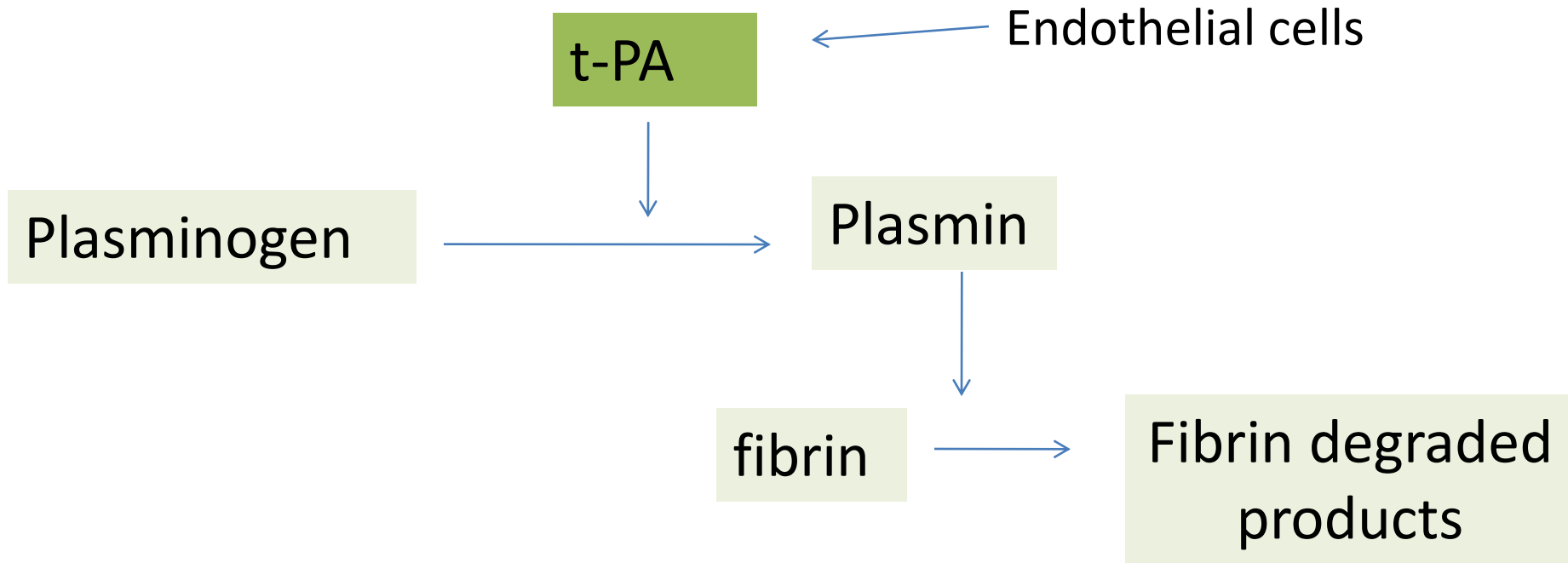


# Fibrinolytics & Antiplatelets

# Fibrinolytic system

- The process of dissolution of clot is called fibrinolysis



Plasminogen



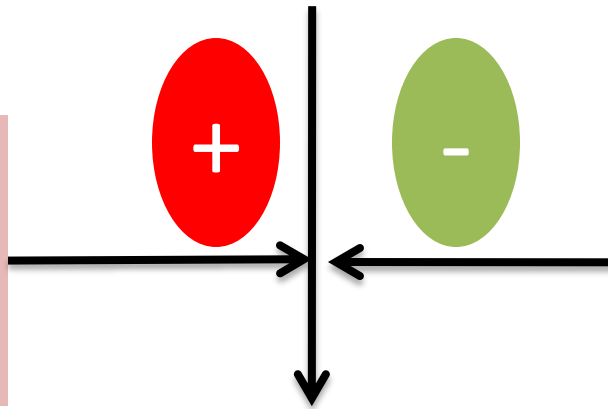
Streptokinase  
Urokinase  
Alteplase

EACA  
Tranexamic acid  
Aprotinin

Fibrinolytics

Plasmin

Antifibrinolytics



# FIBRINOLYTICS

- Used to lyse the thrombi / clot to recanalize the occluded blood vessel (mainly coronary artery)
- Work by **activating the Fibrinolytic system**
  - **STREPTOKINASE**
  - **UROKINASE**
  - **RETEPLASE** (analogue of alteplase)
  - **ALTEPLASE** (t- PA )
  - **TENECTEPLASE**

# Streptokinase

- Obtained from  $\beta$ -hemolytic streptococci
- Binds with circulating plasminogen to form complex that activates plasminogen to plasmin
- $t_{1/2} = 30 - 80$  min
- Antigenic ,Pyrogenic
- Destroyed by circulating antistreptococcal Antibodies
- Hypotension & arrhythmia can occur



# Streptokinase

## Uses

- Acute myocardial infarction
  - 7.5 to 15 lac IU; I.V over 1 hr period
- Deep vein thrombosis , Pulmonary embolism

## Adverse effects

- Bleeding, hypotension, allergic reactions, fever, arrhythmias

## Contraindications

- Recent trauma, surgery, abortion, stroke, severe hypertension, peptic ulcer, bleeding disorders

# Urokinase

- Enzyme isolated from human urine, now prepared from cultured human kidney cells
- **Direct plasminogen activator**
- $t_{1/2}$  of 10 to 15 min
- **Non antigenic, Non allergenic**
- Fever can occur but hypotension rare
- Indicated in patients in whom streptokinase has been for an earlier episode

# Alteplase

- recombinant tissue Plasminogen Activator(rt-PA)
- Selectively activates plasminogen bound to fibrin
- Non antigenic ,not destroyed by antibodies
- Rapid acting, more potent
- Superior in dissolving old clots
- Short half life 4-8 min
- Nausea, mild hypotension, fever may occur
- Expensive



# Newer recombinant tissue plasminogen activators

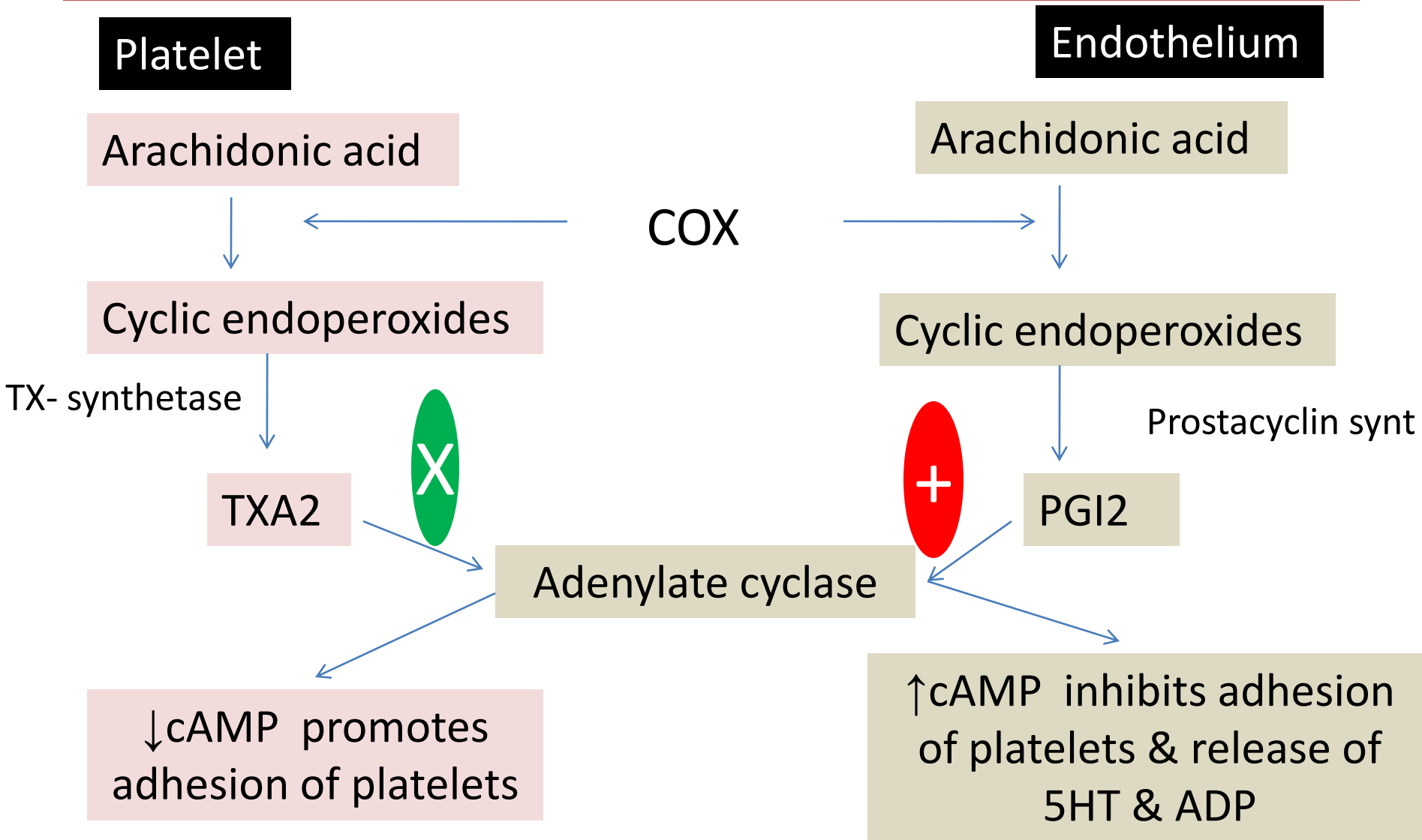
- **Retepase :**
  - Modified rt-PA
  - Longer half life 15 -20 min, but less specific for fibrin bound plasminogen
- **Tenecteplase:**
  - **Genetically engineered** mutant form of alteplase
  - Higher fibrin selectivity and longer half life – 2 hrs
  - Single bolus dose 0.5 mg/kg sufficient
  - Very expensive

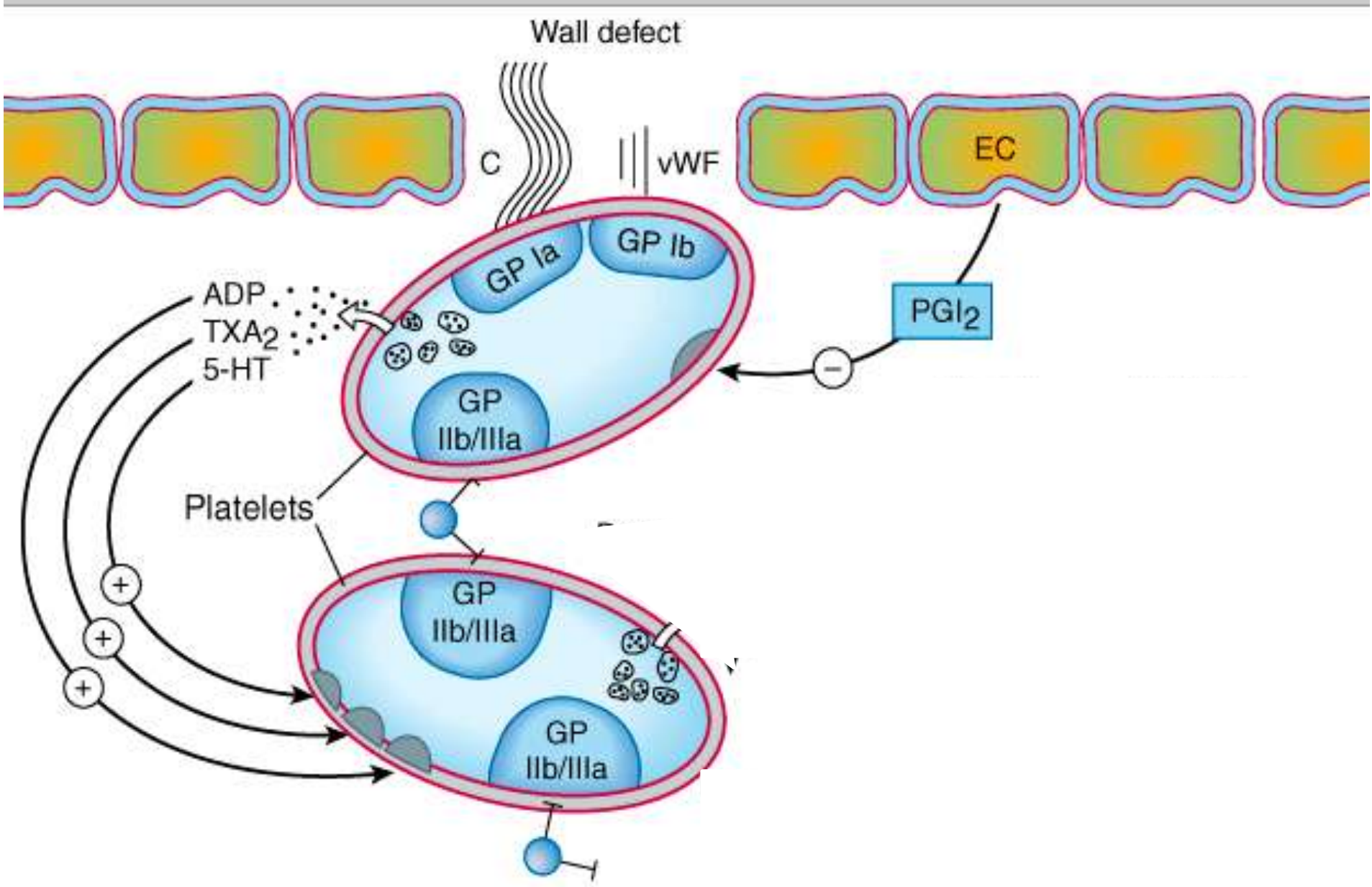
# Uses of fibrinolytics

- Acute myocardial infarction
- Deep vein thrombosis
- Pulmonary embolism
- Peripheral arterial occlusion
- Ischemic Stroke

# Antiplatelet drugs

# Mechanism of platelet aggregation and inhibition

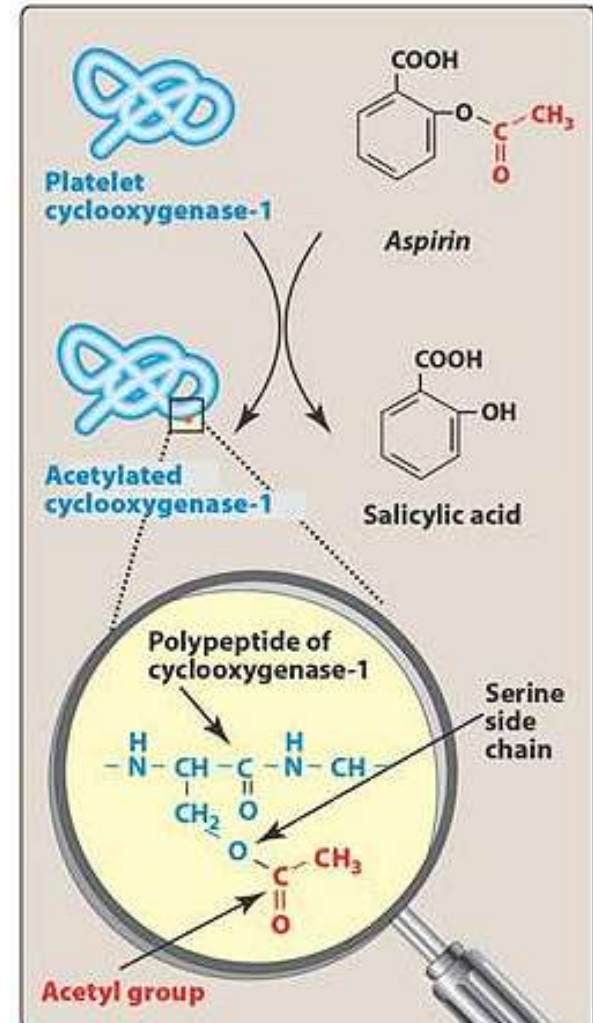
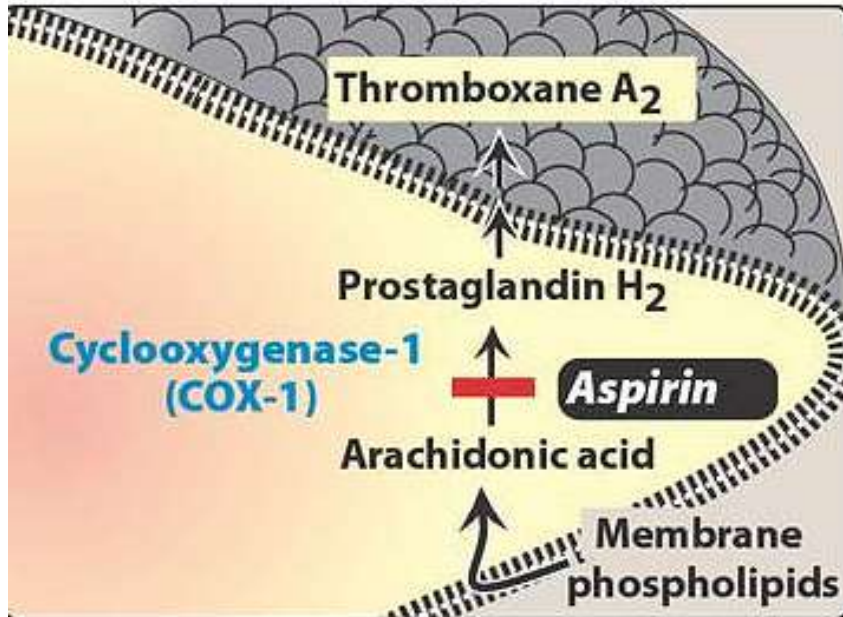




# Antiplatelet drugs (Classification)

- TXA<sub>2</sub> synthesis inhibitor:
  - Low dose **aspirin**
- Phosphodiesterase inhibitor:
  - **Dipyridamole**, cilostazole
- Thienopyridine derivatives (ADP antagonists):
  - **Ticlopidine, clopidogrel**
- Gp-IIb/IIIa receptor antagonists
  - **Abciximab**, eptifibatide, tirofiban
- Others
  - PGI<sub>2</sub>, daltroban, dazoxiben, clofibrate

# Aspirin



# Dipyridamole

- Coronary vasodilator and relatively weak antiplatelet drug
- Mechanism of action
  - Potentiates effect of endogenous prostacycline
  - In high conc inhibits Phosphodiesterase, so  $\uparrow$ cAMP
- Dose = 100 mg BD/TDS
- used with aspirin to prevent ischemic stroke in patients of TIA



# Ticlopidipine & clopidogrel

- **ADP antagonists**, inhibit binding of ADP to its receptors **irreversibly**
- Also Inhibit fibrinogen induced platelet aggregation with out modifying GPIIb/IIIa
- Synergistic action with aspirin
- Both are prodrugs have long duration of antiplatelet effect
- Clopidogrel a congener of ticlodipine is safer and better tolerated

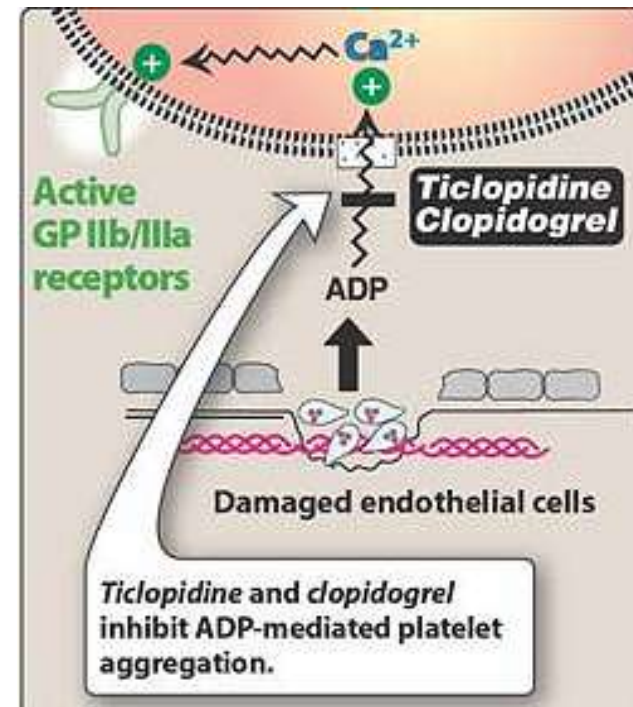
# Ticlopidine Vs clopidogrel

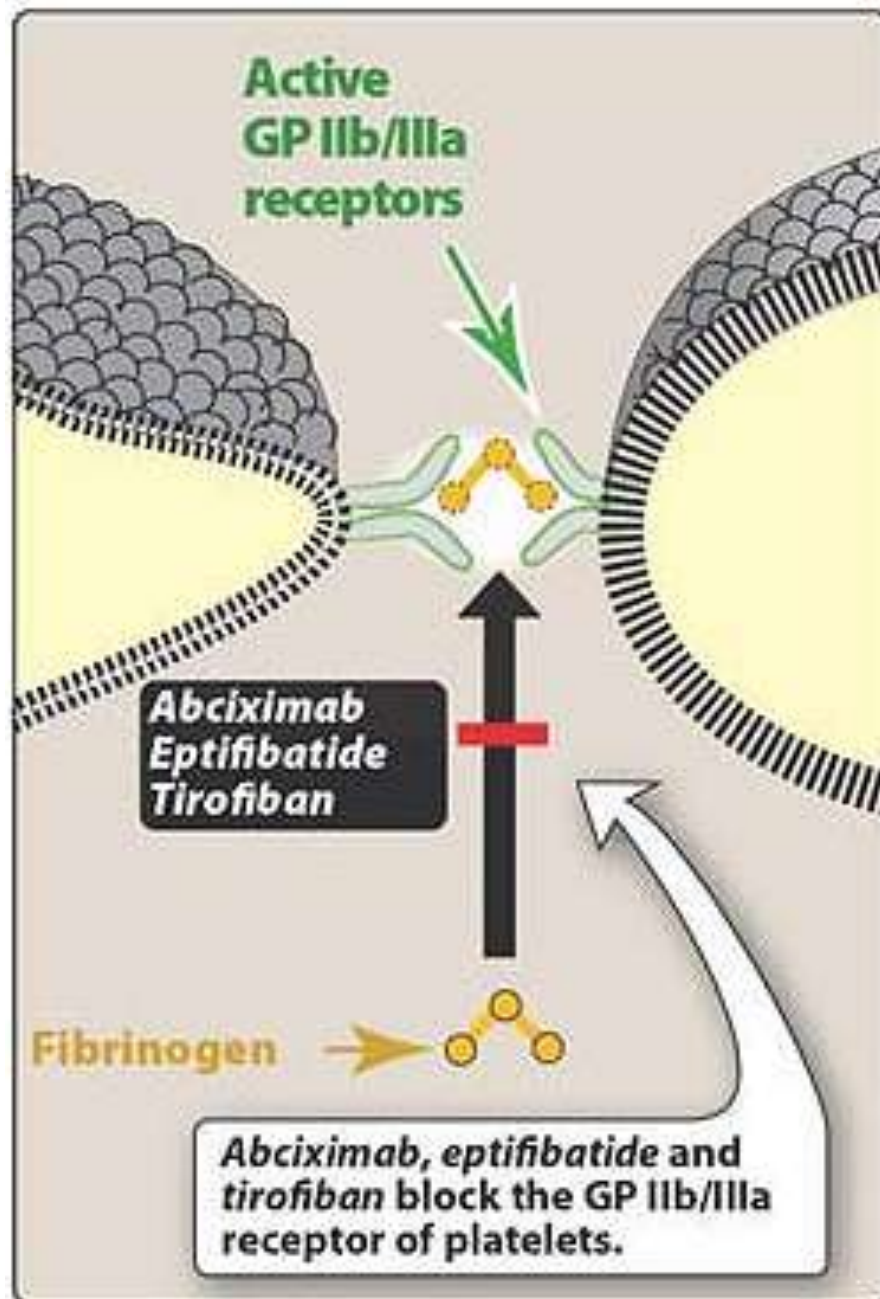
## Ticlopidine

- Adverse effects:
  - Diarrhoea, vomiting, abdominal pain
  - Headache, tinnitus, skin rash
  - **Bleeding, neutropenia, thrombocytopenia**
- dose= 250 mg BD

## Clopidogrel

- Adverse effects
  - Bleeding most IMP
  - Less bone marrow toxicity
  - Diarrhoea, epigastric pain, rashes
- Dose = 75 mg OD





# Abciximab

- Fab fragment of Chimeric monoclonal antibody against GP-IIb/IIIa.
- Used to prevent platelet aggregation in patients having PCI, administered along with aspirin & heparin or LMW heparin
- Most common A/E is bleeding
- May cause thrombocytopenia, hypotension, bradycardia
- Non antigenic
- Dose: 0.25 mg/kg IV before PCI followed by 10 µg/min for 12 hrs

# Uses of antiplatelet drugs

- Prosthetic heart valves & A-V shunts
- Peripheral vascular disease
- Coronary artery diseases
  - Myocardial infarction
  - Unstable angina
  - Primary & secondary prevention of MI
- Coronary angioplasty, stents, bypass implants
- Cerebrovascular transient Ischemic attacks
- Venous thrombo-embolism