BLOOD PHYSIOLGY

Haemostasis and blood Coagulation

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Lecture Content

Platelets synthesis and function .1

Haemostasis .2

Capillaries vasoconstriction .3

Platelets Plug .4

Clot formation (intrinsic & externsic .5 pathway) thrombin function

Fibrinolysis and plasmin .6

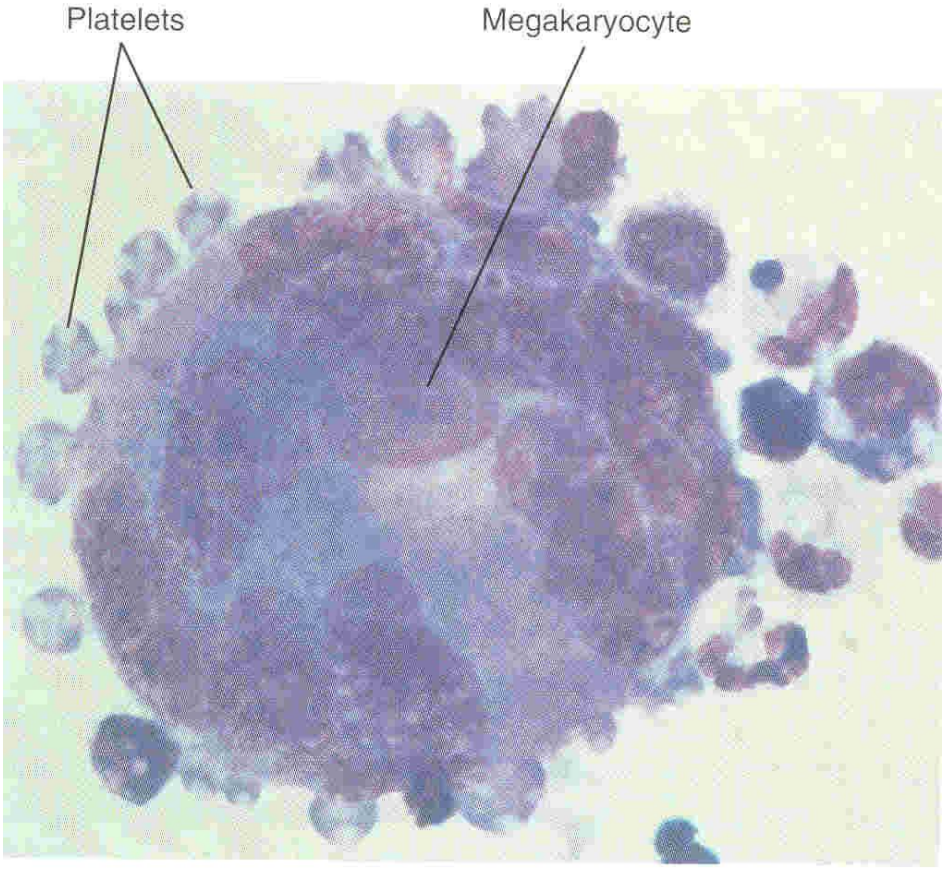
Platelets & Megakaryocyte (Thrombocytes)

- **Platelets:**
  - **are round disc formed in bone marrow**
  - **Stem cells → Promegakaryocyte → megakaryocyte → breaking pieces of cytoplasm (platelets)**
  - **Platelet count = $150x10^3$-$300x10^{3/}$ml,**
  - **life span 8-12 days**
  - **Active cells contain contractile protein,**
  - **Contain high calcium storage & rich in ATP**
  - **Coated by a glycoprotein layer which prevent its sticking to normal endothelial cells**

Platelets & Megakaryocyte (Thrombocytes)

- **Platelets Functions:**
  - **Adhere to injured site of blood vessel to stop bleeding**
  - **Secretes substances which are important for clot formation**

Platelets



Haemostasis

Mechanisms that prevent blood loss

1. Vasoconstriction
2. Platelet plug
3. Blood clot formation

Vasoconstriction

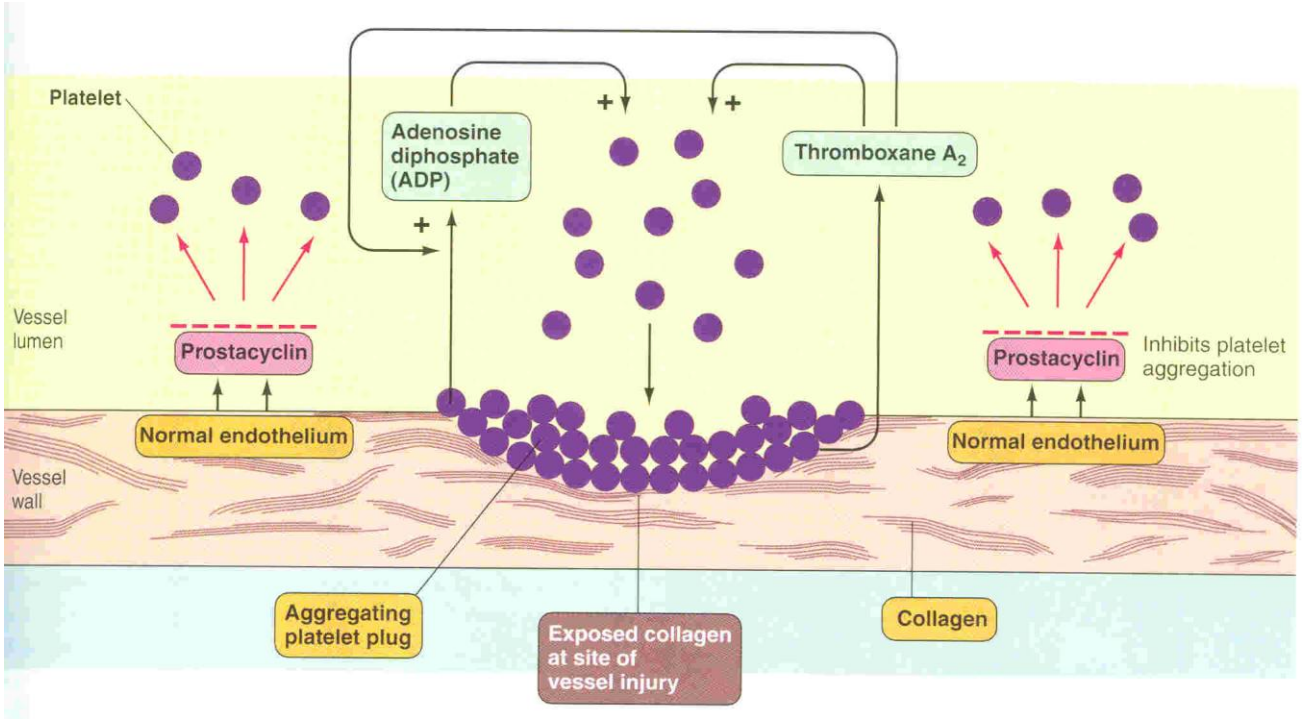
Immediately After injury a localize constriction of blood vessels occurs due to:

1. **Hurmoral factors: local release of thromboxane A2 by platelets, systemic release of adrenaline**
2. **Nervous factors**
3. **Myogenic contraction**

Platelet Plug

- **Platelets in contact with exposed collagen from injured endothelial, platelets swells and contract to release several substances such as 5HT, ADP, thromboxane A2**
- **The released substances increases the stickiness of platelets leading to platelets aggregation and plugging of the cut vessel**
- **These substances are also vasoconstrictor**

Platelets aggregation

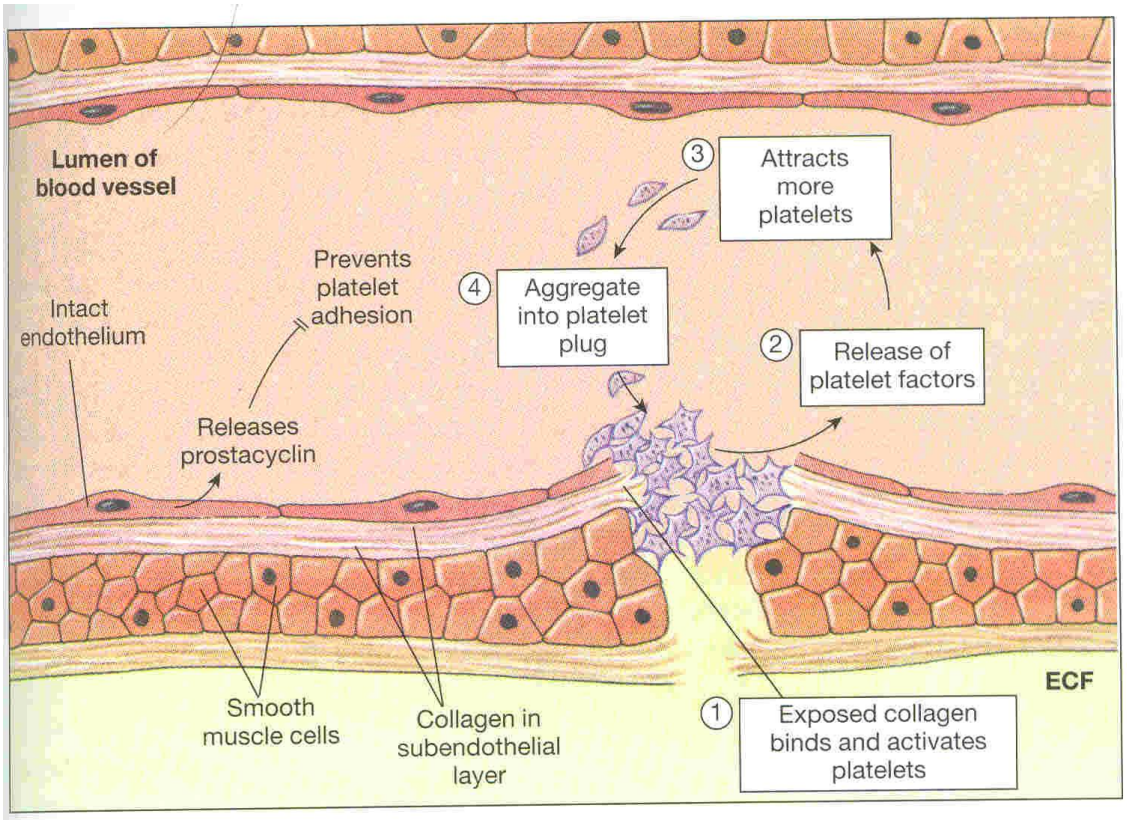


Activated platelet

Secrets:

1. **5HT → vasoconstriction**
2. **ADP → aggregator**
3. **Platlet phospholipid (PF3) needed for clot formation**
4. **Thromboxane A2 (TXA2) is a prostaglandin formed from arachidonic acid causes vasoconstriction and aggregator. Inhibited by aspirin**

Platelet Plug



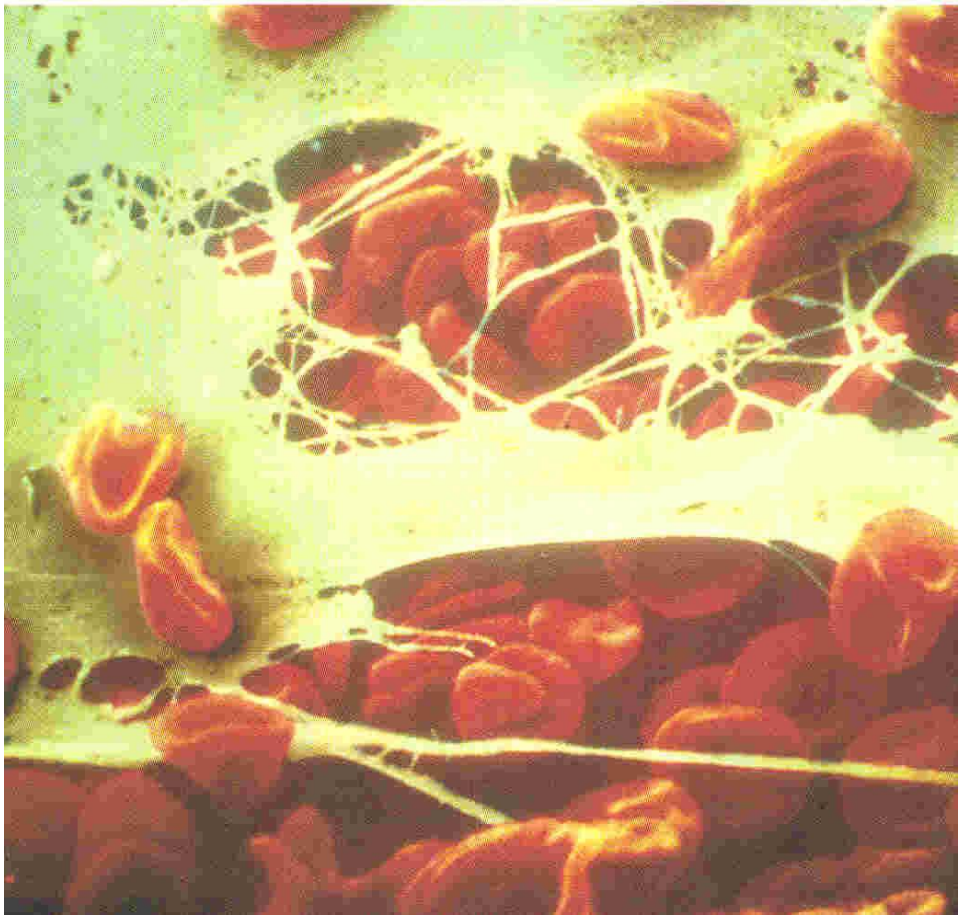
Blood coagulation (clot formation)

- A series of biochemical reaction leads to the formation of blood clot within few second after injury
- This reaction leads to the activation of thrombin enzyme from inactive form prothrombin
- Thrombin will change fibrinogen (plasma protein) to fibrin (insoluble protein)
- Prothrombin (inactive thrombin) is activated by a long intrinsic or short extrinsic pathways
- Activation cascade reaction involve 12 clotting factors, circulating in inactive precursor forms

Clotting Factors

Factors	Names
I	Fibrinogen
II	Prothrombin
III	Thromboplastin
IV	Calcium
V	Labile factor
VII	Stable factor
VIII	Antihemophilic factor
IX	Antihemophilic factor B
X	Stuart-Power factor
XI	Plasma thromboplastin antecedent (PTA)
XII	Hagman factor
XIII	Fibrin stablizing factors

Blood clot



Intrinsic pathway

- **The trigger is the activation of factor XII by contact with foreign surface, injured blood vessel, and glass.**
- **Activate factor (XIIa) will activate XI**
- **Xla will activate IX**
- **IXa + VIII + platelet phospholipid + Ca activate X**
- **Following this step the pathway is common for both**

Extrinsic pathway

- **Triggered by material released from damaged tissues (tissue thromboplastin)**
- **tissue thromboplastin + VII + Ca → activate X**

<u>Common pathway</u>

- **Xa + V +PF3 + Ca (prothrombin activator) it is a proteolytic enzyme activate prothrombin → thrombin**
- **Thrombin act on fibrinogen → insoluble thread like fibrin**
- **Factor XIII + Ca → strong fibrin (strong clot)**

Intrinsic Pathway	Exterinsic pathway
Contact activation ↓ XII →XIIa ↓ XI →XIa ↓ IX → IXa ↓VIII, Ca,P X → Xa	Tissue factor ↓ ↓ VII,Ca ↓ ↓ Xa ← X

Xa
↓
↓ V, Ca, P
Prothrombin (II) → Thrombin (IIa)
↓
Fibrinogen (I) → Fibrin (soluble)
↓ XIII, Ca
insoluble fibrin

Coagulation

- **Both pathway are needed for normal haemostasis**
- **Both pathways are activated when blood come in contact with tissues outside blood vessel**
- **Thrombin is important factor in both**
- **Extrinsic pathway is faster (15 sec) while intrinsic may take up to 1-6 min**

Thrombin

- **Thrombin change fibrinogen to fibrin**
- **Thrombin is essential in platelet morphological changes to form primary plug**
- **Thrombin stimulate platelet to release ADP & thromboxaneA2 bothe stimulate further platelets aggregation**
- **Activate factor V**

BLOOD PHYSIOLGY

FIBRINOLYSIS

Fibrinolysis

- **Formed blood clot can either become fibrous or dissolve**
- **Fibrinolysis (dissolving) = Break down of fibrin by naturally occurring enzyme plasmin therfore prevent intravascular blocking**
- **There is balance between clotting and fibrinolysis**
  - **Excess clotting → blocking of Blood Vessels**
  - **Excess fibrinolysis → tendency for bleeding**

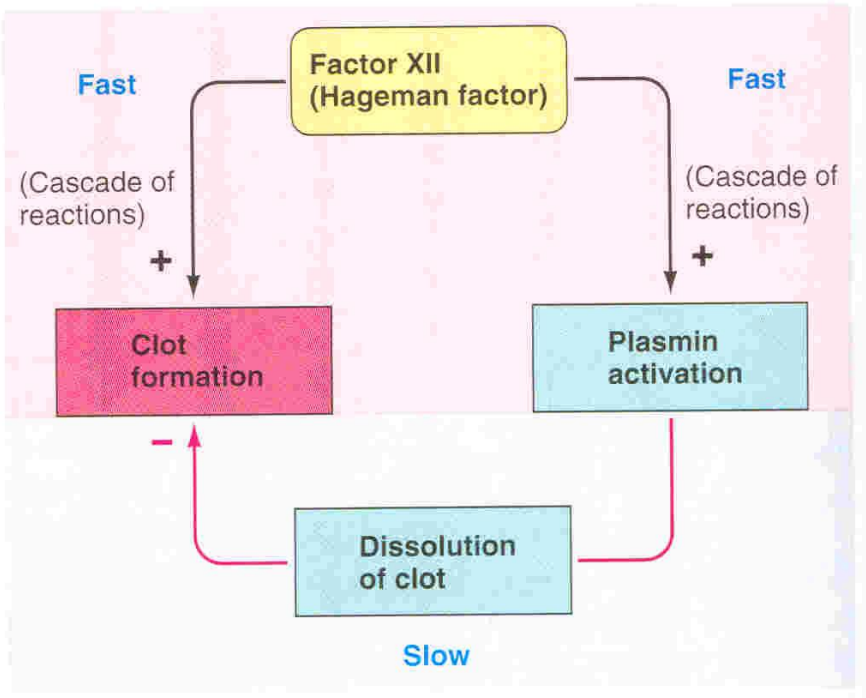
Plasmin

- **Plasmin is present in the blood in inactive form plasminogen**
- **Plasmin is activated by tissue plasminogen activators (t-PA) in blood.**
- **Plasmin digest intra & extra vascular deposit of Fibrin → fibrin degradation products (FDP)**
- **Unwanted effect of plasmin is the digestion of clotting factors**

Plasmin

- **Plasmin is controlled by:**
  - **Tissue Plasminogen Activator Inhibitor (TPAI)**
  - **Antiplasmin from the liver**
- **Uses:**
  - **Tissue Plasminogen Activator (TPA) used to activate plasminogen to dissolve coronary clots**

Coagulation balance



Objectives

At the end of this lecture student should be able to:

1. **Describe formation and development of platelet**
2. **Recognoize different stages of haemostasis**
3. **Describe the role of platelets in haemostasis.**
4. **Recognize different clotting factors**
5. **Describe the cascade of clotting .**

Objectives

At the end of this lecture student should be able to:

5. **Describe the cascade of intrinsic pathway.**
6. **Describe the cascade of extrinsic and common pathway.**
7. **Recognize the role of thrombin in coagulation**
8. **Recognize process of fibrinolysis and plasmin**