MLS 411 - Coagulation
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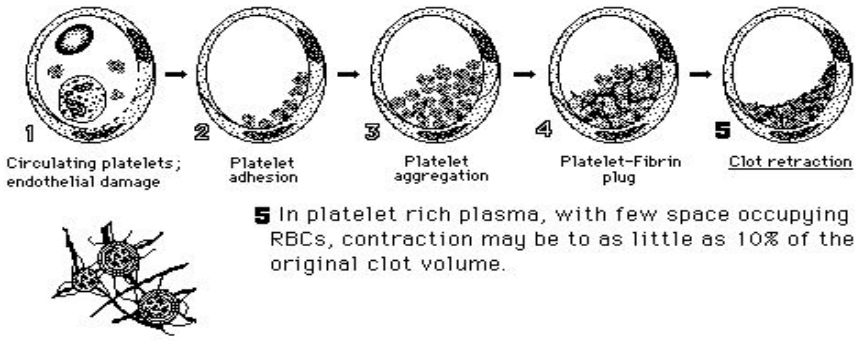
Notice: These notes are just a summary of the text. For detailed information please read the corresponding chapters!

Topic 1: Introduction to Hemostasis and Primary Hemostasis

- Hemostasis - Process of maintaining blood circulating throughout the body in a fluid state. Requires two processes.
  - Coagulation - clotting of blood - bodies response to cut.
  - Fibrinolysis - break down of clot - restores normal blood flow.
- Body maintains balance of coagulation and fibrinolysis. If tilt the scale toward coagulation, would bleed too much. If tilt the scale toward fibrinolysis, thrombosis - clot formed under abnormal conditions - would occur.
- Two major steps in the cessation of bleeding when tissue is injured.
  - Primary hemostasis - involves platelets and blood vessels, which stop the initial blood flow by forming loose plug at site of vessel breach.
  - Secondary hemostasis - involves circulating inactive enzymes, called coagulation factors, that stabilize the loose plug to form a permanent plug.



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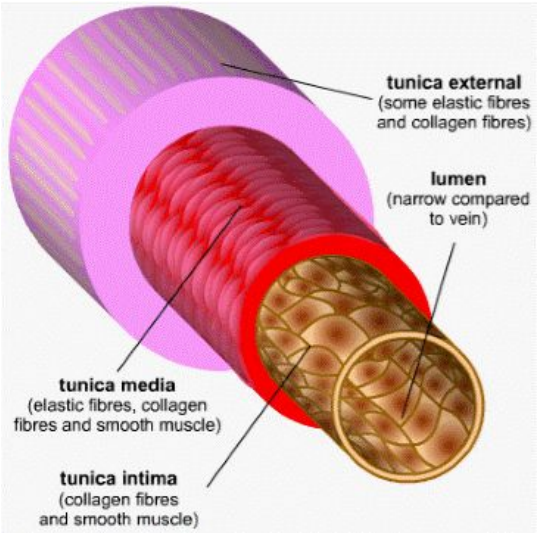
- Two major components of primary hemostasis:
  - Vascular System - blood vessels
    - Arterioles, venules, and capillaries - microvasculature - small vessels; primary site of hemostasis.
    - If have breach in large vessel such as femoral artery, blood flow is too much and blood pressure is too high for the body to stop bleeding.
  - Platelets - small disc-like structures found in blood.
- Structure of Blood Vessels
  - Walls of arteries and veins consist of three layers of tissue that vary in thickness and composition. Arteries, which carry blood away from the heart, are thicker than veins, which carry blood to the heart.



- Function of Blood Vessels in Hemostasis
  - First response of vessel upon injury is to constrict, narrow the lumen, and restrict blood flow to the area.
  - Vasoconstriction also brings blood vessel walls closer together, making it easier for hemostasis to occur.
  - Endothelial cells lining lumen of vessels are nonthrombogenic, meaning they do not trigger coagulation unless they are damaged. Platelets, which plug the vessel breach, do not adhere to a vessel wall unless it is damaged and exposes certain substances. This is the body's way of preventing clots from spontaneously occurring and blocking blood flow.
  - Once endothelial cells are damaged, they become thrombogenic, and are able to trigger platelet activation and initiate coagulation.

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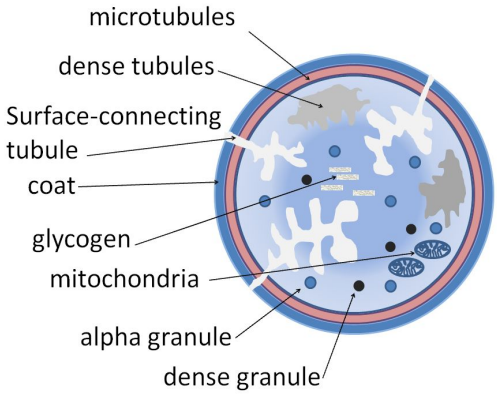
- Platelet Structure
  - Platelets are disc-shaped fragments of cytoplasm that circulate in the blood 7-10 days - as long as they are not used in the coagulation process. They circulate in a resting state, and repel one another due to a net negative surface charge.



  - Platelet ultrastructure is divided into four zones: peripheral, structural, organelle, and membrane system. Each section plays an important role in the platelets function.
  - The peripheral zone contains the membrane and glycocalyx.
    - Glycocalyx gives surface negative charge; consists of glycoproteins and other proteins
    - Membrane is a phospholipid bilayer. It contains receptors important in platelet adhesion to blood vessels and interaction with other platelets.
  - The structural zone contains microtubules and the cytoskeleton. They are involved in platelet shape change.
  - The organelle zone contains mitochondria (provides energy from glucose), alpha granules, dense granules, glycogen (source of glucose which platelet uses for energy), and lysosomes. Each granule has a specific function in platelet activation and coagulation.
    - Alpha - contains coagulation factors and Von Willebrand's Factor (vWF).
    - Dense - contains ATP and calcium.
  - The membrane system contains surface-connecting tubules that make up the open canalicular system - granule contents are released to the outside of the platelet through the OCS.

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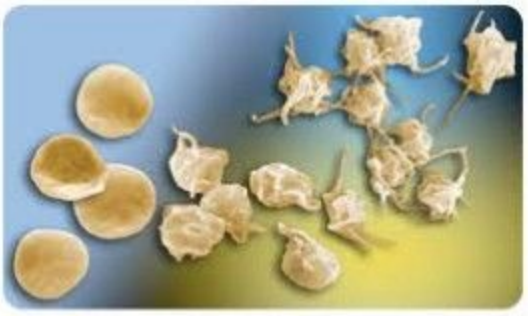
- Formation of the Primary Hemostatic Plug - Platelet Plug
  - Formation of platelet plug requires platelets to undergo *adhesion, shape change, secretion,* and *aggregation*.
  - *Adhesion* - the attachment of platelets to exposed collagen and subendothelium of injured blood vessel. Glycoprotein (GP) Ia/IIa and GPVI, which are on the platelet membrane, are responsible for the initial binding of platelets to the vessel. To strengthen adhesion, vWF acts as a bridge between collagen and the platelet surface receptor GP Ib/IX. Adhesion triggers shape change. Adhesion is also reversible.
  - *Shape Change* - activation of platelets causes them to change shape from a flattened disc to spiny spheres with long projections. This shape change gives the platelets a larger surface area for contact with other platelets and for secondary hemostasis to occur. The membrane surface receptors involved in aggregation are also exposed when the platelets change shape. If platelets do not receive a strong enough stimulus they revert to their disc shape and may release from the vessel wall.



Activated platelets show little cell feet called pseudopodia.

  - *Secretion* - aka platelet release reaction, is the discharge of platelet granule contents into the surrounding area.
  - *Aggregation* - the attachment of platelets to one another. As new platelets enter the site of vessel damage, ADP and thromboxane (TXA2) released from other activated platelets, activate more platelets. Fibrinogen serves as a bridge, cross-linking GPIIb/IIIa receptors on two adjacent platelets. Calcium (Ca++) is required for aggregation to occur. Like adhesion, aggregation is reversible, but only for 10-30 minutes.

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After that, it is irreversible. Granule contents release substances such as ADP and TXA2 that recruit more platelets. Secretion also causes the release of serotonin, which promotes vessel healing. Ca++, vWF, and factor V of the coagulation cascade are also released. Platelets not only initially stop the bleeding, but they aid in secondary hemostasis as well. Aggregation has two phases, primary and secondary. Secondary aggregation occurs after secretion. If secretion does not occur primary aggregation is reversible, and the platelet plug could break loose.

- The platelets eventually form a barrier - the primary hemostatic plug - that seals the vessel breach and prevents further blood loss. The primary plug is just a bandaid. Without secondary hemostasis it could be pulled off and bleeding would resume.

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