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

No vessel damage: Endothelial cells secrete

a. Nitric Oxide (EDRF)

⇒

b. Prostacyclin:

⇒ Prevents:

- Expose underlying collagen:
  a. Platelets adhere to:

Vessel Damage:

1. Endothelial Cell damage:
   a1. Reduce Nitric Oxide secretion
   a2. Release Endothelin (peptide):

⇒ Increased:

b. Reduce Prostacyclin:

⇒ Increased:

- Expose underlying collagen:
  a. Platelets adhere to:
Aided by: von Willebrand factor

- Glycoprotein: produced by
- Links:

Begins:

b. Platelets Activated by binding vWF:

- Activated platelets:
  
  "Platelet release reaction"

- Secrete: Prothrombins: Promote:
  
  ADP, Thromboxane A₂

Promote:

1. Platelet:
2. Platelet activation and

Stimulate more:

Platelet Plug: Multi-layer:

"Positive Feedback Loop"

3. Coagulation: Fibrin web" formation

  - Platelet plug reinforced and stabilized by:

a. Soluble fibrinogen converted into:

  => Two Clotting Pathways; 1. Intrinsic & 2. Extrinsic

  1. Intrinsic Pathway:

    => Clot produced by:

    a. Initiation: Vessel damage & exposure to:

    * Collagen proteins:

    => Contact pathway

b. Factor XII activated (XIIa) by:

c. XIIa initiates a long cascade of plasma protein factor:

  => Result: Activates:
  
  => Converts: Prothrombin to active:

  => Converts: Soluble Fibrinogen into insoluble:
2. **Extrinsic Pathway**: “Short-cut”

   - Damages tissue:
     - a. Tissue Thromboplastin (III):
       * Bypasses steps in :
       * Activates:

     - b. Factor Xa: Converts Prothrombin to :

     - c. Thrombin: Converts Fibrinogen to

       * Conversion to *insoluble fibrin* occurs :

**Anticoagulents**: ANY Factor preventing :

   **“Blood Thinners”**

1. **Aspirin**: Inhibits prostaglandin production

   - Inhibit Thromboxane A₂: Inhibit :

     Therapeutic: Stroke, DVT (deep vein thrombosis)

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

2. **EDTA**: Ethylenediaminetetracetic Acid

   - Chelate (bind to) **calcium**

     Inhibit clotting cascade
3. **Heparin**: Activates Antithrombin III

**Fibrinolysis**: Clot breakdown:
- Activated Plasmin: *Fibrin* :
  - Activated from: Plasma plasminogen
  - Activated by:
    1. Damaged endothelium factors
      a. Tissue plasminogen Activator (t-PA)
      b. Urokinase
    3. Activated clotting factors: aXII, aXI, Kallikrein

**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

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**Study Questions**: 
1. Define hemostasis. What are the three main steps in hemostasis?
2. When vessels are not damaged, what helps prevent vasoconstriction and platelets aggregation (activation)?
3. What affect does endothelial damage have on vasoconstriction and platelet adherence and activation?
4. Initially what do the platelets start binding to during platelet plug formation?
5. What are the two pathways leading to a blood clot? What is the common step in both pathways? What is the last step in both pathways? And how does this help stop bleeding?
6. What are the major differences between the two pathways: which is shorter / quicker? which is mediated entirely with plasma constituents upon activation of collagen exposure? Which pathway utilizes vessel damage?
7. Do “blood thinners” actually thin the blood? What are blood thinners? What are some common anticoagulants and how do they function?
8. How are blood clots eventually removed once formed? Therapeutically How are tPA and urokinase used?