Hemostasis

↳ Primary : vasoconstriction
platelet plug

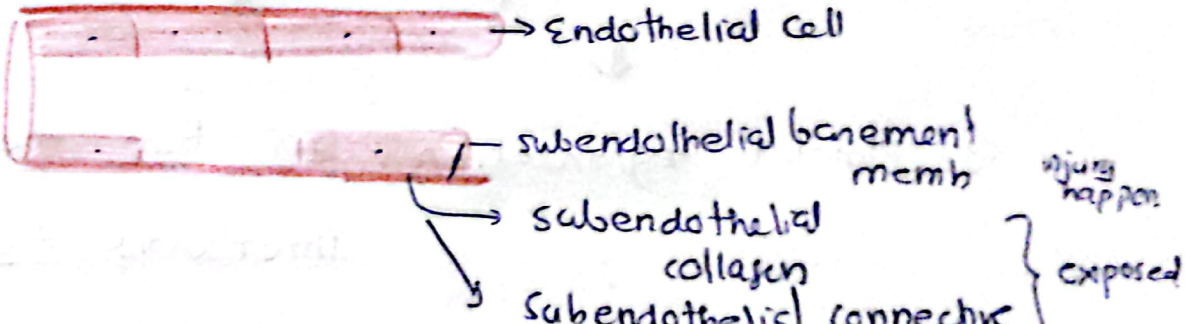
→ secondary : Blood clot

on an endothelial injury

① vasoconstriction : Transient
② Platelet plug formation
③ definitive clot

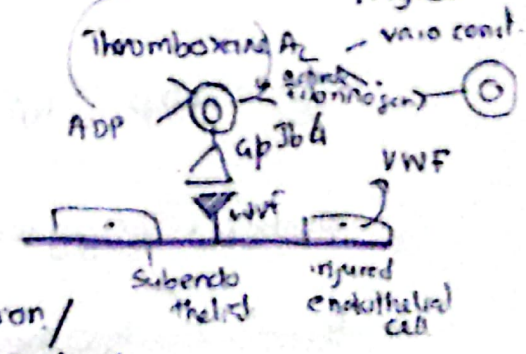
Vasoconstriction

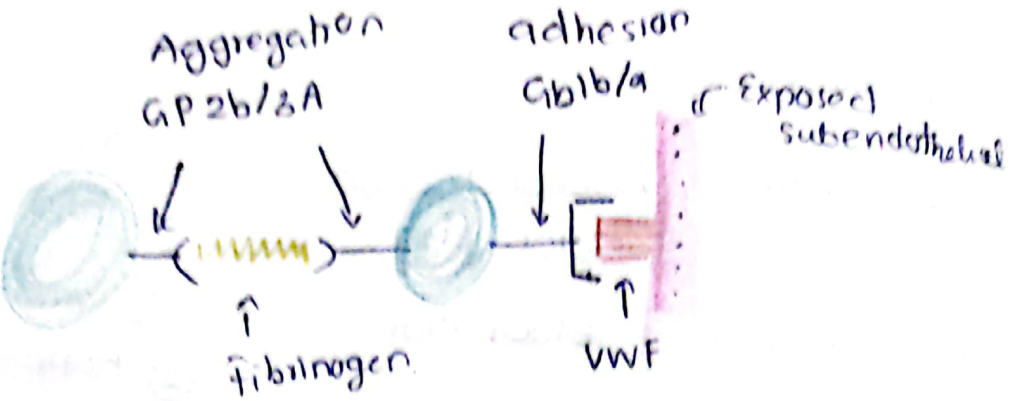
- local myogenic spasm initiated by direct effect of injury on vascular smooth muscle
- Nervous reflexes initiated by activation of nociceptors and other sensory ending.
- Local autocoid factors released from traumatised tissue and platelet :
  1) Serotonin.
  2) Thromboxane A_2.



Platelet plug Formation

Platelet plug
- → VWF bind to collagen
- → Platelet adhesion.
- → Platelet degranulation / activation.
- → Platelet aggregation.





① von willebrand factor bind to collagen

↓

source

↓ platelet

α- granule

↓ endothelial cell

Weibal palade bodies.

⇓

② Platelet adhesion.

on VMF binds platelets :

via Gp 1b/a receptor.

⇓

③ Platelet degranulation

ⓐ Release

: ADP : from dense granules

: Thromboxane A_2

: platelet Cox product.

ⓑ ADP upregulate Gp 2b/3a receptor

④ Platelet aggregation

Bind each other with GP2b/3a Fibrinogen is linear molecule

platelet → Thromboxane A₂ ⟨ V C ; Platelet aggregation

endothelial → Prostaglandin I₂ (Prostacyclin) ⟨ V.D ; ↘ inhibition.

Blood coagulation

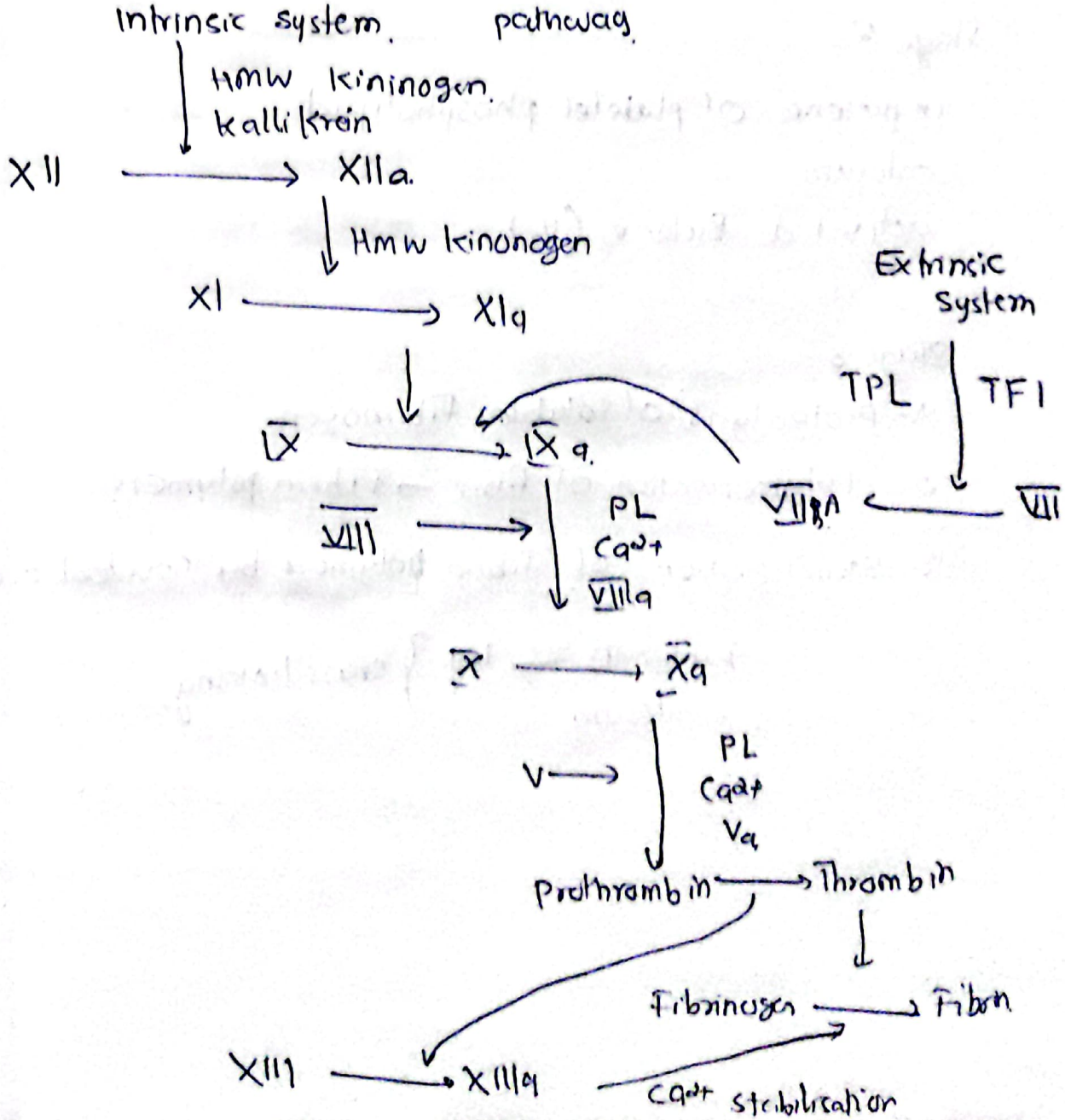
Stage 1 : Activation of factor 10 (Formation of prothrombin activator)

Stage 2: Formation of thrombin from prothrombin

Stage 3: Formation of fibrin from fibrinogen.

Stage 1 :

Achieved by two pathways : the intrinsic and extrinsic



Intrinsic pathway

intrinsic mechanism of prothrombin activation occurs in four steps:

Step 1 (Activation of XII)

Step 2 (Activation of XI)

Step 3 (Activation IX)

Step 4 (Activation of X)

Activation of intrinsic pathway starts with contact of Hagerman Factor with a negatively charged charged surface or exposed collagen of injured vessel wall

high molecular weight (HMW) Kininogen & kallikrein act as cofactors to facilitate the activation of factor XII

Stage 2:

in presence of platelet phospholipid
calcium
activated factor V (V_a)

Stage 3:

1. Proteolysis of soluble fibrinogen
2. Polymerisation of fibrin → Fibrin polymers
3. Stabilization of fibrin polymers by covalent cross linking

Factor 13 → 13a. } cross linking.
- calcium

clot retraction.

clot shrinks expressing serum out of it. This phenomenon is called clot retraction

- ✓ clot retraction is function of platelets.
- ✓ Retracted clot decreases the efficiency of thrombolysis

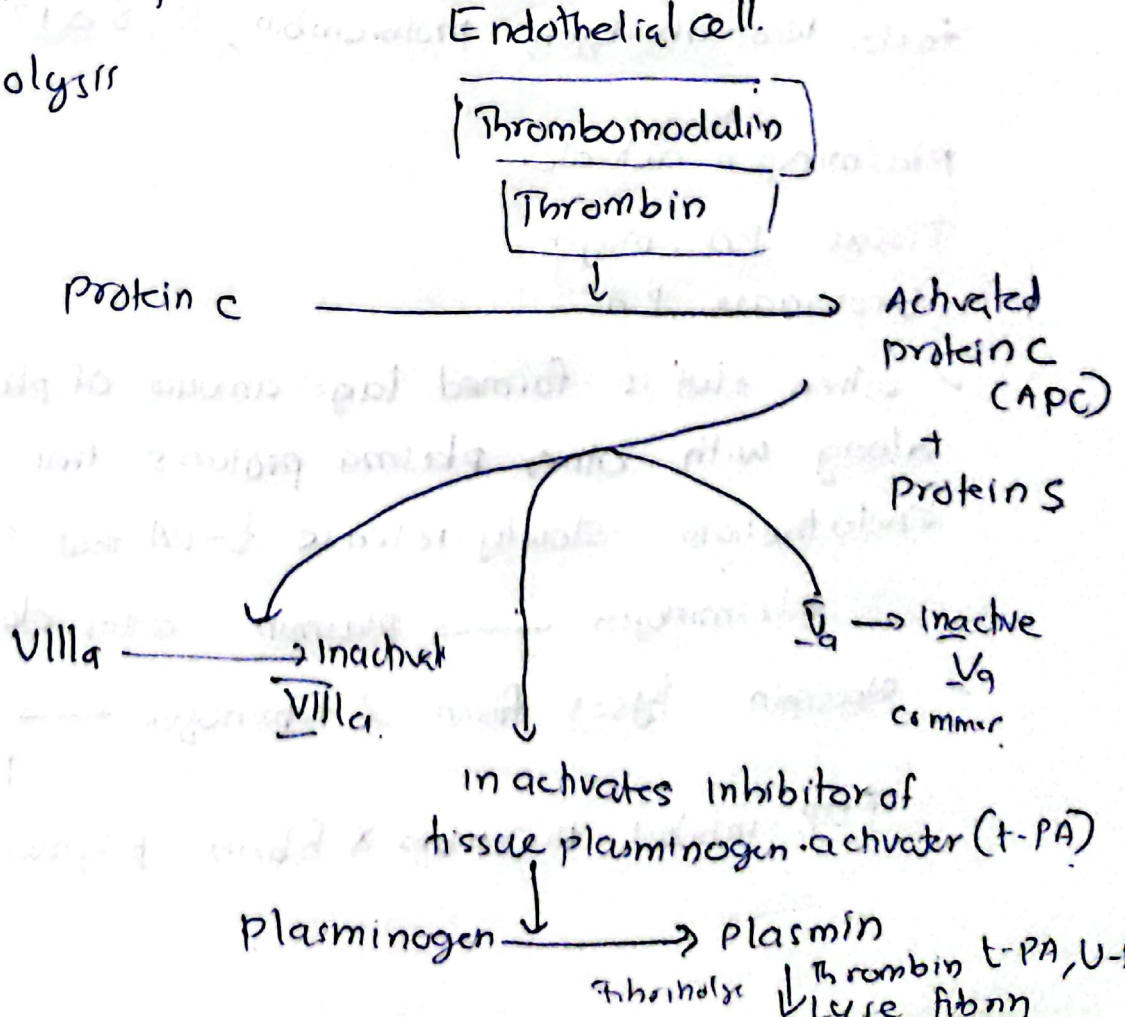
Function of clot Retraction.

1. Retracted clot (thrombus) strong seals injured vessel.
2. It facilitate wound healing
3. It prevents thrombolysis.

Anti clotting mechanism

Fibrinolysis occur in 3 steps

1. Activation of protein C
2. Activation of plasmin
3. Fibrinolysis



Fibrinolytic system

- Plasminogen - globin produced in liver
- Plasmin
  - plasminogen activater
  - plasminogen inactivater inhibiter
  - plasmin inhibiter.

Plasminogen

- It's a globin produced in liver
- circulate in plasma
- ~~In~~ it is inactived
- Active form is plasmin.

Plasminogen activater.

plasminogen ⟶ Plasmin

Plasmin

proteolytic enzyme that lysis fibrin as well as other clotting factor like fibrinogen, prothrombin, 5, 8 & 12.

Plasminogen activater

Tissue PA - major

Urokinase PA.

✓ when clot is formed large amount of plasminogen is trapped along with other plasma proteins that injured vascular endothelium slowly release t-PA that convert

Plasminogen ⟶ plasmin after clot has stopped bleeding.

- Plasmin lyses fibrin & fibrinogen ⟶ Fibrin derived pdts (FDP)
- FDP inhibit thrombin & fibrin polymerisation,

Fibrinolytic system regulated by

- plasminogen activator inhibitor (PAI)
- Plasmin inhibitors

↑ FDP - Blood clot

D.I.C measure.

plasmin inhibitors

α-2 antiplasmin (produced by liver)

- inactivate plasmic

Clinical

For MI - streptokinase PA given. (streptokinase)