## Hematinics, Coagulants and Anticoagulants

**Hematinics:** These are substances demanded in the formation of blood, and are used for the treatment of anemias.

- Essential haematinics: Iron, vitamin B 12, folic acid.

Etiology

- Anemia occurs when:

(a) Blood loss (acute or habitual)

(b) Crippled red cell conformation due to:

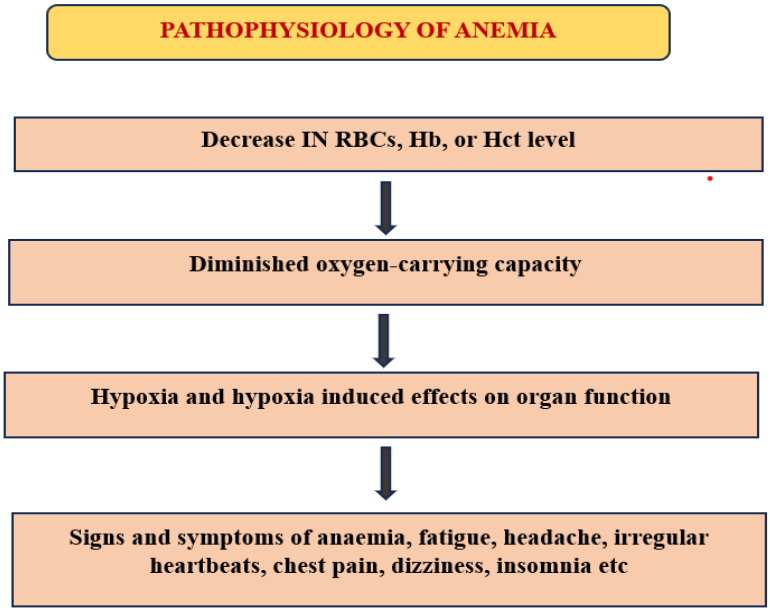
Deficiency of essential factors, i.e., iron, vitamin B-12, and folic acid.

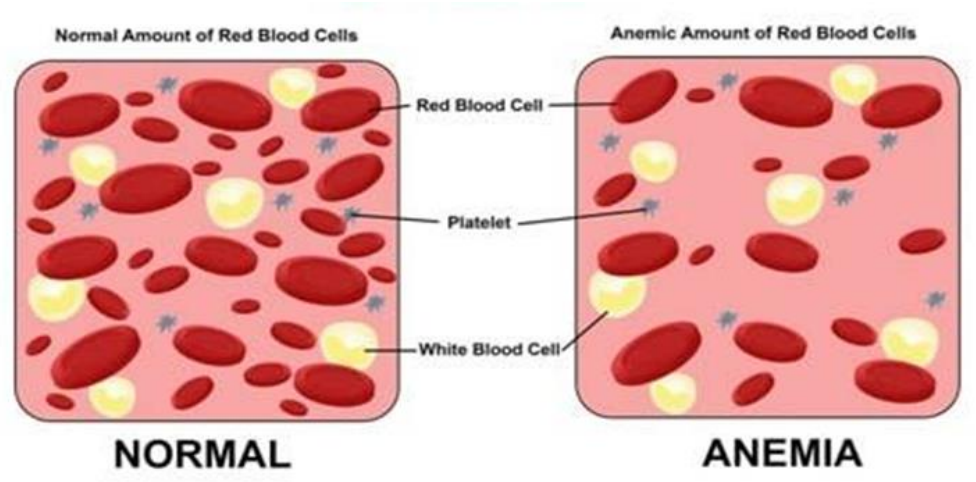
Bone gist depression, erythropoietin insufficiency.

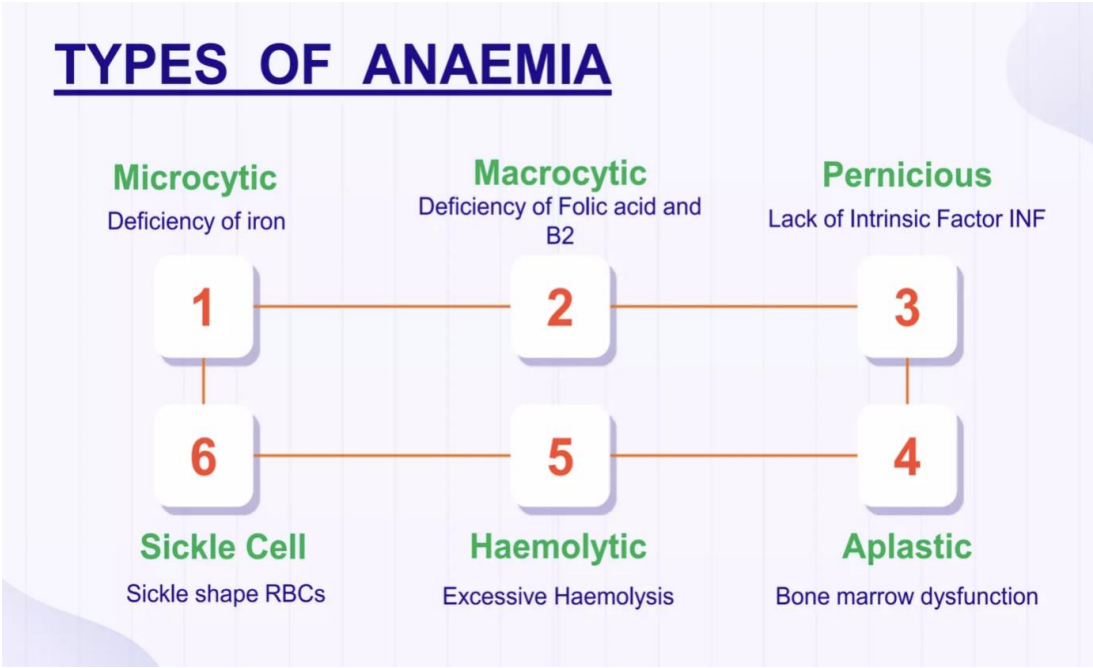
(c) Increased destruction of RBCs

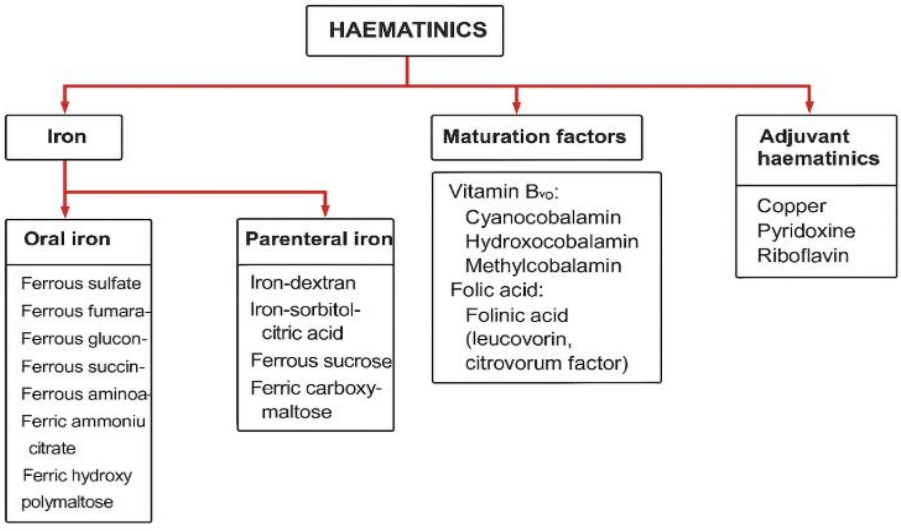
**Anemia**

Anemia is a drop in the RBC count, hemoglobin, or hematocrit values, resulting in a lower capability for the blood to carry oxygen to body tissues.




Normal Amount of Red Blood Cells
Anemic Amount of Red Blood Cells
Red Blood Cell
Platelet
White Blood Cell
NORMAL
ANEMIA


TYPES OF ANAEMIA
Microcytic
Deficiency of iron
Macrocytic
Deficiency of Folic acid and B2
Pernicious
Lack of Intrinsic Factor INF
1
2
3
6
5
4
Sickle Cell
Sickle shape RBCs
Haemolytic
Excessive Haemolysis
Aplastic
Bone marrow dysfunction


HAEMATINICS
Iron
Oral iron
Ferrous sulfate
Ferrous fumara-
Ferrous glucon-
Ferrous succin-
Ferrous aminoa-
Ferric ammoniu citrate
Ferric hydroxy polymaltose
Parenteral iron
Iron-dextran
Iron-sorbitol-citric acid
Ferrous sucrose
Ferric carboxy-maltose
Maturation factors
Vitamin B12:
Cyanocobalamin
Hydroxocobalamin
Methylcobalamin
Folic acid:
Folinic acid (leucovorin, citrovorum factor)
Adjuvant haematinics
Copper
Pyridoxine
Riboflavin

**Iron**

Distribution of iron in the body

- Hemoglobin (Hb). 66%
- Iron stores as ferritin and hemosiderin. 25%
- Myoglobin (in muscles). 7%
- Enzymes (cytochromes, etc.) 6%

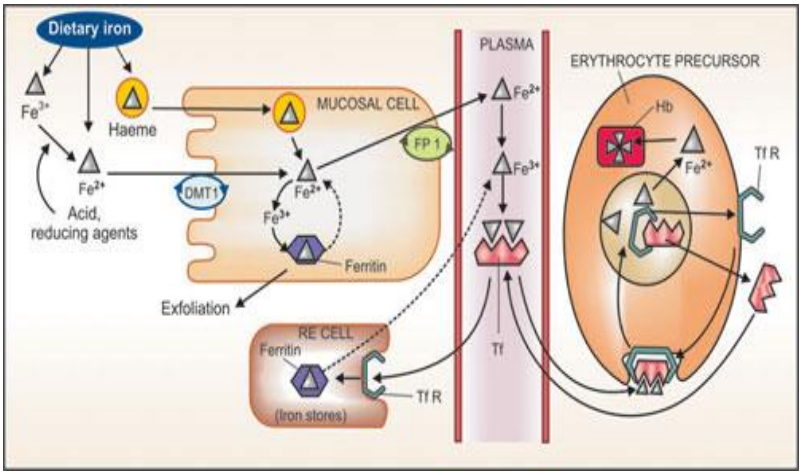
**Daily Iron requirement**

- Adult manly: 0.5-1 mg
- Adult womanish: 1-2 mg (menstruating)
- Children: 25 micro gm /kg
- Gestation: 3-5 mg

**Salutary sources of iron-rich**

- Liver, egg thralldom, dry fruits, wheat, spinach, Meat, funk, fish, banana, apple.
- Two different iron transporters in the intestinal mucosal cells accomplish iron uptake.
- **divalent metal transporter 1** (DMT1) carries ferrous iron into the mucosal cell
- **ferroportins** are bound with ferrous iron & pass through the mucosal cell directly into the bloodstream

**Mechanism of Iron absorption, transportation, utilization & storage**



**Mechanism**

- On entering plasma, Ferrous is immediately converted to the ferric form and forms a complex with a glycoprotein, transferrin (Tf), which has two binding spots for ferric ions.
- Iron is transported into erythropoietic and other cells through attachment of transferrin to specific membrane-bound transferrin receptors (TfRs).
- The complex is engulfed by the receptor through endocytosis. Iron detaches from the complex at the acidic pH of the intracellular vesicles.
- Released iron used for Hb synthesis.
- Tf & TfR come back to the cell surface to carry another.

**Storage**

Liver, (spleen, bone gist) as well as in hepatocytes and myocytes as ferritin and hemosiderin.

**Excretion**

- In adult males is 0.5- to 1mg, substantially as molted, i.e., mucosa cells, some RBCs, and in bile (lost in feces)
- In menstruating women, monthly loss of – 0.5-1mg per day
- Other routes – skin (urine and sweat)

**Therapeutic uses**

- Gestation
- Iron-deficient anemia
- Premature babies
- Blood loss
- Malabsorption syndrome
- GI bleeding due to ulcers.

**Iron preparations & brand names**

- Oral preparations- ferrous sulfate (Feosol)

- Parenteral preparations- iron dextran (imferon)

**Folic acid**

Pteroyl glutamic acid (PGA) (pteridine + Para para-aminobenzoic acid (PABA) + glutamic acid.)

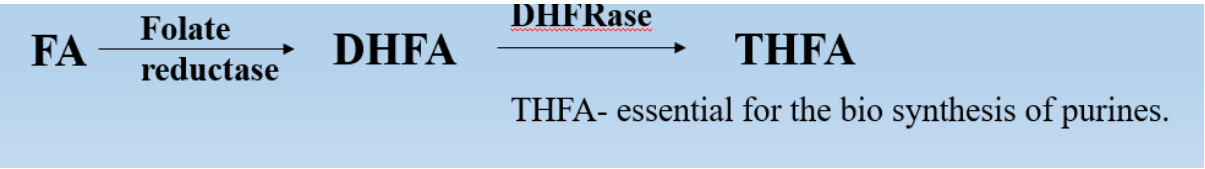
•Salutary sources Liver, green lush vegetables(spinach), incentive, egg, milk.

• Present in food as poly-glutamates

• Absorption: in the duodenum and jejunum

• Transported in the blood as methyl-THFA by active and passive transport.

• Stored in cells as polyglutamate, the Liver takes up a large part and secretes methyl-THFA in bile.




**Therapeutic Uses of Folic Acid**

Megaloblastic anemia

Folic acid insufficiency

Cover epithelial cell

Growth in infants

In gestation

**Preparations and dose:**

- Folic acid: -liquid oral, Injectable
- Folinic acid: -CALCIUM LEUCOVORIN 3 mg/ml inj.

**Quotidian demand:** 0.2 mg per day (0.8 mg in gestation & lactation mothers)

**Vitamin B12 (Cyanocobalamin)**

Complex cobalt-containing compounds, Cyanocobalamin, and hydroxocobalamin

• Synthesized by microorganisms, plants, and animals acquired it from them.

**Dietary sources**: Fish Liver, saltwater fish, eggs, chicken, meat, cheese.

Two active coenzyme forms of B12 are deoxyadenosyl-cobalamin (DAB12) and methyl-cobalamin (methyl B12).

**Functions**

- Vit. B12 act as cofactor in following reactions -
- Conversion of homocysteine to methionine - methionine is methyl group donor in metabolic responses.
- Purine and pyrimidine conflation- demanded for DNA conflation.
- Malonic acid DAB12 Succinic acid important for propionic acid metabolism (Carbohydrate and lipid metabolism)
- for cell growth and addition.

**Dosage and Uses of Vitamin B12**

- Vit B12 is well absorbed after i.m. or deep s.c. injection
- Cyanocobalamin: 35 micro gm/5 ml liq.,
- Hydroxocobalamin: 500 mg. 1000 mg

**Therapeutic Uses**: Treatment of Vitamin B12 deficiency

i. Megaloblastic anaemia: defects in the metabolism of vitamin B12 or folic acid.

ii. Pernicious anaemia: the body can't absorb vitamin B12 orally due to a lack of natural factor, so given parenterally IM or SC

iii. Prophylaxis: 3-10 micro gm daily

iv. Neurological conditions like: Neuropathies, trigeminal neuralgia, Multiple sclerosis, psychiatric disorders.

**COAGULANTS**

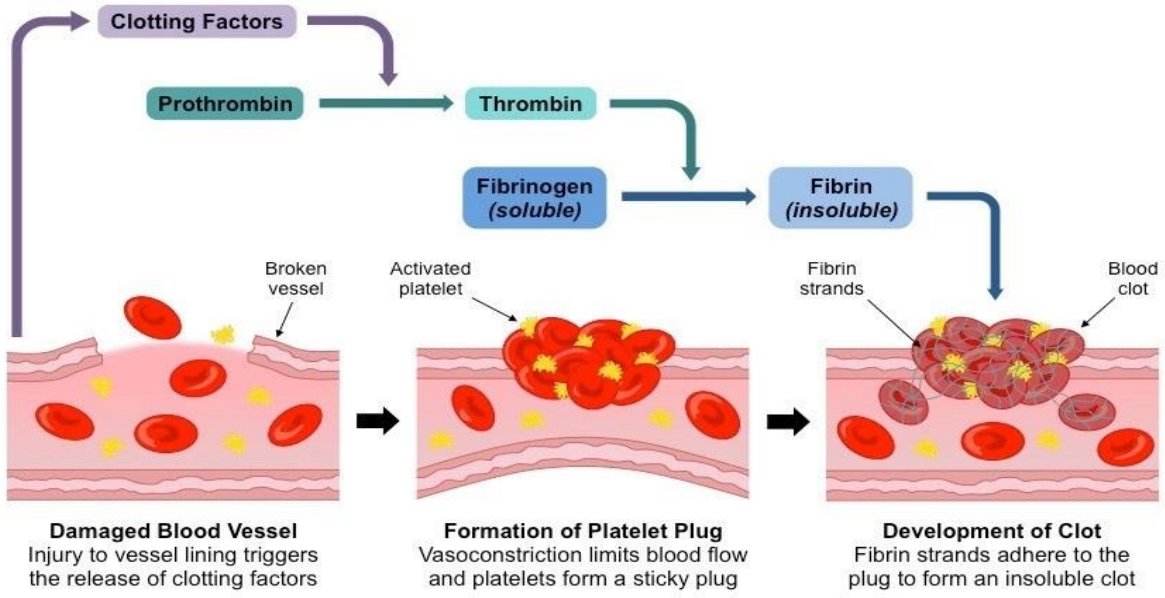
**Introduction**:

Hemostasis- cessation of bleeding from a damaged blood vessel.

3 basic mechanisms that prevent blood loss:

a. Initially vasospasm of small capillaries- Vasoconstriction

b. Platelet plug conformation




**Blood clotting:**

**Coagulation** is the process by which a liquid, particularly blood, changes into a semi-solid or solid state. In the context of blood, coagulation is part of hemostasis, the body's mechanism to help inordinate bleeding after an injury. It involves transformation of blood from liquid to gel, forming a clot.

Disorders of coagulation can lead to an increased threat of bleeding or clotting (thrombosis).

**3 stages of coagulation:**

- Intrinsic/extrinsic
- Thrombin formation
- Fibrin Formation

**Coagulants**

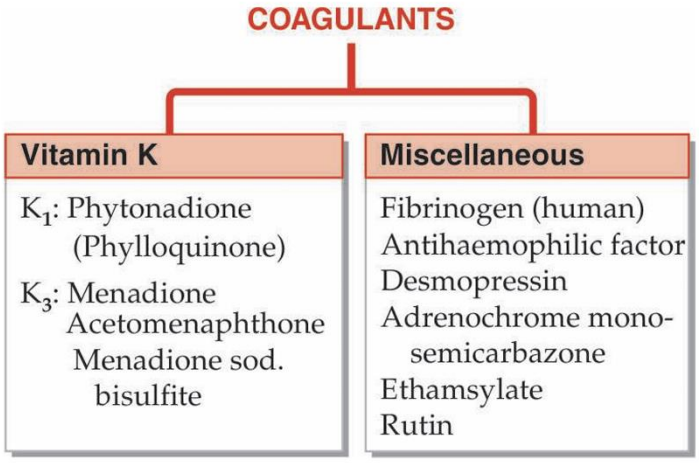
Coagulants are drugs that promote coagulation and control bleeding.

Coagulants are also called hemostatics.

- Systemically
- locally (styptics)

In Hemorrhagic states - Hemophilia, Von Willebrand's disease

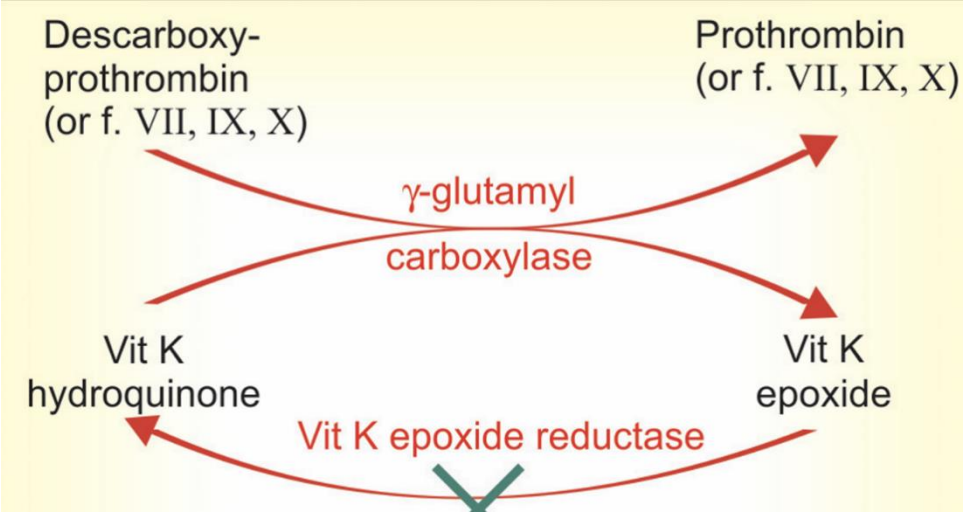
Fresh whole blood or plasma - the best therapy provides all the factors demanded for coagulation Act immediately.




**Vitamin K (**Phytonadione and Menadione)

**Mechanism of Action:**

Vit K acts as a cofactor at a late stage in the synthesis of coagulation proteins - prothrombin (II). VII, IX and X by liver. The vit K dependent changes, capability to bind Ca2+ and to get bound to phospholipids and properties essential for participation in the coagulation cascade.




**Therapeutic uses:**

- Dietary deficiency
- Liver disease
- Malabsorption
- Long term antimicrobial therapy
- Newborn babies lack intestinal flora and have low level of clotting factors:
- Overdose of oral anticoagulants

**Adverse effects:**

- Allergic reactions are very rare.
- Dizziness
- Rapid and Weak Pulse
- Profuse Sweating
- Brief Hypotension
- Pain, Swelling, and Tenderness at the Injection Site

**Contraindications:**

- Severe anaphylaxis reactions can occur on i.v. inj of emulsion; this route should not be used.
- During Surgeries.

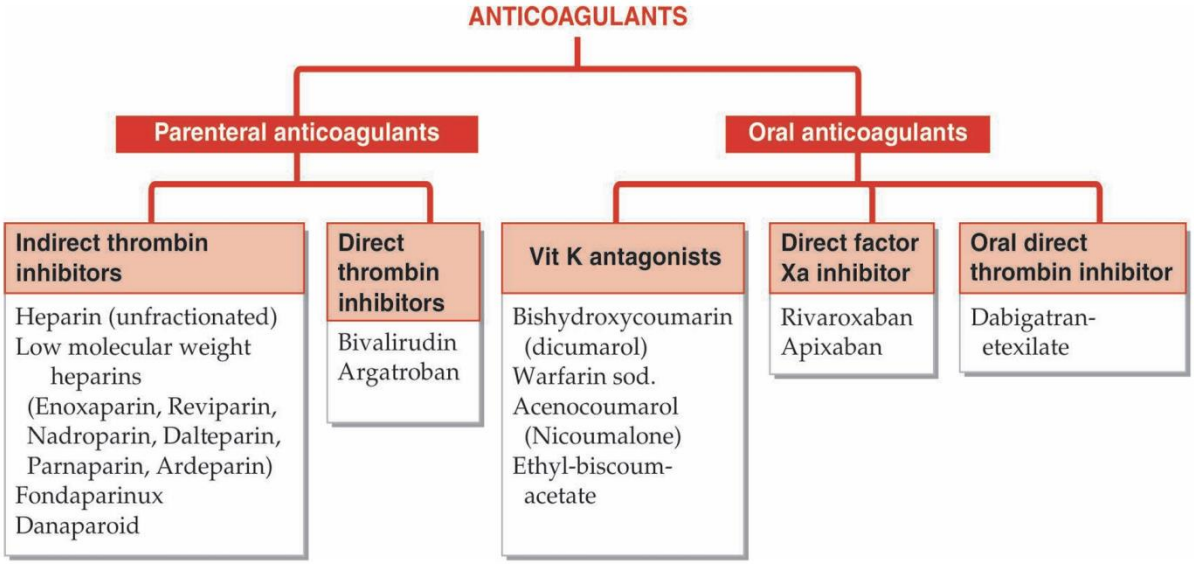
- Vitamin K may interfere with the effectiveness of anticoagulants, such as **warfarin.**

**Dosages and brand names:**

- Phytonadione: VITAMIN-K, KVI, K-WIN 10 mg/ml for i.m. injection.
- Acetonaphthone: ACETOMENADIONE 5, 10 mg tab; KAPILIN 10 mg tab.

**Anti-Coagulants**

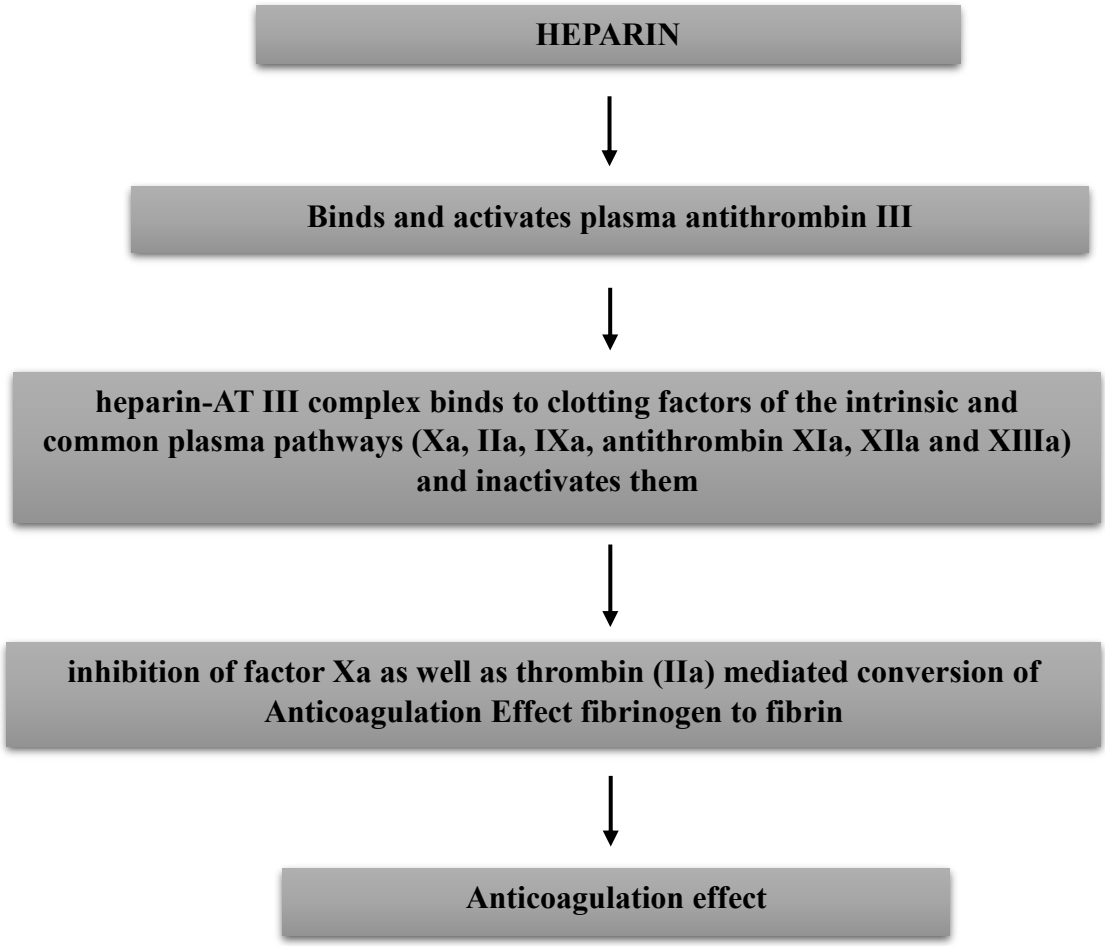
- The drugs that are used to reduce the coagulability of blood are known as anti-coagulants

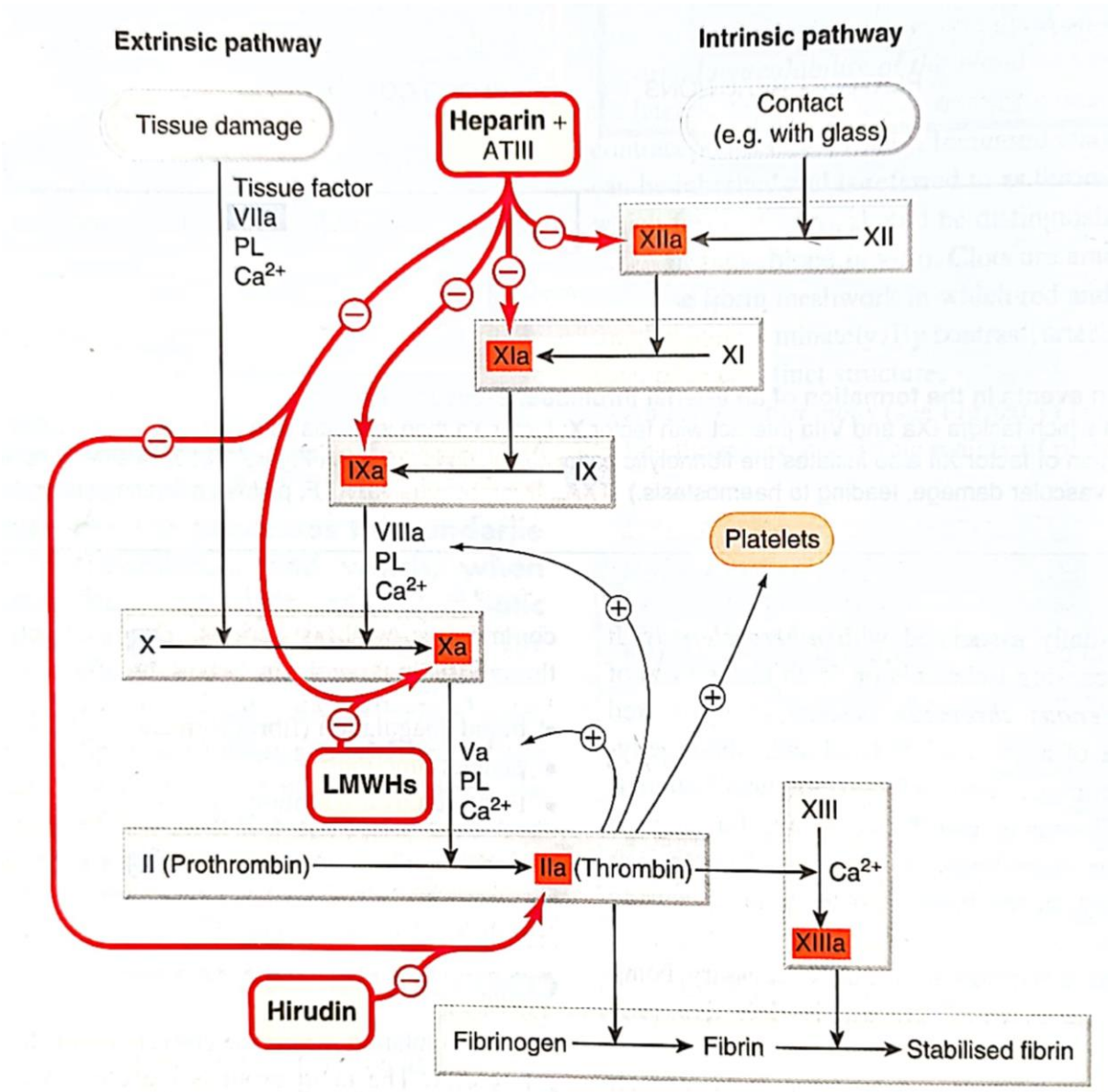



**Heparin**

- McLean, a medical student discovered that liver contains a powerful anticoagulant, in 1916.
- Howell and Holt named it HEPARIN obtained from liver Mixture of mucopolysaccharides with MW 10,000 to 20,000 (D-glucosamine-L-iduronic acid & D-glucosamine - D-glucuronic acid)
- Strongest organic acid present in the body.
- Found in the mast cells of lung, liver and intestinal mucosa Commercially obtained from-ox lung and pig intestinal mucosa.

**Heparin mechanism of action:**






**Pharmacological actions:**

- **On Blood:**

**Anticoagulation**: Heparin prevents blood clot formation by binding to antithrombin III (ATIII) and accelerating its inactivation of coagulation enzymes, including thrombin (factor IIa) and factor Xa

**Thromboprophylaxis:** Heparin is indicated for prophylaxis.

- **On Platelets:**

**Inhibits** platelets aggregation and **increases** the bleeding time.

- **On Cardiovascular System**:

**Prevents embolisms** in patients with atrial fibrillation and also used as an adjunct antithrombin therapy in patients with unstable angina and acute coronary artery syndrome.

- **Respiratory System**:

**Pulmonary Embolism**: Heparin reduces thrombosis associated with pulmonary embolism**.**

- **Renal System**:

**Kidney Dialysis**: Heparin prevents blood clotting during kidney dialysis.

**Pharmacokinetics**

- Large MW, highly ionized molecule: therefore not absorbed orally.
- If injected i.v - acts instantaneously. After s.c injection anticoagulant effect develops after ~ 60 min
- Does not cross blood-brain barrier or placenta.
- Safe in pregnancy
- Metabolized in liver by heparinase

**Adverse Effects:**

• Bleeding due to overdose -serious complication- hematuria (Ist sign)

• Thrombocytopenia

• Transient and reversible alopecia

• Osteoporosis - On long-term use

• Hypersensitivity reactions

**Contraindications**

- Bleeding disorders
- Heparin induced thrombocytopenia
- Endocarditis

- Ulcers in gut
- Severe hypertension (risk of cerebral hemorrhage)
- large malignancies (risk of bleeding in the central necro sed area of the tumor)