Blood Coagulation

* In normal condition blood does not clot due to ① presence of HEPARIN → synthesized in → Most cells of connective tissue
  - Basophils
  - Liver (mainly)
* ② -ve charge of both endothelium & blood platelets
* Blood coagulate → on exposure to air (O_2)
  → contact with rough surface { BV → No ; air, Smoo ; Surface }
* On exposure to air blood coagulate within 3-5 minute in humans.

① Best & Tailer's theory :-

* 4 clotting factors responsible
* Most accepted view until 13 factor theory.

① **Prothrombin** —(Ca^{+2}, Thromboplastin)→ Thrombin
- Synthesized in Liver
- Vit K is required for its synthesis.

② Ca^{+2} → In blood plasma

③ **Thromboplastin** – Released by blood platelets which are fragments of megakaryocytes, produced in Red bone marrow.

④ **Fibrinogen** :- • Found in whole blood, even in lymph
• Synthesized in Liver.

Fibrinogen —(Thrombin)→ Fibrin (insoluble) (At site of injury)
(Soluble).

Vit K → Prothrombin
↓ Ca^{+2} / Thromboplastin
Thrombin
Fibrinogen —(↓)→ Fibrin.

② Howell's Theory :- (dbt)

- Basic mechanism is same as described by Best & Tailor except that the conversion of Prothrombin into thrombin requires only Thromboplastin only not Ca^{+2}
- This view is rejected because he totally rejected the role of Ca^{+2}.

(3) Enzyme Cascade theory or 13 factor's theory

Given by Mc Farllin

* most accepted theory & approved by ICBC (International committee for blood coagulation)

(I) – Fibrinogen :- • Glycoprotein, • Soluble, • M.wt – 3,40,000
• synthesized in liver

Fibrinogen (Soluble) Polymer —depolymerisation→ Fibrin (soluble) Monomer —Re-polymerisation→ Fibrin (Insoluble) polymer

(II)

(III) – Tissue thromboplastin or Tissue factor – (TF) :
- Extrensic thromboplastin.
- Lipoprotein
- Released by injured tissue & damaged blood capillaries.
- phospholipid greatly enhanced its action (especially Cephalin)
- Activate prothrombin

(IV) → Ca^{+2} (II) Prothrombin
- Glycoprotein • soluble • M.wt – 17,000 D;
- synthesized in liver
- Human prothrombin has 9% Carbohydrate normally hexose, hexosamine, Neuraminic acids.

(IV) → Ca^{+2}
- Co-factor of blood clotting
- Required for formation of thromboplastin (both extrensic & intrensic)
- Activation of prothrombin

(V) → Labile factor or Pro accelerin
- Glycoprotein • tnt in plasma • Synthesized in liver
- Helps in Complete conversion of prothrombin into thrombin
- Autocatalysis

(VI) Accelerin →
- Hypothetic active form of pro accelerin
- Not existed now, but included in 13 list of factors

(VII) SPCA → Stable factor → Pro convertin
↳ (Serum prothrombin accelerator proconvertin)
- ~~Antihaemophilic factor~~
- Accelerates the formation of extrensic thromboplastin (III) IV
- Plasma protein, Synthesized from Vit 'K' in liver
- Absence → Genetic defect → Worn billy disease.

VIII → Anti Haemophilic [illegible]

- Protein, - Formed from Vit 'K' in liver.
- Transfusion of PET cells (only blood platelets in 0.9% Salt soln. NaCl, or Isolated blood protein in 0.9 salt sol.) some time in above condition frequently increased the B.C. and small blush patches are formed all over the body beneath skin (PETECHAE & PURPURA)
- Its deficiency cause Haemophilia 'A'

IX → PTC → Christmas Factor → HAE 'B'

↳ ~~Prothrombin component~~ Prothromboplastin component

- Deficiency of blood platelets below 15,000/ (Normal No 1-3 lakh/ml) results in delayed clotting time. This condition is called Hypothromboplastynemia. Such patient immediately required [illegible].
- Glycoprotein, Synthesized in liver (Vit k)
- Main source of Intrensic thromboplastin (Platelets)
- Activity of this factor is governed by 4 platelet factors Pf-1, Pf-2, Pf-3, Pf-4.

X → ~~Stuart~~ Stuart Power Factor

- Glycoprotein
- Its deficiency causes Nose bleeding (Epistaxis) Also bleeding in joints & tissue.

XI → PTA → HAE 'C'

Prothromboplastin ~~Antecedent~~ Antecedent

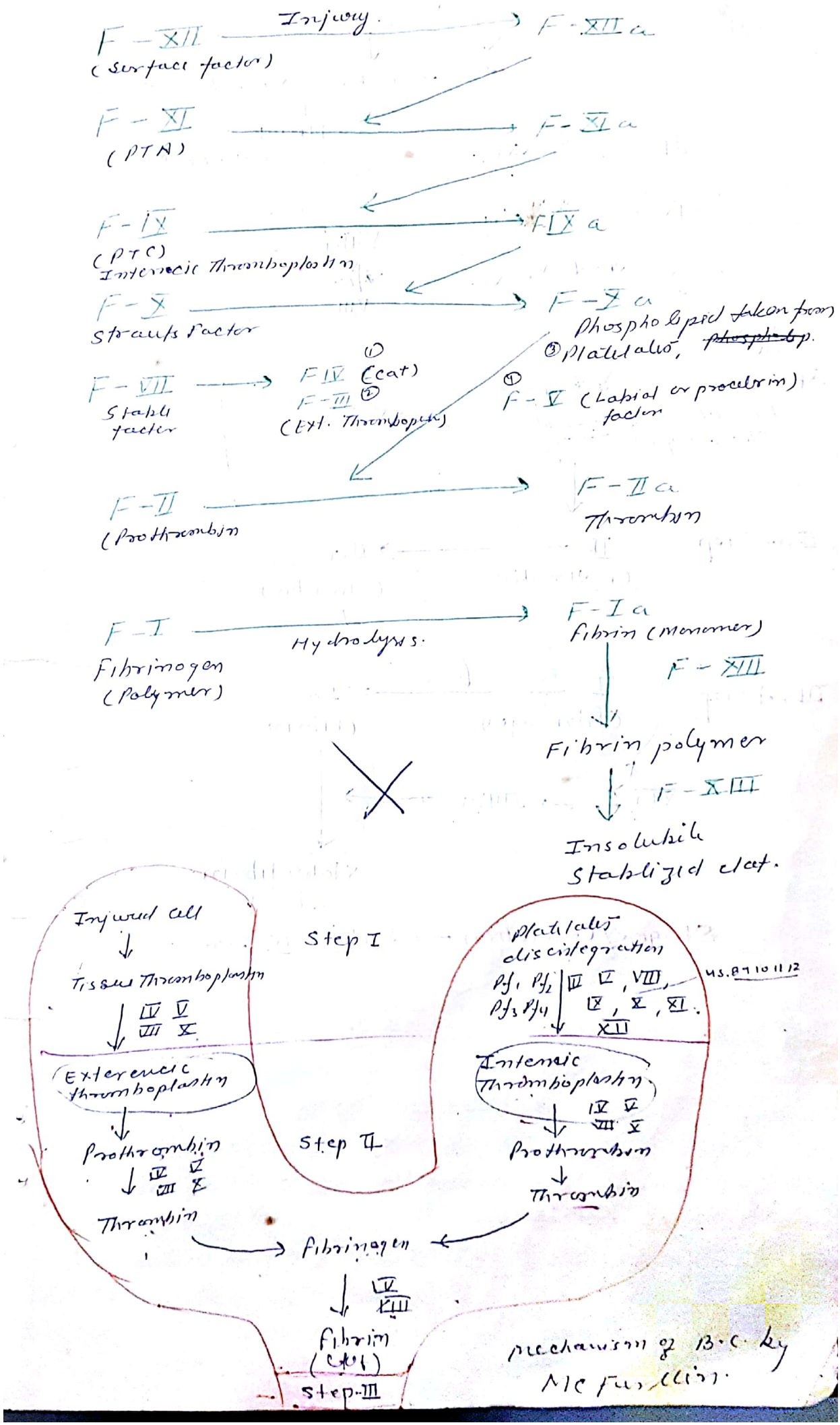
- Glycoprotein
- Synthesized in liver

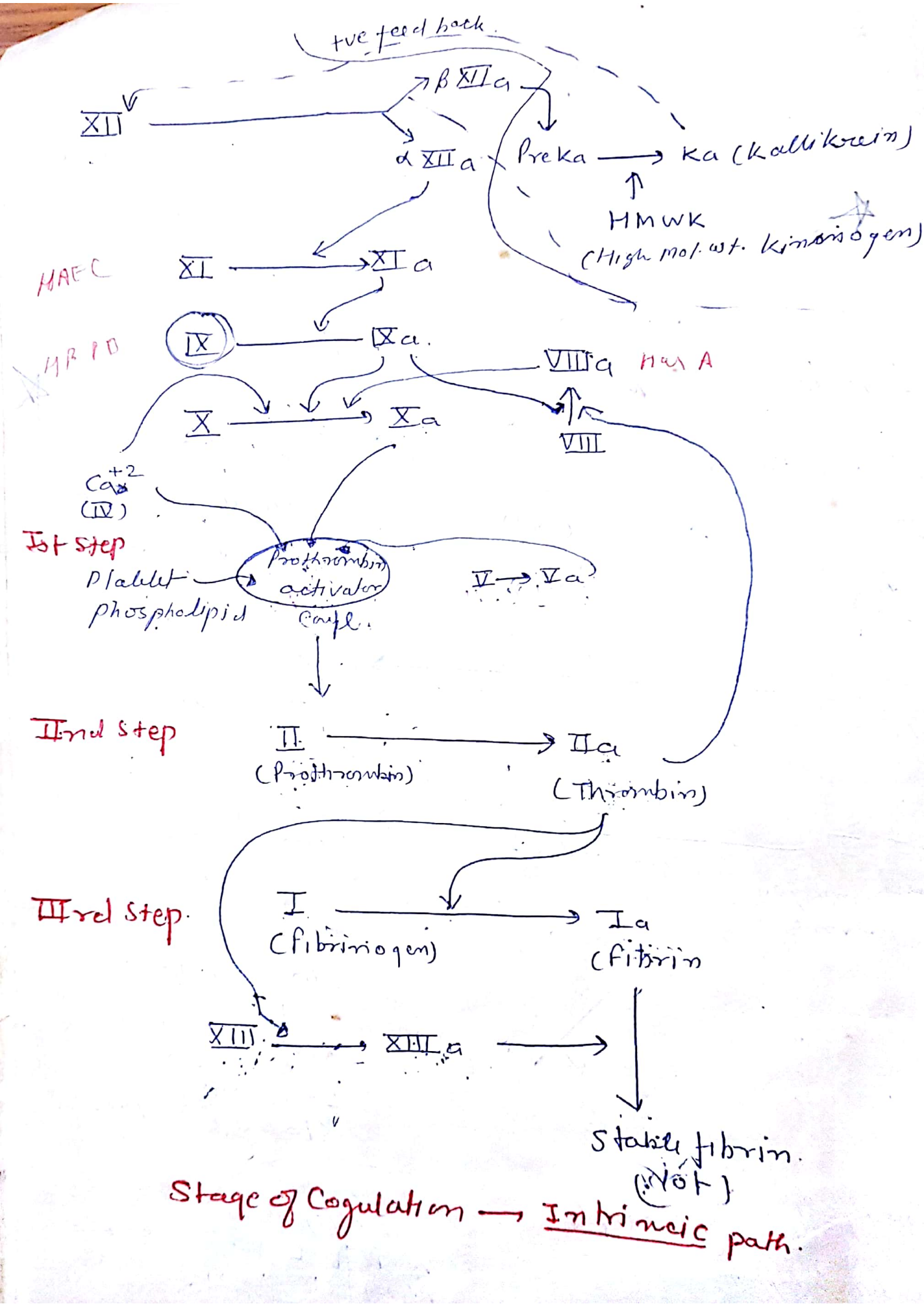
XII → Hagmen's or Surface factor or Glass Contact factor

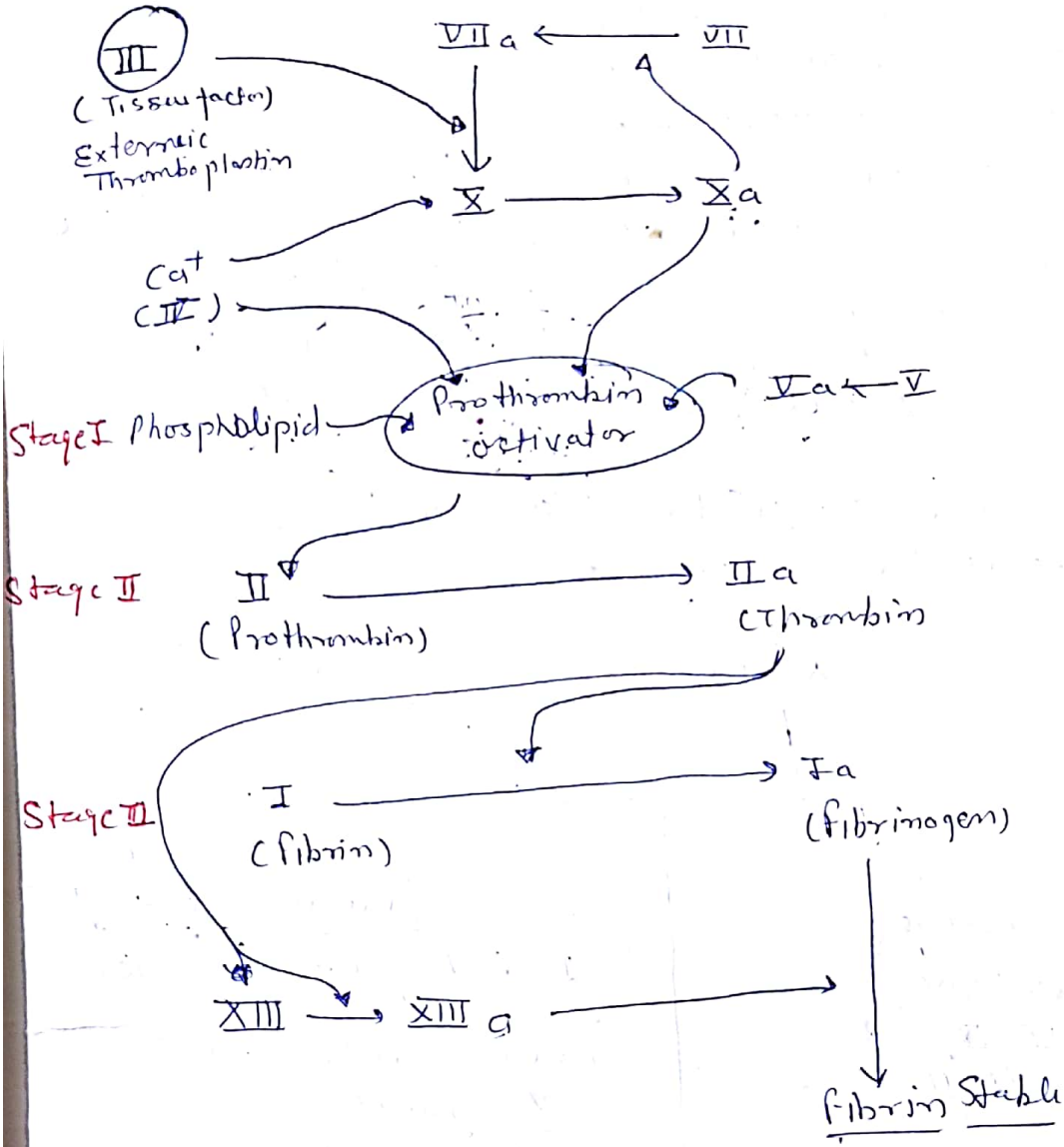
- Activated on contact of rough surface
- Initiate the B.C. at the site of B. injury
- Discovery of this factor explain the rendicape of Best theory.

XIII → FSF (Fibrin Stablising Factor)

- It has enzymatic action & called fibrinase, which converts the fibrin (monomer) in its soluble form.







Step's of B.C. by ~~Extrinsic~~ Extrinsic Path.

★ The Procoagulant factor:- 13 factor

★ factor V, VII, VIII, IX, X, XI, XII, XIII → Exist normally in blood but in inactive form.

★ when process of coagulation starts, they begin to become active & act as enzymes. These activated procoagulant factor are proteolytic enzymes & hence also called as "protease". All these protease (except VIII) are synthesized in liver.

★ Some of them require vit 'K' for their synthesis and hence called 'vit. K dependent procoagulant factors'

The triggering mechanism →

The contact of blood with -vely charged subendothelial tissue is the trigering mechanism.

The activation of the factor →

- Activation process required, Ca^{++} & phospholipid
- The source of phospholipid is platelet. For this reason, it is presumed that clotting of blood occurs on the surface of the platelets which have been adhered & aggregated locally to form the platelet plug.

Role of ① Vit K ② Liver ③ Vascular wall in hemostasis & coagulation →

Role of.

Vit K.

Helps in Synthesis of

Ⓐ Procoagulants, factors VII, IX, X & prothrombin (II).

Ⓑ Circulatory anticoagulant, Protein C.

Vit K deficiency causes hemorrhage disorder.

Vascular wall

I- Sub endothelial layer is highly thrombogenic. contact with blood triggers of coagulation

II- Endothelial layer is primarily opposing clotting as it is a barrier between blood & subendothelial layer But also release some procoagulants

III - Vaso passm is an aid aid to hemostasis.

Liver

Synthesize, some

Ⓐ Procoagulants like V, VII, IX, X; prothrombin (II), fibrinogen as well as

Ⓑ Anticoagulants, heparin, Antithrombin III & Protein C.

Liver failure thus can cause signs & symptoms of hypocoagulability as well as hypercoagulability.

Blood Store in blood banks —

- Time → For 21 days at 4°C
  → for long storage of blood
  ↓
  Powder is formed by drying

* when transfusion, powder is mix in 0.9% saline or glucose (18-20 mg/100ml) solution.

* An individual requiring blood transfusion may not need the whole blood but in no. of disease only parted components of blood are needed. for ex —
  An anemic needs only R.B.Cs, A Thrombocytopenic needs only pet cells,

Anticoagulants → 5 types

① Decalcifying agent
- Citrate & Oxilate of Na & NH_3
- EDTA (Ethylene diamene tetra acetate)

→ Citrate blood used for blood transfusion because in liver citrate separate from Ca^{+2} & blood have become normal property.

→ For Laboratory tests → Oxilate blood used

② Antiprothrombin → Inhibit the activation of prothrombin

Saliva → Leach (Hirudine)
Lempray (Lampridin)

Heparin – commercially obtained from cattles.

Coumerin → • Present in clove
• Plaferon is its synthetic derivative.

③ Antithrombin →
Ex – chemicals like thiol (-SH) derivative

④ Antithromboplastins
Ex → • Protamines (clupin, cellmin, salpin, & Stugein) → • found in milt of fishes
• Histones

⑤ Antifibrinogen →
KMnO4 & Natural Salts.

Fibrinolysis → Process of dissolving clot (fibrin)

Plasminogen ——→ Plasmin
Inactive
(Seminal fluid & blood).

Clot ——→ Soluble

Thrombosis

- Stationary clot (large)
- Clot in intact b.V.
- occurs in patient suffer from hypercalostermia as a result of which diameter of b.V. decreas.
- Coronary thrombosis results in heart attack

Amboliism

Moving clot (small)

- Due to activation of some cloting factor, some time small clot form in b.V. which move with blood (ambolus)
- It is fatal when it block the small b.v. of brain causing nervous damage (Paralysis).