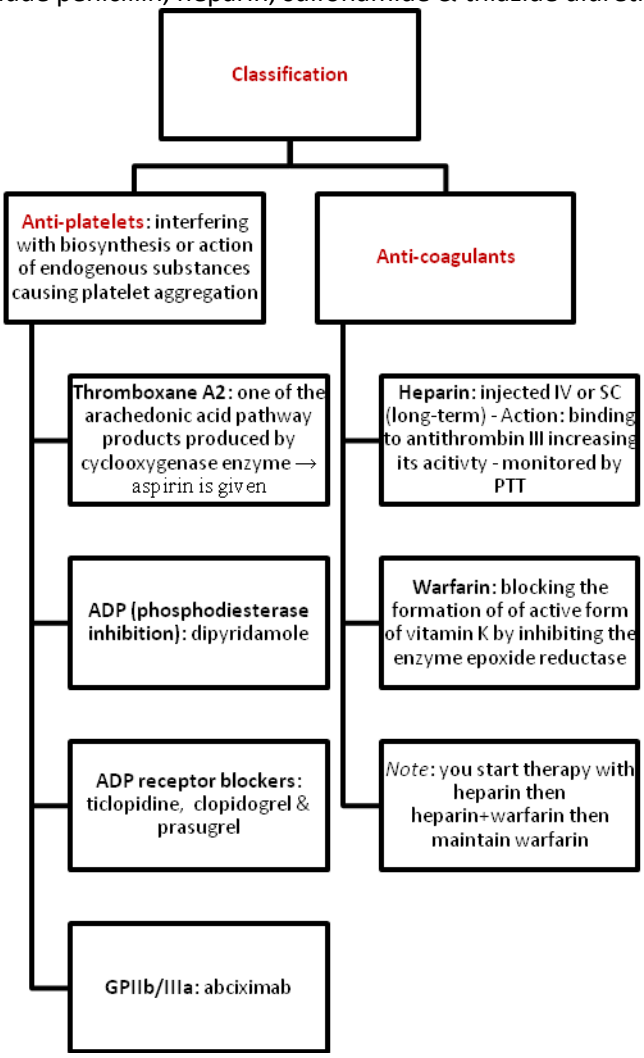
- **ITP**: is the formation of autoantibodies against platelets GPIIb/IIIa leading to platelets destruction and increased turnover by macrophages of the RE system in the spleen.
- Platelets interact with vascular endothelium when it is damaged and this will lead to the formation of platelet plug.
- Platelets have short lifespan (7-10 days) with constant turnover and production (from megakaryocytes in the bone marrow) → balanced state.
- Platelets are non-nucleated & are incapable of producing their own proteins and enzymes.
- **Drugs that can cause thrombocytopenia:**
  - Immunologically-mediated.
  - Bone marrow suppression (such as in cancer chemotherapy).

  Note: these drugs include penicillin, heparin, sulfonamide & thiazide diuretics.

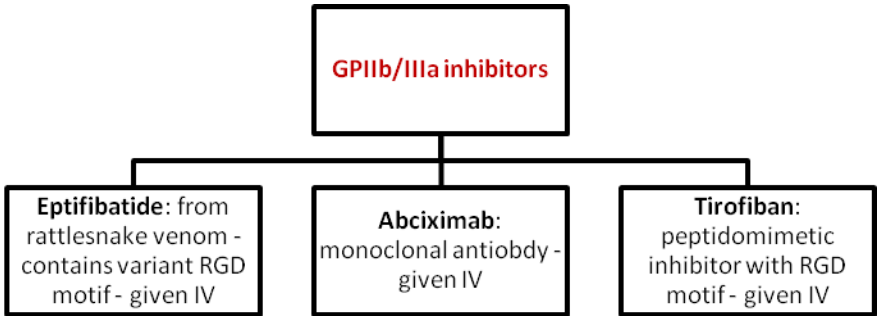


- Membrane phospholipids are broken down by phospholipase A_2 to arachidonic acid. Arachidonic acid can go to two pathways:
  - **Either cyclooxygenase pathway**: which will produce PG, prostacyclin (preventing platelet aggregation) and thromboxane A2 (activating platelets).

    Note: COX is inhibited by aspirin.
    Thromboxane A2 is inhibited by low disease of aspirin.
  - **Lipoxygenase pathway.**
- **Aspirin and platelet function:**
  - **Another name**: acetylsalicylic acid and it is belonging to NSAIDs.
  - ↓$t_{1/2}$ but the effect can persist for 7-10 days.
  - Irreversible inhibition of COX.
  - Can be used as prophylaxis for MI and secondary prevention of vascular events.

- **ADP receptor blockers:**
  - Normally, ADP promotes platelet activation and aggregation.
  - They block the receptors irreversibly.
  - They are also called thienopyridines and include 3 generations:
    - ✓ *First generation*: ticlopidine.
    - ✓ *Second generation*: clopidogrel (used after coronary stenting and angioplasty).
    - ✓ *Third generation*: prasugrel

    Note: as you go from the first generation to the third, the duration of effects is prolonged and there is better safety.
  - They have rapid onset and the maximal effect is seen after 1 week.
  - A rapid effect is achieved by giving a loading dose.
  - **ADR**: upper GI-related adverse effects. In patients given ticlopidine, 2-5% can develop neutropenia.
  - Combined with aspirin for unstable angina, NSTEMI, MI & stroke.
- **Platelet GPIIb/IIIa inhibitors:**



- **Phosphodiesterase inhibitors:**
  - **Dipyridamole**: is inhibiting the enzyme & adenosine –powerful platelet aggregator- uptake. This helps the RBCs to squeeze through small blood vessels. This drug is combined with aspirin for cerebrovascular ischemia. Also, it is used to prevent thromboembolism in patients with prosthetic heart valves.
  - **Cilostazole**: newer phosphodiesterase inhibitor, vasodilator and platelet aggregation inhibitor, used for intermittent claudication.
- **Antifibrinolytic drugs:**
  - used in DIC to prevent fibrinolysis.
  - EACA and tranexamic acid → preventing conversion of plasminogen to plasmin (plasminogen activation inhibitors).
  - Aprotinin: plasmin inhibitor.
- **Drugs used in bleeding disorders:**
  - Vitamin K (K3: water soluble). It is important to the production of prothrombin, factors VII, IX, & X
  - Recombinant factor VIII for hemophilia-A.
  - Factor IX for hemophilia-B.
  - Desmopressin (SC/intranasal) increases factor VIII activity in hemophilia & VWD.