

Antiplatelet Drugs (Anti-thrombotics)

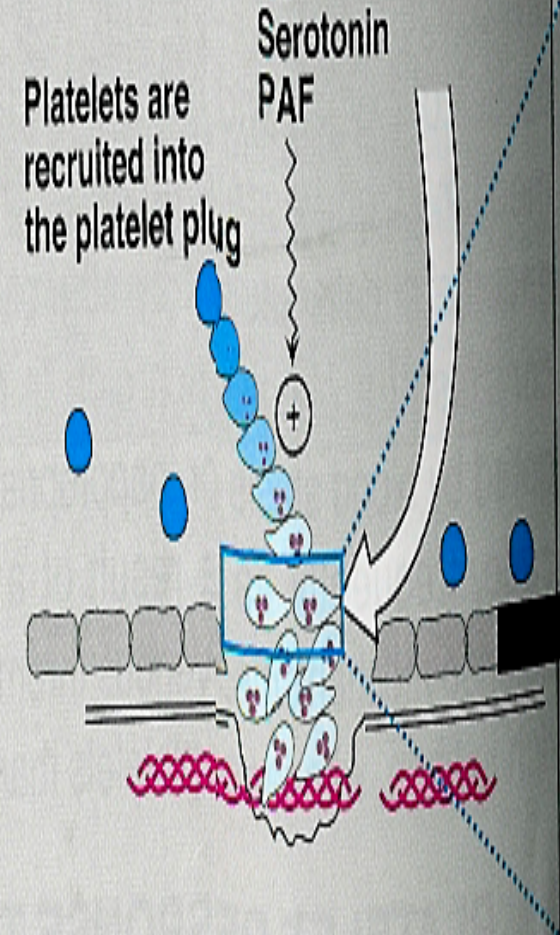
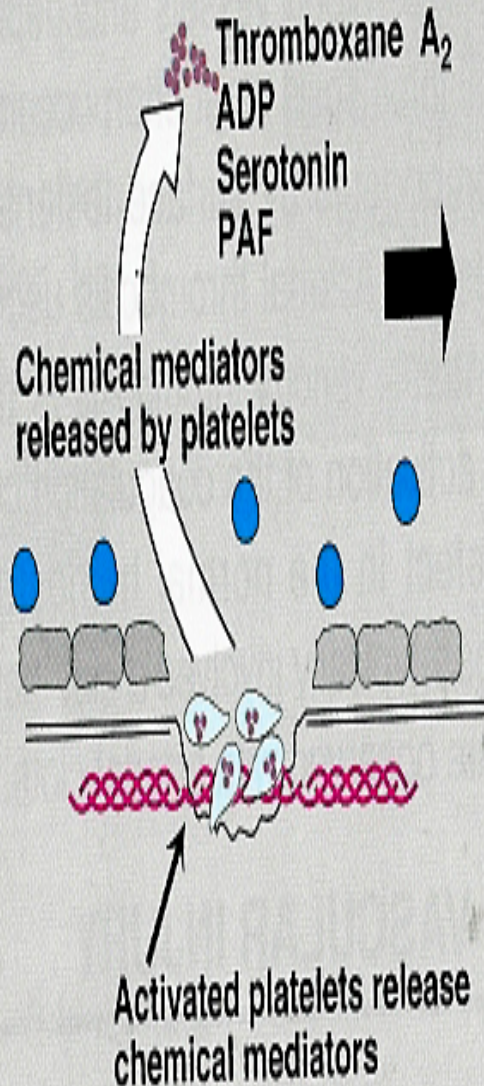
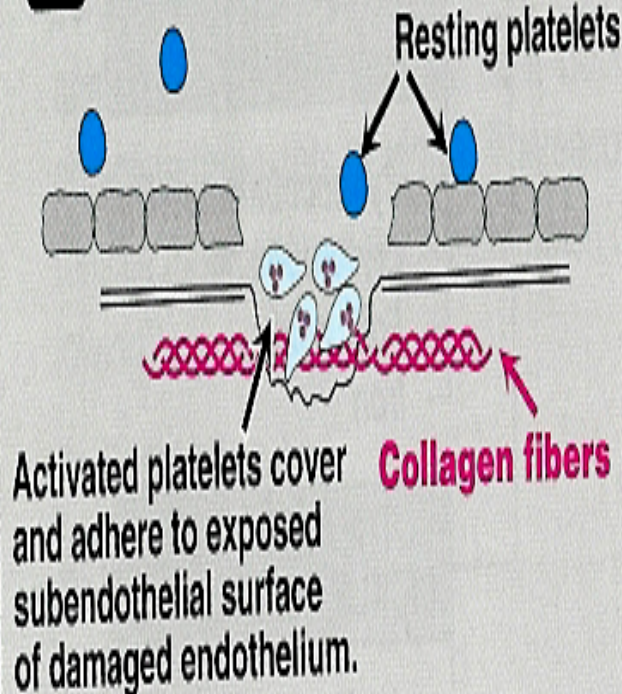
Classification

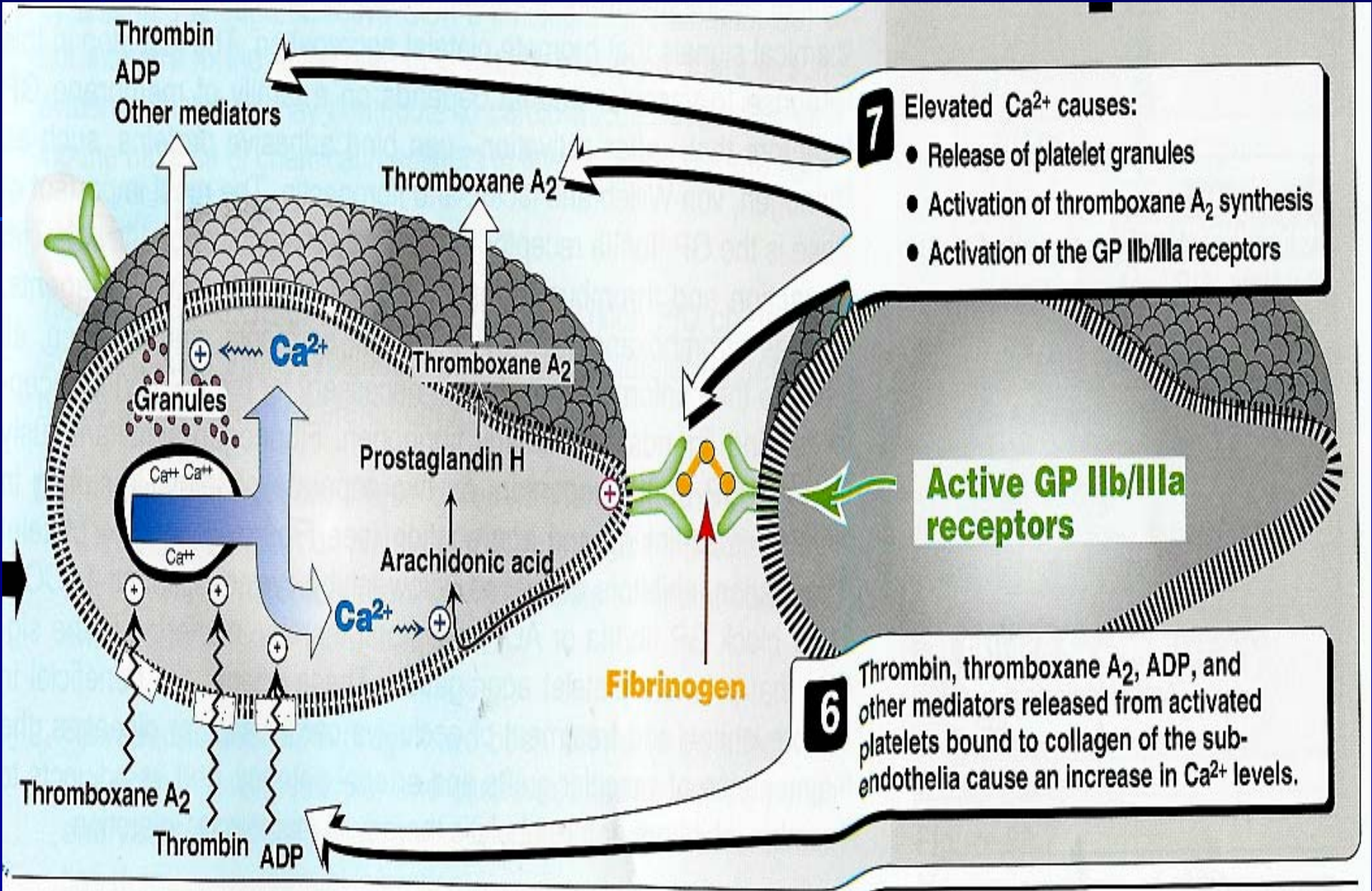
1. Arachidonic acid pathway inhibitors e.g **aspirin**
2. Phosphodiesterase inhibitors e.g. **dipyridamol**
3. ADP pathway inhibitors.
Ticlopidine- Clopidogrel
4. Glycoprotein IIb/IIIa inhibitors.
Abciximab, tirofiban

Platelet aggregation

Release of granules containing platelet aggregation agents or Ca^{2+} .

3 Platelet adhesion

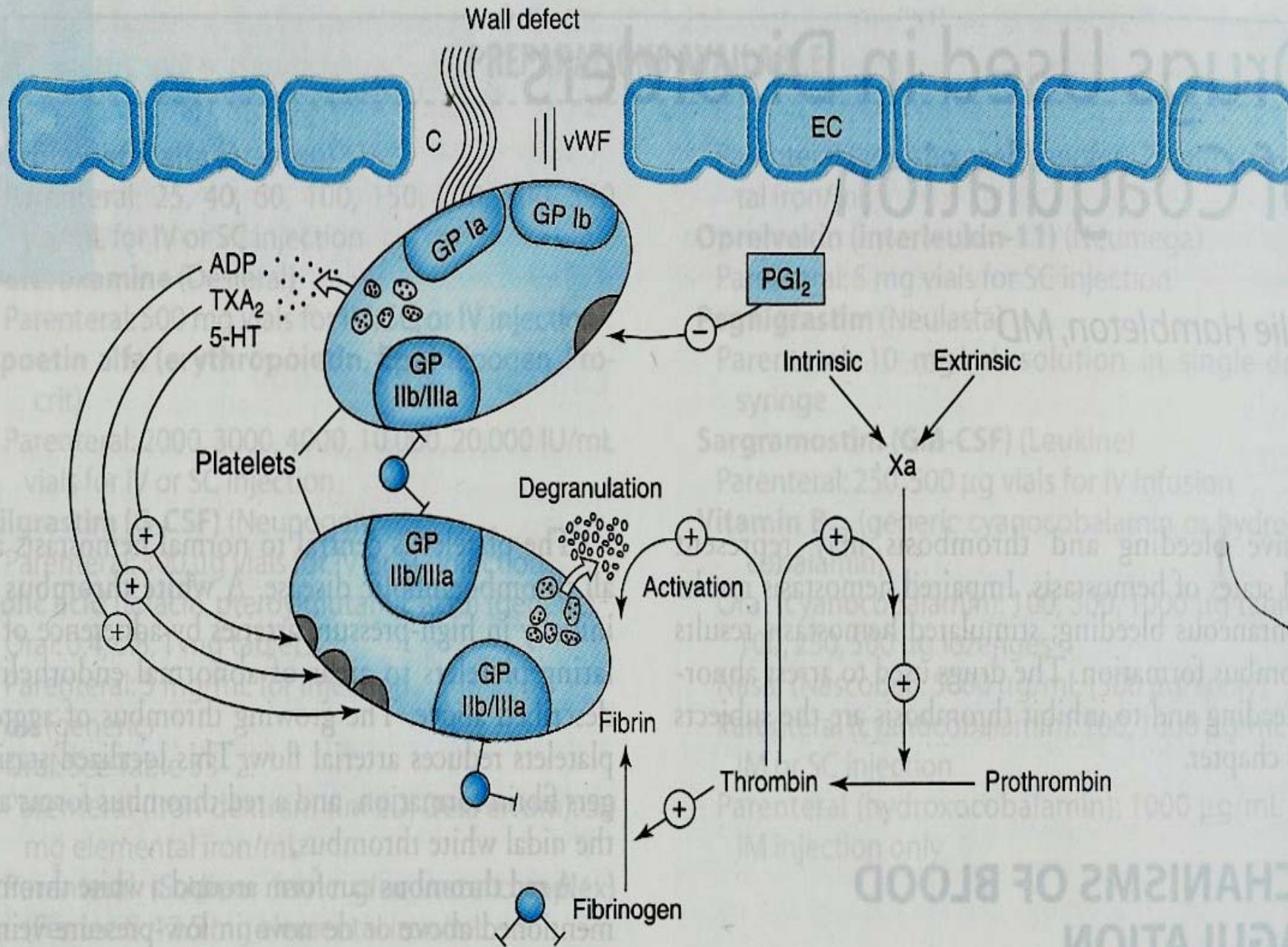




7 Elevated Ca^{2+} causes:

- Release of platelet granules
- Activation of thromboxane A₂ synthesis
- Activation of the GP IIb/IIIa receptors

6 Thrombin, thromboxane A₂, ADP, and other mediators released from activated platelets bound to collagen of the sub-endothelium cause an increase in Ca^{2+} levels.



Uses

- 1. Prophylaxis of venous thrombosis.**
- 2. Transient cerebral ischemic attacks.**
- 2. Following coronary artery bypass grafting.**
- 3. Prevention of myocardial infarction.**
- 4. Following coronary artery angioplasty.**
- 5. Prosthetic heart valves.**
- 6. Chronic disseminated intravascular coagulation.**

Aspirin (Acetylsalicylic Acid)

Mechanism of Action

- 1. Irreversible inhibition of cyclooxygenase enzyme via acetylation.**
- 2. Small dose inhibits thromboxane synthesis in platelets (TXA₂) But not prostacyclin (PGI₂) synthesis in endothelium (larger dose).**

Dose : Low dose 75 - 150 mg / day.

Side effects

- 1. Peptic Ulcer.**
- 2. Increased incidence of GIT bleeding**

Uses

Prophylaxis of myocardial infarction

ADP pathway inhibitors

Ticlopidine & Clopidogrel

Mechanism of Action

Inhibits the binding of ADP to its platelet receptor by irreversibly modifying the platelet ADP receptor.

Pharmacokinetics

Given orally.

Extensively bound to plasma proteins.

Metabolized in the liver to give active metabolites.

Slow onset of action (3 - 5 days).

is taken twice (250 mg twice daily).

Adverse Effects

- 1. Severe neutropenia.**
- 2. Bleeding (Prolong bleeding time).**
- 3. CYT P450 inhibitors**
- 4. G.I.T : Diarrhoea, Nausea, Dyspepsia.**
- 5. Allergic Reactions.**

Monitoring of blood count every month is essential.

Drug interaction: Increased plasma levels of drugs as Phenytoin, Carbamazepines

Clopidogrel

- 1. Clopidogrel is more potent.**
- 2. Less side effects (less neutropenia).**
- 3. Less Frequency (75 mg once daily).**
- 4. Bioavailability is unaffected by food.**

Clinical Uses

Alternative prophylactic therapy to aspirin in secondary prevention of stroke and myocardial infarction and unstable angina.

Glycoprotein IIb/ IIIa receptor inhibitors

Glycoprotein IIb/ IIIa receptor

- **Is a receptor for fibronectin, fibrinogen, vitronectin and von Willebrand factor.**

Glycoprotein IIb/ IIIa receptor inhibitors

1. Abciximab

- a chimeric monoclonal antibody that inhibits glycoprotein IIb/ IIIa receptor.
- It inhibits all the pathways of platelet activation (**Final common pathway**).
- Given I.V. infusion
- adjuncts to heparin and aspirin for prevention of cardiac ischemic complications.

Glycoprotein IIb/ IIIa receptor inhibitors

2. Tirofiban

- inhibits glycoprotein IIb/ IIIa receptor at site that interacts with Arginine-Glycine-Aspartic sequence of fibrinogen (by occupancy of the receptor).
- Non peptide drug.
- Acute coronary syndromes to decrease incidence of thrombotic complications
- Excreted unchanged by the kidney.

Dipyridamole

Phosphodiesterase inhibitor thus \uparrow cAMP in the blood platelets \rightarrow inhibition of platelet aggregation.

Uses

- Taken orally.
- Primary prophylaxis in patients with prosthetic heart valves (in combination with warfarin).
- As prophylactic therapy to treat angina pectoris in combination with aspirin .

Disadvantages : Headache

Advantage : No excess risk of bleeding