Hemostasis
Lecture 19

HEMOSTASIS: Cessation of Bleeding

- Hemo = “Blood” ; stasis = “standing”

3 major steps in Hemostasis:

1. **Vasoconstriction**: Decrease downstream blood flow and subsequent blood loss
2. **Platelet plug**: Form temporary seal over vessel opening
3. **Coagulation**: “Fibrin Web” secures platelet plug

How does blood clot?

Usually, every time you have a cut or bruise, your blood clots to stop the bleeding.
No vessel damage: **Endothelial cells secrete**

a. **Nitric Oxide** (EDRF)
   - Strong vasodilator

b. **Prostacyclin**:
   - Prevents Platelet aggregation

c. **Enzyme CD39**: Converts plasma ADP to AMP
   - Prevents Platelet activation

*NOTE: ADP promotes platelet aggregation*
Vessel Damage:

1. **Endothelial Cell damage:**
   a. Reduce Nitric Oxide secretion
   b. Release Endothelin (peptide) ➔ *Increased vasoconstriction*
   c. Reduce Prostacyclin: ➔ *Increased platelet “stickiness”*
   d. Less Active CD39: ➔ *Increased ADP; Platelet Activation*
   e. Secrete vonWillebrand Factor (vWF) ➔ *Bind Platelets and collagen*

2. **Exposes underlying collagen:**
   a. Platelets adhere to collagen & other platelets ➔ Aided by von Willebrand factor
      • GLYCOPROTEIN: Produced by endothelial & CT cells
      • Links platelets & collagen

   ➔ *Begin Platelet plug formation*
b. **Platelets Activated by binding vWF:**

- Activated platelets **Degranulate:**
  
  "Platelet release reaction"

- Secrete: **Prothrombins: promote clot formation**

Prothrombins: **ADP & Thromboxane A_2**

Promote:
1. Platelet cross linking
2. Platelet activation and platelet release Rxn

- Secrete:

  * Stimulate: **further platelet activation & binding**
Platelet Plug: Multi-layer platelet formation (thrombocyte)

“Positive Feedback Loop”

Platelet Plug Formation

HEMOSTASIS

1. Vessel Injury
2. Vascular Spasm
3. Formation of Platelet Plug
4. Coagulation
3. **Coagulation**: “Fibrin web” formation
   - Platelet plug reinforced and stabilized by Fibrin web
   - Clot formation
     - Soluble fibrinogen converted into insoluble Fibrin
     - Two Clotting Pathways
       1. Intrinsic
       2. Extrinsic

Coagulation Cascade
1. **Intrinsic Pathway**:  
   - Clot produced by blood constituents
   
a. **Initiation**: Vessel damage & exposure to negatively charge surface
   - Collagen proteins: Exposed connective tissue
   - **Contact Pathway**

b. **Factor XII**: Activated (XIIa) by collagen
c. **XIIa initiates a long cascade of plasma protein factor activation**
   - Result: Activates **Factor X**
   - Converts: Prothrombin to **active Thrombin**
   - Converts: **Soluble Fibrinogen into insoluble Fibrin**

2. **Extrinsic Pathway**: "Short-cut"
   - **Damaged tissue initiates pathway**
     a. **Tissue Thromboplastin (III):** Vessel wall glycoprotein
        - *Bypasses steps in intrinsic cascade*
        - *Activates: Factor X (Common step)*
     b. **Factor Xa** : Converts Prothrombin to Thrombin
c. **Thrombin**: Converts Fibrinogen to Fibrin
   - *Conversion to insoluble fibrin occurs more quickly*
### Anticoagulents: ANY Factor preventing Clot Formation

**Blood Thinners**

1. **Aspirin**: Inhibits prostaglandin production
   - Inhibit Thromboxane A₂: Inhibit platelet plug

   **Therapeutic**: Stroke, DVT (deep vein thrombosis)

   **BUT**: Prolongs Bleeding: Don’t use after surgery or last trimester of pregnancy

2. **EDTA**: Ethylenediaminetetraacetic Acid
   - Chelate (bind to) calcium

   Inhibit clotting cascade

3. **Heparin**: Activates Antithrombin III
Fibrinolysis: Clot breakdown

- **Plasmin**: *Fibrin digesting enzyme*
  - Converted from: inactive *Plasma plasminogen*
  - Activated by:
    1. Damaged endothelium factors
      - a. Tissue plasminogen Activator (t-PA)
      - b. Urokinase
    2. Activated clotting factors: aXII, aXI, Kallikrein

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Therapeutically: tPA & Urokinase

- “Clot Busters”: Catheter directed Thrombolysis
  - DVTs: Deep Vein Thrombosis
  - PE: Pulmonary Embolisms
  - MI: Myocardial infarct
  - Ischemic Stroke
  - IV Catheter restoration: 25% blocked by clots