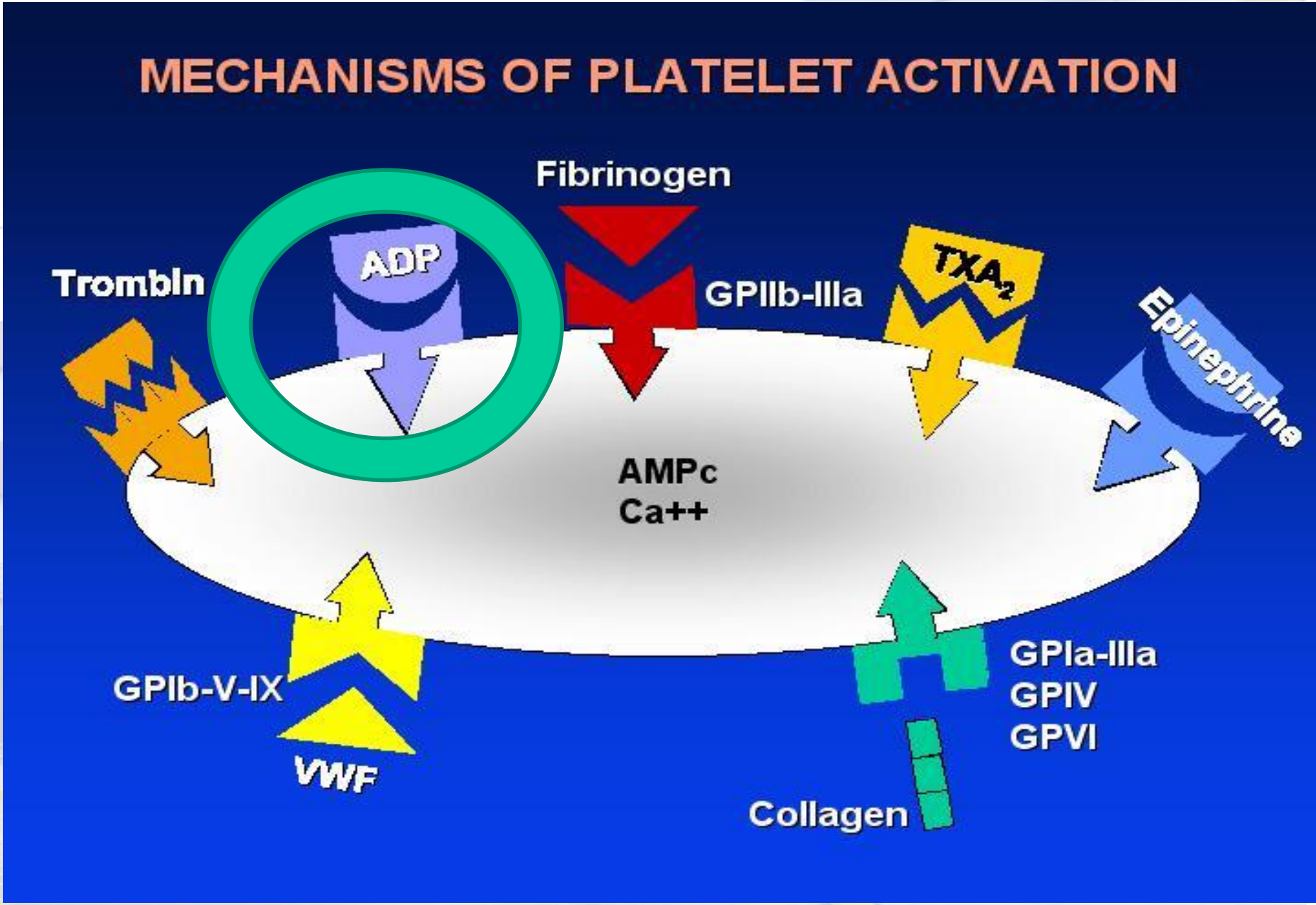

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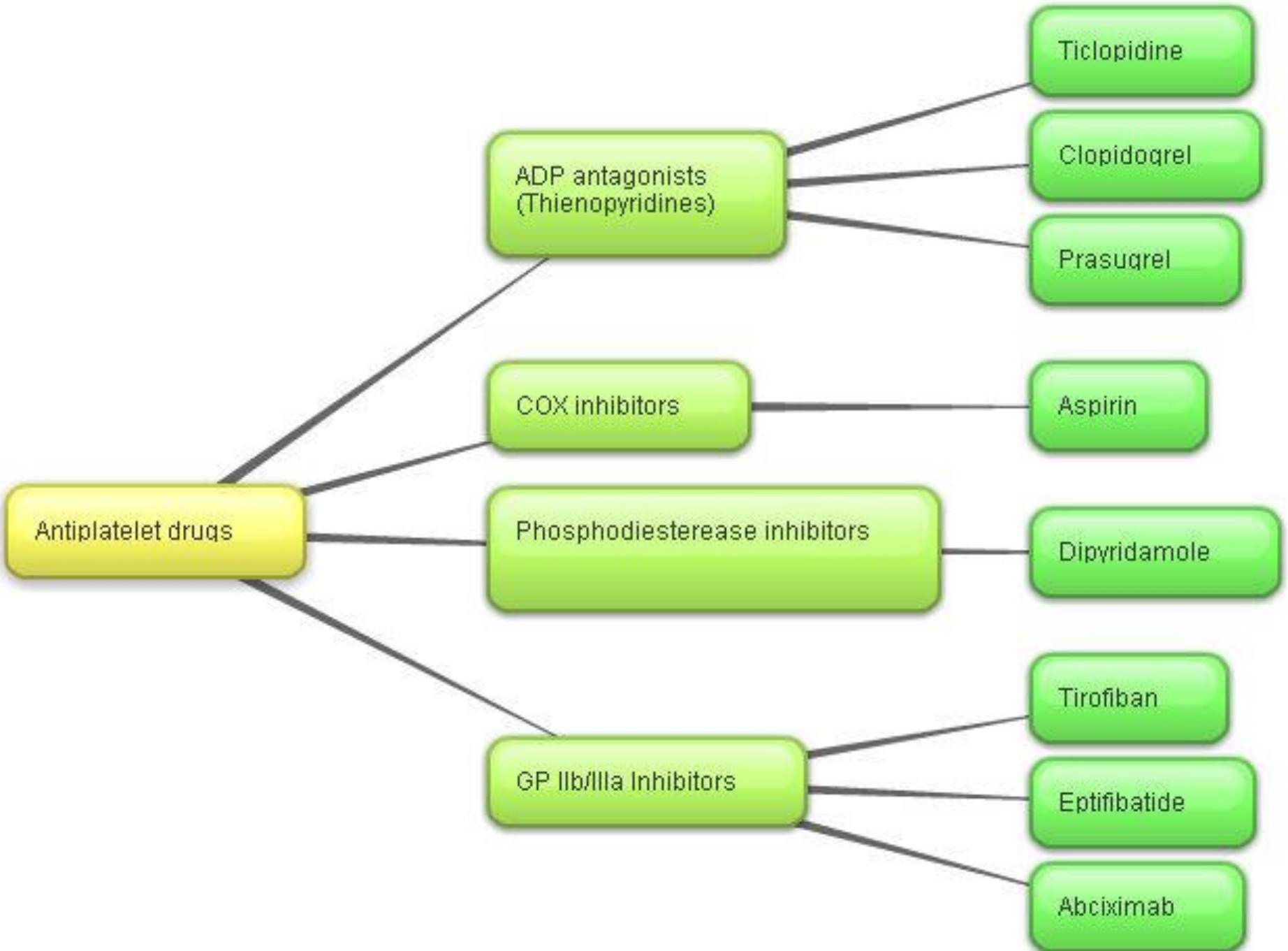
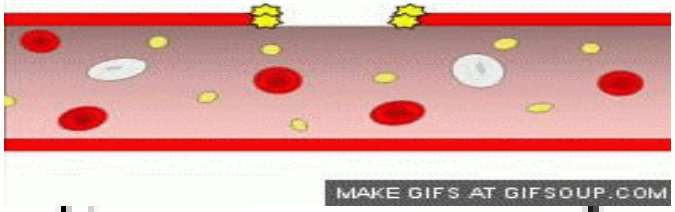

Antiplatelet drugs
ADP antagonists (Thienopyridines)
Ticlopidine
Clopidogrel
Prasugrel
COX inhibitors
Aspirin
Phosphodiesterease inhibitors
Dipyridamole
GP IIb/IIIa Inhibitors
Tirofiban
Eptifibatide
Abciximab

Diphosphoesterase inhibitor e.g.dipyridamole

Platelet ADP receptor inhibitor e.g. clopidogrel, ticlopidine



Cyclo-oxygenase inhibitor e.g. aspirin

Platelet GP IIb/IIIa receptor antagonists e.g.tirofiban, lamifiban, eptifibatide, abxicimab

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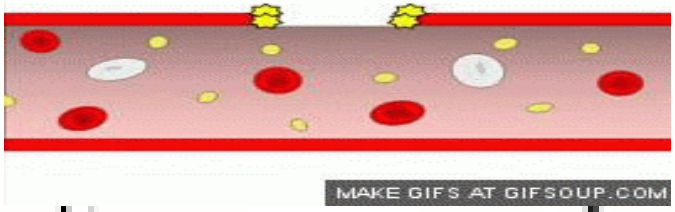
Diphosphoesterase inhibitor e.g.dipyridamole

Platelet ADP receptor inhibitor e.g. clopidogrel, ticlopidine



Cyclo-oxygenase inhibitor e.g. aspirin

Platelet GP IIb/IIIa receptor antagonists e.g.tirofiban, lamifiban, eptifibatide, abxicimab

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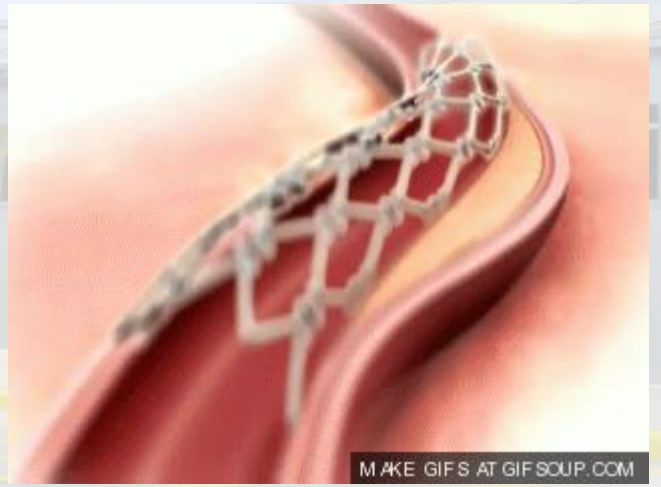
TIENOPIRIDINAS Y TRIAZOLOPIRIDINAS



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INHIBIDORES DE P2Y12

TIENOPIRIDINAS

- Clopidogrel
- Prasugrel
- y nuevos Greles

TRIAZOLOPIRIDINAS

- Ticagrelor
- Nuevos Grelores

Inhibidores P2Y12

Características	Clopidogrel	Prasugrel	Ticagrelor
Clase	Tienopiridina	Tienopiridina	Triazolopirimidina
Reversibilidad	Irreversible	Irreversible	Reversible
Activación	2 pasos	1 paso	Activo
Comienzo	2-4 hs	30 min	30 min
Duración (dias)	3-10	5-10	3-4
Días susp. Cir	5	7	5

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Mecanismo de acción de las tienopiridinas

Meadows TA, et al. *Circ Res.* 2007;100(9):1261-1275; Beitelshees A, et al. *Arterioscler Thromb Vasc Biol.* 2006;26:1681-1683; Wiviott S, et al. *Circulation.* 2010; 122: 394-403; Cattaneo M. *Eur Heart J.* 2008;10(Suppl I):I33-I3; Ibanez B, et al. *Eur Heart J.* 2006:8:G.3

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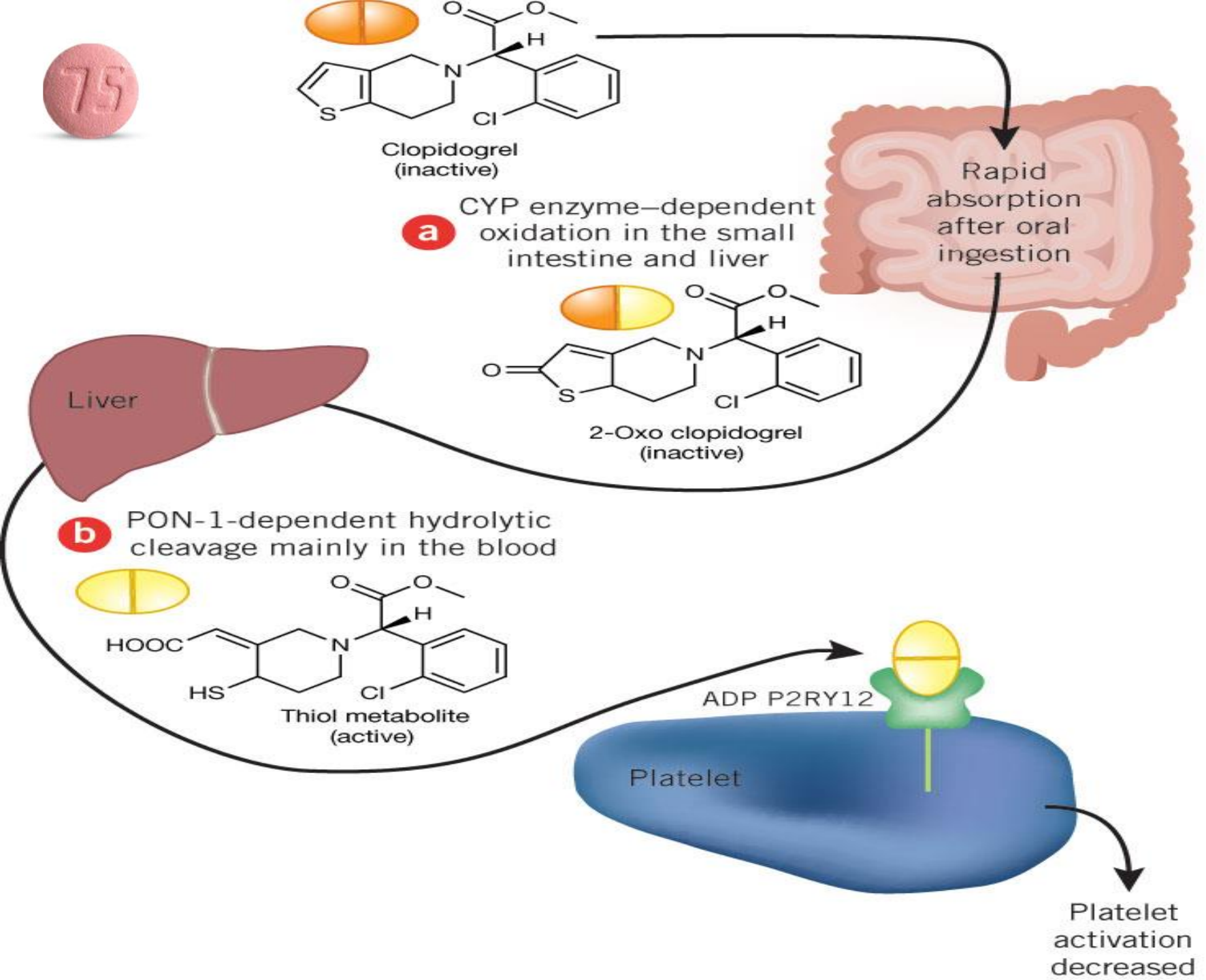
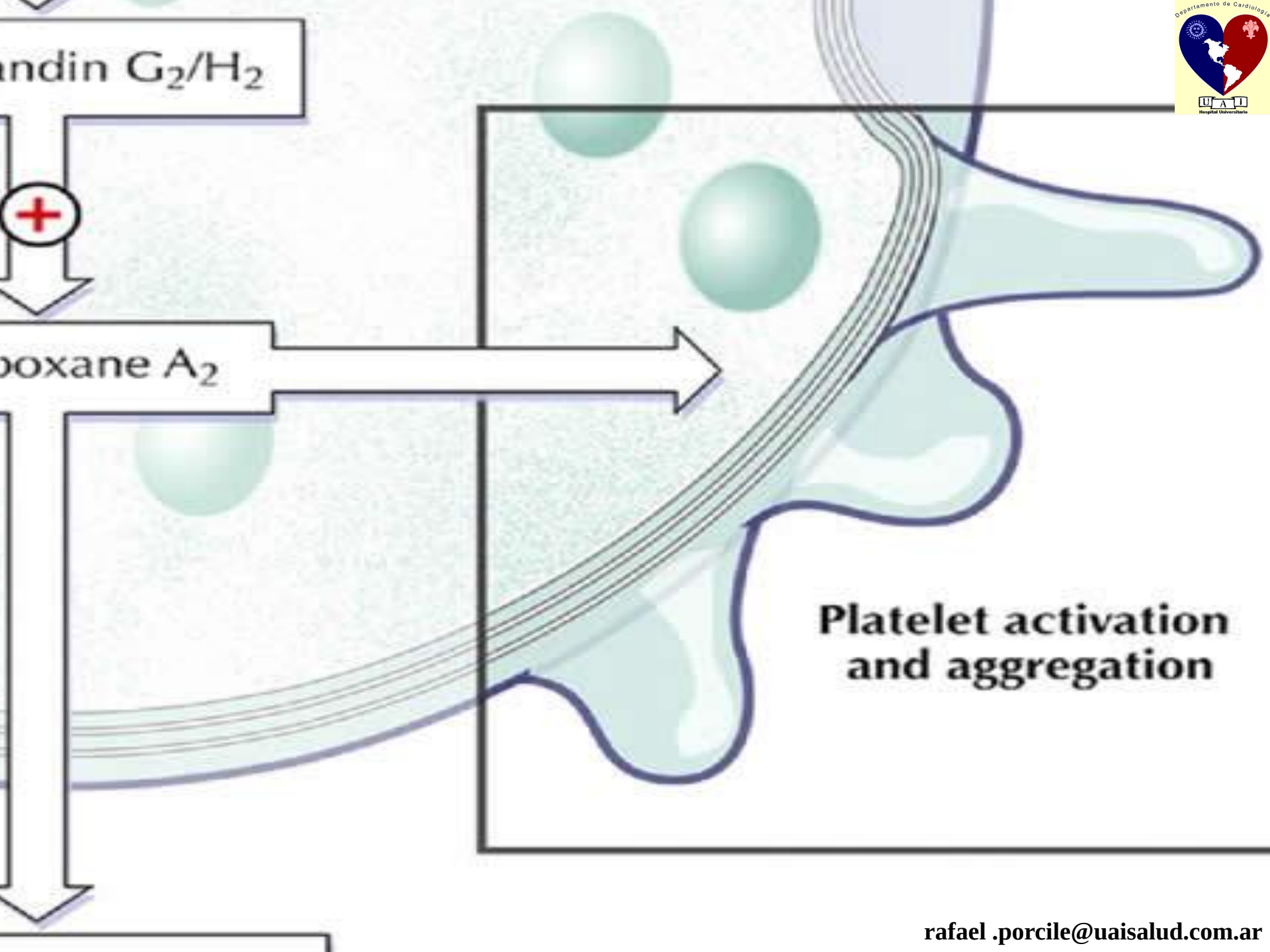

75
Clopidogrel
(inactive)
Rapid
absorption
after oral
ingestion
a
CYP enzyme–dependent
oxidation in the small
intestine and liver
2-Oxo clopidogrel
(inactive)
Liver
b
PON-1-dependent hydrolytic
cleavage mainly in the blood
Thiol metabolite
(active)
ADP P2RY12
Platelet
Platelet
activation
decreased



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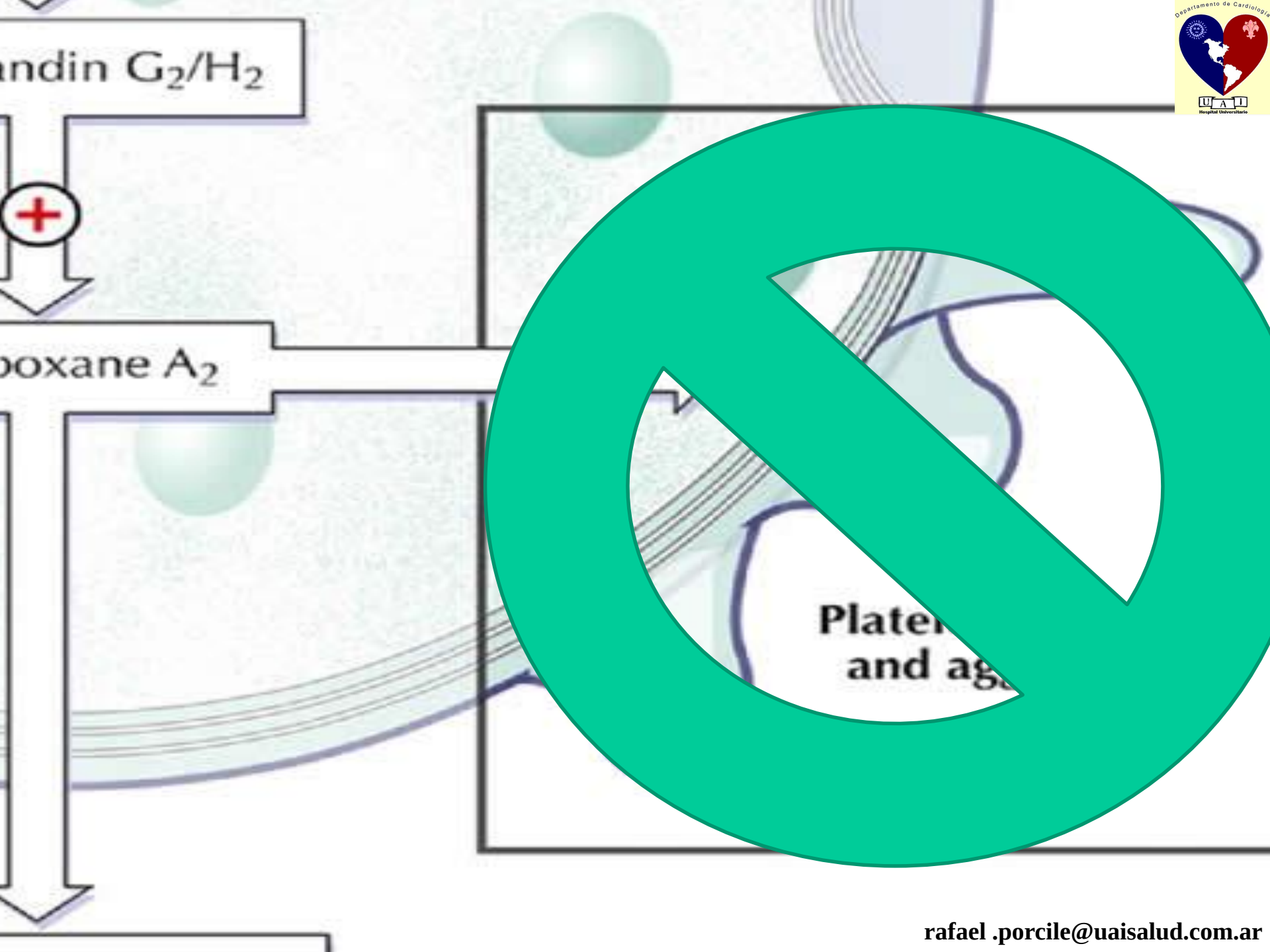

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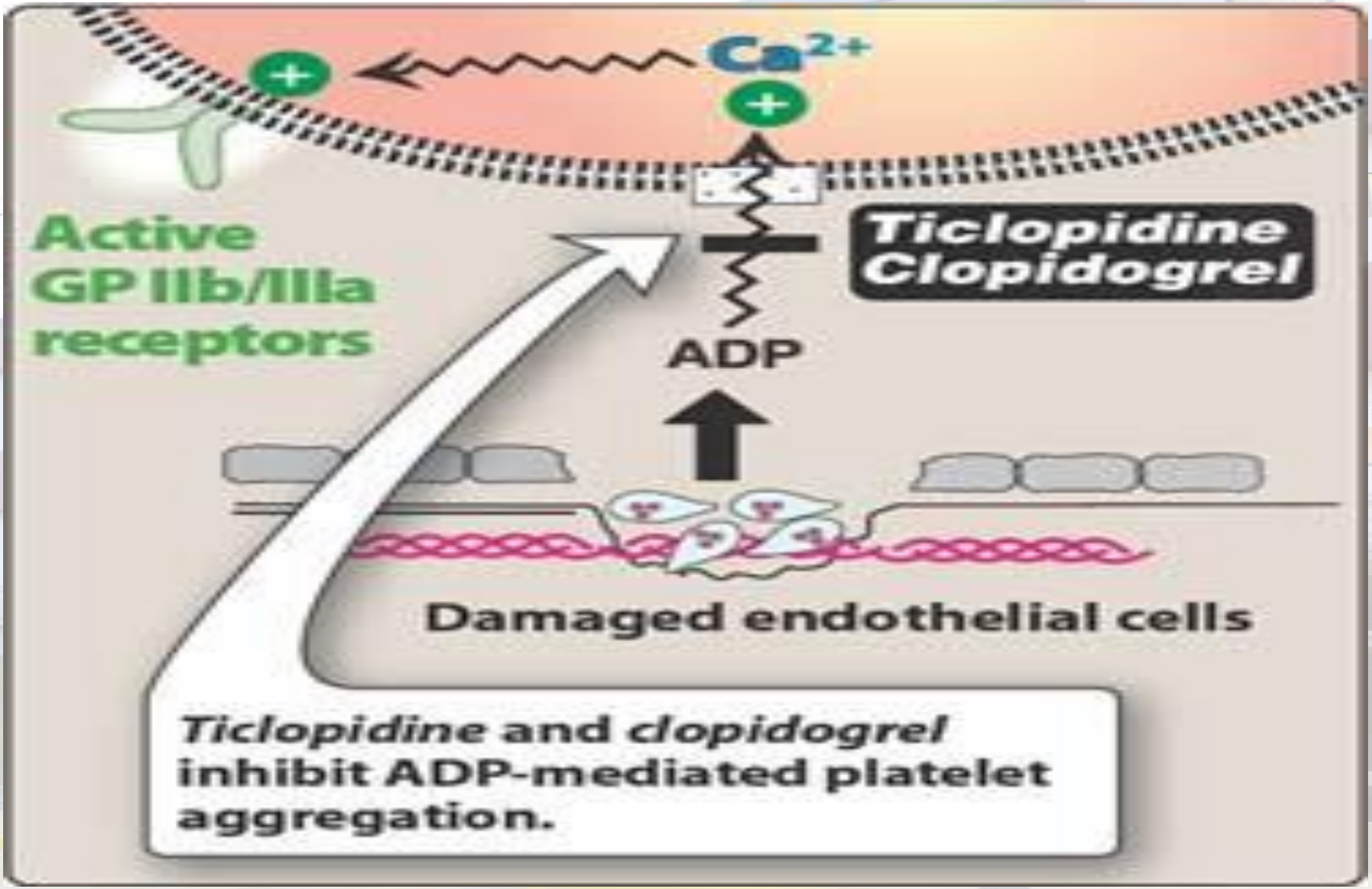

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VEAMOS LA BIBLIOGRAFIA

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¿Clopidogrel o aspirina?

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CAPRIE : CLOPIDOGREL vs ASPIRINA EN PACIENTES CON RIESGO DE EVENTOS ISQUEMICOS

LANCET 1996:348:1329

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.: Outcome Events in the CAPRIE Primary Analysis

	Clopidogrel bisulfate	aspirin
Patients	9599	9586
IS (fatal or not)	438 (4.6%)	461 (4.8%)
MI (fatal or not)	275 (2.9%)	333 (3.5%)
Other vascular death	226 (2.4%)	226 (2.4%)
Total	939 (9.8%)	1020 (10.6%)

Outcome Events in the CAPRIE Primary Analysis

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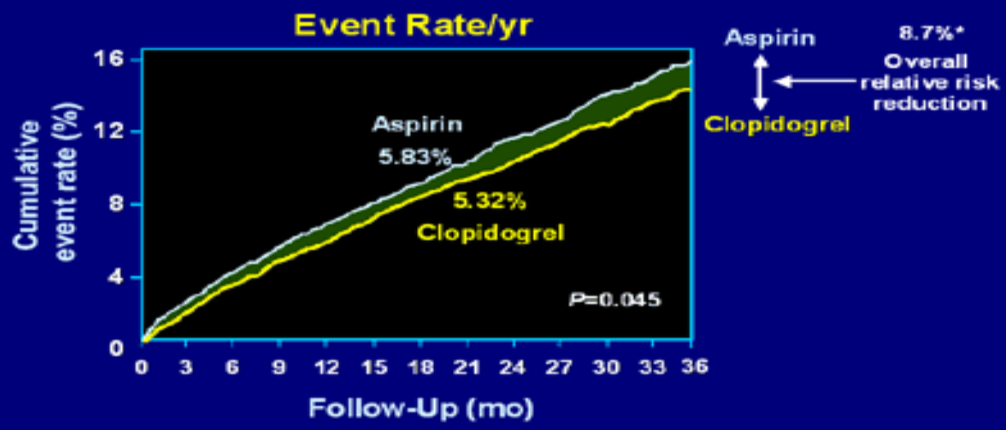
CAPRIE Study

Efficacy of Clopidogrel vs Aspirin in MI, Ischemic Stroke, or Vascular Death (n=19,185)

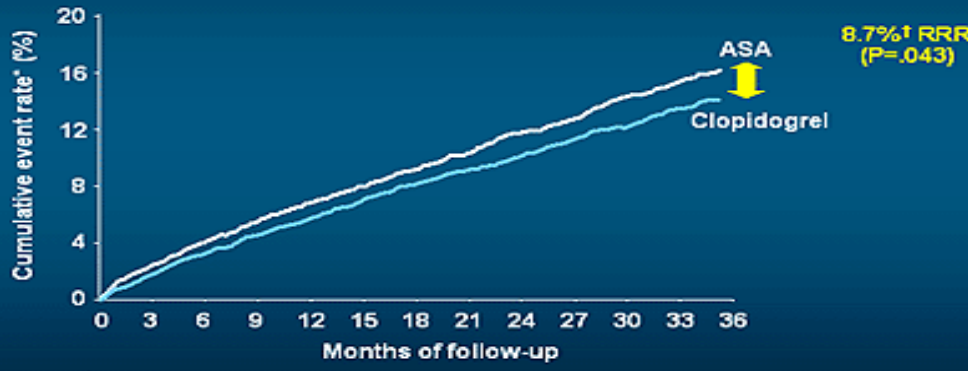


*ITT analysis

Adapted with permission from CAPRIE Steering Committee. *Lancet*. 1996;348:1329

CAPRIE: Superior Efficacy of Clopidogrel versus ASA

Patients with Recent ischemic stroke, recent MI, or symptomatic PAD



*MI, ischemic stroke or vascular death

†Intent-to-treat analysis (n=19,185)

CAPRIE Steering Committee. *Lancet* 1996; 348: 1329–1339. (A)

CHARISMA

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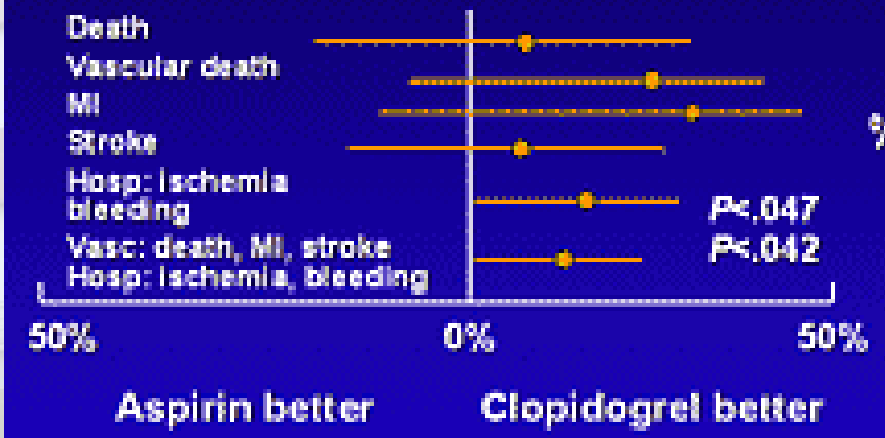
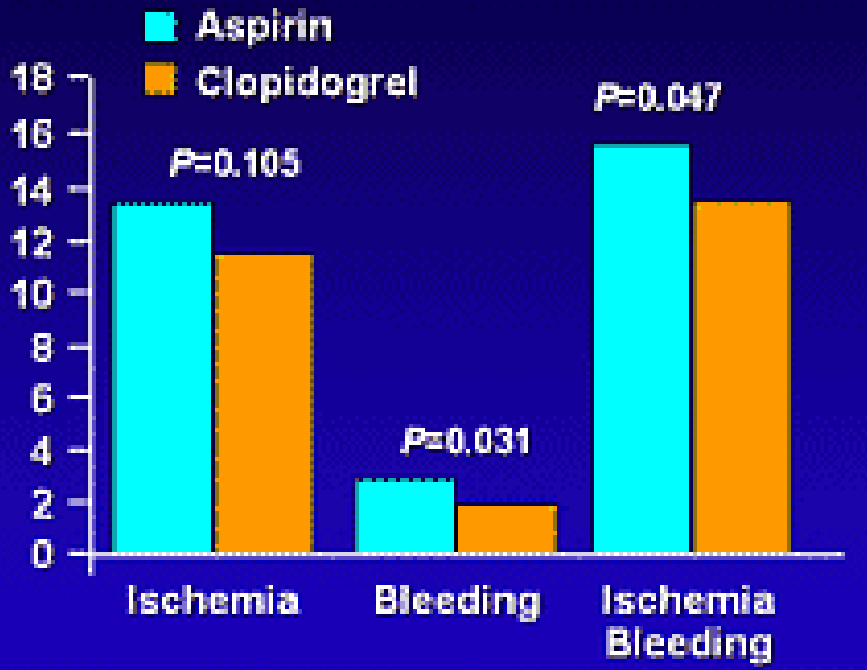
Superiority of Clopidogrel vs Aspirin in Patients With Diabetes Mellitus: CAPRIE

Relative Risk Reduction



Rehospitalization



	Aspirin	Clopidogrel
Nondiabetic (n)	7954	7639
Diabetic (n)	1952	1914

Adapted with permission from Bhatt DL et al. *J Am Coll Cardiol.* 2000;35(suppl A):409A

CAPRIE
EL CLOPIDOGREL PREVIENE 24 EVENTOS CLINICOS MAYORES CADA 1000 PACIENTES Y LA ASPIRINA 19 CADA 1000

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En el estudio **CAPRIE**, clopidogrel ligeramente más eficaz que la aspirina, pero con
un NNT elevado (NNT=196, necesidad de tratar 196 pacientes al año para evitar un evento arteriosclerótico adicional)

Pone en cuestión la relevancia clínica de la superioridad de clopidogrel sobre aspirina.

¿El escaso beneficio derivado del tratamiento con clopidogrel frente a aspirina justifica la diferencia de coste?

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¿Clopidogrel y aspirina?

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2001

The New England Journal of Medicine

EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION

THE CLOPIDOGREL UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS TRIAL
N Engl J Med, Vol. 345, No. 7 August 16, 2001

*

The CURE study

12,562 patients with acute coronary syndrome without ST segment elevation

Patients were required to have either ECG changes compatible with new ischemia (without ST segment elevation)

or elevated cardiac enzymes or troponin I or T to at least twice the upper limit of normal.

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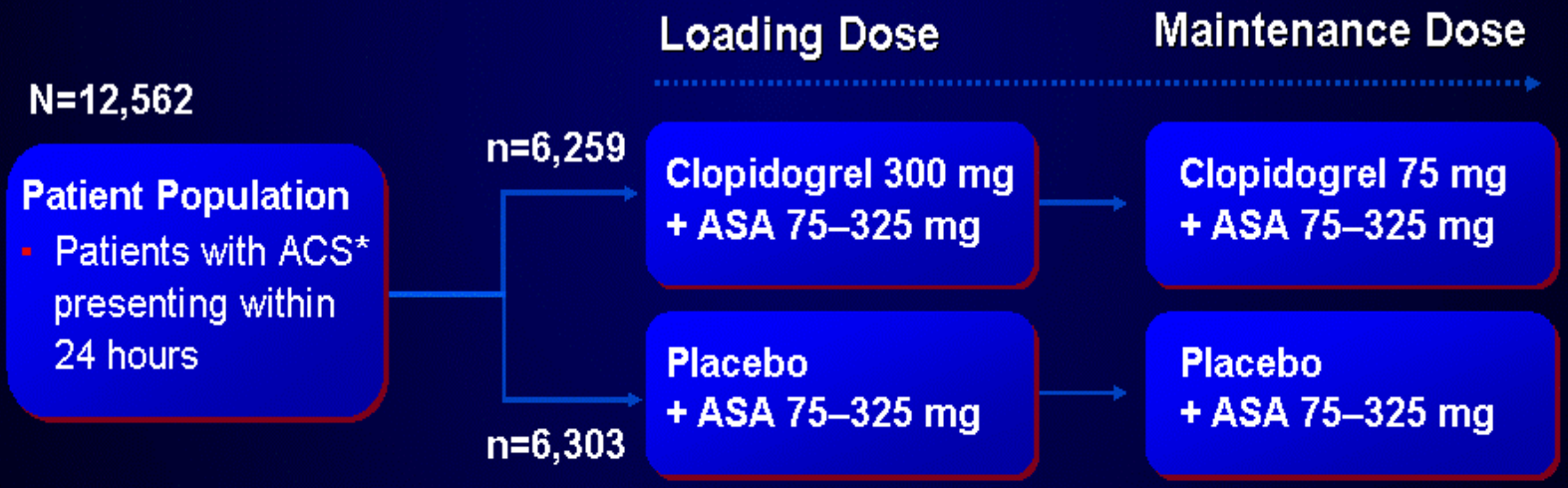
CURE: Clopidogrel in Unstable Angina to Prevent Recurrent Events



Primary End Point
- Composite of death from cardiovascular causes, nonfatal MI, or stroke

Coprimary End Point
- Composite of death from cardiovascular causes, nonfatal MI, stroke, or refractory ischemia

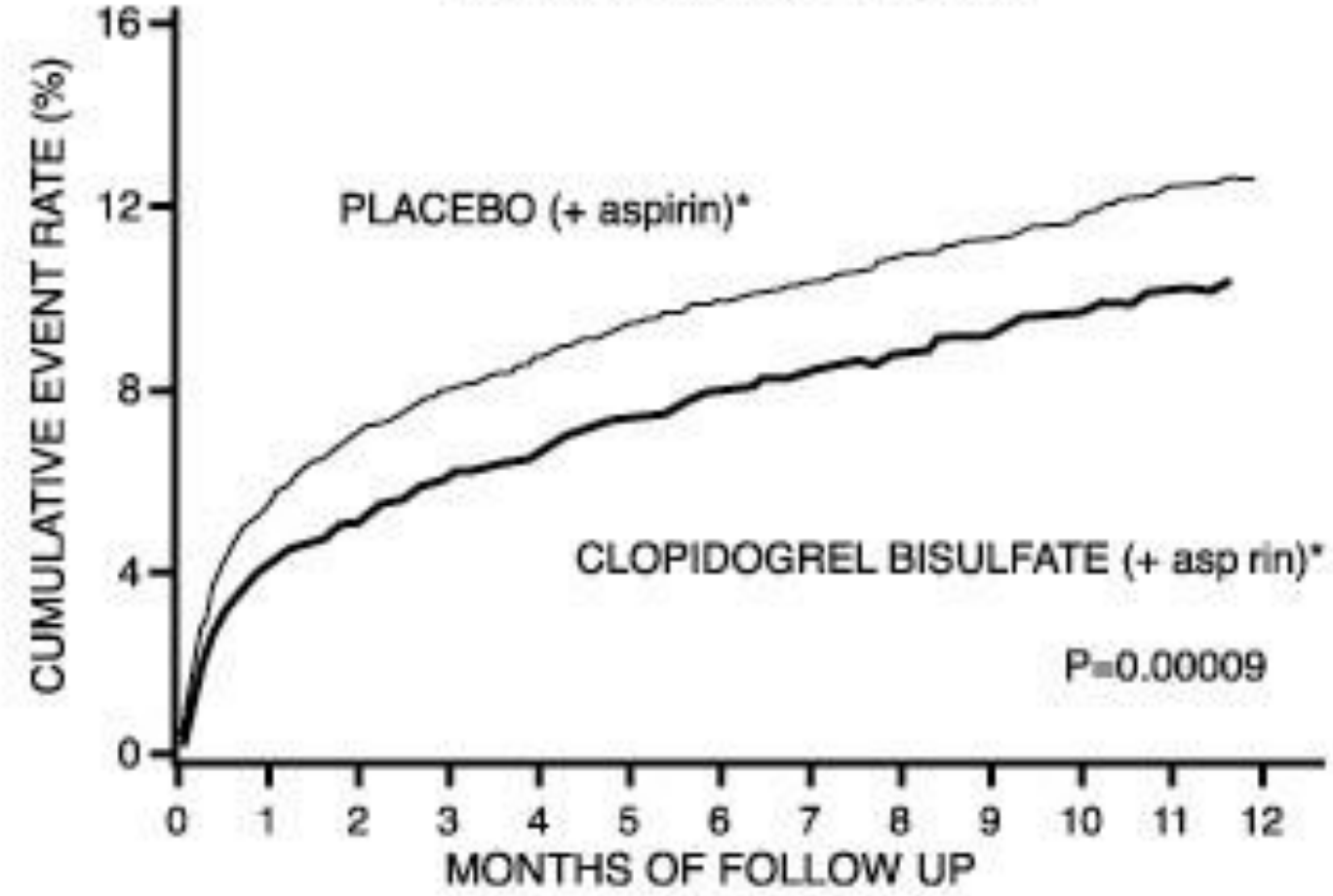
482 centers
28 countries

SIN ELEVACION DEL ST

* UA/NSTEMI.

CURE Trial Investigators. *N Engl J Med.* 2001;345:494-502.

CARDIOVASCULAR DEATH, MYOCARDIAL INFARCTION, STROKE



*Other standard therapies were used as appropriate

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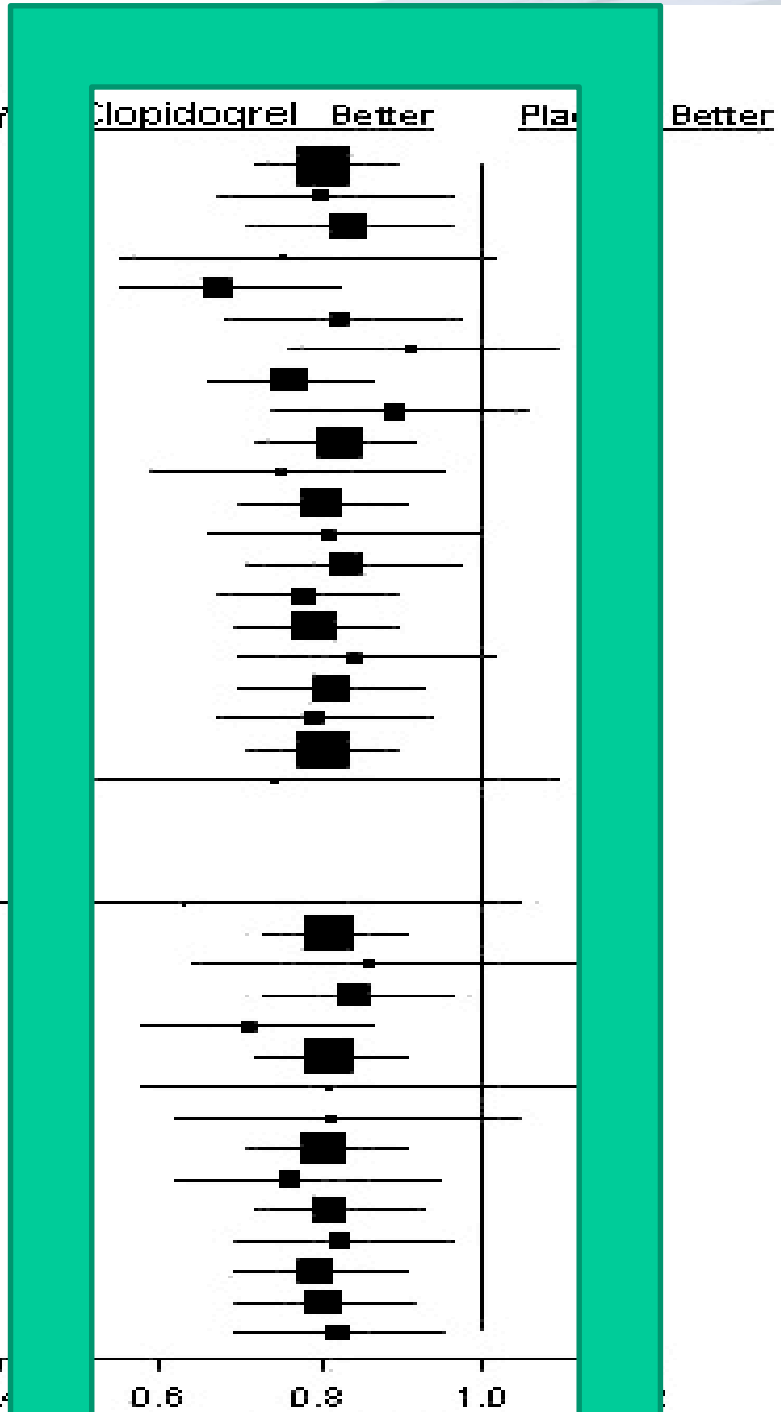
Baseline Characteristics		N	Percent Events Clopidogrel (+aspirin)*	Placebo (+aspirin)*
Overall		12562	9.3	11.4
Diagnosis	Non-Q-W	3295	12.7	15.5
	Unst Ang	8298	7.3	8.7
	Other	968	15.1	19.7
Age	< 65	5996	5.2	7.6
	65-74	4136	10.2	12.4
	≥ 75	2430	17.8	19.2
Gender	Male	7726	9.1	11.9
	Female	4836	9.5	10.7
Race	Caucas	10308	9.1	11.0
	Non-Cauc	2250	10.1	13.2
Elev Card Enzy	No	9381	8.8	10.9
	Yes	3176	10.7	13.0
ST Depr >1.0mm	No	7273	7.5	8.9
	Yes	5288	11.8	14.8
Diabetes	No	9721	7.9	9.9
	Yes	2840	14.2	16.7
Previous MI	No	8517	7.8	9.5
	Yes	4044	12.5	15.4
Previous Stroke	No	12055	8.9	11.0
	Yes	506	17.9	22.4
Concomitant Medication / Therapy				
Heparin/LMWH	No	951	4.9	7.7
	Yes	11611	9.7	11.7
Aspirin	<100mg	1927	8.5	9.7
	100-200mg	7428	9.2	10.9
	>200mg	3201	9.9	13.7
GPIIb/IIIa Antag	No	11739	8.9	10.8
	Yes	823	15.7	19.2
Beta-Blocker	No	2032	9.9	12.0
	Yes	10530	9.2	11.3
ACEI	No	4813	6.3	8.1
	Yes	7749	11.2	13.5
Lipid-Lowering	No	4461	10.9	13.1
	Yes	8101	8.4	10.5
PTCA/CABG	No	7977	8.1	10.0
	Yes	4585	11.4	13.8

*Other standard therapies were used as appropriate



Purpura Trombotica trombocitopenica (TTP)

TTP has been reported rarely following use of clopidogrel bisulfate, sometimes after a short exposure (<2 weeks). TTP is a serious condition that can be fatal and requires urgent treatment including plasmapheresis (plasma exchange). It is characterized by thrombocytopenia, microangiopathic hemolytic anemia (schistocytes [fragmented RBCs] seen on peripheral smear), neurological findings, renal dysfunction, and fever

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PACIENTE con TROMBOCITOPENIA: EXAMEN FISICO

1º EVALUAR PRESENCIA DE PURPURA

- *Seca:* petequias, equimosis, hematomas
- *Húmeda:* sangrado mucoso
- Signos premonitorios de sangrado mayor: ampollas hemorrágicas en cav. oral y/o sangrado al F. O.

2º BUSCAR ENFERMEDAD SUBYACENTE

- Hepato y/o esplenomegalia
- Estigmas de insuficiencia hepática
- Adenopatías

BENEFICIOS Y PERJUICIOS DE LA DOBLE ANTIAGREGACION

¿Clopidogrel a todos los síndromes coronarios agudos al ingreso a la unidad coronaria?

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The American Journal of Cardiology
Volume 115, Issue 8, April 2015, Pages 1019–1026

Prognostic Impact of Clopidogrel Pretreatment in Patients With Acute Coronary Syndrome Managed Invasively

Analyzed the prognostic impact of clopidogrel pretreatment in a large cohort of invasively managed patients with ACS. In hospital,

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The American Journal of Cardiology
Volume 115, Issue 8, April 2015, Pages 1019–1026

Prognostic Impact of Clopidogrel Pretreatment in Patients With Acute Coronary Syndrome Managed Invasively

Pretreatment with clopidogrel reduced the occurrence of death and thrombotic outcomes at the cost of minor bleeding. Those benefits exclusively affected ST-elevation myocardial infarction cases. **The potential benefit of routine upstream pretreatment in patients with non–ST-elevation ACS should be reappraised at the present.**

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Reappraisal of thienopyridine pretreatment in patients with non-ST elevation acute coronary syndrome: a systematic review and meta-analysis

BMJ 2014; 349 doi: http://dx.doi.org/10.1136/bmj.g6269
(Published 24 ***October 2014****) Cite this as: BMJ 2014;349:g6269*

Conclusion In patients presenting with non-ST elevation ACS, pretreatment with thienopyridines is associated with no significant reduction of mortality but with a significant excess of major bleeding no matter the strategy adopted, invasive or not. Our results **do not support a strategy of routine pretreatment in patients with non-ST elevation AC**

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Ojo sin supra del ST

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Clopidogrel NO a los síndromes coronarios agudos sin elevación del ST al ingreso a la unidad coronaria

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DOBLE ANTIAGREGACIÓN aspirina y clopidogrel

esta indicado en:

- Pacientes sometidos a intervención coronaria percutánea con colocación de stent.
- SCA con elevación del segmento ST.

Mantener el tratamiento con clopidogrel tras la **implantación de un stent, ya que lasuspensión precoz se ha relacionado con episodios de trombosis.**

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Clopidogrel

- No requiere ajuste por edad o función renal.
- En PTCA se da una dosis de carga de 300 mgs y luego se continua con 75 mgs c/d por al menos 1 año.
- Se asocia menos frecuentemente a neutropenia y PTT pero incrementa el riesgo de sangrado SNC.

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ANTIAGREGACÍON POST ANGIOPLASTIA CON STENT MEDICAD

DAT

Dual antiplatelet therapy (aspirin), which is the combination of aspirin and a $P2Y_{12}$ receptor blocker to reduce the risk of myocardial infarction (MI) or death. **For most patients, we recommend aspirin 75 to 100 mg daily plus clopidogrel 75 mg daily for at least 12 months and we continue DAPT for at least an additional 18 months in many of those who have tolerated such therapy**

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Seis meses…

Un año….

Dos años

Toda la vida….

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Impact of clinical presentation on ischaemic and bleeding outcomes in patients receiving 6- or 24-month duration of dual-antiplatelet therapy after stent implantation: a pre-specified analysis from the PRODIGY (Prolonging Dual-Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia) trial

Francesco Costa , Pascal Vranckx , Sergio Leonardi , Elisabetta Moscarella , Giuseppe Ando , Paolo Calabro , Giuseppe Oreto , Felix Zijlstra , Marco Valgimigli *DOI: http://dx.doi.org/10.1093/eurheartj/ehv038 First published online:*

25 February 2015

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This analysis suggests that clinical presentation may be a treatment modifier with respect to DAPT duration after stenting consistent with the hypothesis that SCAD—but not ACS—patients are exposed to a significant increase in bleeding and net adverse clinical events when treated with 24-month compared with 6-month therapy

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AN UPDATE META-ANALYSIS OF RANDOMIZED TRIALS COMPARING SHORT-TERM AND LONG-TERM DUAL ANTIPLATELET THERAPY FOLLOWING DRUG-ELUTING STENTS

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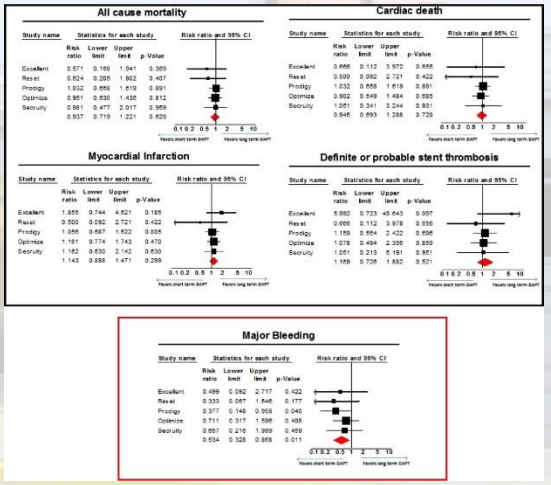
From: AN UPDATE META-ANALYSIS OF RANDOMIZED TRIALS COMPARING SHORT-TERM AND LONG-TERM DUAL ANTIPLATELET THERAPY FOLLOWING DRUG-ELUTING STENTS

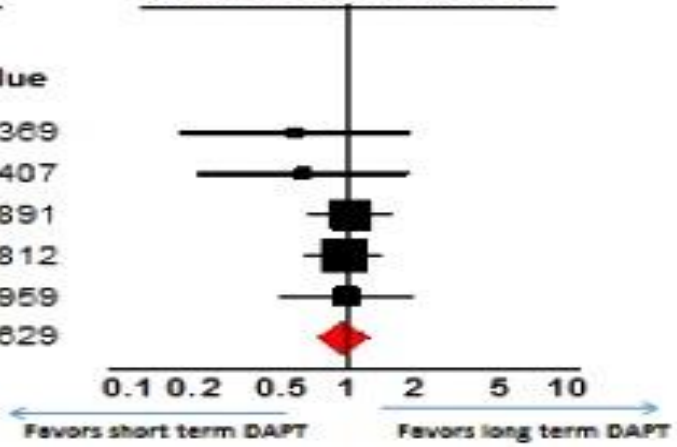
J Am Coll Cardiol. 2015;65(10_S). doi:10.1016/S0735-1097(15)61639-4

Updated meta-analysis of randomized trials to assess the efficacy and safety of ≤ 6 months versus ≥ 12 months DAPT after implantation of DES



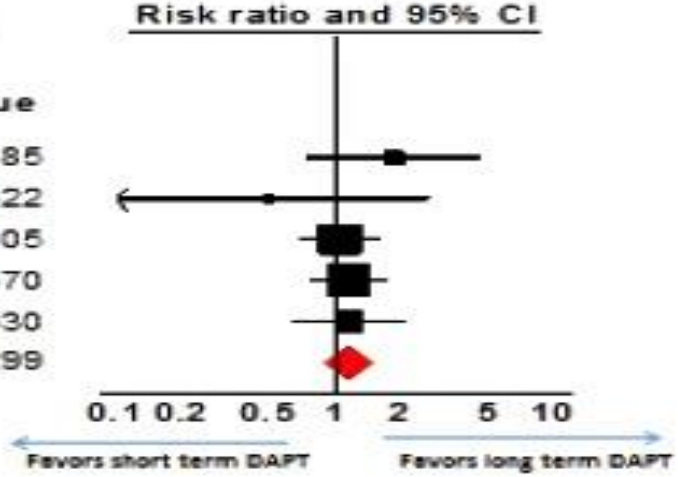
All cause mortality

Study name	Risk ratio	Lower limit	Upper limit	p-Value
Excellent	0.571	0.168	1.941	0.369
Reset	0.624	0.205	1.902	0.407
Prodigy	1.032	0.658	1.619	0.891
Optimize	0.951	0.630	1.436	0.812
Secruity	0.981	0.477	2.017	0.959
	0.937	0.719	1.221	0.629



Myocardial Infarction

Study name	Risk ratio	Lower limit	Upper limit	p-Value
Excellent	1.855	0.744	4.621	0.185
Reset	0.500	0.092	2.721	0.422
Prodigy	1.056	0.687	1.622	0.805
Optimize	1.161	0.774	1.743	0.470
Secruity	1.162	0.630	2.142	0.630
	1.143	0.888	1.471	0.299



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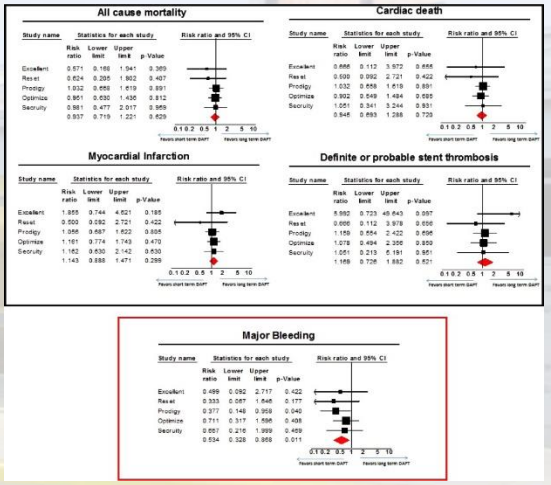
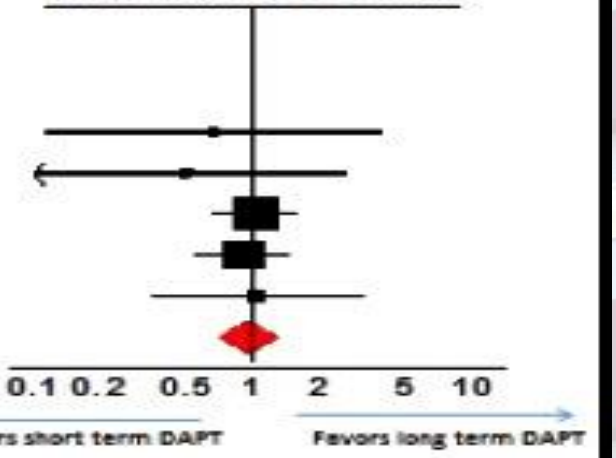


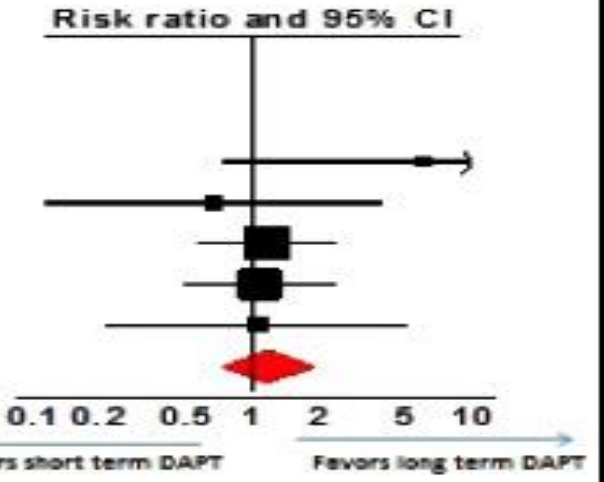
Cardiac death

Study name	Risk ratio	Lower limit	Upper limit	p-Value
Excellent	0.666	0.112	3.972	0.655
Reset	0.500	0.092	2.721	0.422
Prodigy	1.032	0.658	1.619	0.891
Optimize	0.902	0.549	1.484	0.685
Secruity	1.051	0.341	3.244	0.931
	0.945	0.693	1.288	0.720



Definite or probable stent thrombosis

Study name	Risk ratio	Lower limit	Upper limit	p-Value
Excellent	5.992	0.723	49.643	0.097
Reset	0.666	0.112	3.978	0.656
Prodigy	1.159	0.554	2.422	0.696
Optimize	1.078	0.494	2.356	0.850
Secruity	1.051	0.213	5.191	0.951
	1.169	0.726	1.882	0.521

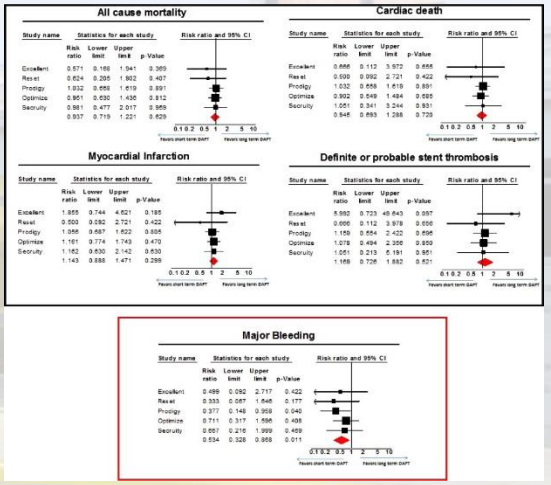


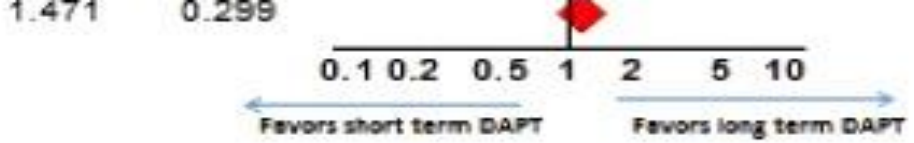
Major Bleeding

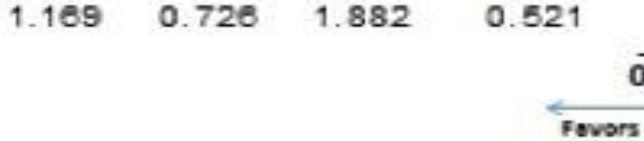
From: AN UPDATE META-ANALYSIS OF RANDOMIZED TRIALS COMPARING SHORT-TERM AND LONG-TERM DUAL ANTIPLATELET THERAPY FOLLOWING DRUG-ELUTING STENTS

J Am Coll Cardiol. 2015;65(10_S). doi:10.1016/S0735-1097(15)61639-4

Updated meta-analysis of randomized trials to assess the efficacy and safety of ≤ 6 months versus ≥ 12 months DAPT after implantation of DES

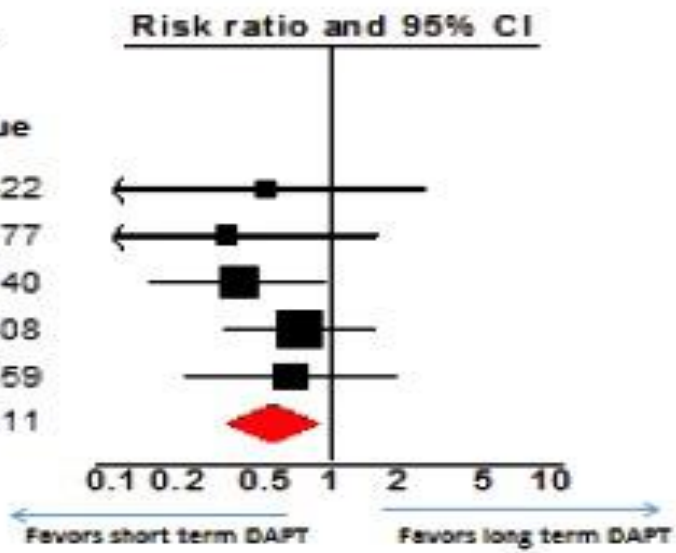






Major Bleeding

Study name	Risk ratio	Lower limit	Upper limit	p-Value
Excellent	0.499	0.092	2.717	0.422
Reset	0.333	0.067	1.646	0.177
Prodigy	0.377	0.148	0.958	0.040
Optimize	0.711	0.317	1.596	0.408
Secruity	0.657	0.216	1.999	0.459
	0.534	0.328	0.868	0.011



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Extended-duration DAPT was not associated with cardiovascular or mortality benefits after implantation of DES, although the risk of major bleeding was significantly lower with shorter duration of therapy.

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Seis meses…

Un año….

Dos años

Toda la vida….

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Seis meses…

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From: Resistance to clopidogrel: A review of the evidence

J Am Coll Cardiol. 2005;45(8):1157-1164. doi:10.1016/j.jacc.2005.01.034

Extrinsic mechanisms

1. Patient non-compliance
2. Under-dosing or inappropriate dosing of clopidogrel
3. Drug-drug interactions involving CYP3A4

Intrinsic mechanisms

1. Genetic variables
   a. Polymorphisms of $P2Y_{12}$ receptor
   b. Polymorphisms of CYP3As
2. Increase release of ADP
3. Alternate pathways of platelet activation:
   a. Failure to inhibit catecholamine-mediated platelet activation (epinephrine)
   b. Greater extent of $P2Y_1$-dependent platelet aggregation
   c. Up-regulation of $P2Y_{12}$-independent pathways (thrombin, thromboxane A_2, collagen)

5 minutos …

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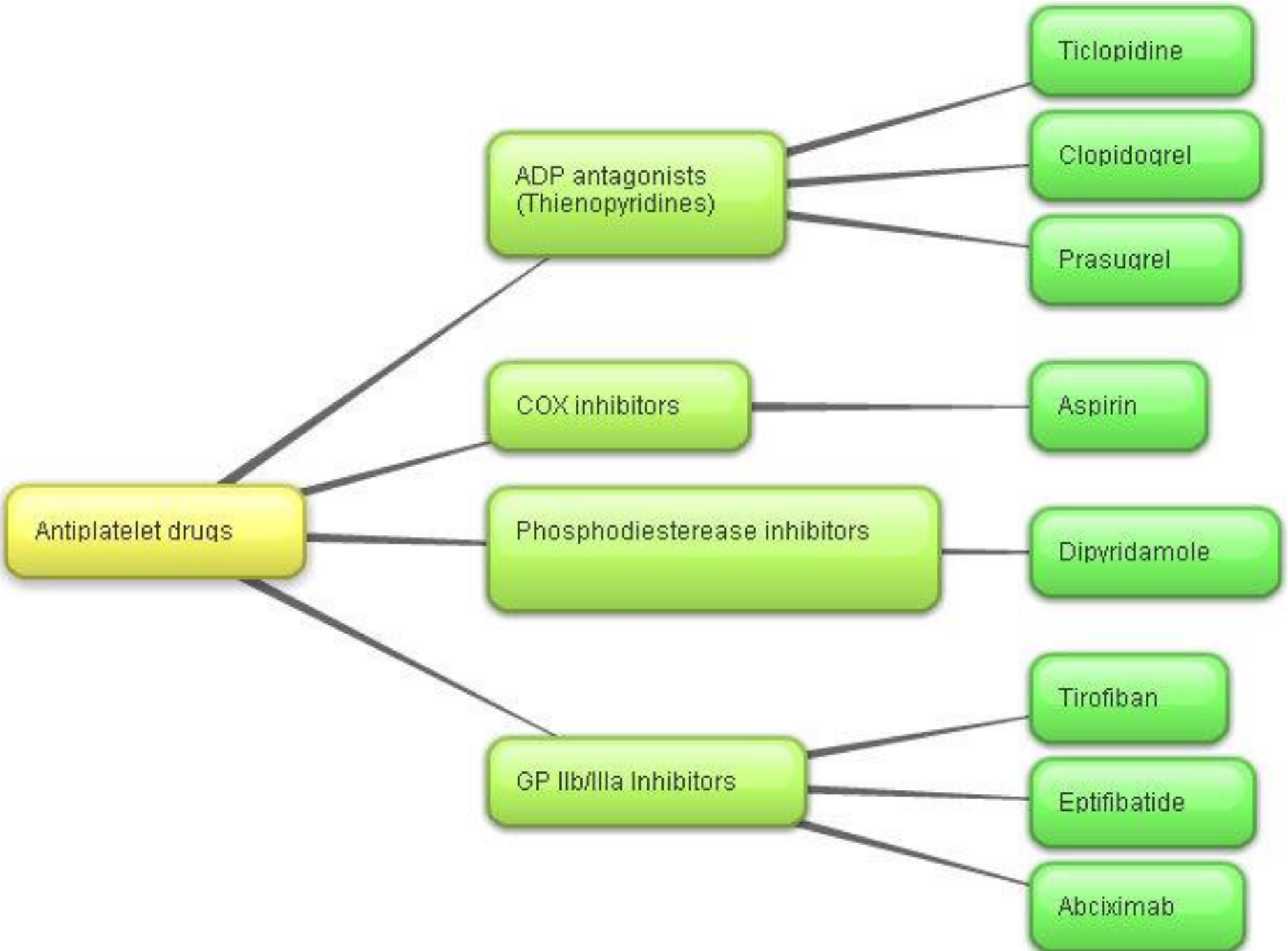
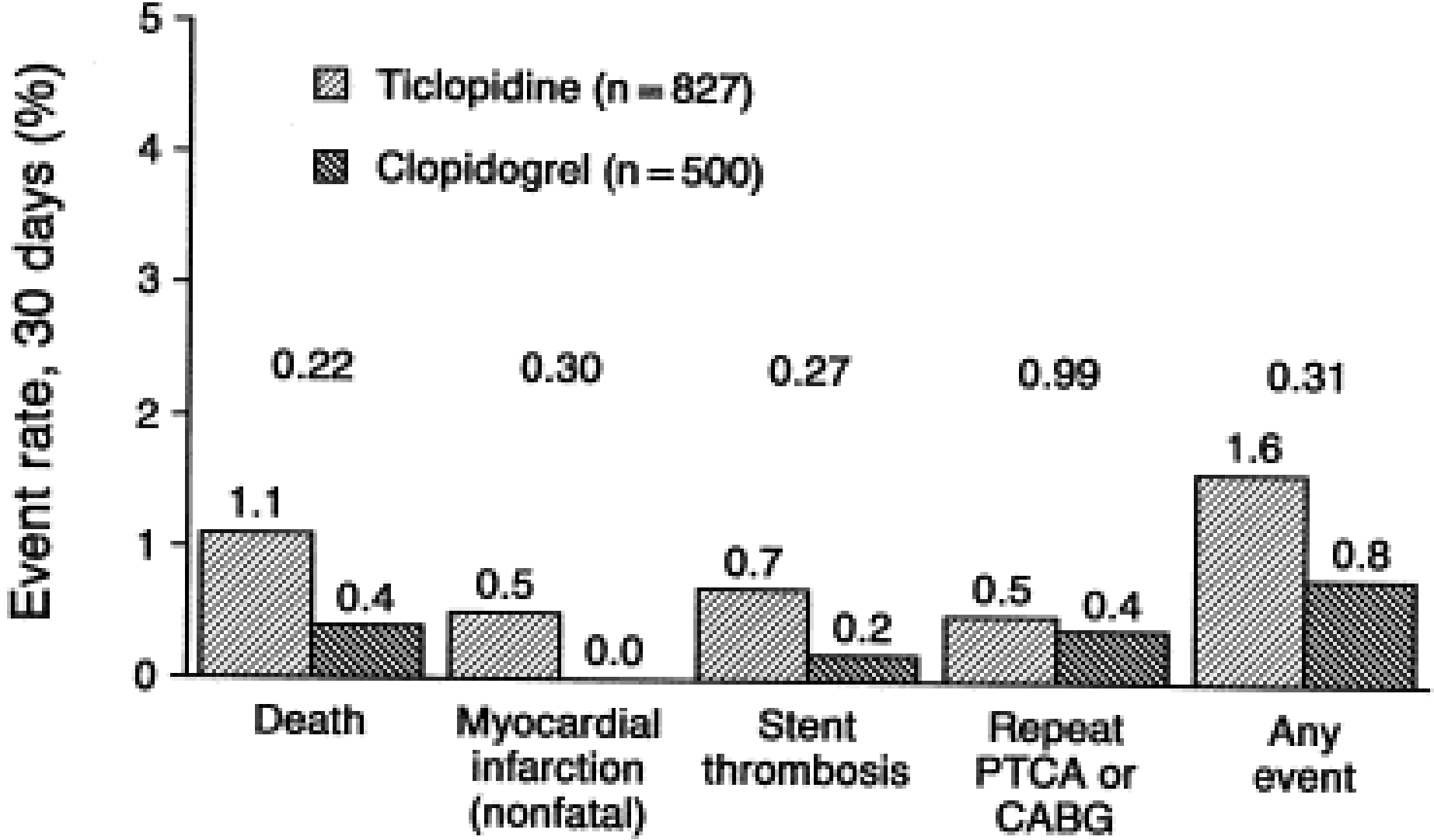
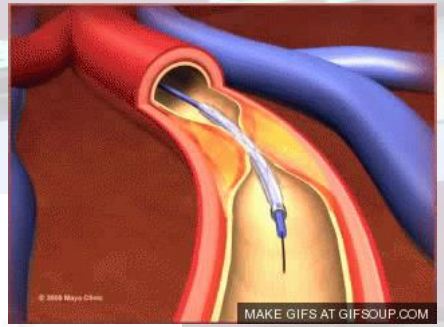

Antiplatelet drugs
ADP antagonists (Thienopyridines)
Ticlopidine
Clopidogrel
Prasugrel
COX inhibitors
Aspirin
Phosphodiesterease inhibitors
Dipyridamole
GP IIb/IIIa Inhibitors
Tirofiban
Eptifibatide
Abciximab

Ticlopidina/Clopidogrel



Prasugrel/Clopidogrel



Evaluar cuantitativamente la relación riesgo/beneficio para prasugrel.

Por cada 1000 pacientes tratados con prasugrel en lugar de con clopidogrel se evitarán 22 IM no fatales, pero se producirán 5 sangrados con compromiso vital, de los que 3 fallecerán.

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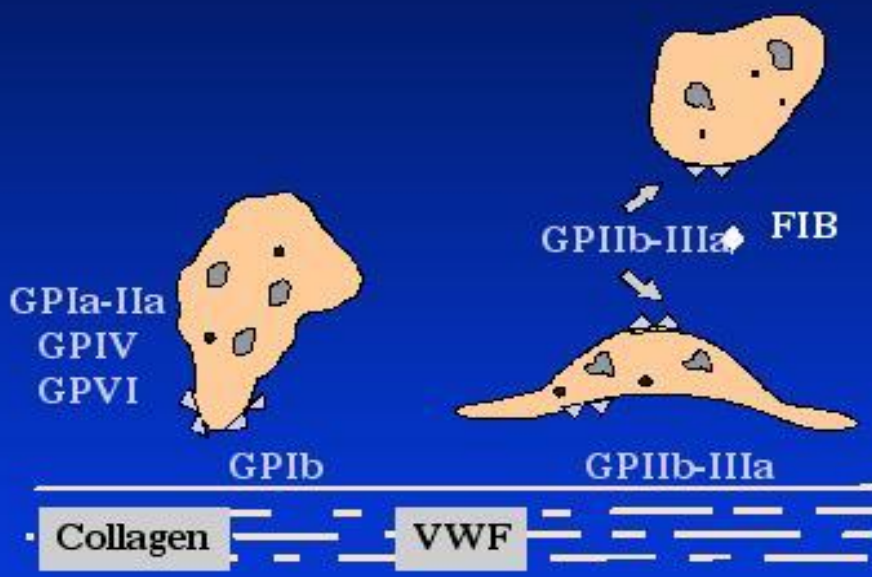
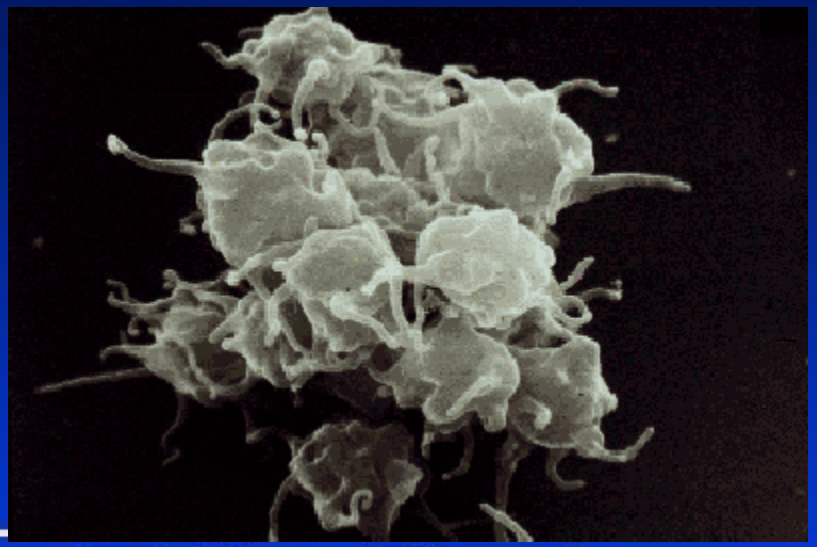
PLATELET FUNCTIONS





CONTACT ADHESION AGGREGATION AND RELEASE

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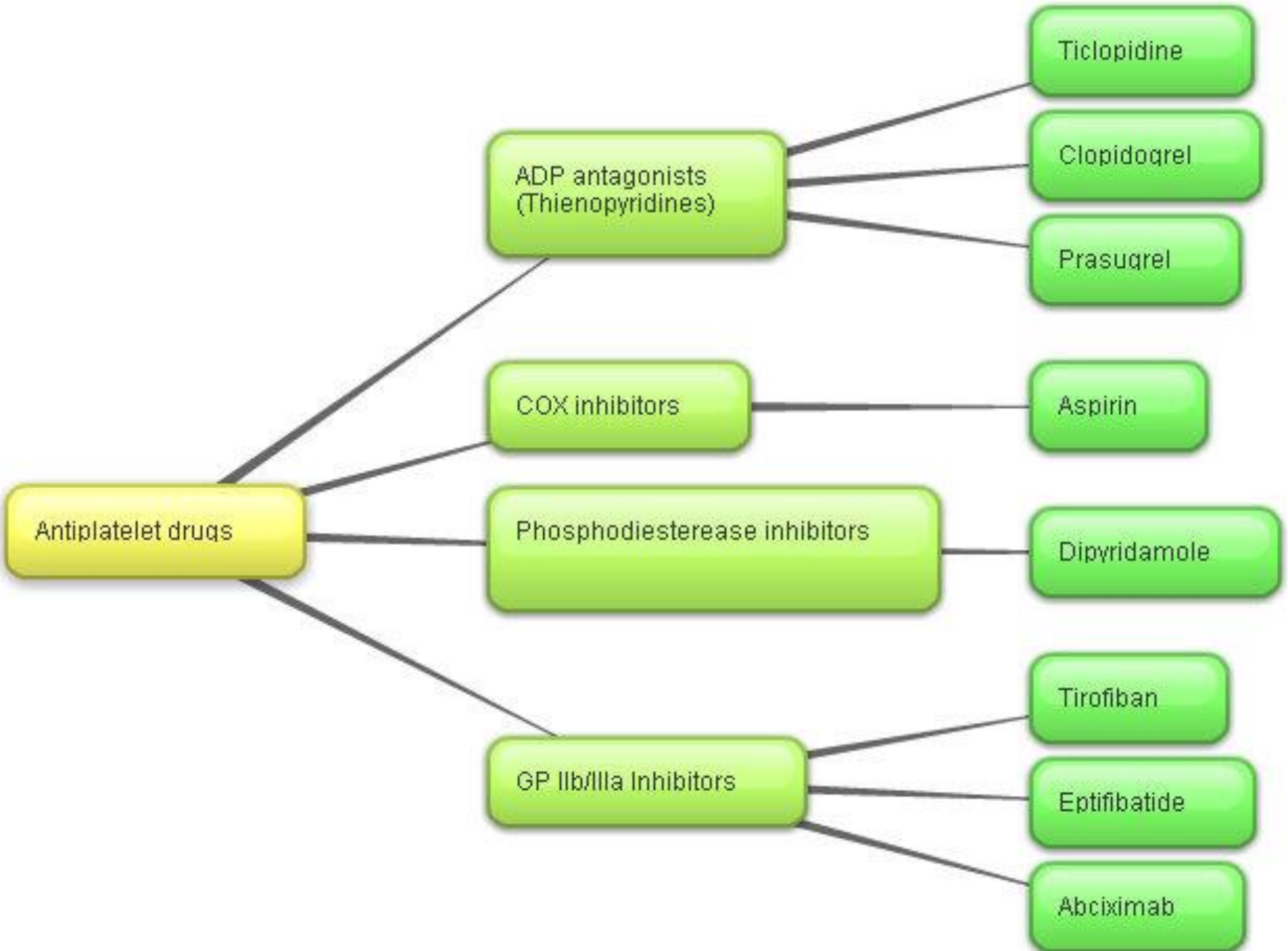
Antiplatelet drugs
ADP antagonists (Thienopyridines)
Ticlopidine
Clopidogrel
Prasugrel
COX inhibitors
Aspirin
Phosphodiesterease inhibitors
Dipyridamole
GP IIb/IIIa Inhibitors
Tirofiban
Eptifibatide
Abciximab

INHIBIDORES DE P2Y12

TIENOPIRIDINAS

- Clopidogrel
- Prasugrel
- y nuevos Greles

TRIAZOLOPIRIDINAS

- Ticagrelor
- Nuevos Grelores

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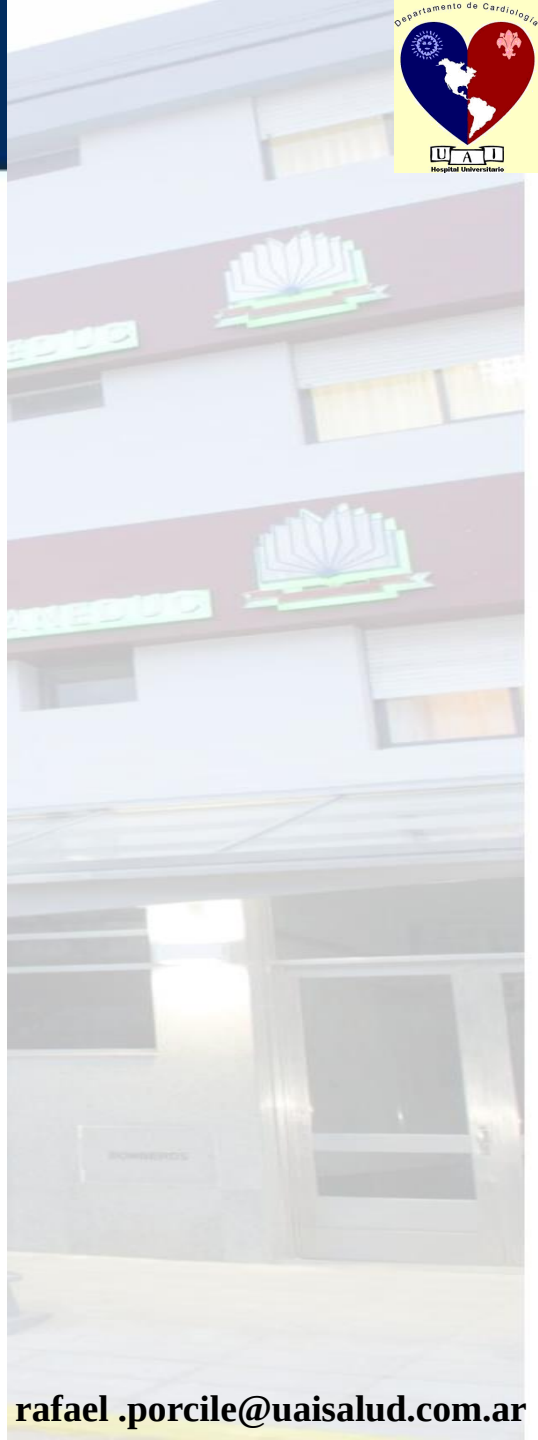
Inhibidores P2Y12

Características	Clopidogrel	Prasugrel	Ticagrelor
Clase	Tienopiridina	Tienopiridina	Triazolopirimidina
Reversibilidad	Irreversible	Irreversible	Reversible
Activación	2 pasos	1 paso	Activo
Comienzo	2-4 hs	30 min	30 min
Duración (dias)	3-10	5-10	3-4
Días susp. Cir	5	7	5



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Inhibidores P2Y12

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Días susp. Cir	5	7	5

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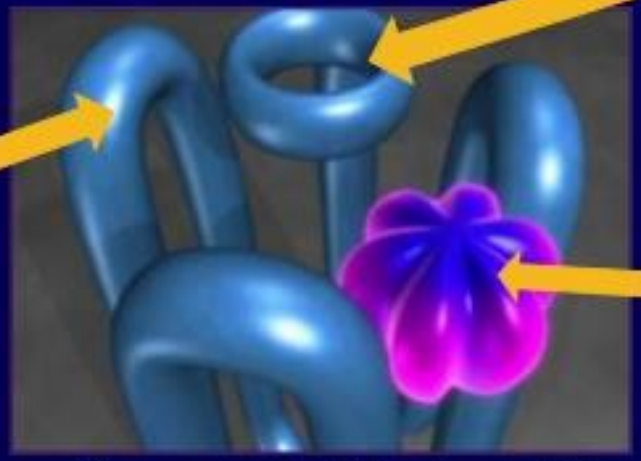
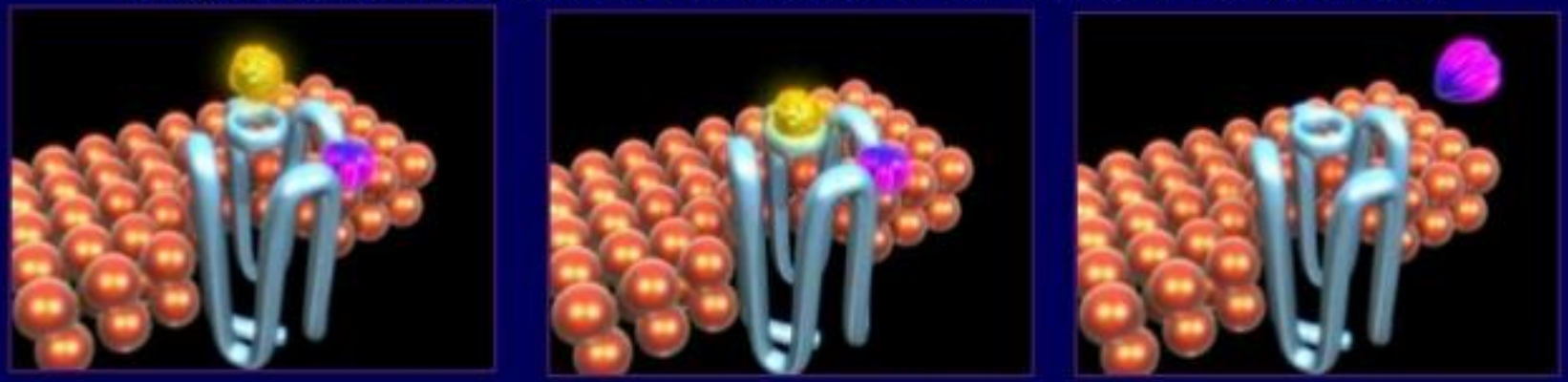
Ticagrelor: mecanismo de acción

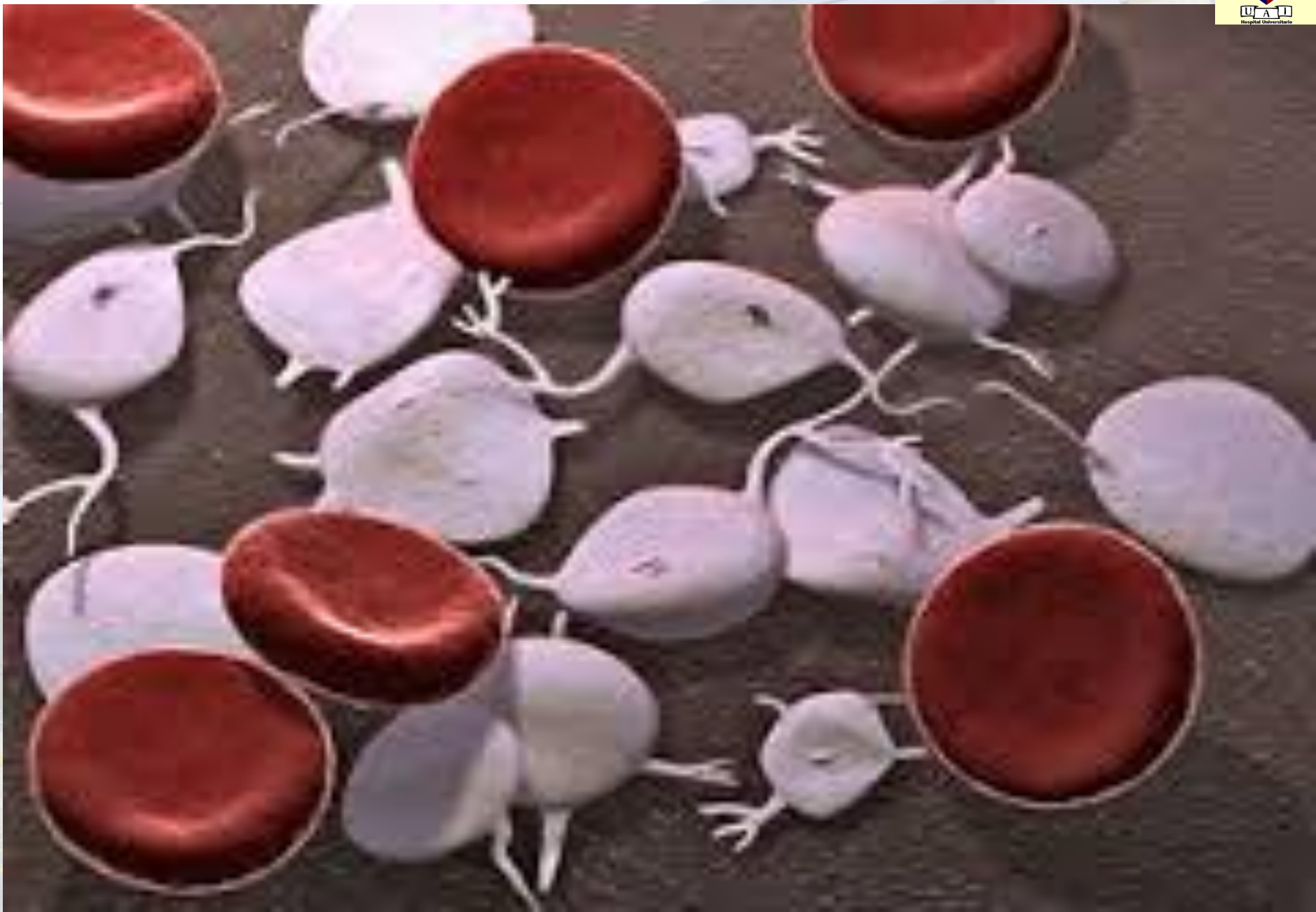


Ticagrelor no interactúa con el sitio de unión del receptor ADP

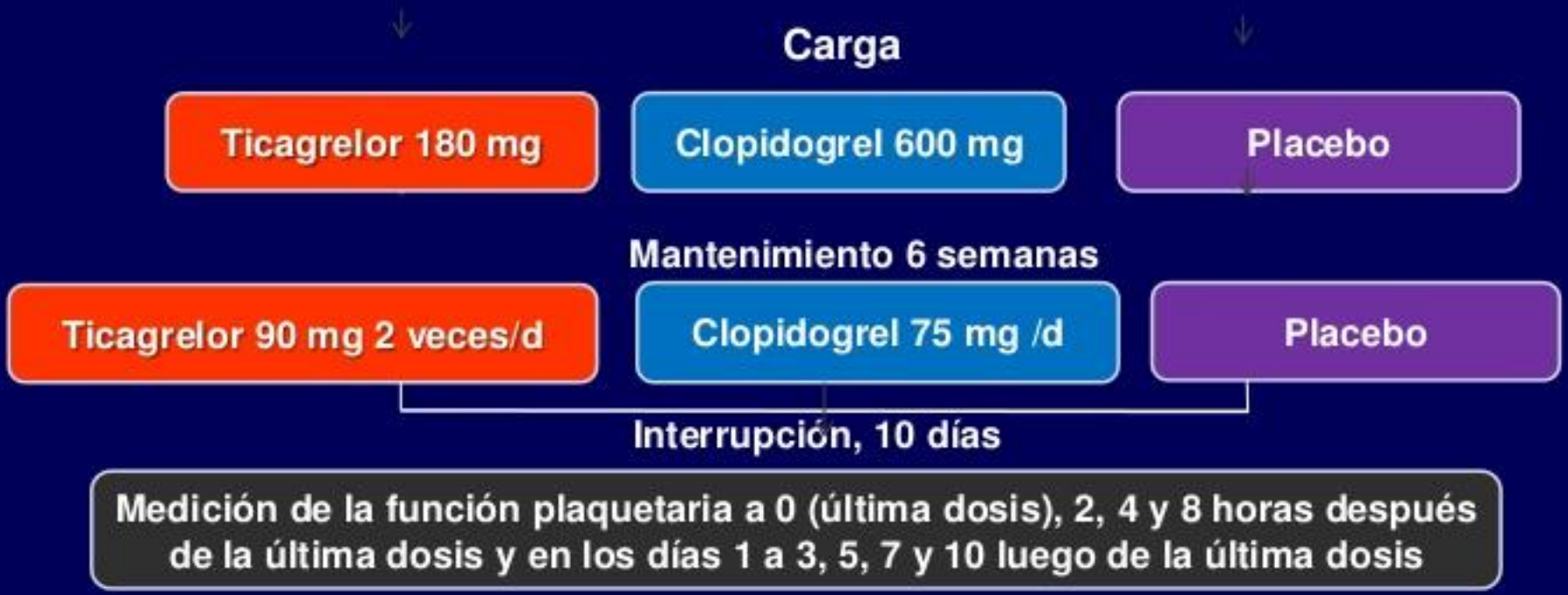


Ticagrelor unión directa al receptor $P2Y_{12}$ en forma reversible: inhibe la agregación y activación plaquetaria

Husted S, et al. *Euro Heart J*. 2006;27:1038–1047.
Gurbel PA, et al. *Expert Opin Drug Metab Toxicol*. 2009;5(8):989–1004.
Van Giezen JJ, et al. *J Thromb Haemost*. 2009;7:1556–1565.



Diseño del estudio ONSET/OFFSET



Bassand JP, et al. *Eur Heart J.* 2007;28:1598-1660.; Plavix® [package insert]. Bridgewater, NJ: Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership;2010; Gurbel PA, et al. *Circulation.* 2009;120:2577-2585.

Conclusiones de ONSET/OFFSET

- El estudio **ONSET/OFFSET** en pacientes con enfermedad coronaria estable, tratados con AAS, demostró que, comparado con clopidogrel:
  - Ticagrelor tiene un comienzo de accion más rápido; A los 30 minutos se observa un efecto antiplaquetario más significativo, (IPA 41% vs 8 %)
  - Ticagrelor presenta un efecto inhibitorio mayor y sostenido durante el mantenimiento.
  - Ticagrelor tiene una pendiente de offset más rápida versus clopidogrel; el IPA de Ticagrelor en el día 3 es comparable a la de clopidogrel en el día 5.

PLATO - diseño del estudio

Pacientes con SCA con AI/NSTEMI (riesgo moderado-alto)
STEMI (en caso de ICP primaria).
Todos recibiendo aspirina (75-100 mg/día); tratamiento previo o no con clopidogrel;
Randomizados dentro de las 24 horas del evento índice (n=18624)

Clopidogrel	Ticagrelor
300 mg de dosis de carga (excepto en pretratados), luego 75 mg 1 vez/día de mantenimiento	180 mg de dosis de carga, luego 90 mg 2 veces/día de mantenimiento

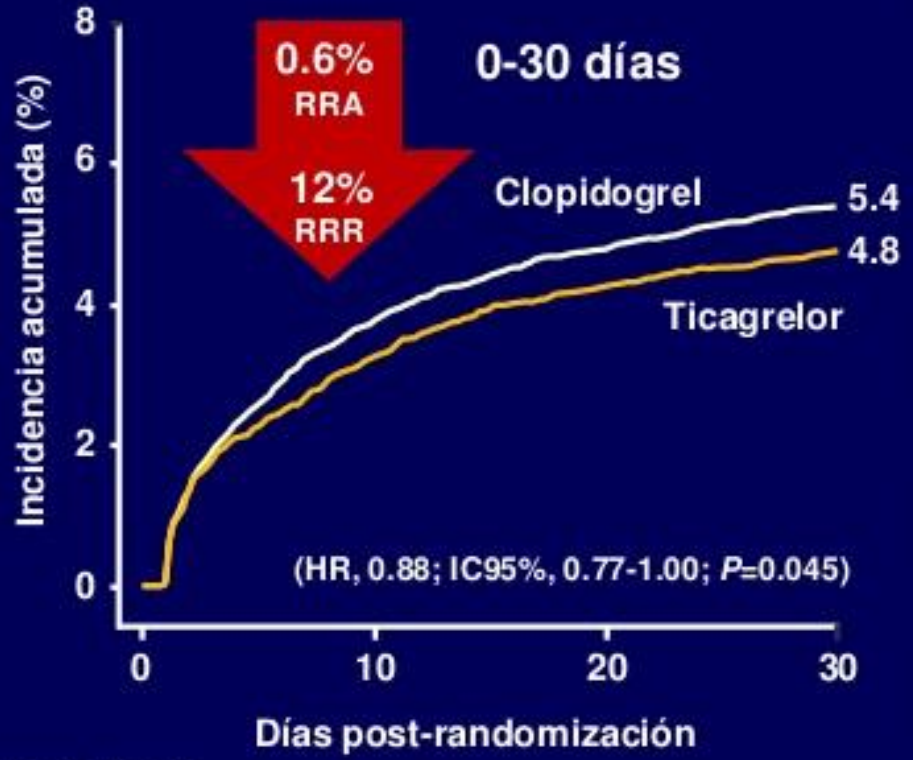
6-12 meses de exposición
Duración promedio 277 días

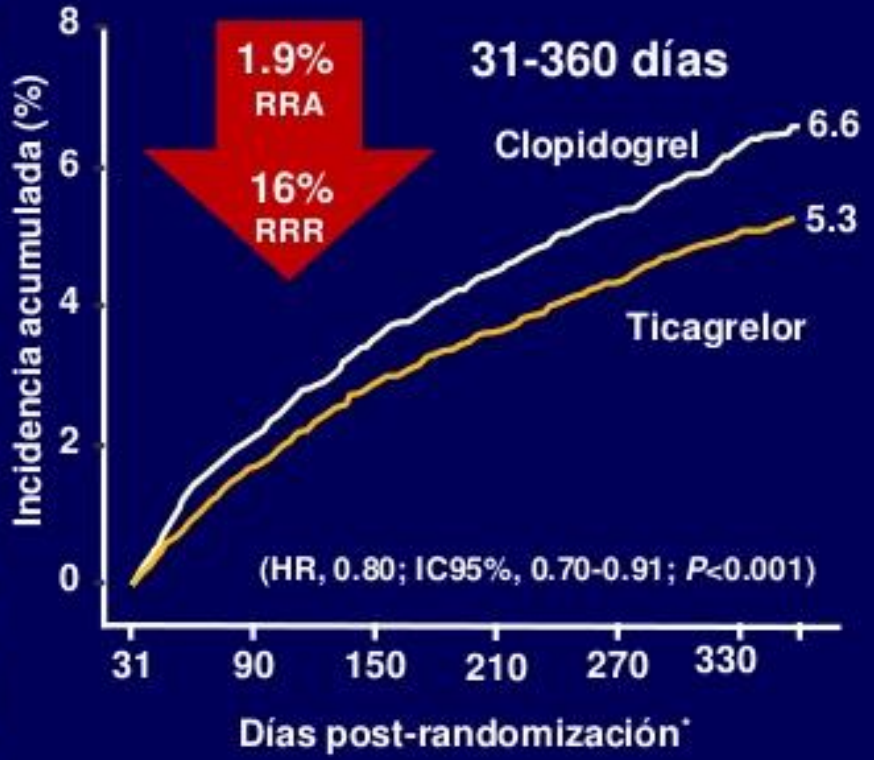
Endpoint primario:	• Combinación de muerte CV, IM o ACV
Edpoints secundarios:	• Muerte CV, IM, ACV en pacientes propuestos para manejo invasivo • Mortalidad total, IM o ACV • Muerte CV, IM, ACV, isquemia recurrente, AIT o evento arterotrombótico • Componentes del criterio primario (Muerte CV, IM y ACV) • Muerte por cualquier causa
Endpoint primario de seguridad:	• Sangrado mayor total

ICP, intervención coronaria percutánea; CV, cardiovascular; AIT, ataque isquémico transitorio, IM, infarto de miocardio, ACV: accidente cerebrovasculartransient ischemic attack .

James S, et al. *Am Heart J.* 2009;157:599-605; Wallentin L, et al. N Engl J Med. 2009;361:1045-1057.

Endpoint primario de eficacia a lo largo del tiempo (compuesto de muerte CV, IM o ACV)





Nro. en riesgo												
Ticagrelor	9333	8942	8827	8763	8673	8543	8397	7028	6480	4822
Clopidogrel	9291	8875	8763	8688	8688	8437	8286	6945	6379	4751

*Excluyendo pacientes con algún evento primario durante los primeros 30 días

Wallentin L. Presented at the European Society of Cardiology Congress 2009, Barcelona, Spain. August 29-September 2: 179.
http://spo.escardio.org/eslides/view.aspx?eevtid=33&id=179 -2.

¿PLAQUETAS INMADURAS?

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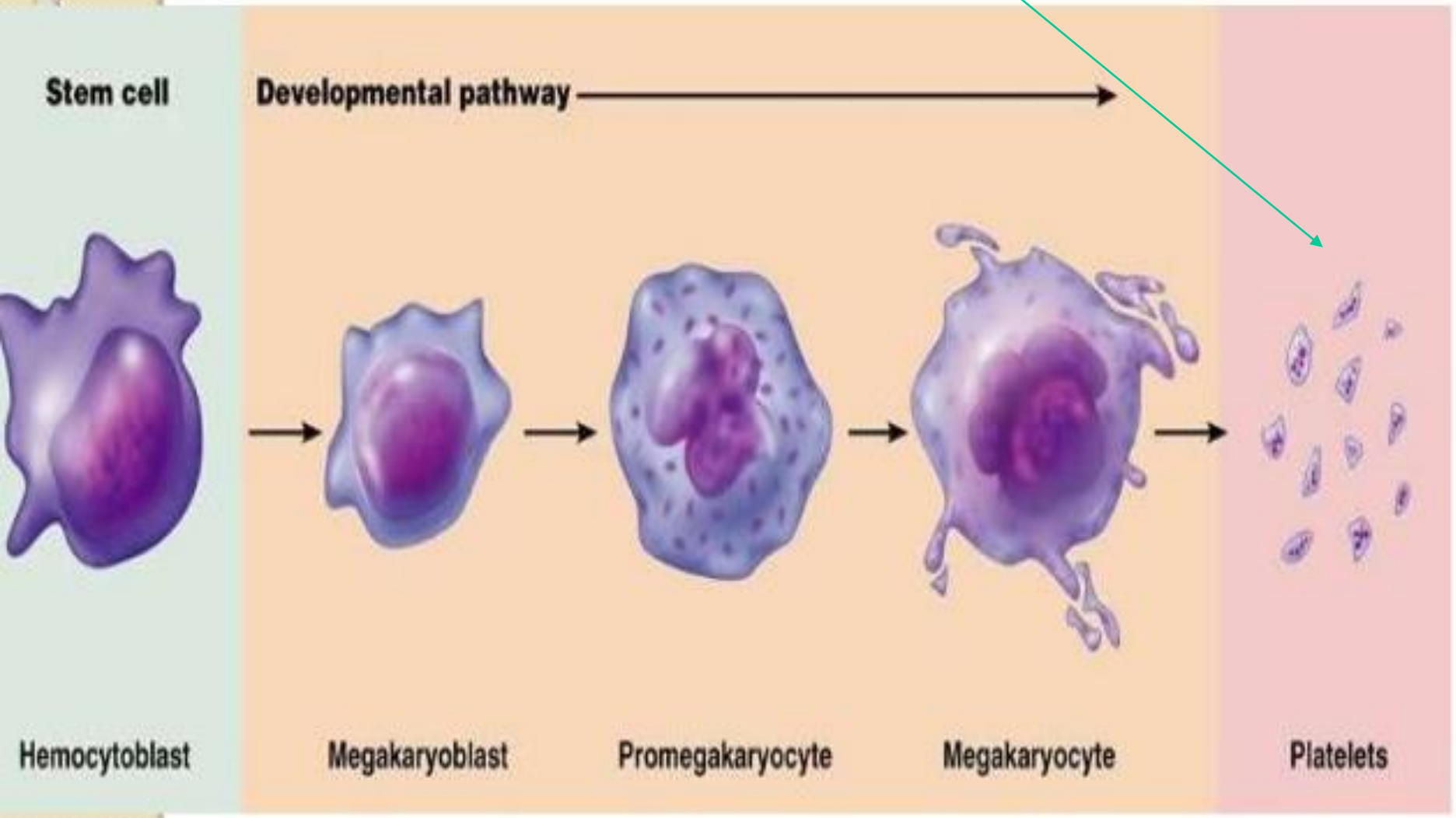
PLAQUETAS RETICULADAS



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Alrededor del 12% del total de las plaquetas circulantes son PR, las cuales suelen ser más grandes y relativamente más reactivas (con mayor poder trombótico) que las plaquetas maduras o viejas

En pacientes con ciertas características, tales como en los diabéticos, o en ciertas situaciones clínicas como en momentos de estrés, de alto consumo plaquetario o de trombosis aguda, se incrementa considerablemente el número de estas plaquetas nuevas en la sangre, por aumento de la renovación (“turn over”) plaquetario

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Impact of immature platelets on platelet response to ticagrelor and prasugrel in patients with acute coronary syndrome

European Heart Journal doi:10.1093/eurheartj/ehv326
Received 5 March 2015; revised 3 **June 2015;** accepted 22 June 2015

Clinical Perspective

Reticulated platelets differently influence adenosine diphosphate-induced platelet aggregation in dependence of the selected $P2Y_{12}$ receptor inhibitor in patients with acute coronary syndrome.

Aiming at a personalized antiplatelet therapy, **measurement of RPs may influence the choice of $P2Y_{12}$ receptor inhibitors** or the timing interval of drug intake especially in patients with a high platelet turnover

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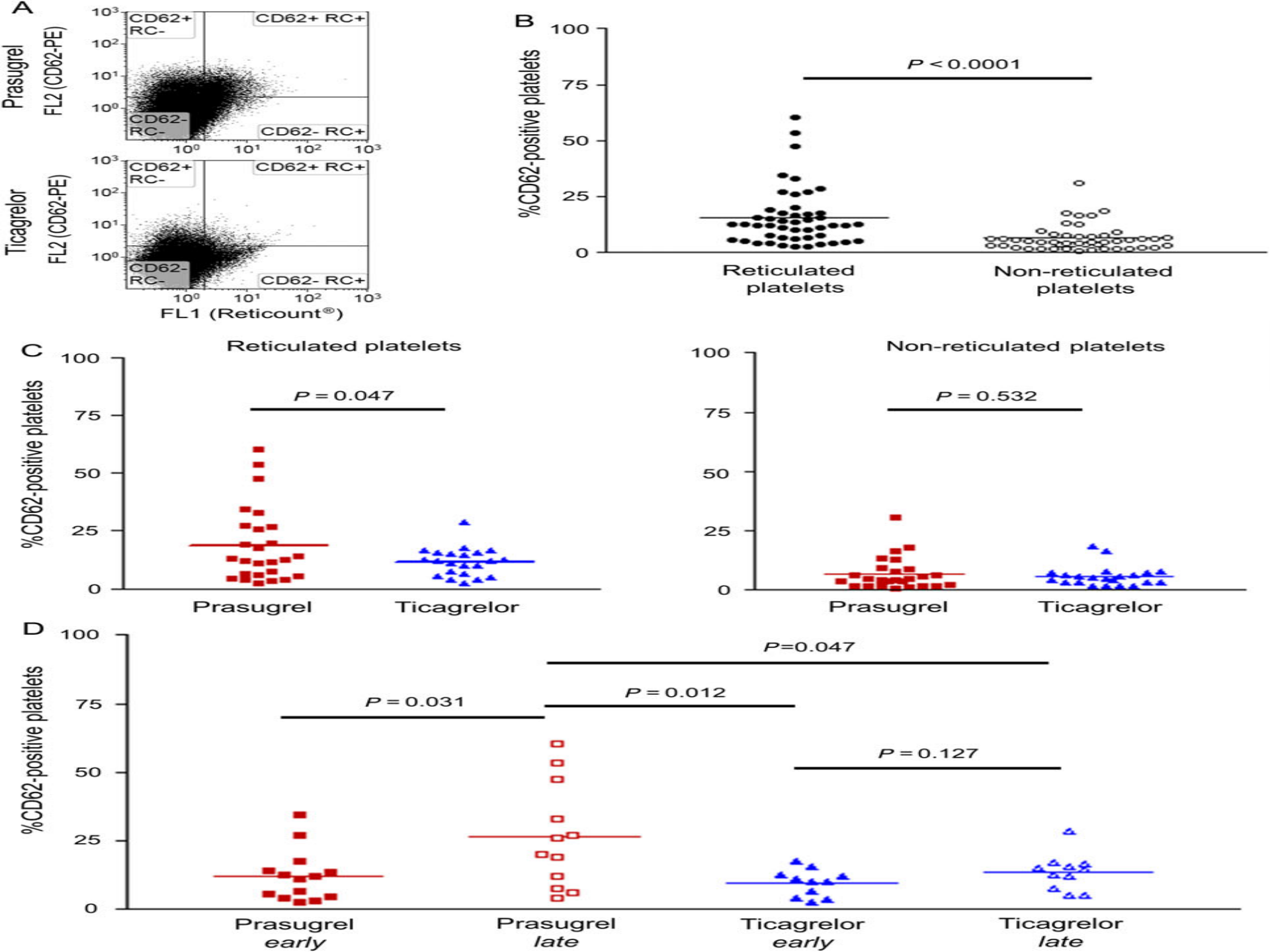
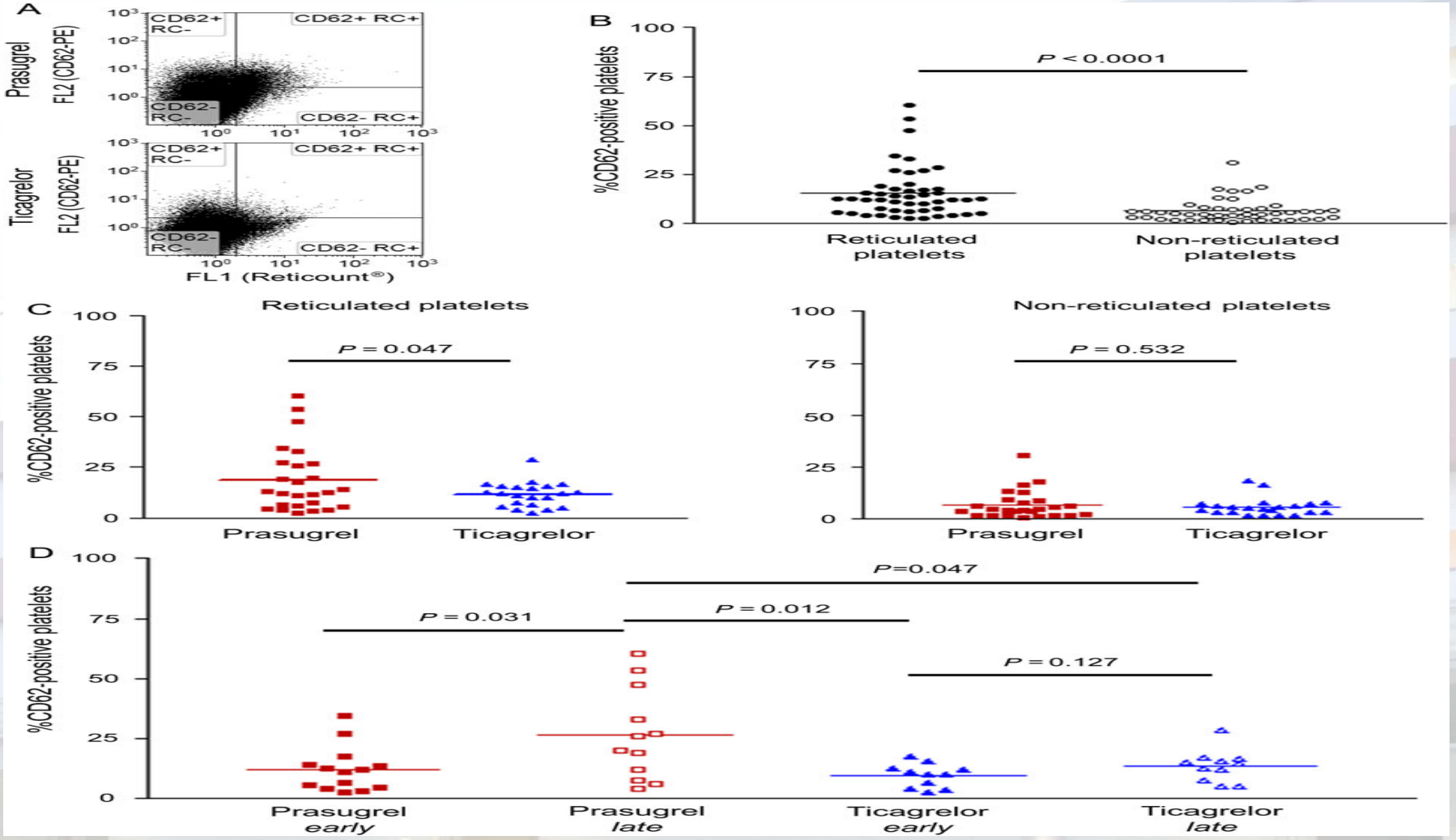

A
Prasugrel
Ticagrelor
FL2 (CD62-PE)
CD62+ RC-
CD62+ RC+
CD62- RC-
CD62- RC+
FL1 (Reticount®)
B
%CD62-positive platelets
P < 0.0001
Reticulated platelets
Non-reticulated platelets
C
Reticulated platelets
P = 0.047
Prasugrel
Ticagrelor
Non-reticulated platelets
P = 0.532
D
P=0.047
P = 0.031
P = 0.012
P = 0.127
Prasugrel early
Prasugrel late
Ticagrelor early
Ticagrelor late



Los inhibidores $P2Y_{12}$ de acción reversible, como el cangrelor y el ticagrelor, actúan en forma dinámica sobre el receptor, uniéndose y desuniéndose continuamente, favoreciendo que haya siempre moléculas activas del fármaco libres en plasma

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Café y preguntas

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2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

Developed in Collaboration with American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists,
and Society of Thoracic Surgeons
Endorsed by Preventive Cardiovascular Nurses Association
and
Society for Vascular Surgery

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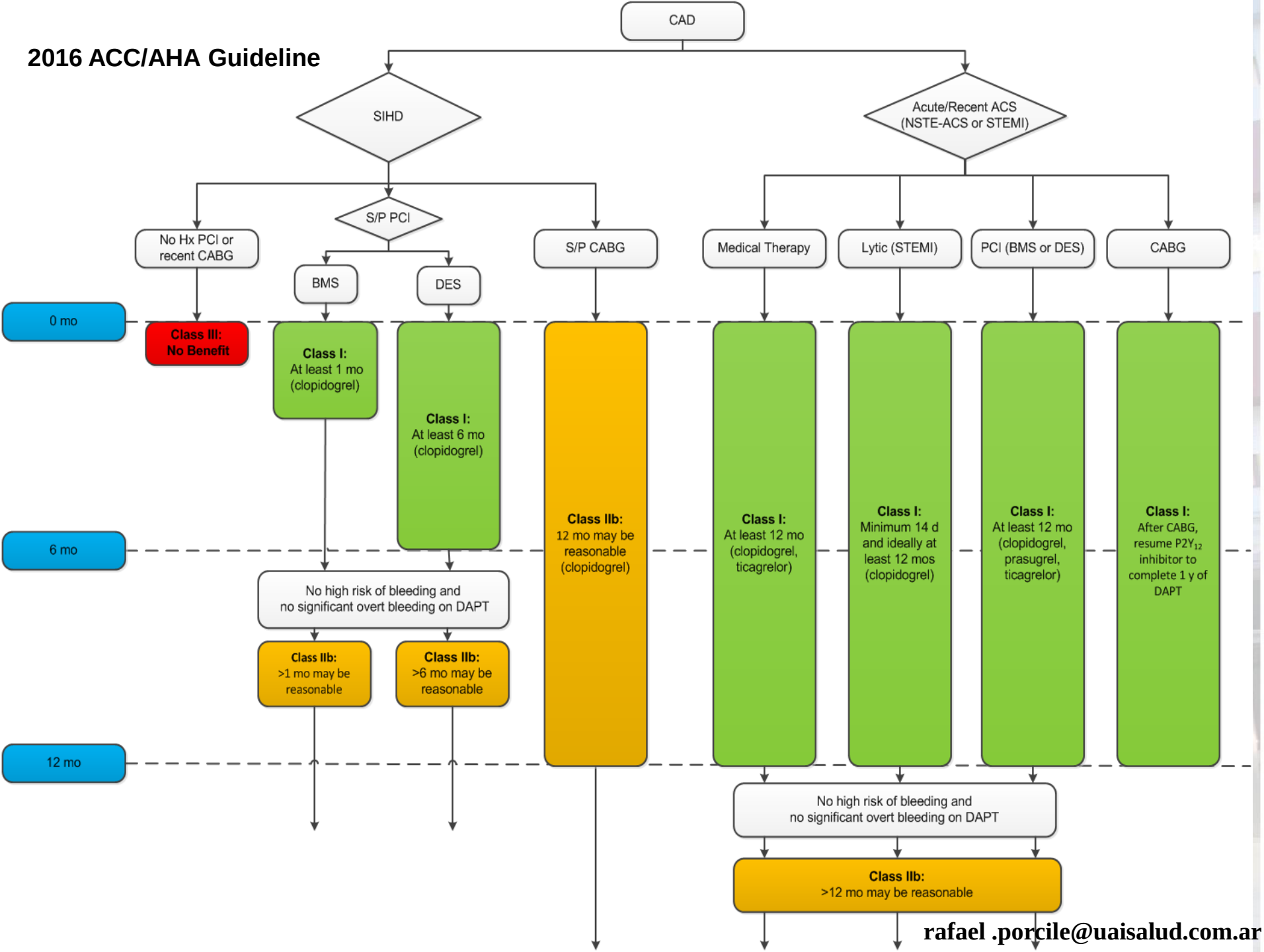
2016 ACC/AHA Guideline



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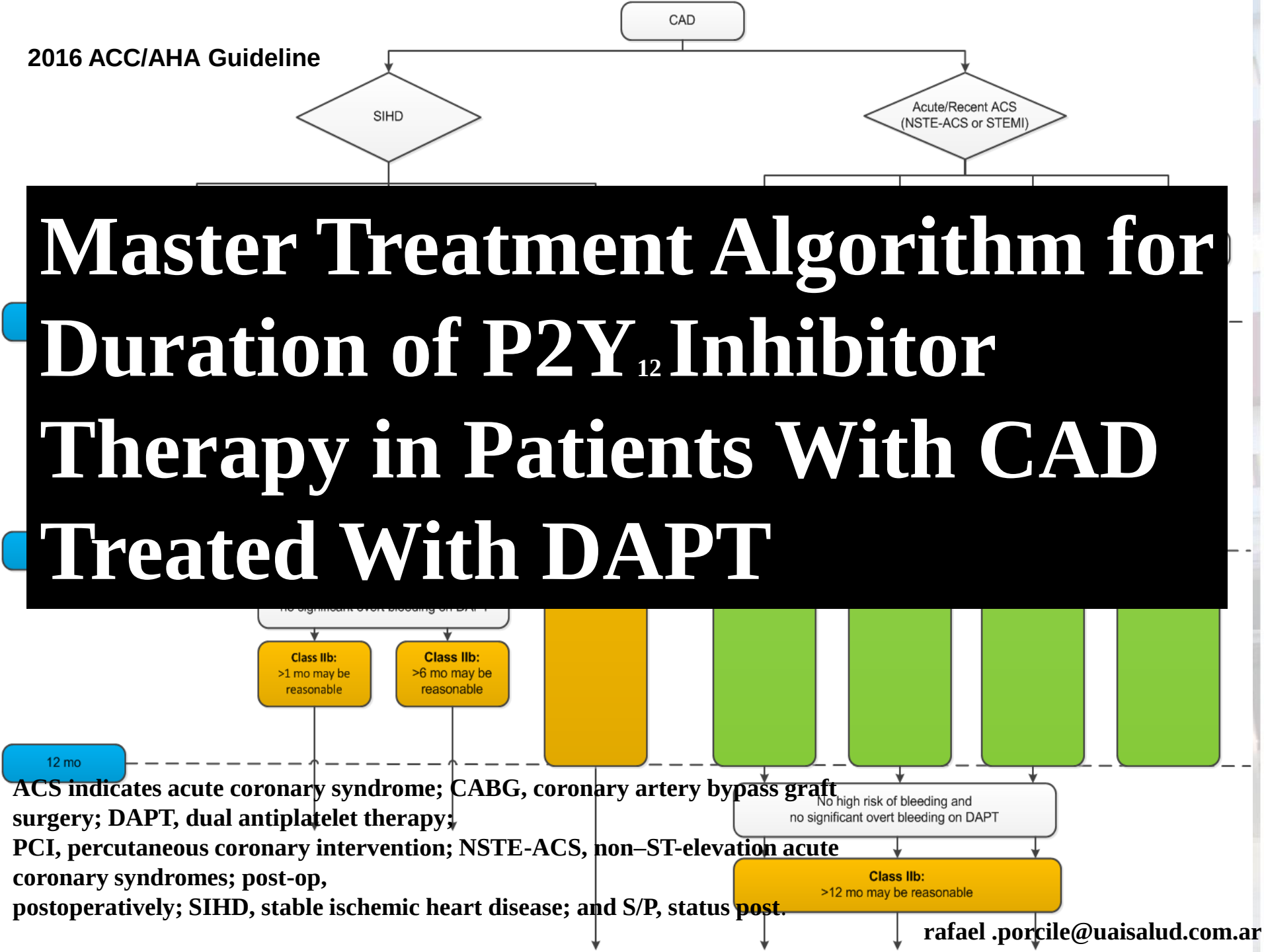
2016 ACC/AHA Guideline

Master Treatment Algorithm for Duration of $P2Y_{12}$ Inhibitor Therapy in Patients With CAD Treated With DAPT



ACS indicates acute coronary syndrome; CABG, coronary artery bypass graft surgery; DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention; NSTE-ACS, non–ST-elevation acute coronary syndromes; post-op, postoperatively; SIHD, stable ischemic heart disease; and S/P, status post.

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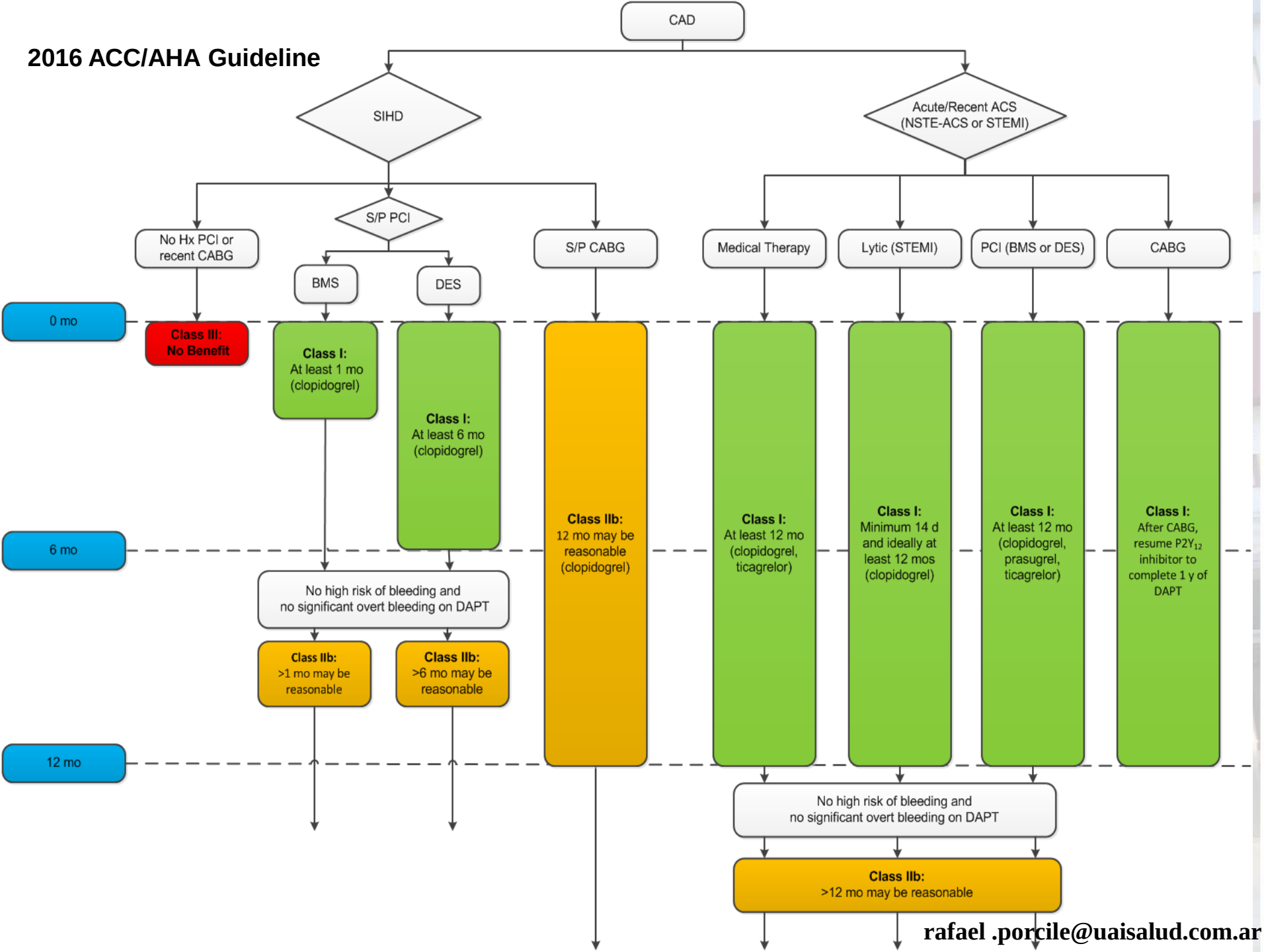
2016 ACC/AHA Guideline



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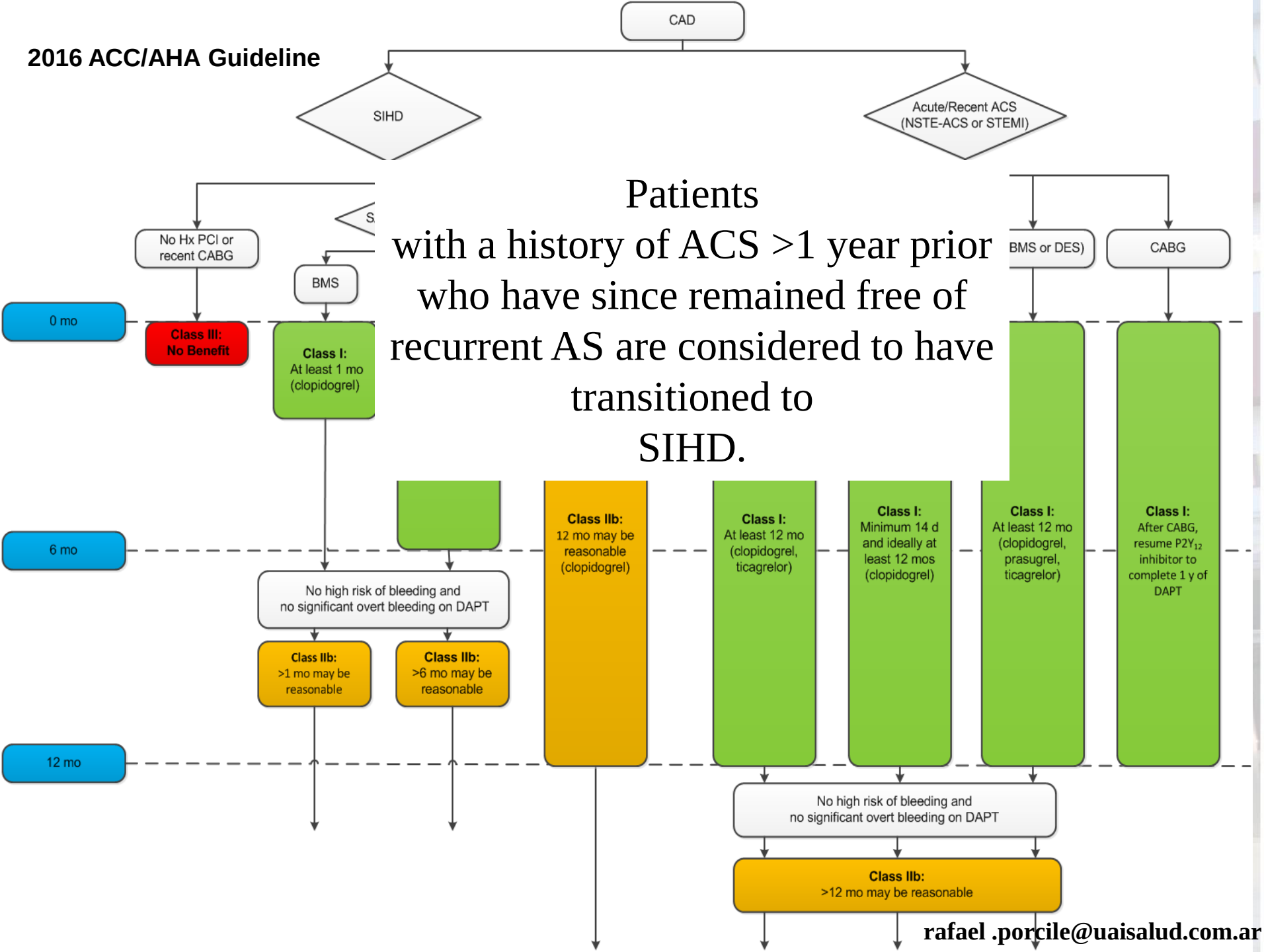
2016 ACC/AHA Guideline



Patients with a history of ACS >1 year prior who have since remained free of recurrent AS are considered to have transitioned to SIHD.

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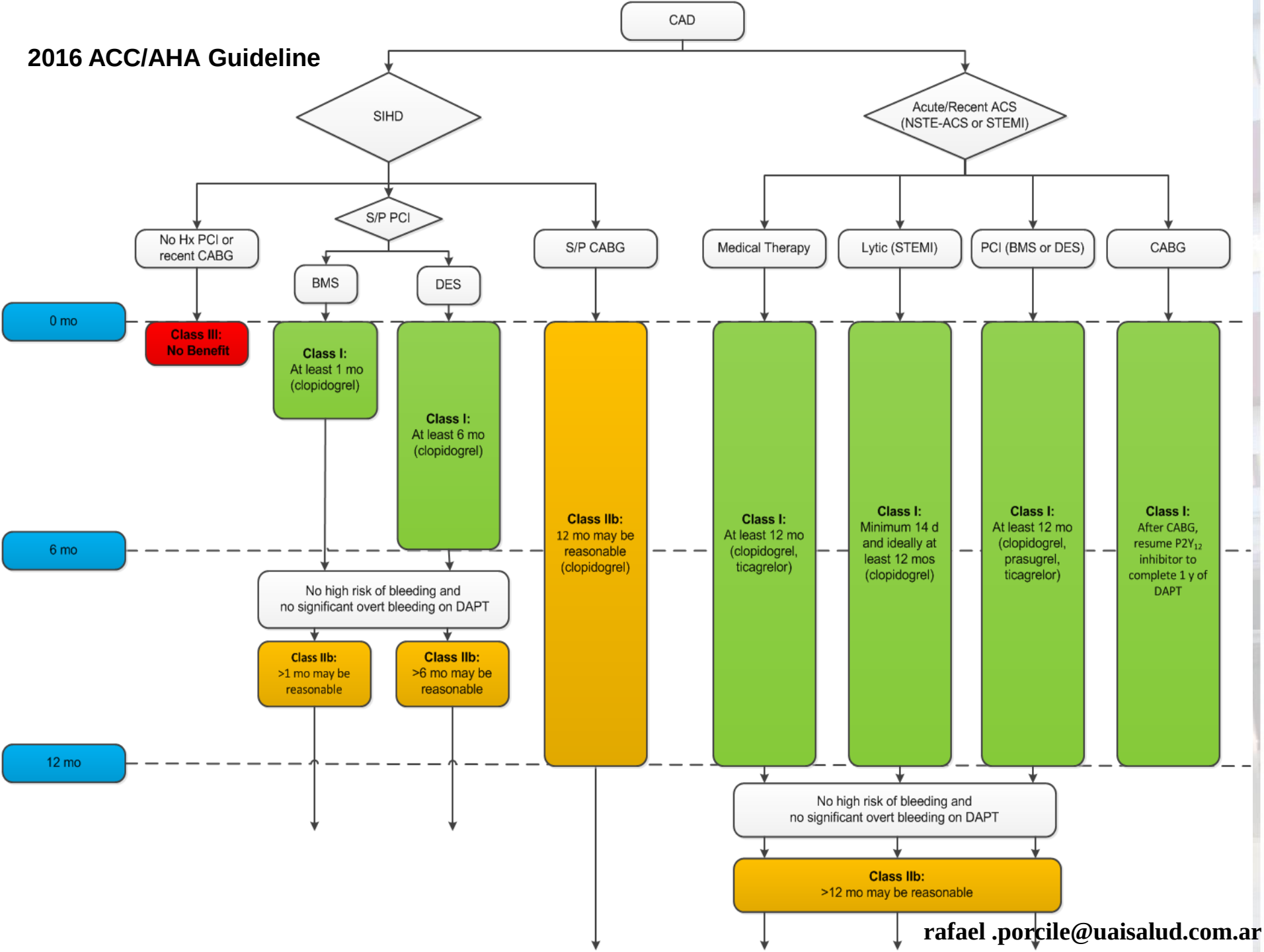

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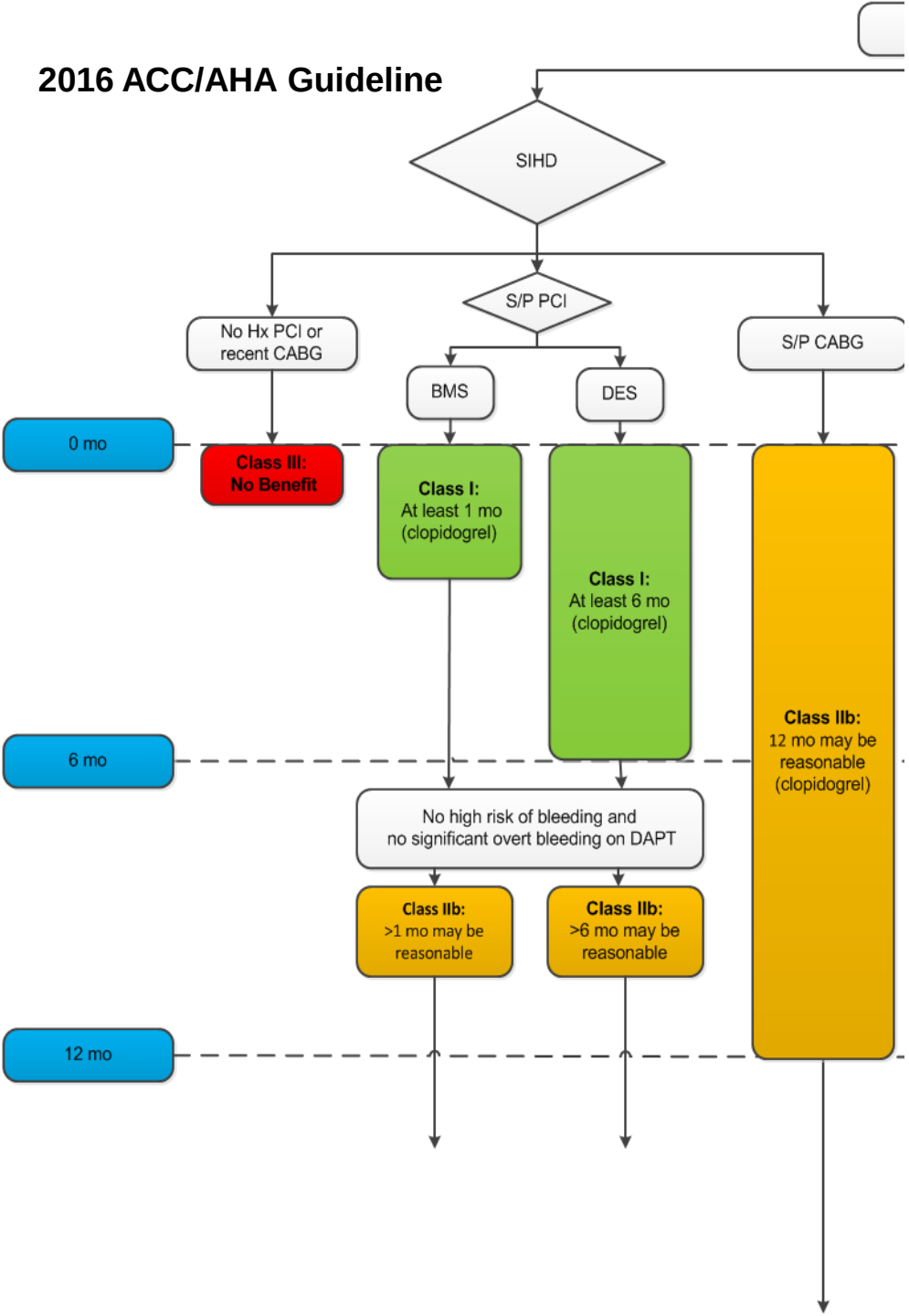
2016 ACC/AHA Guideline

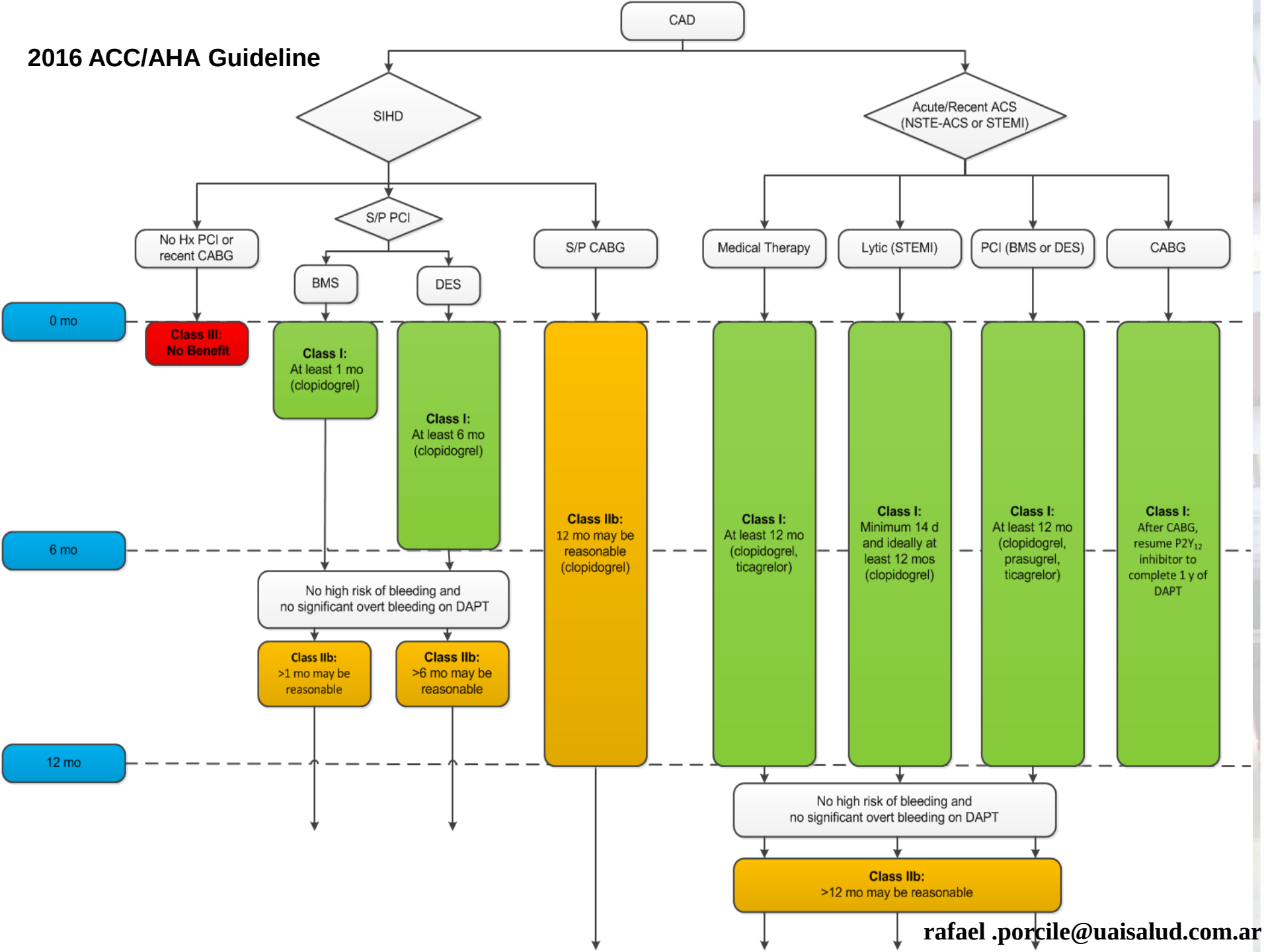


Arrows at the bottom of the figure denote that the optimal duration of prolonged DAPT is not Establishe

DES, drug-eluting stent

BMS, bare metal stent

2016 ACC/AHA Guideline



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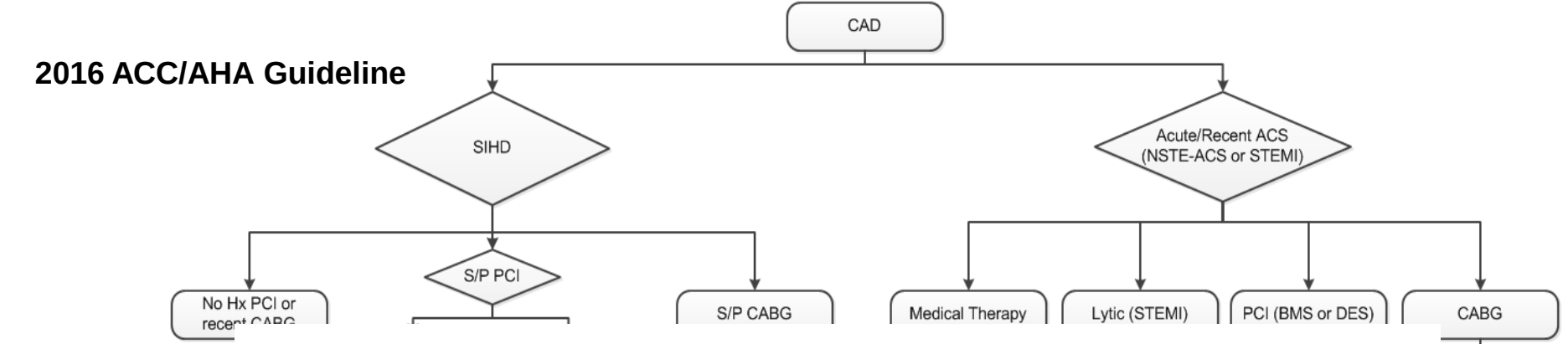
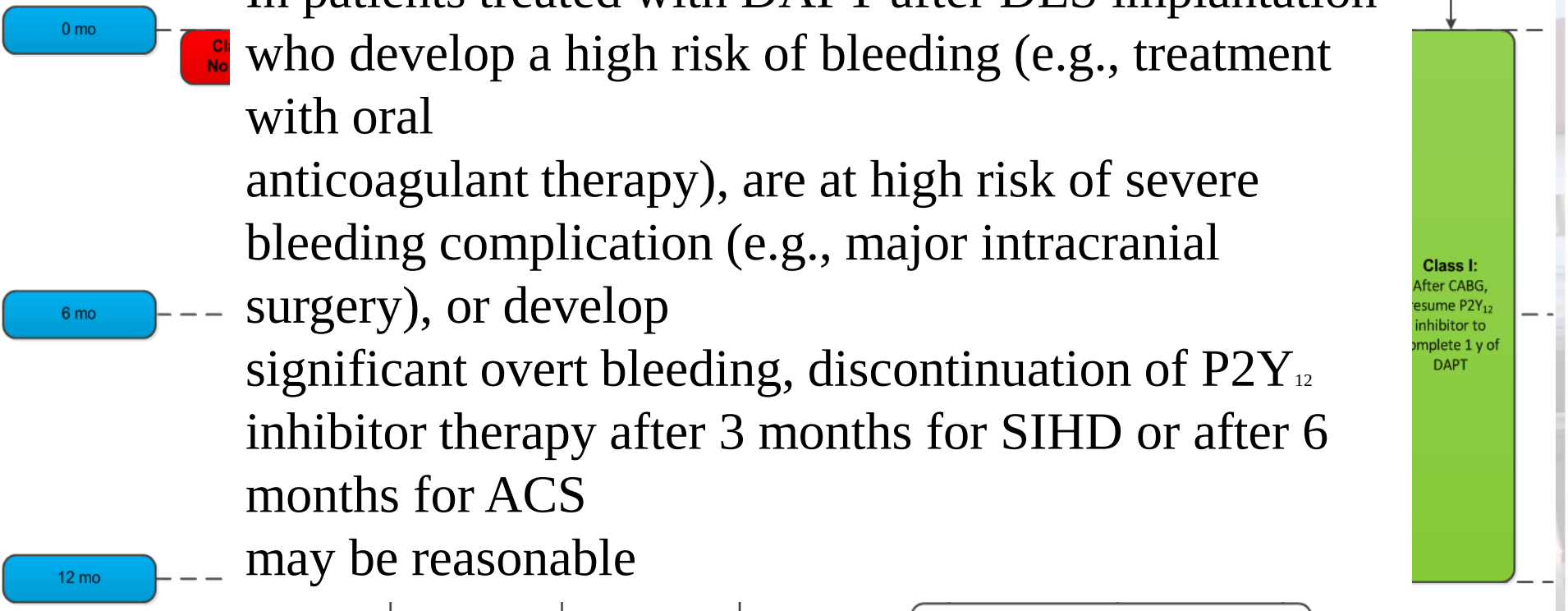
2016 ACC/AHA Guideline



In patients treated with DAPT after DES implantation who develop a high risk of bleeding (e.g., treatment with oral anticoagulant therapy), are at high risk of severe bleeding complication (e.g., major intracranial surgery), or develop significant overt bleeding, discontinuation of $P2Y_{12}$ inhibitor therapy after 3 months for SIHD or after 6 months for ACS may be reasonable



DES, drug-eluting stent;

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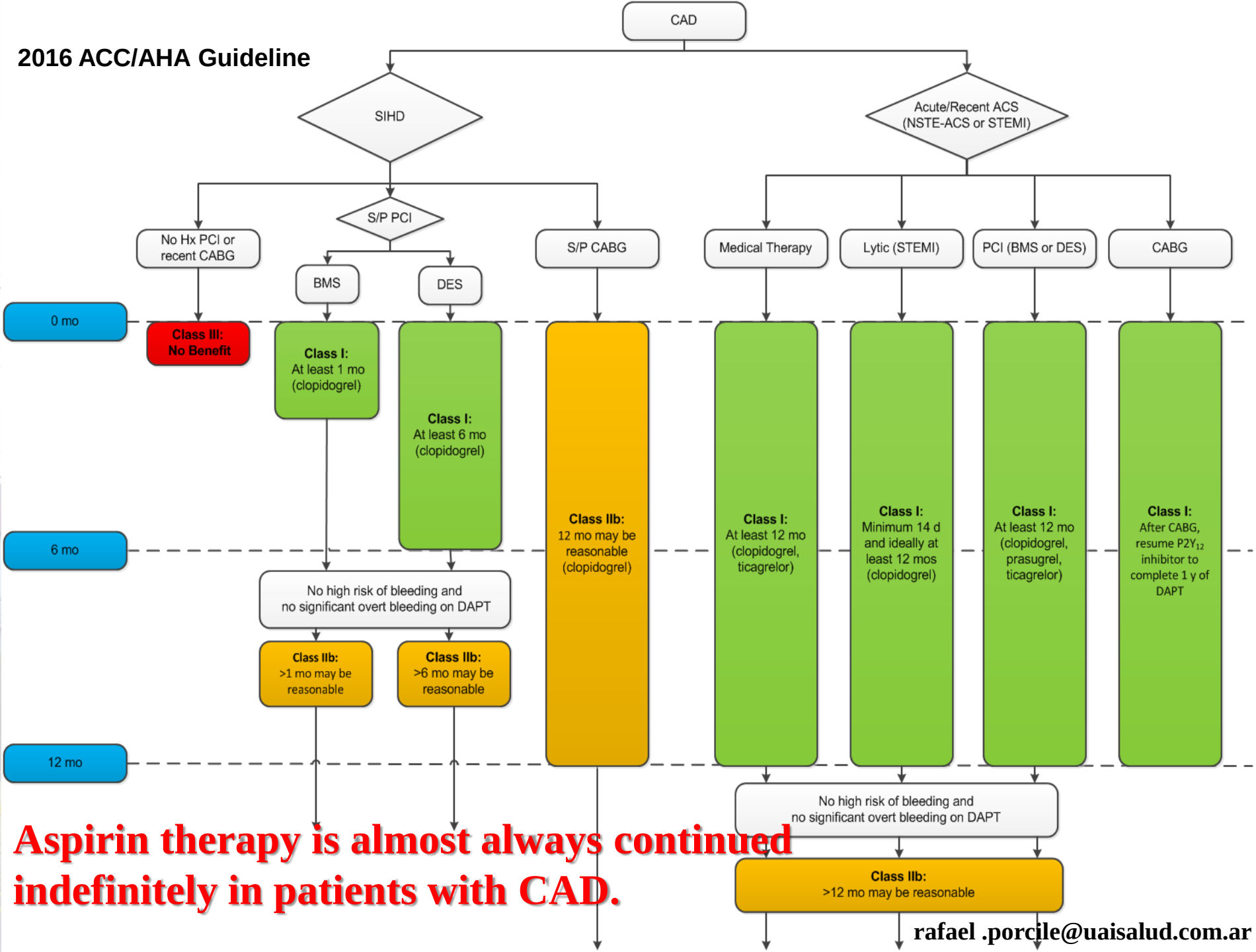

Aspirin therapy is almost always continued indefinitely in patients with CAD.

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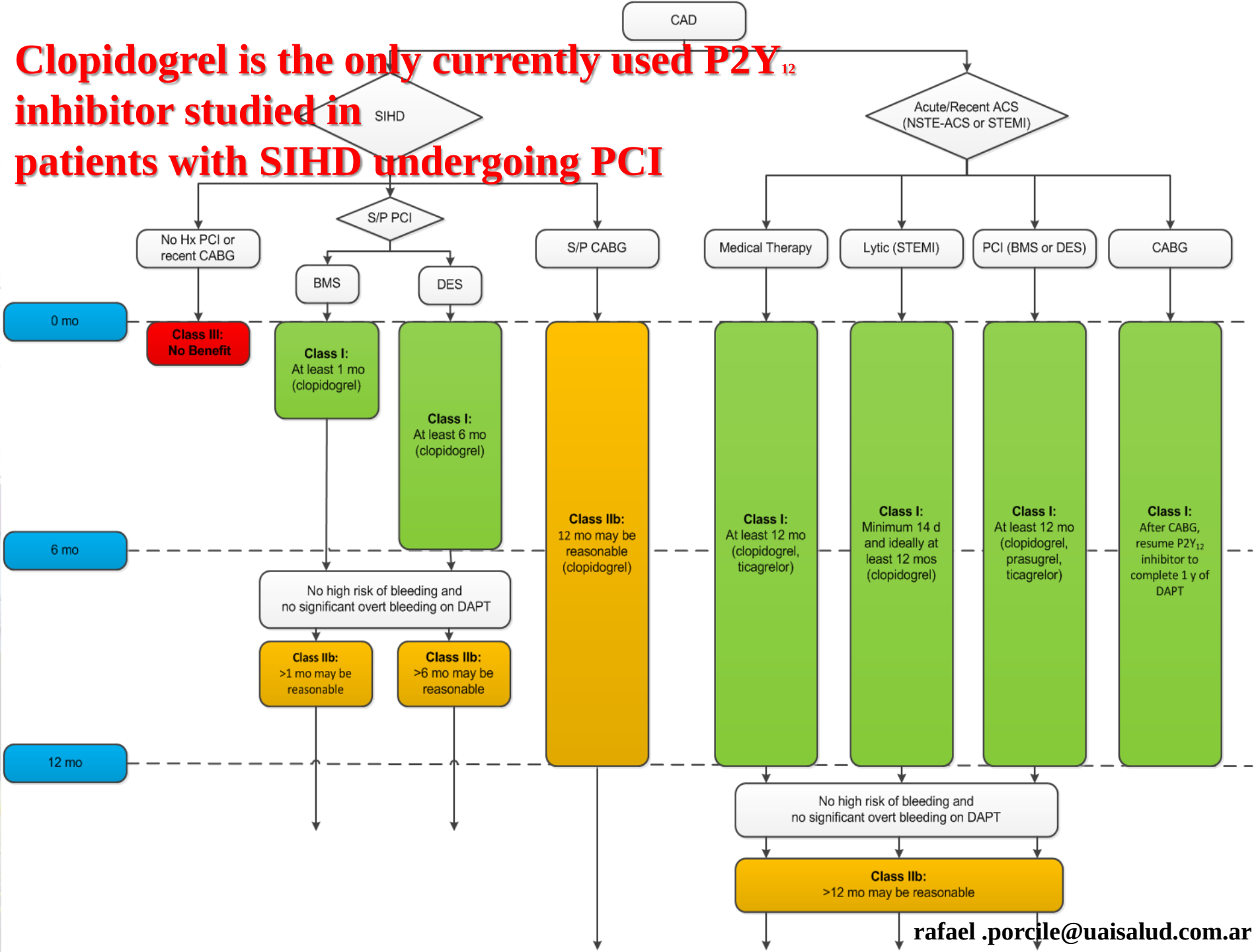
Clopidogrel is the only currently used $P2Y_{12}$ inhibitor studied in patients with SIHD undergoing PCI



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IIa B-R

In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation and in patients with NSTE-ACS treated with medical therapy alone (without revascularization), it is reasonable to use ticagrelor in preference to clopidogrel for maintenance $P2Y_{12}$inhibitor therapy.

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IIa B-R

In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIA, it is reasonable to choose prasugrel over clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy.

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III: Harm B-R

Prasugrel should not be administered to patients with a prior history of stroke or TIA.

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IIa B-R

In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation, it is reasonable to use ticagrelor in preference to clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy

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IIb A SR

In patients with ACS (NSTE-ACS or STEMI) treated with coronary stent implantation who have tolerated DAPT without a bleeding complication and who are not at high bleeding risk (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use), continuation of DAPT (clopidogrel, prasugrel, or ticagrelor) for longer than 12 months may be reasonable

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I B -R

In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after BMS or DES implantation, $P2Y_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) should be given for at least 12 months

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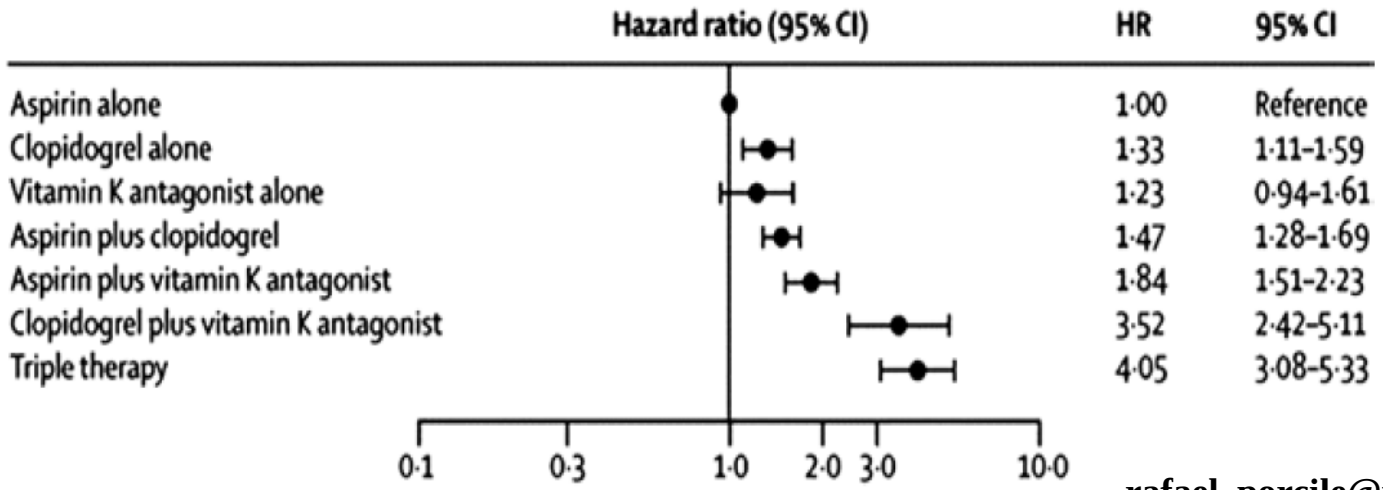
Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction :

e396 *Circulation* **January 29, 2013**



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Condition	Recommended Treatment	Evidence
Primary prevention	aspirin alone for patients in whom benefits outweigh risks	POPADAD, JPAD, USPSTF
Acute coronary syndromes [unstable angina, non-ST-segment elevation MI (NSTEMI), and ST-segment elevation MI (STEMI)]	Undergoing PCI: clopidogrel + aspirin for ≥1 year	CURE, COMMIT, CLARITY
	For some patients, prasugrel + aspirin or ticagrelor + aspirin may be a superior choice	TRITON, PLATO
	Not undergoing PCI: clopidogrel + aspirin for some patients for ≥1 year	CURE, COMMIT, CLARITY
	For some patients, ticagrelor + aspirin may be a superior choice	PLATO
Stable angina or past MI	aspirin	Antiplatelet Trialists' Collaboration, CHARISMA, CAPRIE
Elective PCI	clopidogrel + aspirin for ≥1 year	CREDO
Recent stroke	clopidogrel or aspirin + dipyridamole	MATCH, CHARISMA, ESPS2, ESPRIT, PRoFESS, SPS3
Past stroke	aspirin alone	CHARISMA, ATT
Peripheral artery disease	clopidogrel	CHARISMA, CAPRIE

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MUCHAS GRACIAS POR SU ATENCIÓN

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