HEMOSTASIS (INCLUDING BLOOD CLOTTING)

rvsd 23Feb2016
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 inhhibits)
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**:

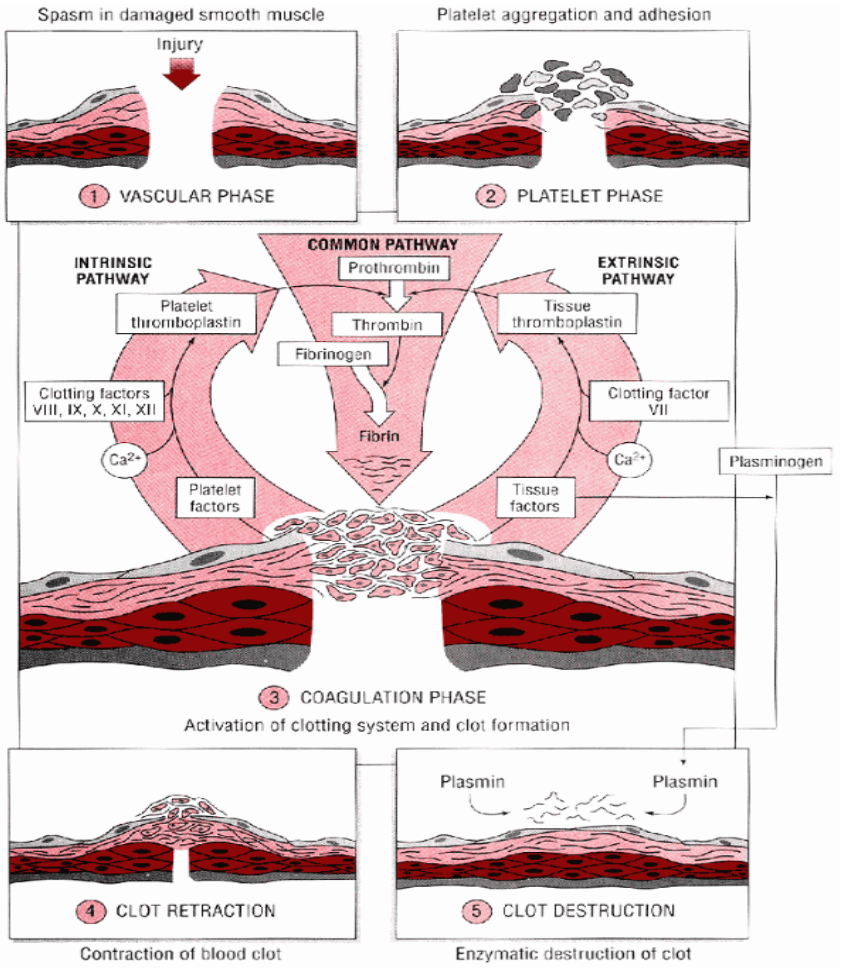
A) COMMON PATHWAY (in blue on p 677)
1 **factor X** catalyzes formation of **thromboplastin** (**prothrombinase or prothrombin activator)**. Catalyzes:
2 **prothrombin converted to thrombin** Catalyzes:
3 **fibrinogen converted to fibrin** Fibrin is stabilized by fibrin stabilizing factor (XIII)

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** (Fxctor III also called tissue factor)
2) Ca^{++} (factor IV) combines with thromboplastin, activates clotting factor VII
3) active tissue factor complex **converts faxctor 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 (hemophiliac 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 O_2, nutrients, caused flaccid heart muscle