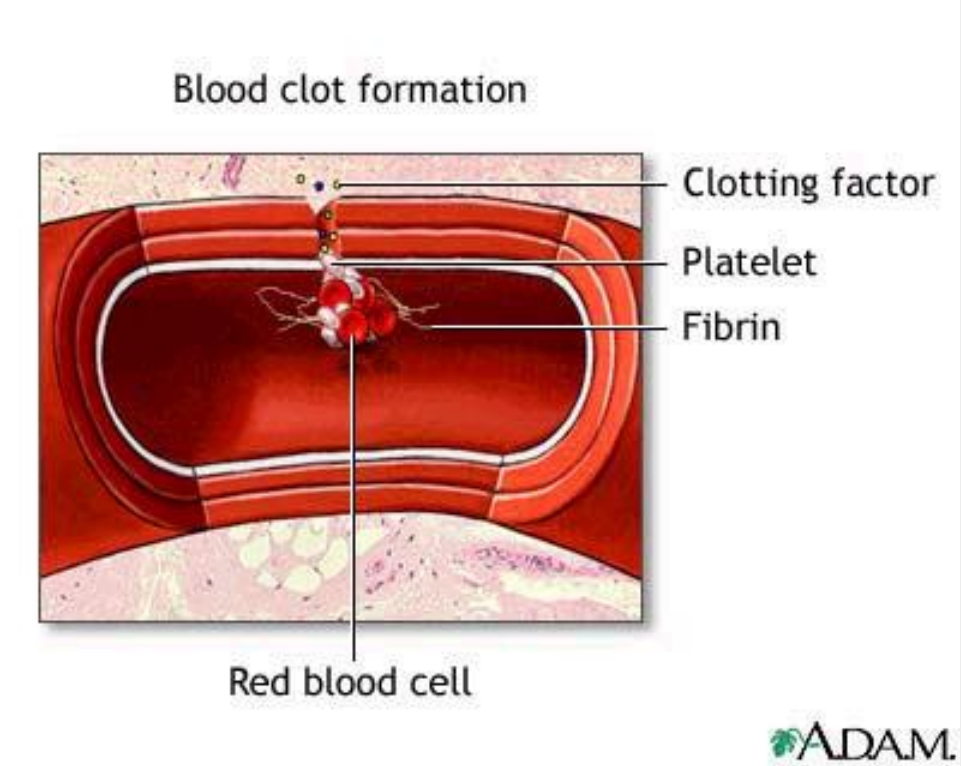
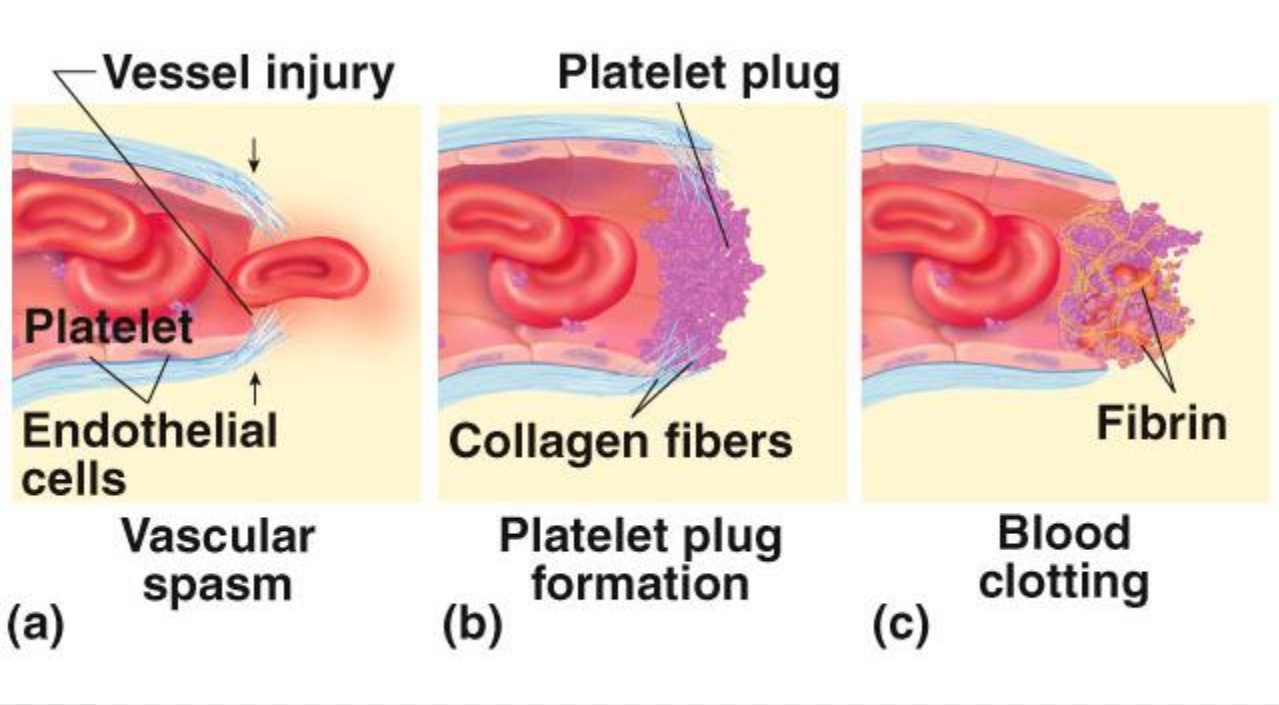
Hemostasis

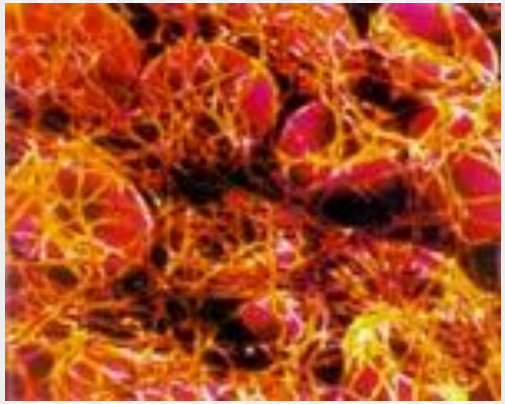

Blood clot formation
Clotting factor
Platelet
Fibrin
Red blood cell
A.D.A.M.

Hemostasis *(„hemo"=blood; sta=„remain")*

is the stoppage of bleeding, which is vitally important when blood vessels are damaged.

Following an injury to blood vessels several actions may help prevent blood loss, including:



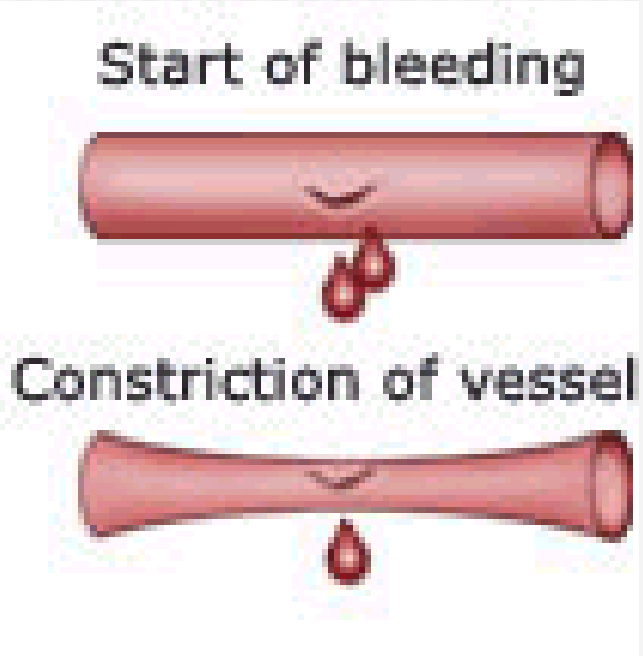


Formation of a clot

Hemostasis

STAGE I

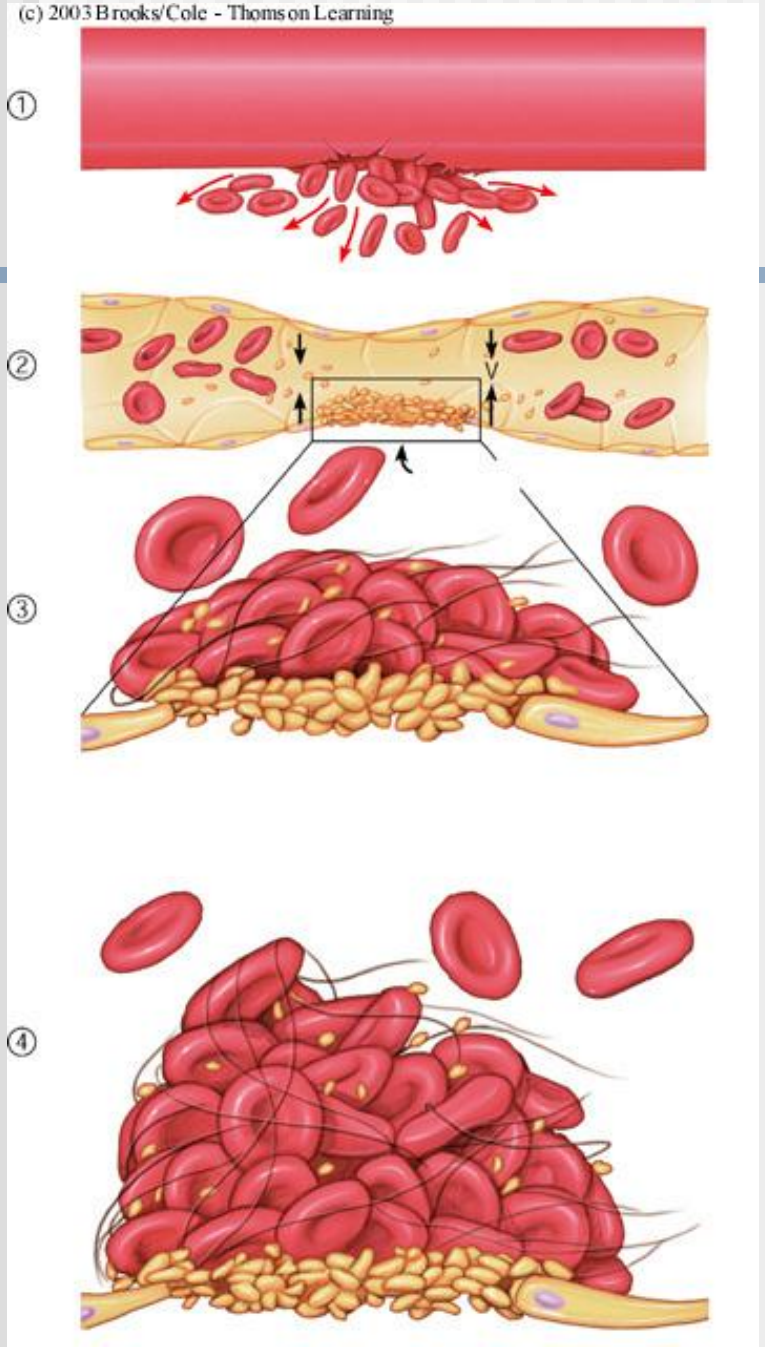
Local vasoconstriction



- is due to local spasm of the smooth muscle (symp. reflex)
- can be maintained by platelet vasoconstrictors

Hemostasis

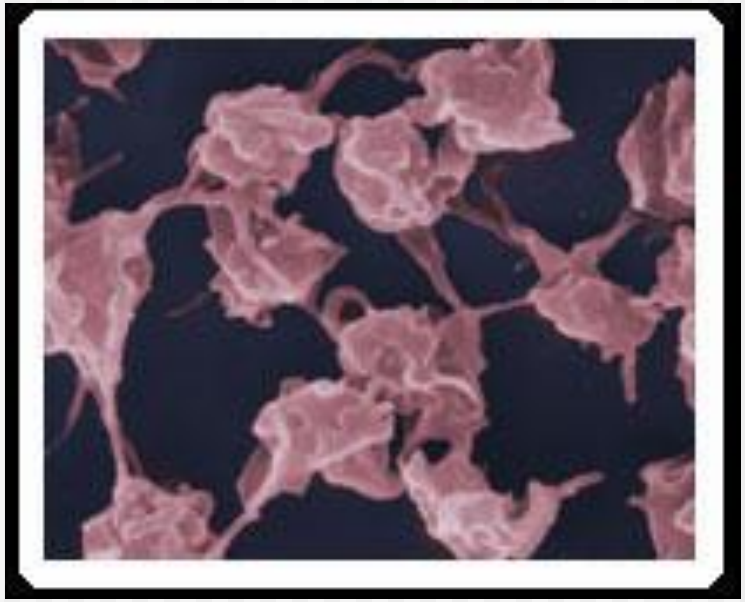
STAGE II

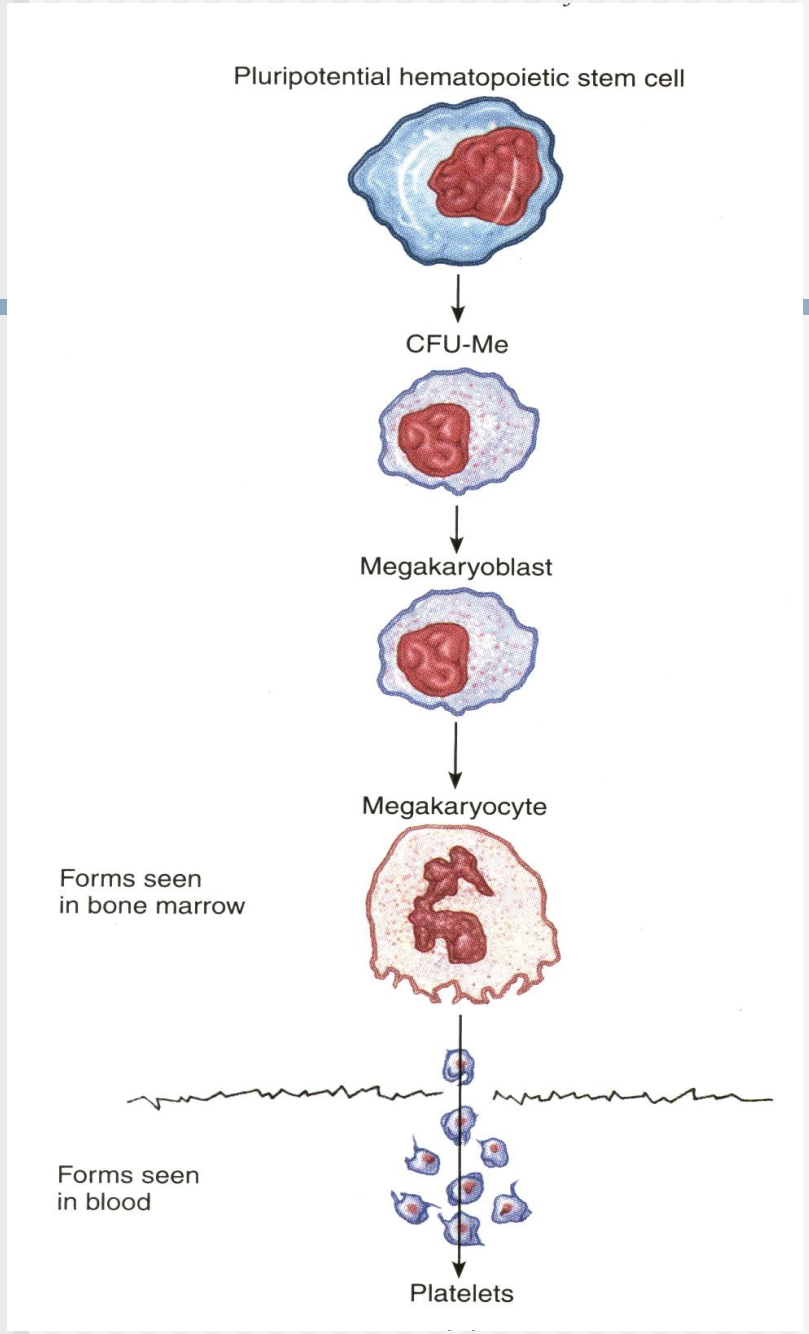


Formation of platelet aggregate

- Injured blood vessel releases ADP, which attracts platelets (PLT)
- PLT comming in contact with exposed collagen release: serotonin, ADP, TXA2, which accelerate vasoconstriction and causes PLT to swell and become more sticky

Platelets

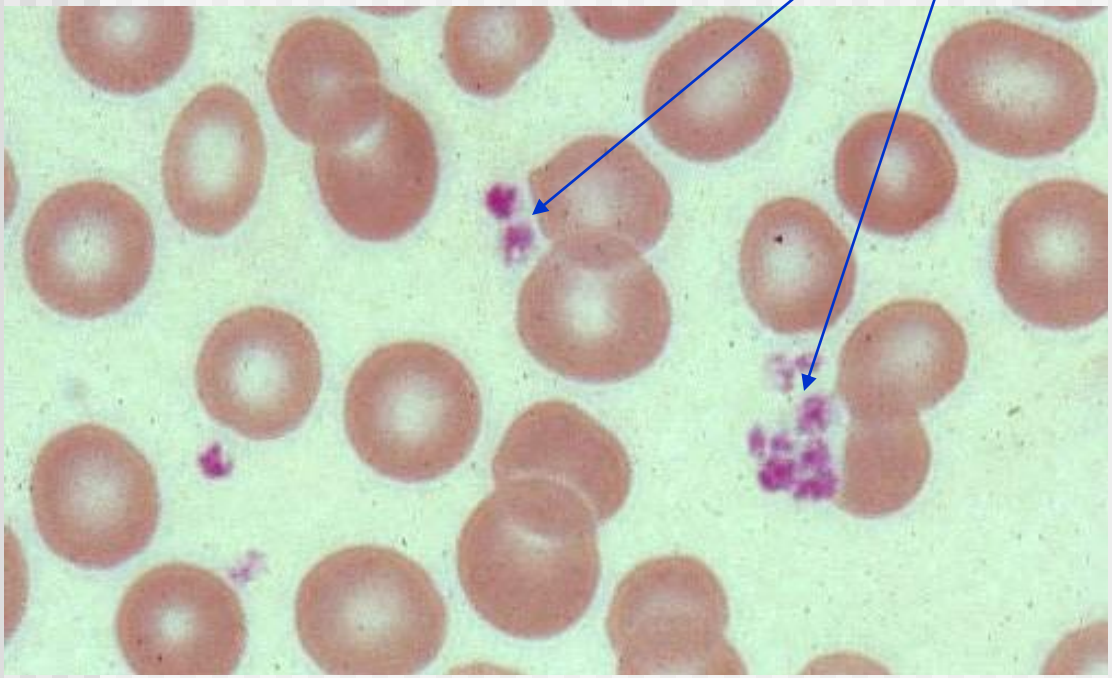


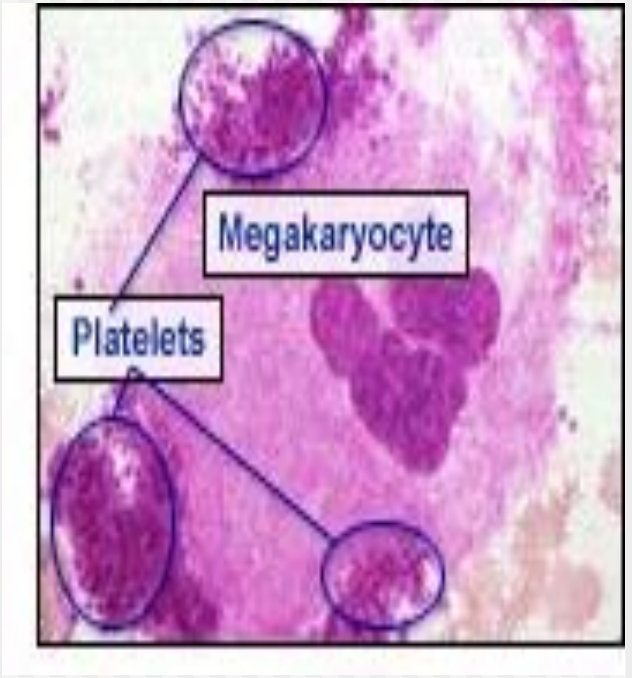


Platelets (thrombocytes)

- thrombocytes, are not true cells, but rather cytoplasmic fragments of a large cell in the bone marrow, the megakaryocyte
- blood normally contains 150,000 to 400,000 per microliter (μl) of platelets

The image shows a number of platelets stained purple associated with some RBC's.



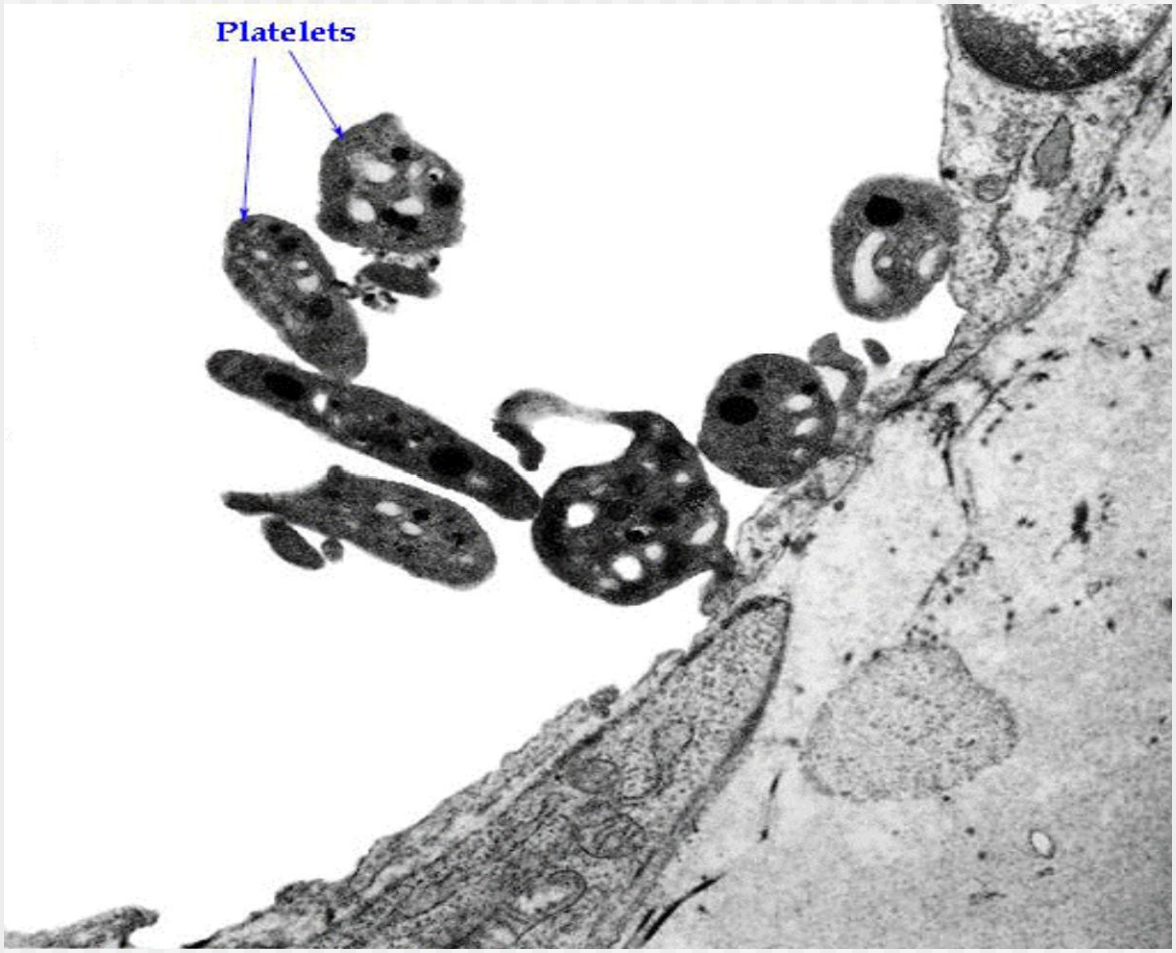


Platelets

- At any one time, about two-thirds of the body's platelets are circulating in the blood and one-third are pooled in the spleen.
- the life span of platelets is between

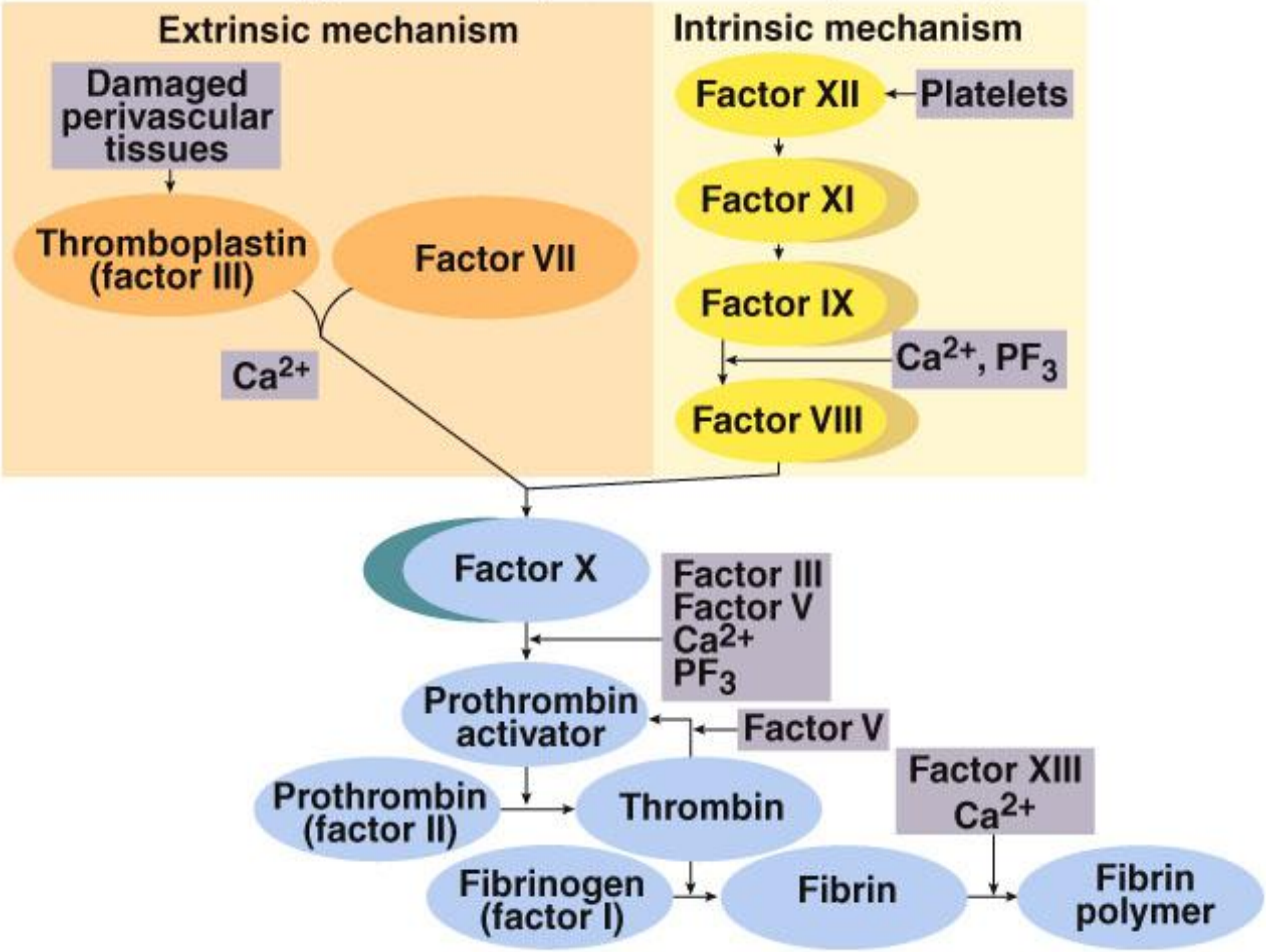
  1 and 2 weeks
- if not consumed in the process of blood clotting, they are destroyed by macrophages in the liver and spleen

The micrograph shows activated platelets adhering to some damaged cells



Hemostasis

STAGE III


Extrinsic mechanism
Damaged perivascular tissues
Thromboplastin (factor III)
Factor VII
Ca^{2+}
Intrinsic mechanism
Factor XII
Platelets
Factor XI
Factor IX
Ca^{2+}, PF_3
Factor VIII
Factor X
Factor III
Factor V
Ca^{2+}
PF_3
Prothrombin activator
Factor V
Prothrombin (factor II)
Thrombin
Factor XIII
Ca^{2+}
Fibrinogen (factor I)
Fibrin
Fibrin polymer

Calcium ions

- Are required for promotion and acceleration of almost all blood clotting reactions
- Except: activation of XII and XI (intrinsic mechanism)

Ca^{2+}

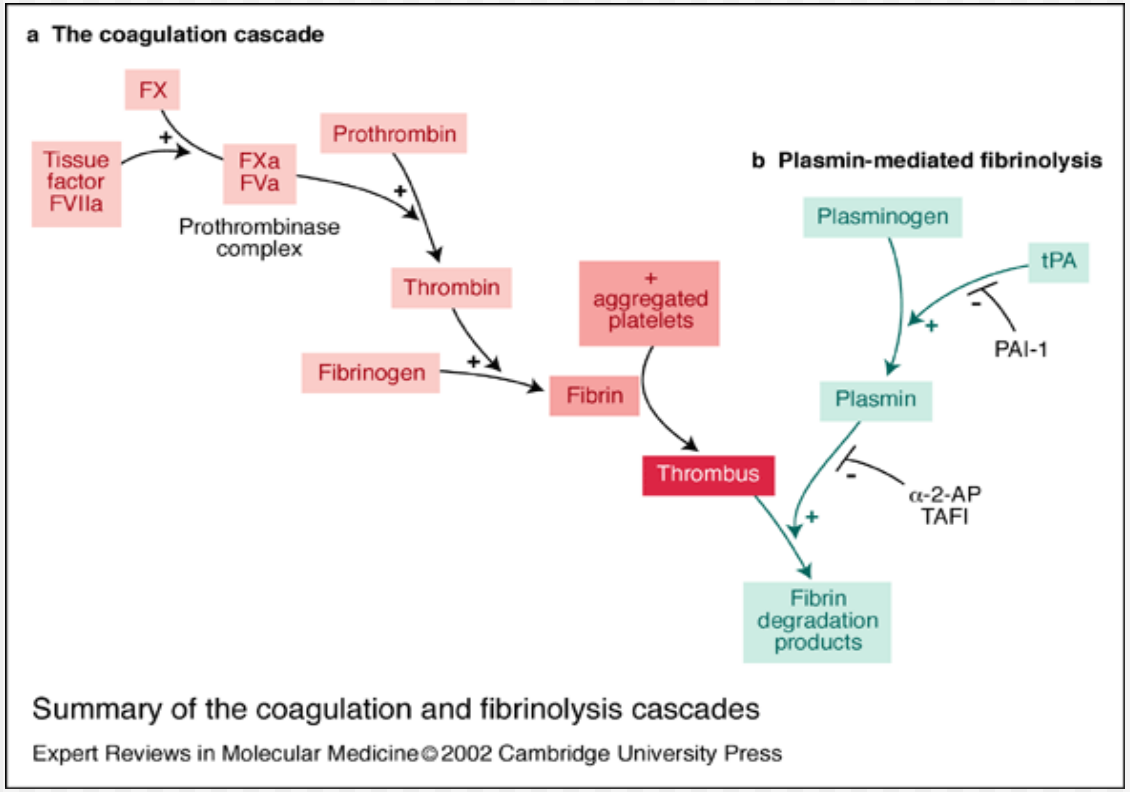
http://www.mhhe.com/biosci/esp/2002_general/Esp/folder_structure/tr/m1/s7/trm1s7_3.htm

Vitamin K

the "K" in Vitamin K came from the Danish word "koagulation"

- Vitamin K is a cofactor needed for the synthesis *(in the liver)* of:
  - factor **II** (prothrombin), **VII**, **IX**, and **X**
  - proteins ***C*** and ***S***
- **deficiency** of Vitamin K predisposes to bleeding.
- Conversely, blocking the action of vitamin K helps to prevent inappropriate clotting (eg. by *Warfarin*)

Fibrinolysis

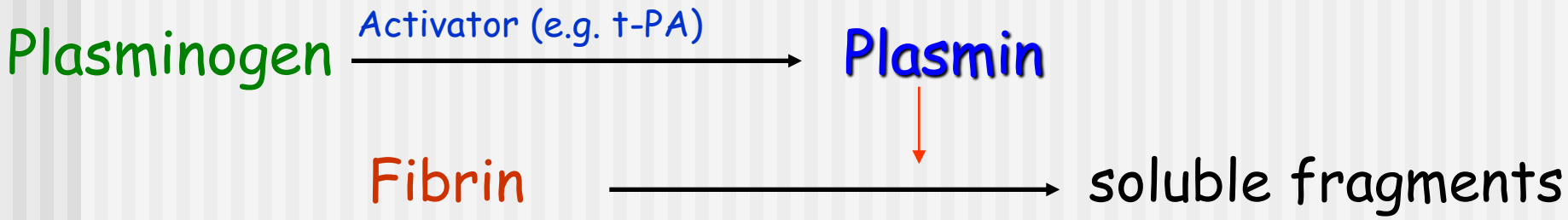


Summary of the coagulation and fibrinolysis cascades

Clot Dissolution

1. Plasmin is formed from plasminogen - enzyme called activator (e.g. enzymes from urine, tears, saliva or bacterial enzyme streptokinase)

2. Plasmin as an enzyme is involved in breaking down fibrin into soluble fragments (fibrinolysis)



Plasminogen may be produced by eosinophils

Anticoagulants

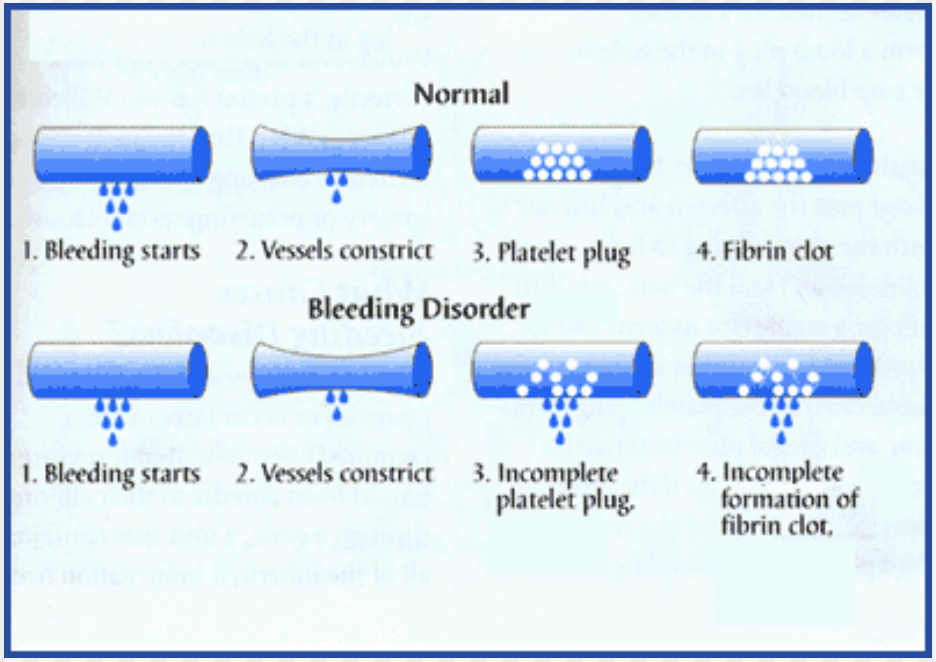
Hirudo medicinalis produce

Hirudin that inhibits Thrombin

Natural anticoagulants

- Antithrombin III – inhibits factor X and thrombin
- **Heparin from basophils and mast cells potentiates effects of antithrombin III (together they inhibit IX, X, XI, XII and thrombin)**
- Antithromboplastin (inhibits „tissue factors" – tissue thromboplastins)
- Protein C and S – activated by thrombin; degrade factor Va and VIIIa

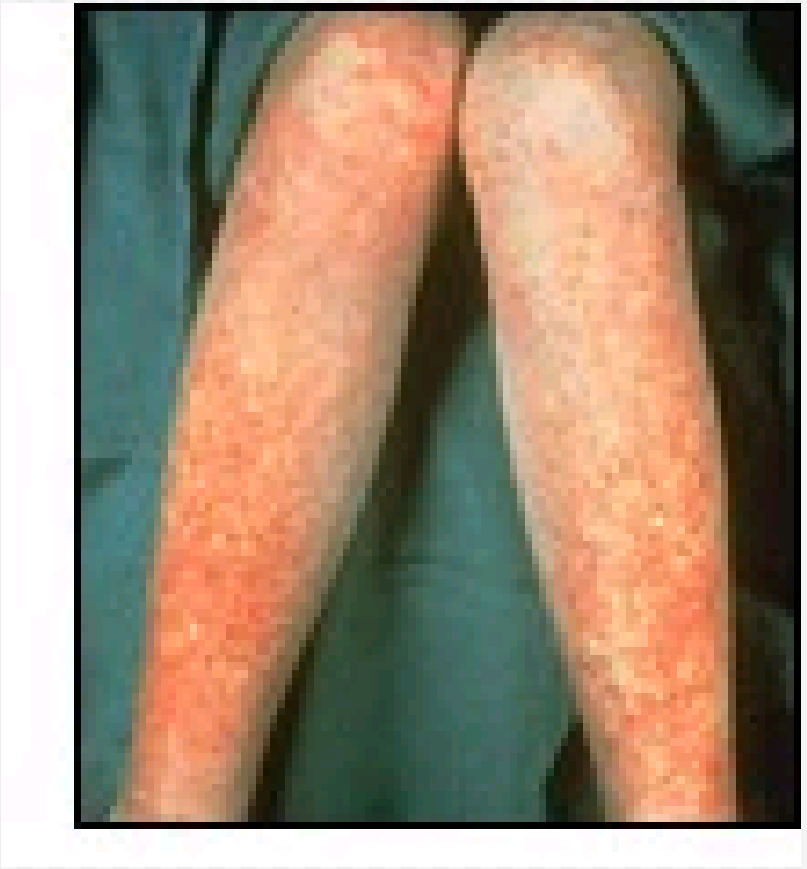
Abnormalities of hemostasis



Thrombocytopenia

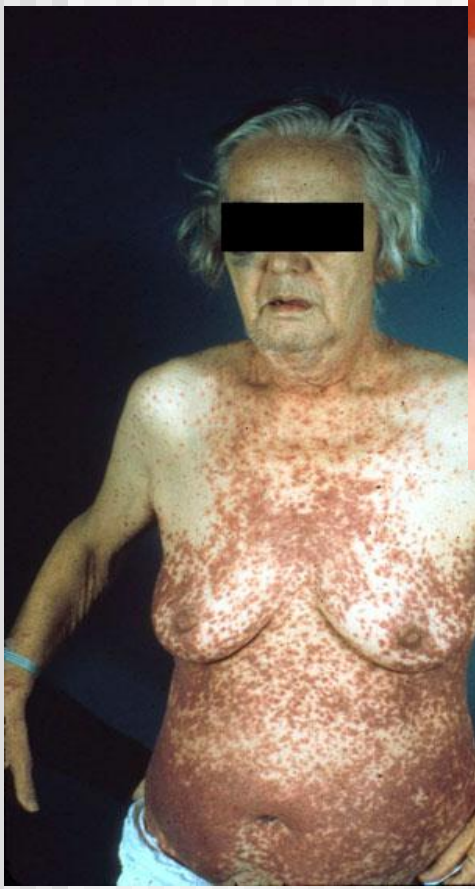
- Severe reduction in the number of PLTs - thrombocytopenia
- this causes spontaneous bleeding as a reaction to minor trauma
- in the skin - reddish-purple blotchy rash
- it may result from:

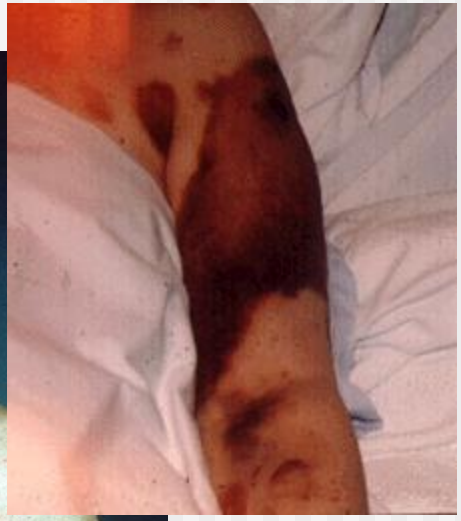
- decreased production (toxins, radiation, infection, leukemias)
- increased destruction (autoimmune processes)
- increased PLTs consumption (DIC)

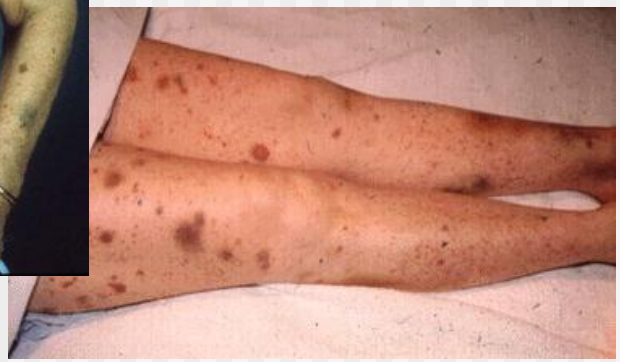


Hemorrhagic spots (petechiae)

Thrombocytopenia

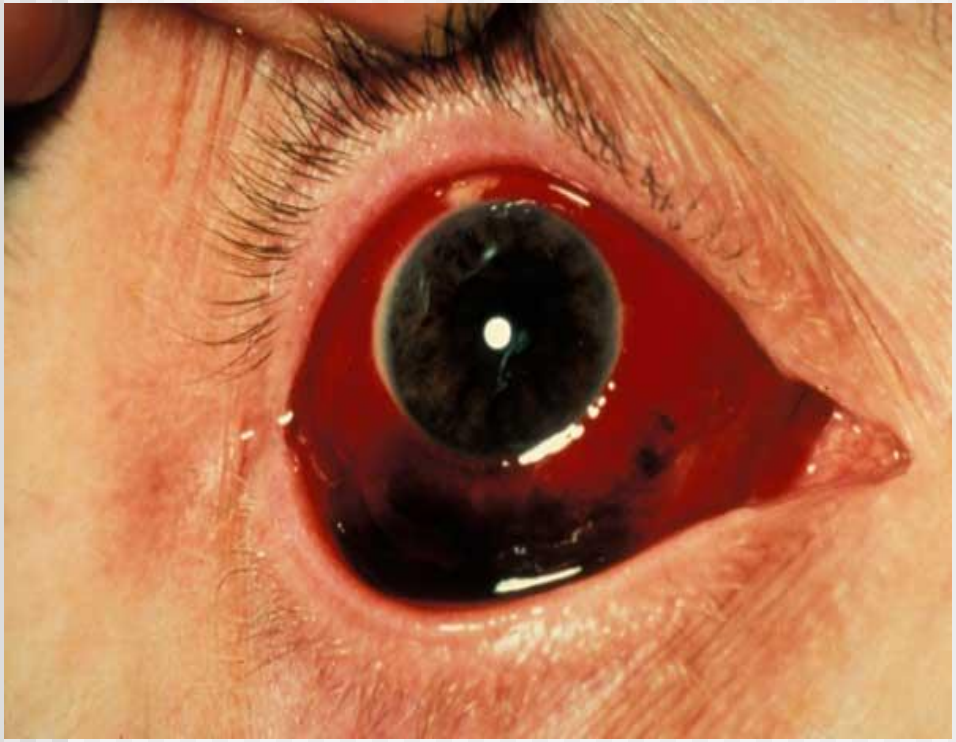






- Lethal when PLTs<10G/L
- Bleeding occurs when PLTs<50G/L
- Norm: 150-400G/L

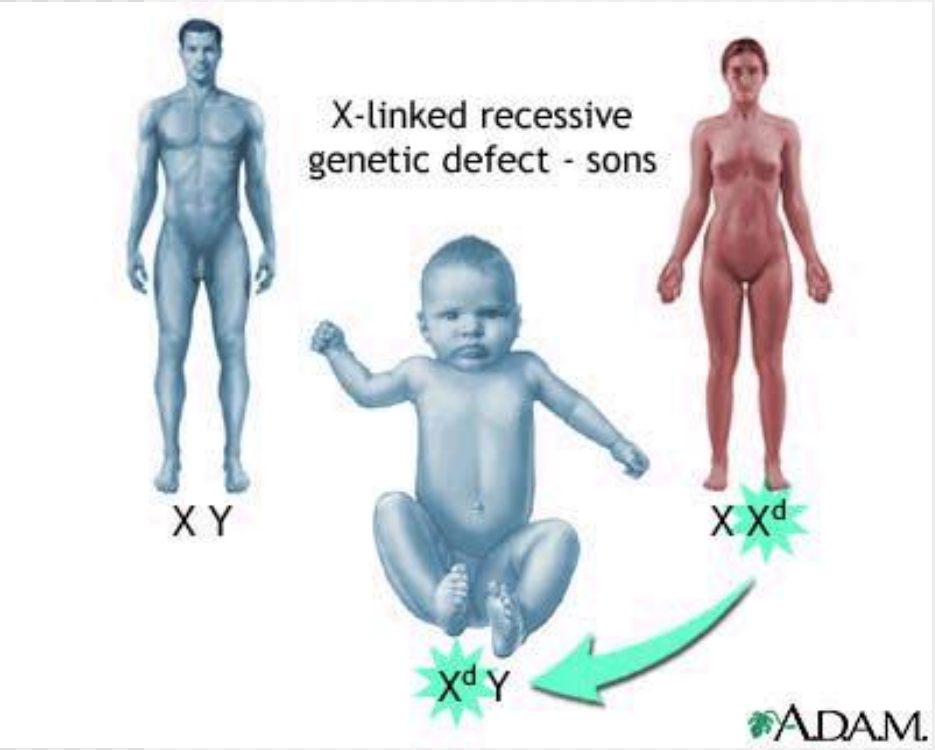
Hepatic failure

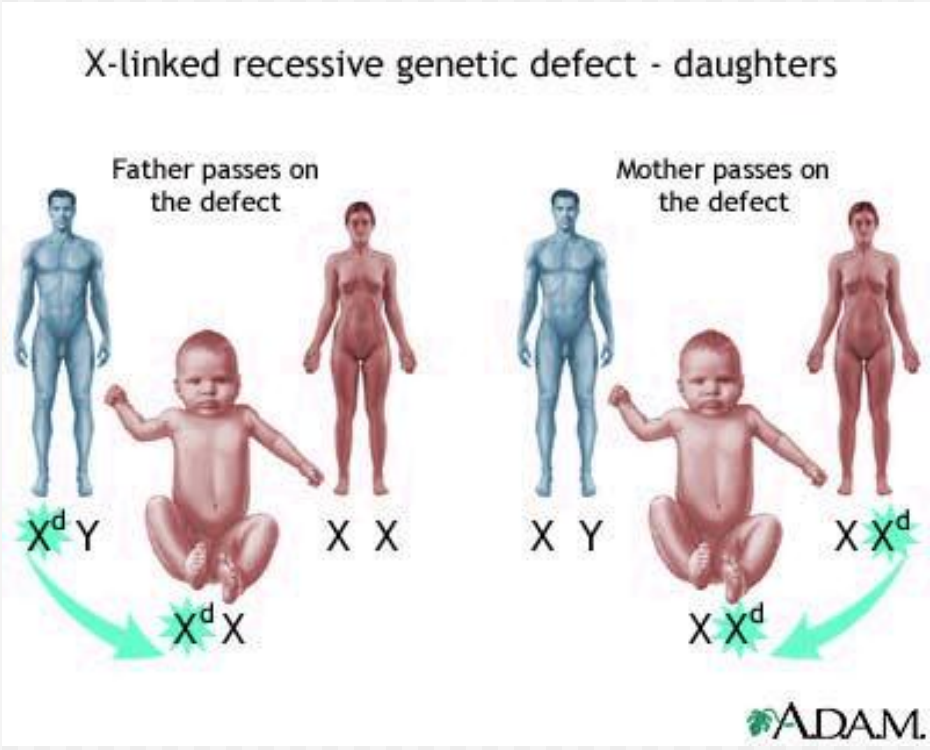


Subconjunctival hemorrhage

- Most of the clotting factors are formed in the liver

Hemophilia A (lack of F VIII) and B (lack of F IX) are transmitted genetically and affect only males. Females carry the gen but do not show symptoms.

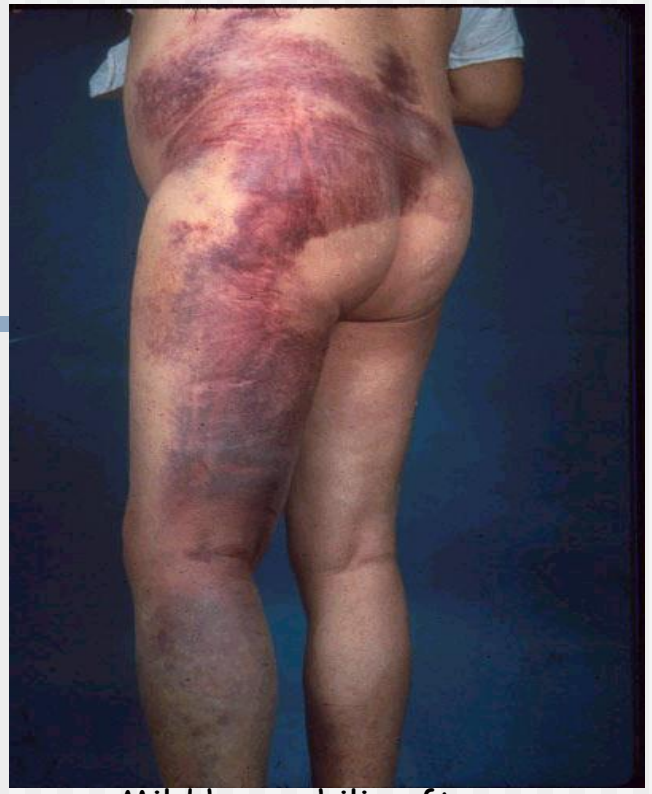




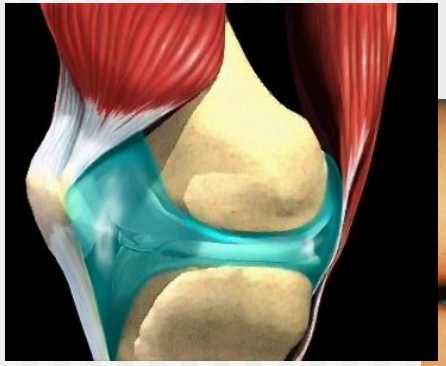
Von Willebrand's disease – loss of large component of fVIII

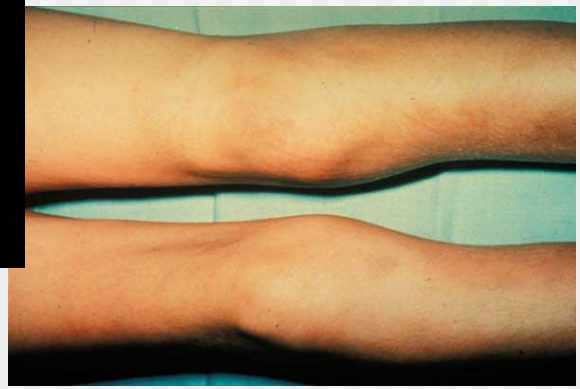
Hemophilia A (lack of F VIII; 85%)

- Spontaneous or traumatic subcutaneous bleeding
- Blood in the urine
- Bleeding in the mouth, lips, tongue
- Bleeding to the joints, CNS, gastrointestinal tract



Mild hemophilia after injection in buttock





Tests of coagulation

Selected causes of abnormal coagulation tests

Partial Thromboplastin Time (aPTT)	Prothrombin Time (PT)	Thrombin Time (TT)	Bleeding Time (BT)
Factor deficiency (except VII)	VII, X, V, II, fibrinogen deficiency	Low or absent fibrinogen	Thrombocytopenia
Antibodies to clotting factors	Antibodies	Dysfibrinogenemia, hypofibrinogenemia	Von Willebrand's disease
Heparin	Warfarin; Vit K defficiency (mild to severe)	Heparin	Drugs (Aspirin, NSAIDs, high dose penicillins, etc.)
Excessive Warfarin	Excessive Heparin		Cirrhosis, Uremia, PLTs dysfunction

International Normalised Ratio (INR)

- The result for the **PT** is expressed as a ratio (prothrombin clotting time for patient plasma divided by time for control plasma);
- Correction factor (International Sensitivity Index) is applied to the prothrombin ratio and the result issued as INR.
- **Therapeutic interval**: Therapeutic interval for oral anticoagulant therapy: 2.0-4.0.
- **Application**: Monitoring oral anticoagulant therapy (eg. Warfarin);
- note that heparin will not prolong INR *(heparinase is included within the INR reagent)!!!!!!!!!!!!*
  For heparin therapy we monitor aPTT and/or aPTT ratio

INR → oral anticoagulants

- Norm:INR about 1.0.

- **For patients on anticoagulants, the INR typically should be between 2.0 and 3.0**
- for patients with atrial fibrillation, or between 3.0
- for patients with mechanical heart valves = 4.0
- be individualized for each patient.
- An INR can be too high; a number
- greater than 4.0 - blood is clotting too slowly (a risk of uncontrolled bleeding)
- INR less than 2.0 may not provide adequate protection from clotting.

Bleeding time - procedure:

- Clean the earlobe with an alcohol
- Prick the earlobe with an automatic lancet
- Note the time when blood first appears on the skin
- After half a minute (30sec) place the edge of the filter paper on the top of the drop of blood.
- Perform the operation at half minute (30 sec) interval
- The end point or bleeding time is the first half minute when no blood is seen on the filter paper.