HEMOSTASIS (INCLUDING BLOOD CLOTTING)

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Mareib, p. 592-597, Martini, pp. 667-676, Martini’s 5th: 645-650, Martini’s 6th: 672-677, 8th: 672-677, 10th: 674-680

HEMOSTASIS: prevent loss of blood from break in vascular wall. Three mechanisms:

1) VASOCONSTRICTION (vascular phase of hemostasis) (vascular spasm) is first response, due in part to local trauma. Endothelin released, stimulate vascular smooth muscle contraction. Does not work well with clean cut. (p 676)

2) PLATELET PLUG: (p 676)
Ruptured endothelium exposes collagen
collagen causes platelets to swell, become spiked, sticky (aggregation) to each other in exposed area,
Bound platelets release thromboxane (similar to prostaglandins synthesized by cyclooxygenase)
Platelets then react by releasing a battery of compounds (a process called degranulation):
thromboxane (a prostaglandin) stimulates further aggregation and vascular spasms (aspirin inhibits)
serotonin enhancing vascular spasm
ADP causes platelet aggregation
Ca++ enhances clotting
Platelets join in positive feedback process, form a platelet plug

3) COAGULATION: (p 677) in outline, three stages. Extrinsic and intrinsic factors make factor X, first in common pathway:

A) COMMON PATHWAY (in blue on p 677)
1 factor X catalyzes formation of thromboplastin (prothrombinase or prothrombin activator). Catalyzes:
2 prothrombin converted to thrombin Catalyzes:
3 fibrinogen converted to fibrin Fibrin is stabilized by fibrin stabilizing factor (XIII)

Balance of procoagulants (I through XIII, p 678) and anticoagulants prevents unwanted clotting:
Most procoagulants are proteins formed in liver

ACTIVATION OF PROTHROMBINASE: TWO PATHWAYS LEAD TO COMMON PATHWAY, both need Ca++

B) EXTRINSIC (factors released from injured tissue):
1) injured cells release tissue thromboplastin (Fctor III also called tissue factor)
2) Ca++ (factor IV) combines with thromboplastin, activates clotting factor VII
3) active tissue factor complex converts factor X to prothrombinase
C) INTRINSIC (factors found and activated in blood):
1) aggregated platelets release platelet factor
2) Ca++ (factor IV) combines, activates clotting factor
3) acts on VIII (hemophilic factor) and IX, which converts X to prothrombinase

ANTICOAGULANT, THERAPEUTIC AGENTS:
Aspirin inhibits thromboxane production (As well as other prostaglandins)
Dicoumarol Vit K analog, prevents prothrombin synthesis (example: warfarin, rat poison)
Heparin inhibits thrombin
Ca++ chelaters prevent formation of clotting complex (Example: EDTA, citrate)
Streptokinase (a fibrinase) dissolves clots

CONDITIONS:
Thrombosis a clot is formed, exists in the vessels
eMBOLUS clot plugs vessel
Infarct ("stuffed") death of heart tissue, due to lack of O2, nutrients, caused flaccid heart muscle