MED 443
King Saud University

Reviewed by
Mohammed AlEssa
Abdulaziz AlFuhayd
Lama AlMutairi

TEAM 443
PHARMACOLOGY

Antiplatelet Drugs

Dr. Asma Alonazi
Dr. Abdulrahman Alshammari

- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

Objectives

- Describe different classes of anti-platelet drugs and their mechanism of action.
- Understand pharmacological effects, pharmacokinetics, clinical uses and adverse effects of anti-platelet drugs.

Platelets, Vessels, & Clots

Platelets & Vessels

- In healthy vessels, nitric oxide (**NO**) and prostacyclin (**PGI2**) (released by endothelial cells lining the blood vessels) inhibit platelet aggregation.
- Damage to the vessel wall leads to interactions between **platelets**, **endothelial** cells and **coagulation factors** which lead to the formation of the **clot**.

Clots

- **Thrombus**: the CLOT that adheres to vessel wall

- **Embolus**: the CLOT that floats in the blood

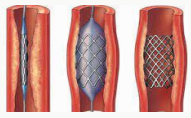
- **THROMBOSIS**: is the formation of an unwanted clot within the blood vessel which blocks blood supply to the affected area leading to cell damage or even death, producing life threatening **conditions such as:**
  - Acute myocardial infarction (MI)
  - Acute ischemic stroke
  - Deep vein thrombosis (DVT)
  - Pulmonary embolism (PE)

Coronary Angioplasty

Females' Slides

- Percutaneous coronary intervention (PCI): is a procedure used to open clogged heart arteries.

- Angioplasty involves temporarily inserting and inflating a tiny balloon to help widen the artery.

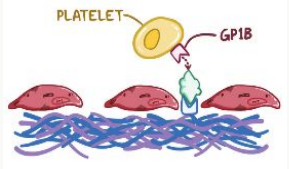


Female slide

The Role of Platelets in Hemostasis

1 adhesion

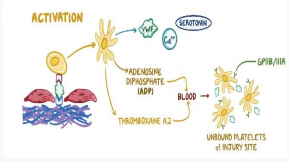
- Following vascular injury, the **von Willebrand factor** binds to collagen in the exposed subendothelium at the site of injury.
- The other side of the **"rod-formed"** von Willebrand factor binds to the platelet receptor GPIb and platelets are thereby anchored to the site of the injured endothelium.



2 Activation

- Following adhesion, agonists such as **collagen**, **thrombin**, **adenosine diphosphate (ADP)**, and **thromboxane A2** activate platelets by binding to their respective platelet receptors.

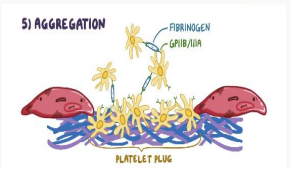
- As a result of agonist binding, platelets undergo a **shape change** and new structures such as **phospholipids and GPIIb/IIIa receptors** are exposed on the cell membrane.



3 Aggregation

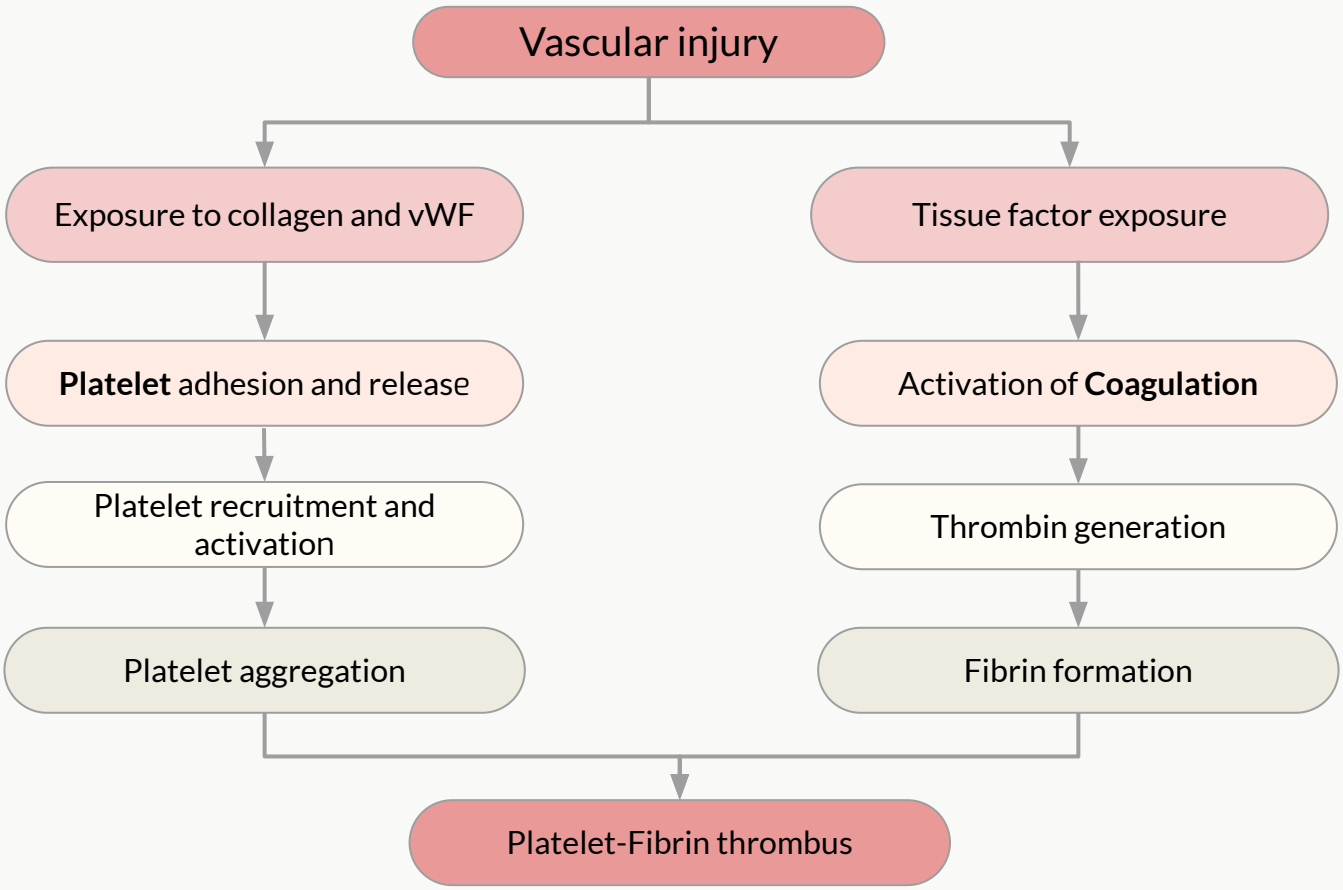
- The third step of platelet response is **aggregation**.

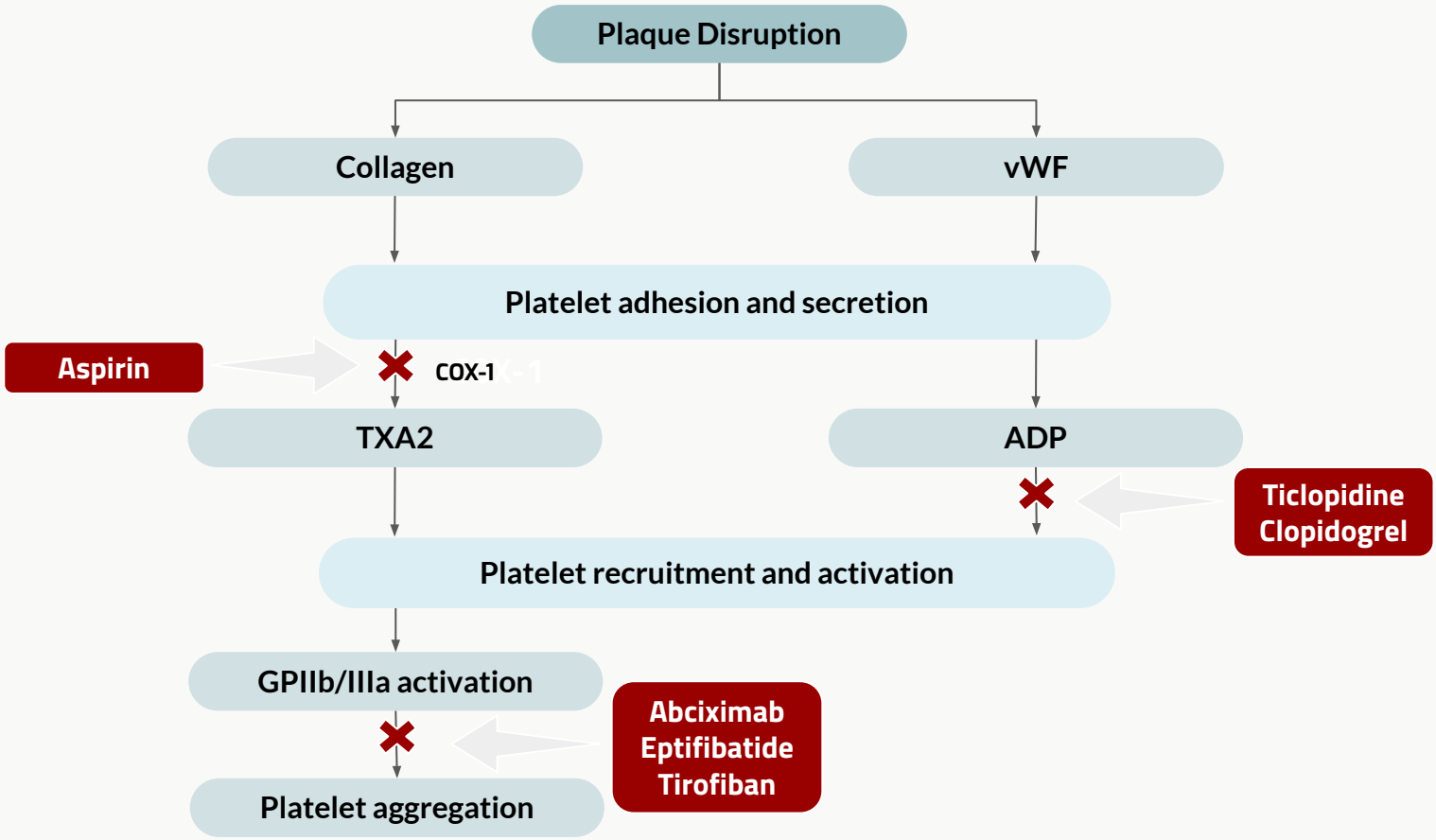
- After activation, binding of **fibrinogen** to **GPIIb/IIIa** causes platelets to adhere to each other into a loose platelet plug.



Female slide

Vascular Injury & M.O.A of Antiplatelet Drugs





Overview

Drugs Used in Thrombosis

Anticoagulants	Antiplatelets	Thrombolytics or Fibrinolytics
Drugs which prevent clotting by inhibiting **clotting factors** (coagulation process).	Drugs which prevent and inhibit **platelet activation and aggregation.**	Act by dissolving existing or already formed thrombi or emboli.
used in **prevention and treatment of thrombosis.**	used as **prophylactic therapy in high risk patients.**	used in the **acute treatment of thrombosis.**

Classification of Antiplatelet Drugs

Drugs	M.O.A	R.O.A
Aspirin	Inhibition of **thromboxane A2** synthesis via inhibiting **COX-1** **(Arachidonic acid pathway inhibitors)**	Oral
Clopidogrel Ticlopidine	**ADP receptor antagonists** (inhibitors)	Oral
Abciximab Tirofiban Eptifibatide	**Glycoprotein IIb/IIIa receptor antagonists** (Inhibitors)	**I.V**
Dipyridamole	**Phosphodiesterase (PDE) inhibitor**	Oral

Arachidonic Acid Pathway Inhibitors

Drug	Aspirin (Acetylsalicylic Acid)
M.O.A	• **Irreversible inhibition of cyclooxygenase enzyme (COX-1) via acetylation** • **A small dose** inhibits the synthesis of thromboxane **(TXA2)** in platelets **but not prostacyclin (PGI2)** synthesis in the endothelium **(larger dose)**.
P.K.	• Low-dose aspirin (81 mg enteric coated tablet/day) is the most common dose used to prevent a heart attack or a stroke.
Uses	• **Prophylaxis** of thromboembolism e.g. **prevention of transient ischemic attack, ischemic stroke, and myocardial infarction** • **Prevention of ischemic events in patients with unstable angina pectoris.** • **Combined** with other antiplatelet drugs: **(clopidogrel)** or anticoagulants **(heparin)**.
ADRs	★★ Risk of peptic ulcer **(#)** • **Epigastric pain & hyperacidity** • ↑ incidence of GIT bleeding (aspirin prolongs bleeding time).

Phosphodiesterase (PDE) Inhibitors

Drug	Dipyridamole
M.O.A.	• **Vasodilator** • Inhibits phosphodiesterase thus increasing cAMP and causing decreased synthesis of TXA2 and other platelet aggregating factors.
P.K.	Given orally
Uses	○ Secondary prevention of **stroke** and transient ischemic attack **with aspirin**. ○ Adjunctive therapy: prophylaxis of thromboembolism in cardiac valve replacement **with warfarin**.
ADRs	• Headache • Postural hypotension

Glycoprotein IIb/IIIa Receptor Inhibitor

Drugs	Abciximab monoclonal antibody	Tirofiban (non-peptide drug)	Eptifibatide (peptide drug)
M.O.A.	**The GP IIb/IIIa receptor** is required for platelets' aggregation with each other and with fibrinogen and von Willebrand factor.		
	Inhibits platelet aggregation by **preventing the binding of fibrinogen, von Willebrand factor, and other adhesive molecules to GP IIb/IIIa receptor sites** on activated platelets.	• Act by **occupying the site on GP IIb/ IIIa receptor that is required to bind the platelet to fibrinogen (act as fibrinogen-mimetic agents).**	
P.K.	Given I.V. infusion	• **Given I.V. for the reduction of the incidence of thrombotic complications during coronary angioplasty (PCI)**	
Uses	With **heparin and aspirin** as adjunct to PCI for the prevention of cardiac ischemic complications.	-	

Adenosine Diphosphate Pathway Inhibitors

Drug	Ticlopidine	Clopidogrel
M.O.A.	• They specifically and **irreversibly inhibit adenosine diphosphate (ADP) receptors of subtype P2Y12**, which is required for platelet activation and thus prevents platelet aggregation • **P2Y12** is purinergic receptor and is a chemoreceptor for adenosine diphosphate **(ADP).**	
P.K.	○ **Pro-drugs**; they have to be activated in the liver ○ Given orally. ○ Have slow onset of action (3 - 5 days). ○ Bound to plasma protein.	
	-	○ More potent than ticlopidine, Bioavailability is unaffected by food ○ Longer duration of action than ticlopidine ○ Less frequency of administration (once daily) ○ Less side effects **(less neutropenia)** ○ **Clopidogrel has replaced ticlopidine**
Uses for your information	◦ **Secondary prevention of ischemic complications after myocardial infarction, ischemic stroke, and unstable angina..**	
		○ **For patients with a history of recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease.** ○ For patients with **acute coronary syndrome** (unstable angina/ MI): either those managed medically or with percutaneous coronary intervention (PCI) with or without stent.
ADRs	○ **GIT:** nausea, dyspepsia, diarrhea. ○ Bleeding (prolongs bleeding time) ★★**Severe neutropenia,** CBC should be done monthly during treatment. ○ Allergic reactions	
DDI	**Inhibit** CYT P450 causing ↑ plasma levels of drugs such as **phenytoin** and **carbamazepine**.	

Female slide

New ADP Pathway Inhibitors

Drug	Prasugrel	Ticagrelor
M.O.A	**Irreversible** inhibitor of the **P2Y12** receptor	**Reversible** inhibitor of the **P2Y12** receptor
P.K.	○ Both have **more rapid** onset of action than clopidogrel ○ Both drugs **do not need hepatic activation** (not prodrugs)	
Uses	↓ the rate of thrombotic cardiovascular events (including stent thrombosis) in patients with acute coronary syndrome who are to be managed by PCI.	
ADRs	○ Both increase bleeding risk ○ **Ticagrelor**: dyspnea	

MCQ ★

★★ which of the following cause neutropenia?			
A. aspirin	B.dipyridamole	C. clopidogrel	D. abciximab
★★ which of the following can lead to peptic ulcers			
A. aspirin	B.dipyridamole	C. clopidogrel	D. abciximab
3. which of the following is the mechanism of action for Aspirin			
A. GPIIb/IIIa inhibitor	B. ADP inhibitor	C. COX-1 inhibitor	D. PDE inhibitor
4. Which of the following is the mechanism of action of dipyridamole			
A. GPIIb/IIIa inhibitor	B. ADP inhibitor	C. COX-1 inhibitor	D. PDE inhibitor
5. which of the following is the mechanism of action of clopidogrel			
A. GPIIb/IIIa inhibitor	B. ADP inhibitor	C. COX-1 inhibitor	D. PDE inhibitor
6. which of the following works on the GPIIb/IIIa receptors			
A. aspirin	B.dipyridamole	C. clopidogrel	D. abciximab

1:C ,2:A ,3:C ,4:D ,5:B ,6:D

SAQ

01

Give 2 examples of antiplatelets, each with MOA and side effect

Aspirin: irreversible inhibition of cyclooxygenase enzyme (COX-1) via acetylation.
SE: Risk of peptic ulcer, Epigastric pain & hyperacidity, ↑ incidence of GIT bleeding
Clopidogrel: irreversibly inhibit (ADP) receptors (P2Y12), thus prevents platelet aggregation.
SE: GIT: nausea, dyspepsia, diarrhea, Bleeding (prolongs bleeding time), Severe neutropenia, Allergic reactions

Team Leaders

Reema Almotairi

Sarah Alajaji

Team members

Maryam Alghannam

Aroub Almahmoud

Layan Sulaiman

Aishah Boureggah

Areej Alquarini

Lama Alotaibi

Jana alshiban

Layan Alruwaili

Sara Alharbi

Fatimah Alghamdi

Alanoud Abdullah

Nourah alarifi

Renad Alotaibi

Wafa Alakeel

Wasan Alanazi

Ayedh Alqantash

Nazmi A Alqutub

Yousef badgesh

Mohammed Alqutub

Fahad Aldhafian

Special thanks to Norah Almania for the amazing logo