

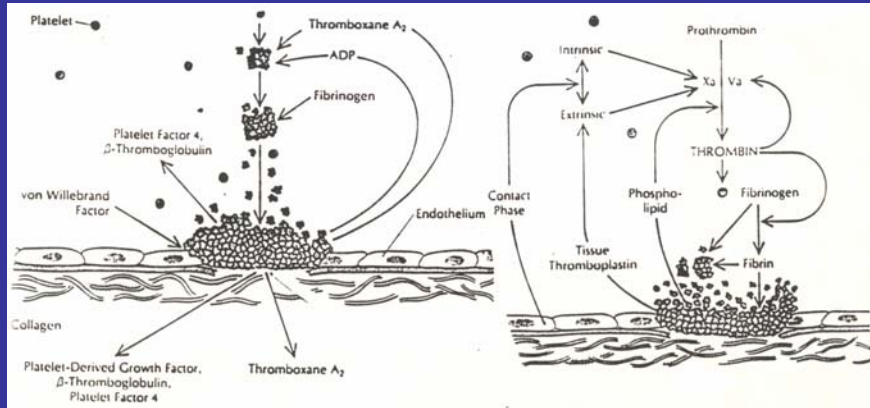
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Anti-thrombotic Drugs

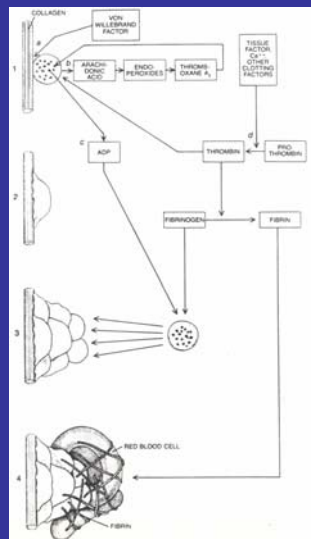
- Hemostasis: physiological process to arrest the blood loss from injured blood vessels
- Thrombosis: pathological complications resulting in the formation of occluding thrombi

Platelet Aggregation

Blood Coagulation

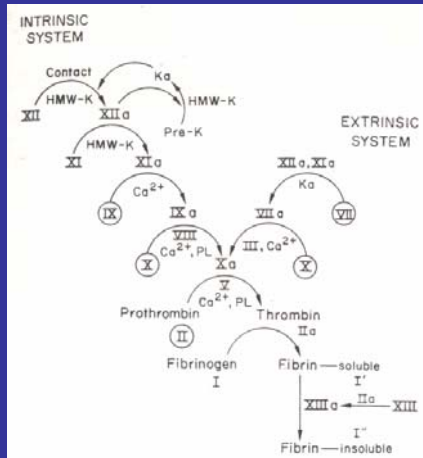


Thrombus Formation



The Coagulation Pathways

- Serine proteases
- Zymogens
- Cascades of proteolytic reactions
- Thrombin generation
- Fibrinogen → Fibrin
- Extrinsic
- Intrinsic



Thrombosis

- Formation of occluding thrombi
- Heart – myocardial infarction
- Brain – stroke
- Leading cause of death
- High incidence groups – prevention

Anti-thrombotic therapy

Anti-coagulant and anti-platelet therapy:

- Prevent propagation
- Prevent thrombus formation

Thrombolytic therapy:

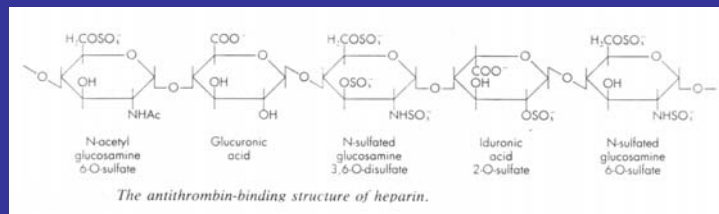
- Lysis of existing thrombi

Anticoagulants

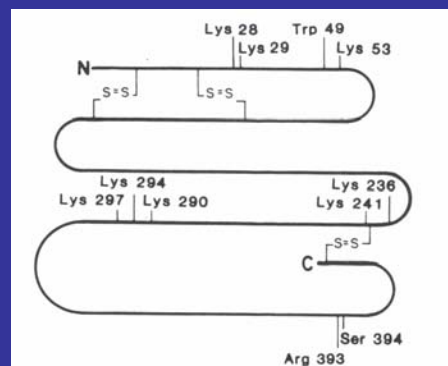
- Heparin
- Coumarins (oral anticoagulants)

Heparin

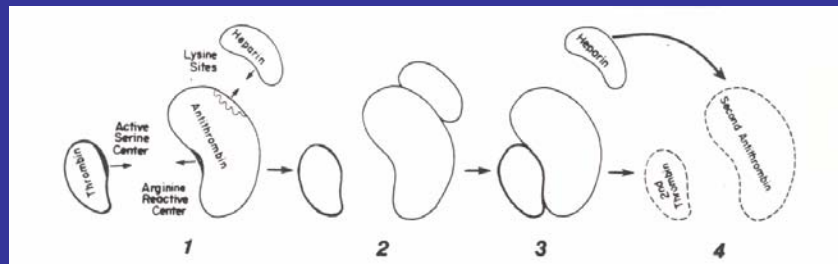
- Anionic mucopolysaccharide
- Glycosaminoglycans
- Activate anti-thrombin III (AT III)



Anti-thrombin III



Heparin Action on Anti-thrombin III



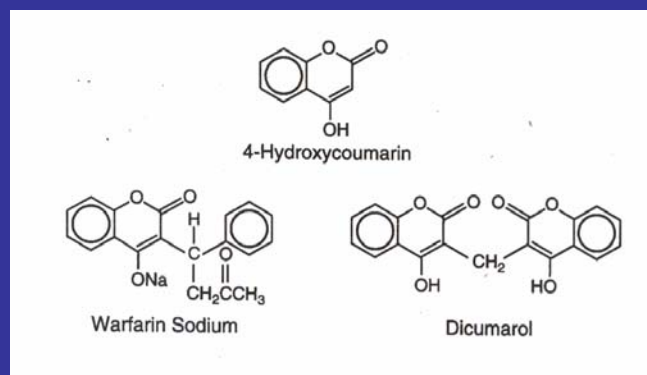
Heparin

- Highly charged, crosses membranes poorly
- Administered parenterally
- Does not cross placenta, given during pregnancy
- Cleared by the reticuloendothelial system
- Metabolized by the liver
- Half-life (0.5-2.5 h) depends on dosage
- Non-toxic
- Minor side effects: allergy, alopecia, osteoporosis
- Major side effects: hemorrhage, thrombocytopenia
- Antidote: protamine sulfate

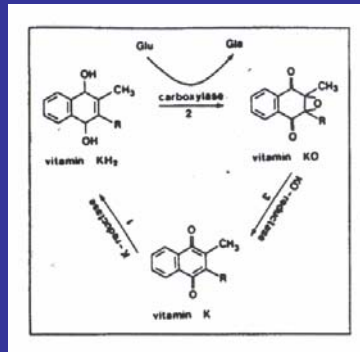
Heparin Dosage

- Full dose
intravenous: bolus injection 5,000 units followed by 700-2,000 units/h by infusion pump delivery
subcutaneous: 7,500-15,000 units/12 h
monitored by aPTT – intrinsic coagulation
26-30 sec → 50-70 sec
- Low dose (prevent thromboembolism)
subcutaneously 5,000 units/8-12 h
does not affect aPTT

Oral Anticoagulants (Coumarins)



Mode of Action of Warfarin



Warfarin

- Given orally
- Peak concentrations reached within 1 h
- A lag phase for effectiveness
- In plasma, 99% bound to albumin
- Drug competes warfarin binding to proteins are contradictory
- Metabolized by liver; half-life ~ 36 h
- Crosses placenta, NOT given during pregnancy
- Major side effect is hemorrhage
- Dosage for adults: 10-15 mg/day for 2-4 days followed by 2-15 mg/day depending on PT time
- Antidote: vitamin K, Plasma infusion