Constituents of Blood

Nutrients:
- O_2
- Glucose
- amino acids
- cholesterol
- vitamins
- triglycerides

Waste products:
- CO_2
- bilirubin
- urea

Ions:
- Na^+
- K^+
- Cl^-
- Ca^{++}
- Mg^{++}
- PO_3^-

Buffers:
- HCO_3^-

Red Blood Cells

Immune Cells and Factors

Hormones & Binding factors

Clotting Factors and Platelets

Disease Diagnostics:
- Liver markers
- cardiac markers
- tumor markers

Composition of Blood

Red Blood Cells

Biconcave discoids. Contain hemoglobin, which binds O_2 and helps transport CO_2. ***Red blood cells not have nuclei, so no DNA! (also no mitochondria)***

White Blood Cells

Immune system cells. Source of DNA for PCR fingerprinting studies using blood.

Platelets

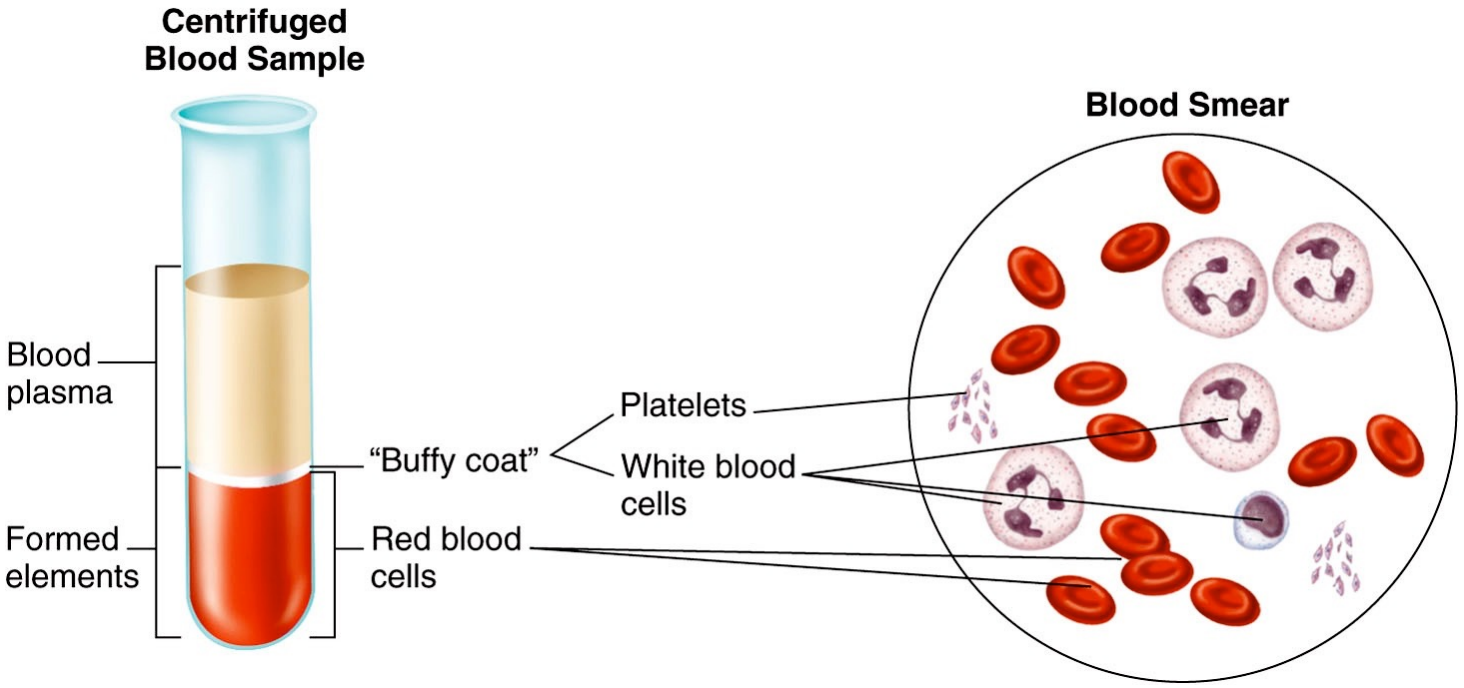
Very small fragments of cells which help in blood clotting.

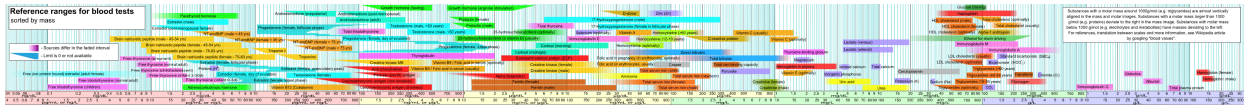
All derived from bone marrow stem cells.

Table 13.2 | Formed Elements of the Blood

Component	Description	Number Present	Function
Erythrocyte (red blood cell)	Biconcave disc without nucleus; contains hemoglobin; survives 100 to 120 days	4,000,000 to 6,000,000 / mm^3	Transports oxygen and carbon dioxide
Leukocytes (white blood cells)		5,000 to 10,000 / mm^3	Aid in defense against infections by microorganisms
Granulocytes	About twice the size of red blood cells; cytoplasmic granules present; survive 12 hours to 3 days		
1. Neutrophil	Nucleus with 2 to 5 lobes; cytoplasmic granules stain slightly pink	54% to 62% of white cells present	Phagocytic
2. Eosinophil	Nucleus bilobed; cytoplasmic granules stain red in eosin stain	1% to 3% of white cells present	Helps to detoxify foreign substances; secretes enzymes that dissolve clots; fights parasitic infections
3. Basophil	Nucleus lobed; cytoplasmic granules stain blue in hematoxylin stain	Less than 1% of white cells present	Releases anticoagulant heparin
Agranulocytes	Cytoplasmic granules not visible; survive 100 to 300 days (some much longer)		
1. Monocyte	2 to 3 times larger than red blood cell; nuclear shape varies from round to lobed	3% to 9% of white cells present	Phagocytic
2. Lymphocyte	Only slightly larger than red blood cell; nucleus nearly fits cell	25% to 33% of white cells present	Provides specific immune response (including antibodies)
Platelet (thrombocyte)	Cytoplasmic fragment; survives 5 to 9 days	130,000 to 400,000 / mm^3	Enables clotting; releases serotonin, which causes vasoconstriction

Figure 13.1


Centrifuged Blood Sample
Blood plasma
Formed elements
"Buffy coat"
Red blood cells
Platelets
White blood cells
Blood Smear


Reference ranges for blood tests
sorted by mass

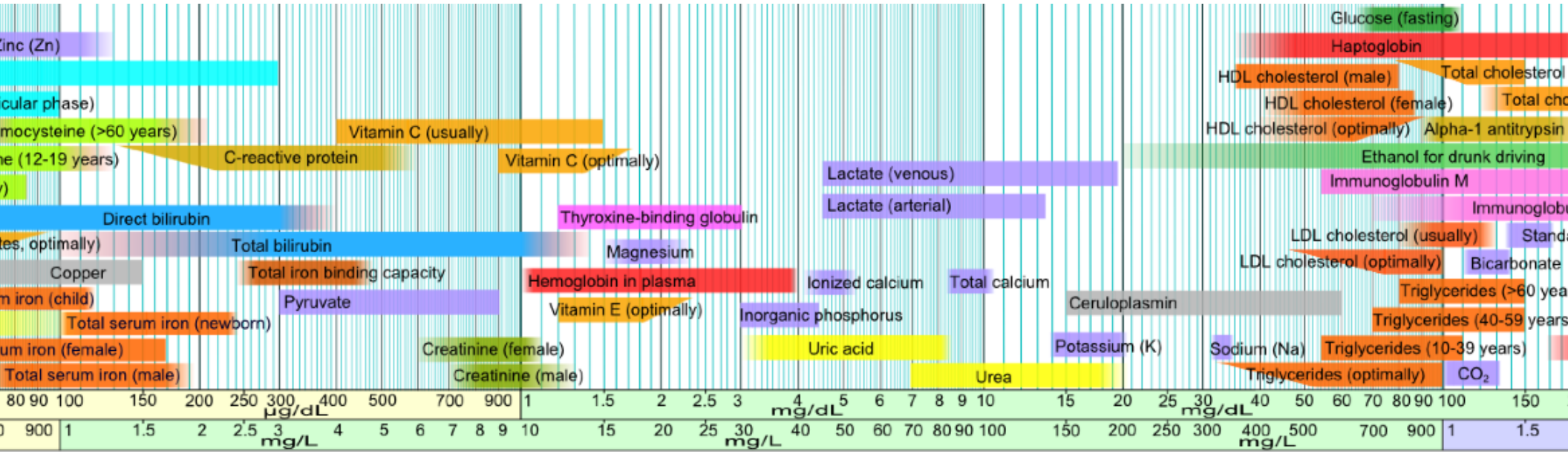

Glucose (fasting)
Haptoglobin
HDL cholesterol (male)
HDL cholesterol (female)
HDL cholesterol (optimally)
Alpha-1 antitrypsin
Ethanol for drunk driving
Immunoglobulin M
Lactate (venous)
Lactate (arterial)
Thyroxine-binding globulin
Vitamin C (usually)
C-reactive protein
Vitamin C (optimally)
Direct bilirubin
Total bilirubin
Magnesium
Copper
Total iron binding capacity
Hemoglobin in plasma
Ionized calcium
Total calcium
Pyruvate
Vitamin E (optimally)
Inorganic phosphorus
Ceruloplasmin
Total serum iron (newborn)
Creatinine (female)
Uric acid
Potassium (K)
Sodium (Na)
Total serum iron (male)
Creatinine (male)
Urea
Triglycerides (optimally)
LDL cholesterol (usually)
LDL cholesterol (optimally)
Bicarbonate
Triglycerides (>60 yea
Triglycerides (40-59 years
Triglycerides (10-39 years)
CO_2
μg/dL
mg/dL
mg/dL
mg/L
mg/L
mg/L

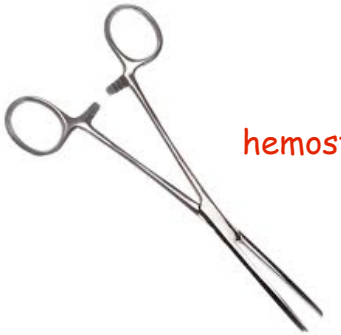
Table 13.1 | Representative Normal Plasma Values

Measurement	Normal Range
Blood volume	80–85 ml/kg body weight
Blood osmolality	285–295 mOsm
Blood pH	7.38–7.44
Enzymes	
Creatine phosphokinase (CPK)	Female: 10–79 U/L Male: 17–148 U/L
Lactic dehydrogenase (LDH)	45–90 U/L
Phosphatase (acid)	Female: 0.01–0.56 Sigma U/ml Male: 0.13–0.63 Sigma U/ml
Hematology Values	
Hematocrit	Female: 36%–46% Male: 41%–53%
Hemoglobin	Female: 12–16 g/100 ml Male: 13.5–17.5 g/100 ml
Red blood cell count	4.50–5.90 million/mm^3
White blood cell count	4,500–11,000/mm^3
Hormones	
Testosterone	Male: 270–1,070 ng/100 ml Female: 6–86 ng/100 ml
Adrenocorticotrophic hormone (ACTH)	6–76 pg/ml
Growth hormone	Children: over 10 ng/ml Adult male: below 5 ng/ml
Insulin	2–20 μU/ml (fasting)

http://en.wikipedia.org/wiki/Reference_ranges_for_blood_tests

Table 13.1

Blood Clotting (hemostasis)



Vasoconstriction, formation of platelet plug, fibrin web.

Intact blood vessel: Endothelial cells inhibit platelet aggregation by
1) physically separating platelets from collagen
2) secreting prostacyclin & nitric oxide (NO), & cause **vasodilation**
3) expressing CD39 enzyme which breaks down ADP in the blood

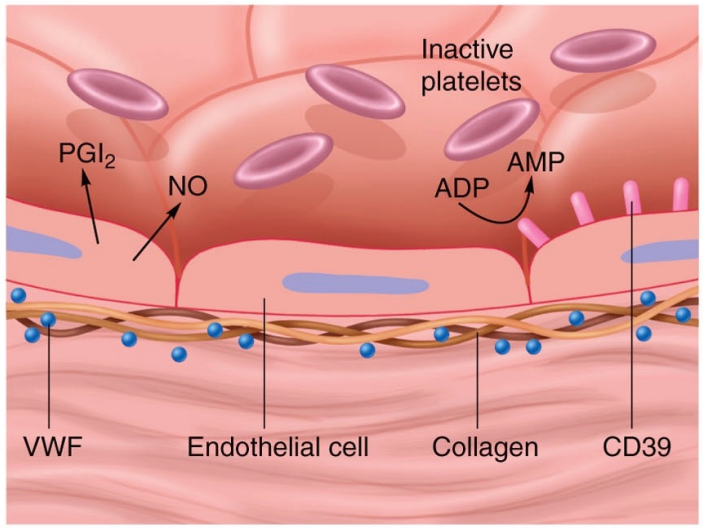
Damaged blood vessel:
1) Platelets bind to collagen and **von Willbrand's factor** (protein produced by endothelial cells that binds platelets and collagen together)

2) Platelets release secretory granules (platelet release reaction):
ADP & thromboxane A -> recruit more platelets to plug
serotonin causes **vasoconstriction** (aspirin inhibits prostaglandin production)

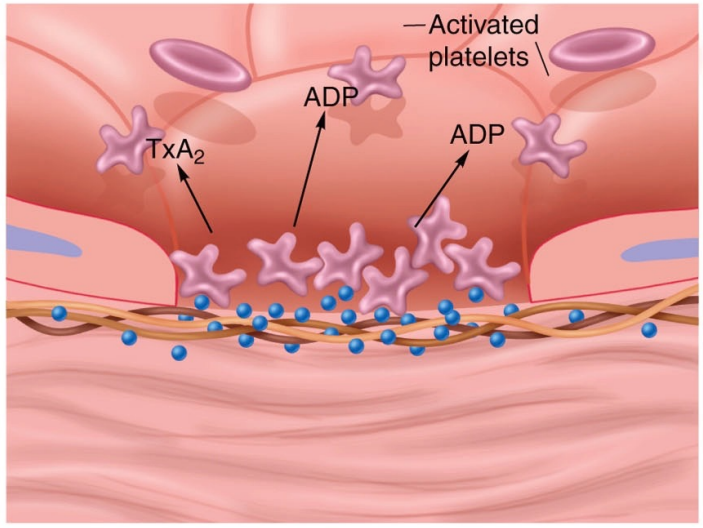
3) Platelets activate **plasma clotting factors**, converting soluble **fibrinogen** -> insoluble **fibrin** -> platelet plug.

hemo- related to blood
hemostasis- preventing blood loss (i.e. stop bleeding)
hemorrhage- bleeding

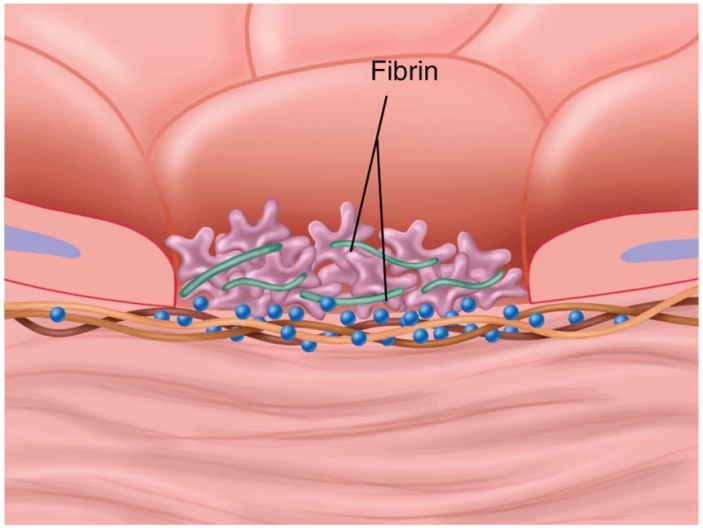
vasodilation- opening blood vessels wider
vasoconstriction - making blood vessels narrower



(a)



(b)

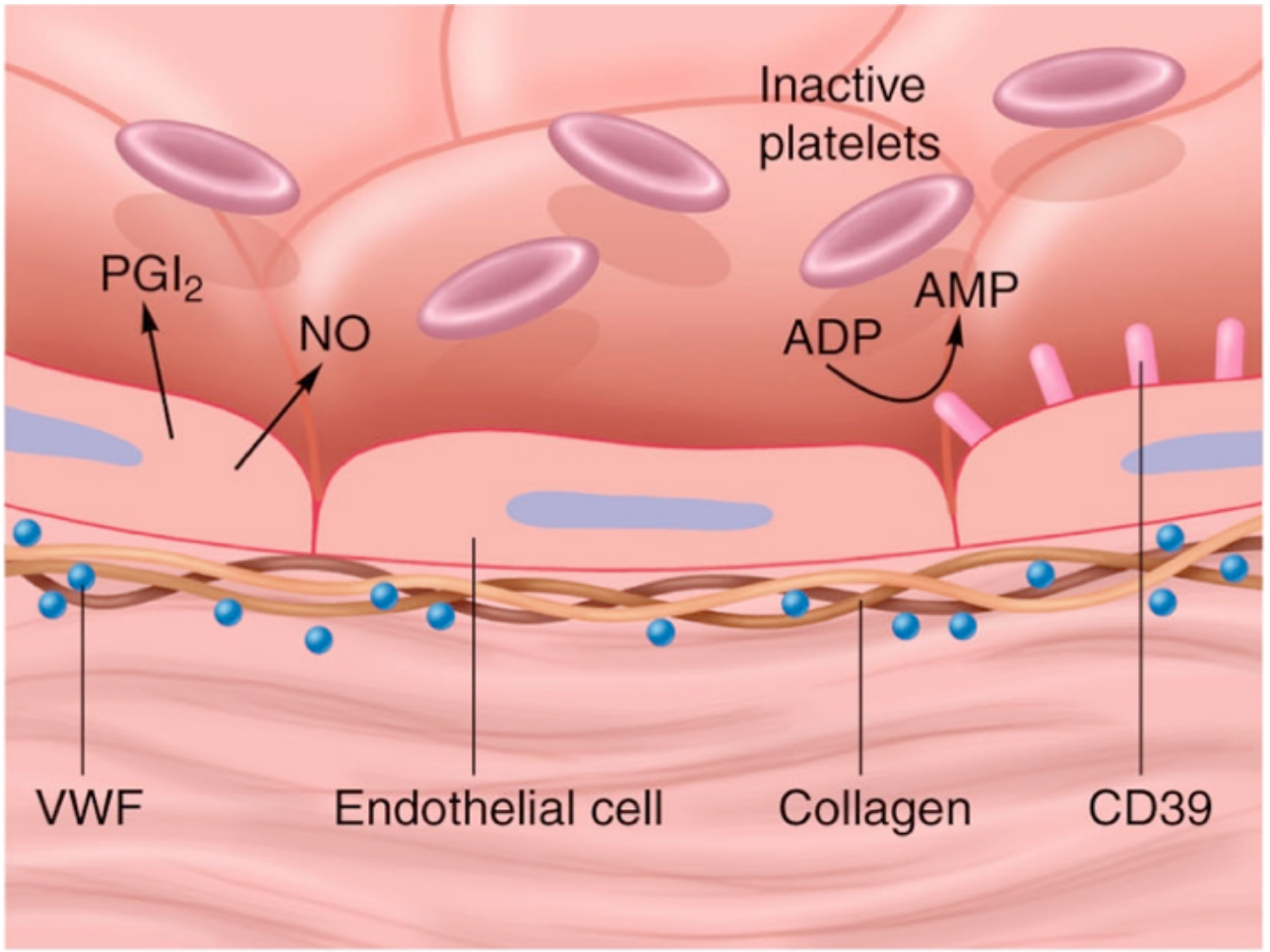


(c)

Figure 13.7

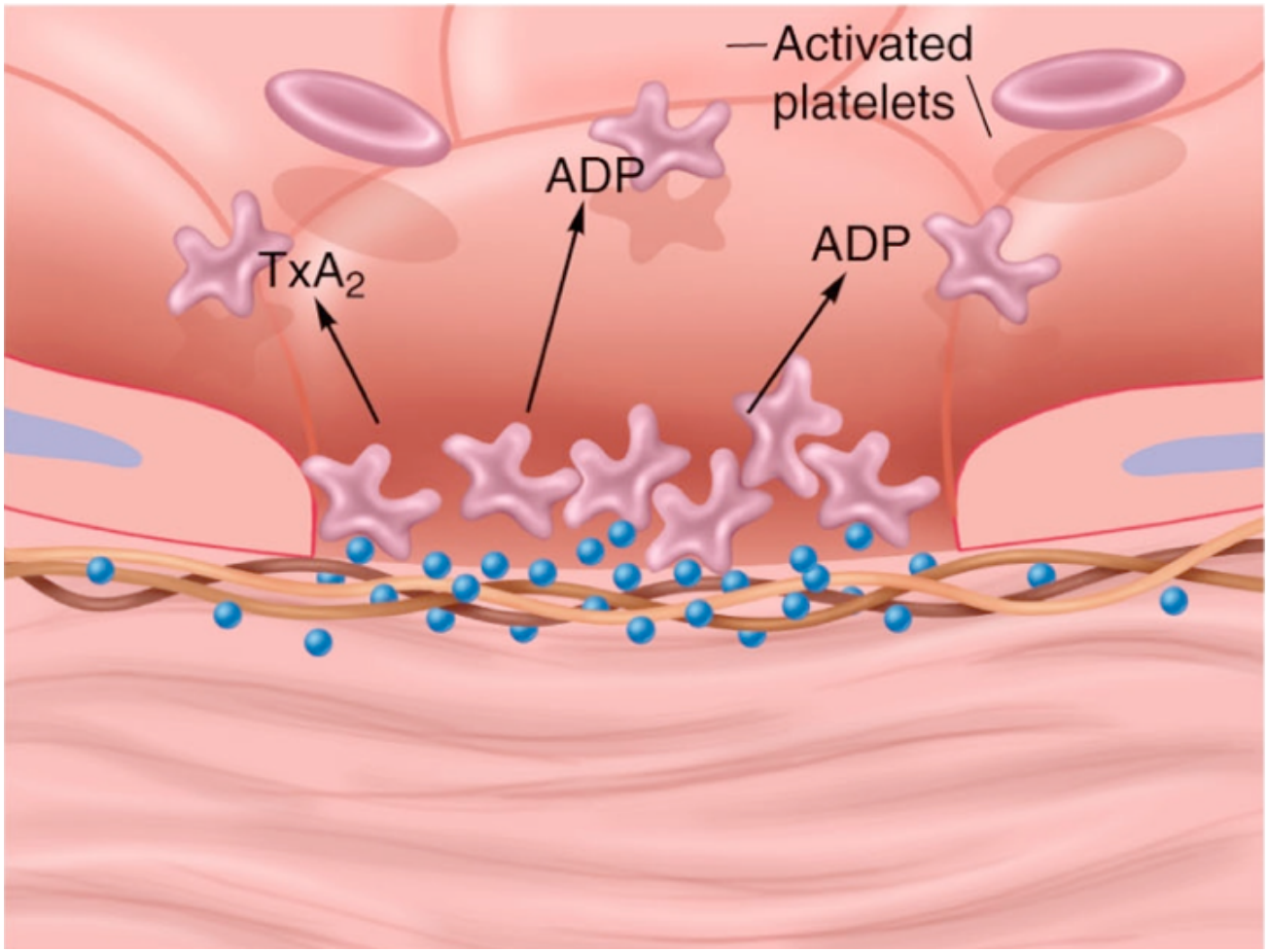
Intact Blood Vessel:

Prostaglandin & NO keep vessel dilated; ADP levels low, so platelets inactive



Damaged Blood Vessel:

Prostaglandin TxA2, high levels of ADP activate platelets.
Activated platelets bind to collagen and von Willebrand's factor



Clot Formation:

Platelet plug forms; activated plasma clotting factors causes fibrin formation to reinforce platelet plug

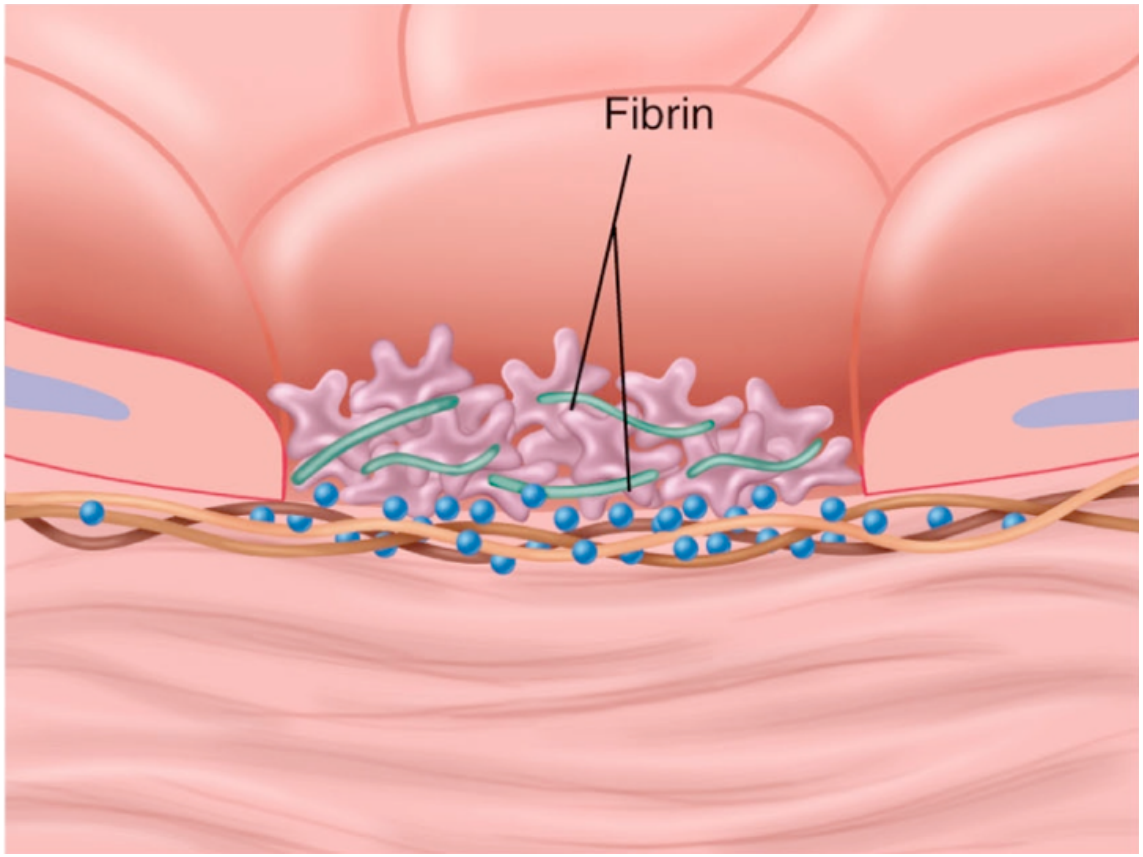
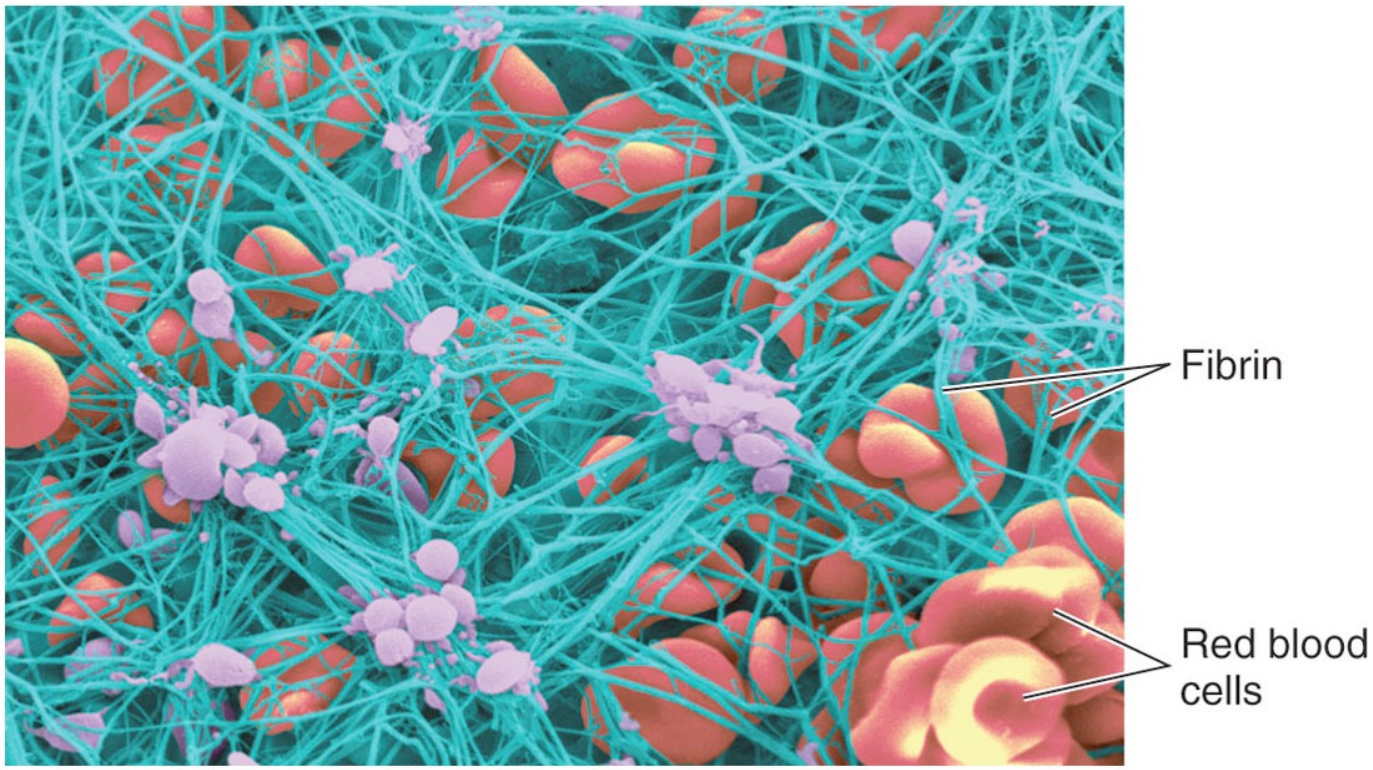


Figure 13.8



From Nature Volume 413, Issue 6855, 4 October 2001, cover. Photo by Dr. John W. Weisel, University of Pennsylvania

Clotting Factors & Fibrin Formation

Intrinsic Pathway: Blood will clot on its own, e.g. in a test tube

Extrinsic Pathway: Damaged tissue releases **tissue factor** that accelerates clotting

Key events of clotting:

Prothrombin converted into **thrombin**, an active enzyme (**thrombosis = clotting)**

Thrombin converts **fibrinogen** to **fibrin**, an insoluble fibrous molecule.

Vitamin K (*Koagulationsvitamin*) converts glutamate residues of clotting factors into gamma-carboxyglutamate, which increases binding of Ca++ to clotting factors. Provided by gut bacteria. Vitamin K deficiency or blockade by drugs leads to decreased clotting ability.

Clot Dissolution:
Factor XII activates Kallikrein (enzyme).
Kallikrein converts plasminogen into plasmin (enzyme).
Plasmin digests fibrin to dissolve clot.
Tissue plasminogen activator (TPA) & streptokinase are synthetic enzymes administered after stroke or cardiac **thrombosis** (vessel blocked by blood clot)

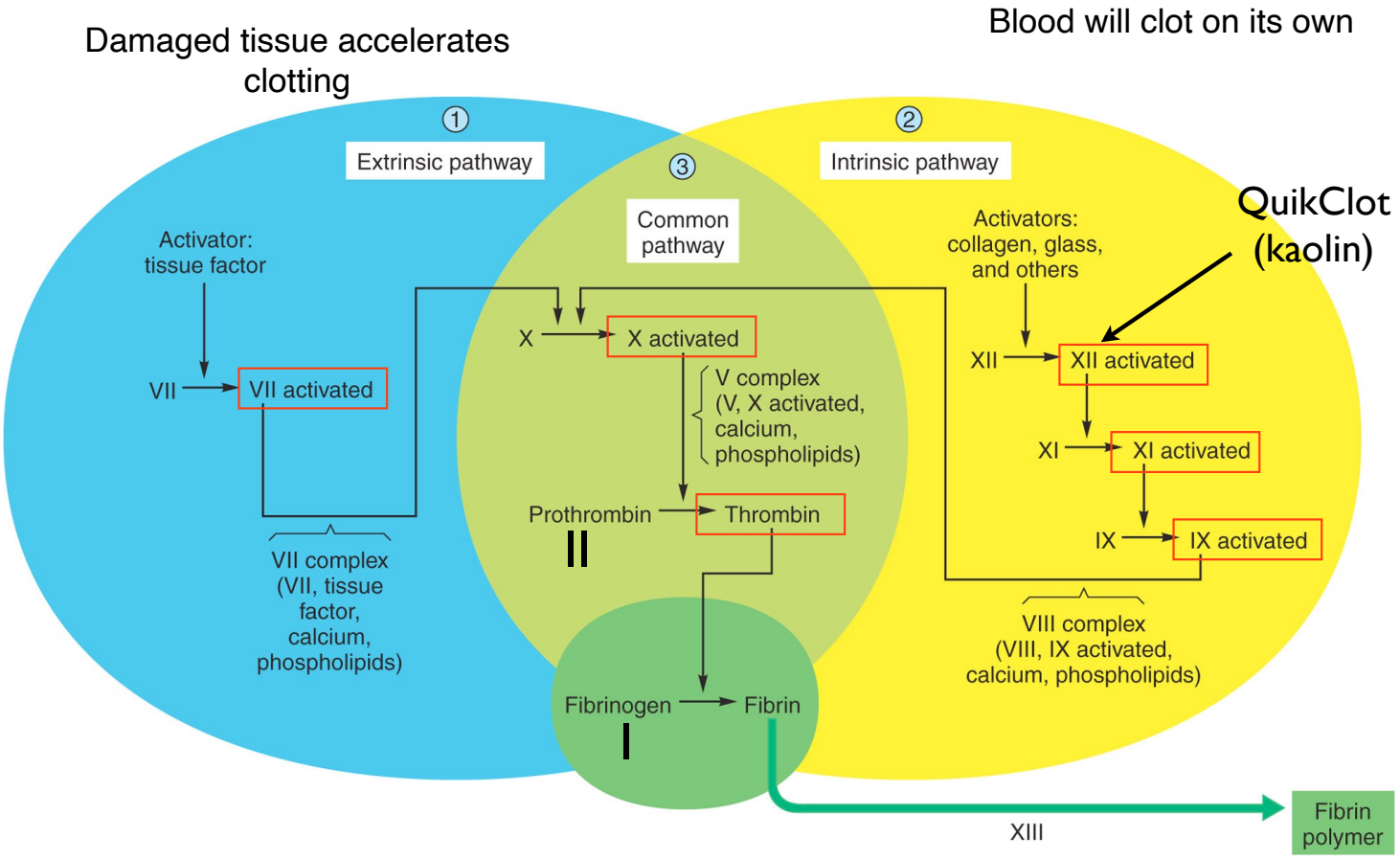
Table 13.4

Table 13.4 | The Plasma Clotting Factors

Factor	Name	Function	Pathway
I	Fibrinogen	Converted to fibrin	Common
II	Prothrombin	Converted to thrombin (enzyme)	Common
III	Tissue thromboplastin	Cofactor	Extrinsic
IV	Calcium ions (Ca^{2+})	Cofactor	all
V	Proaccelerin	Cofactor	Common
VII*	Proconvertin	Enzyme	Extrinsic
VIII	Antihemophilic factor	Cofactor	Intrinsic
IX	Plasma thromboplastin component; Christmas factor	Enzyme	Intrinsic
X	Stuart-Prower factor	Enzyme	Common
XI	Plasma thromboplastin antecedent	Enzyme	Intrinsic
XII	Hageman factor	Enzyme	Intrinsic
XIII	Fibrin stabilizing factor	Enzyme	Common

*Factor VI is no longer referenced; it is now believed to be the same substance as activated factor V.

Figure 13.9



active enzyme

Most enzymes require Ca^{++} (factor IV)

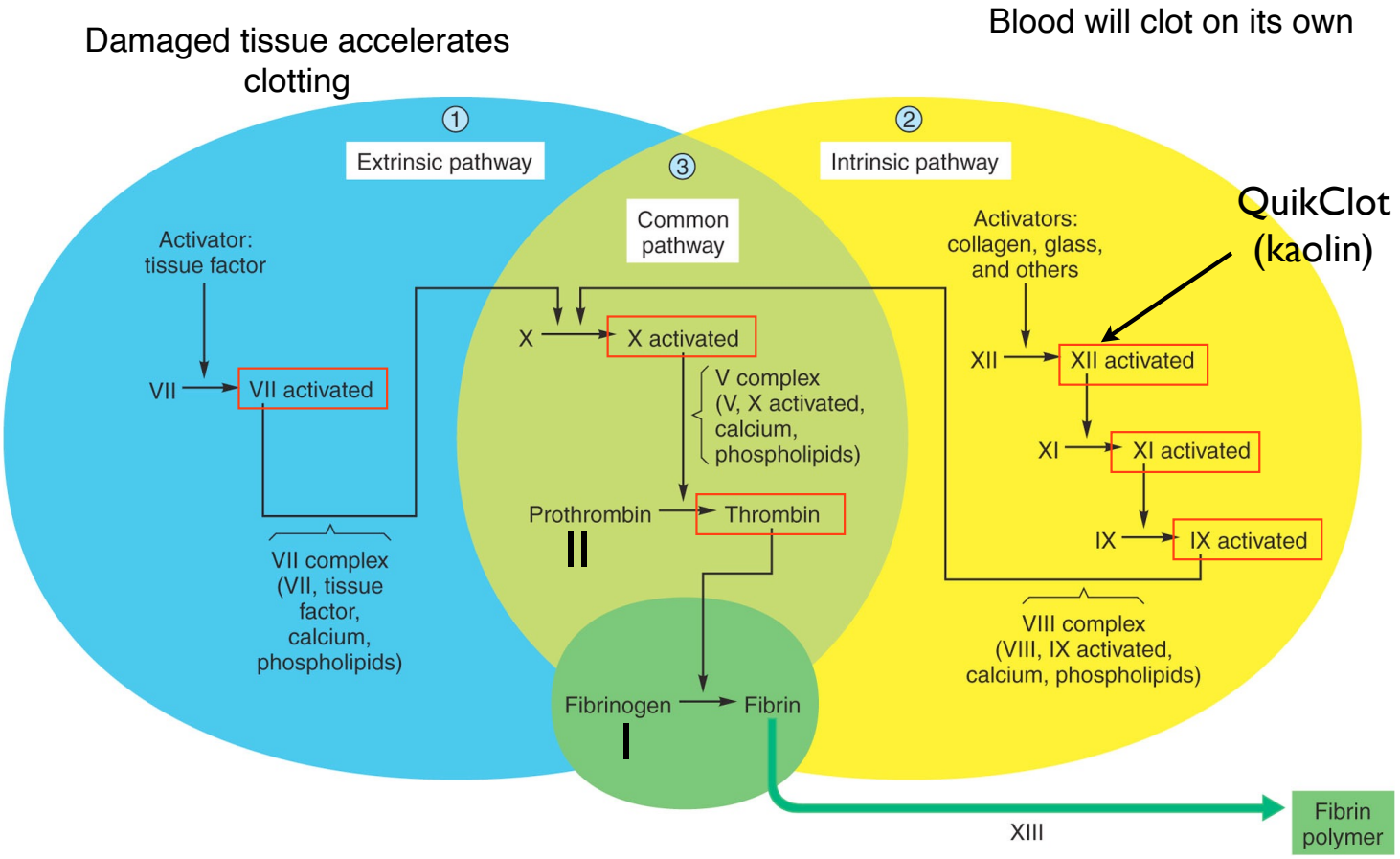
QuikClot Combat Gauze®

Item #: 200

QuikClot Combat Gauze, with kaolin technology, is the CoTCCC hemostatic dressing of choice for the U.S. Department of Defense (DOD).[20]

CONTACT A QUIKCLOT MILITARY SPECIALIST

Figure 13.9



active enzyme

Most enzymes require Ca^{++} (factor IV)

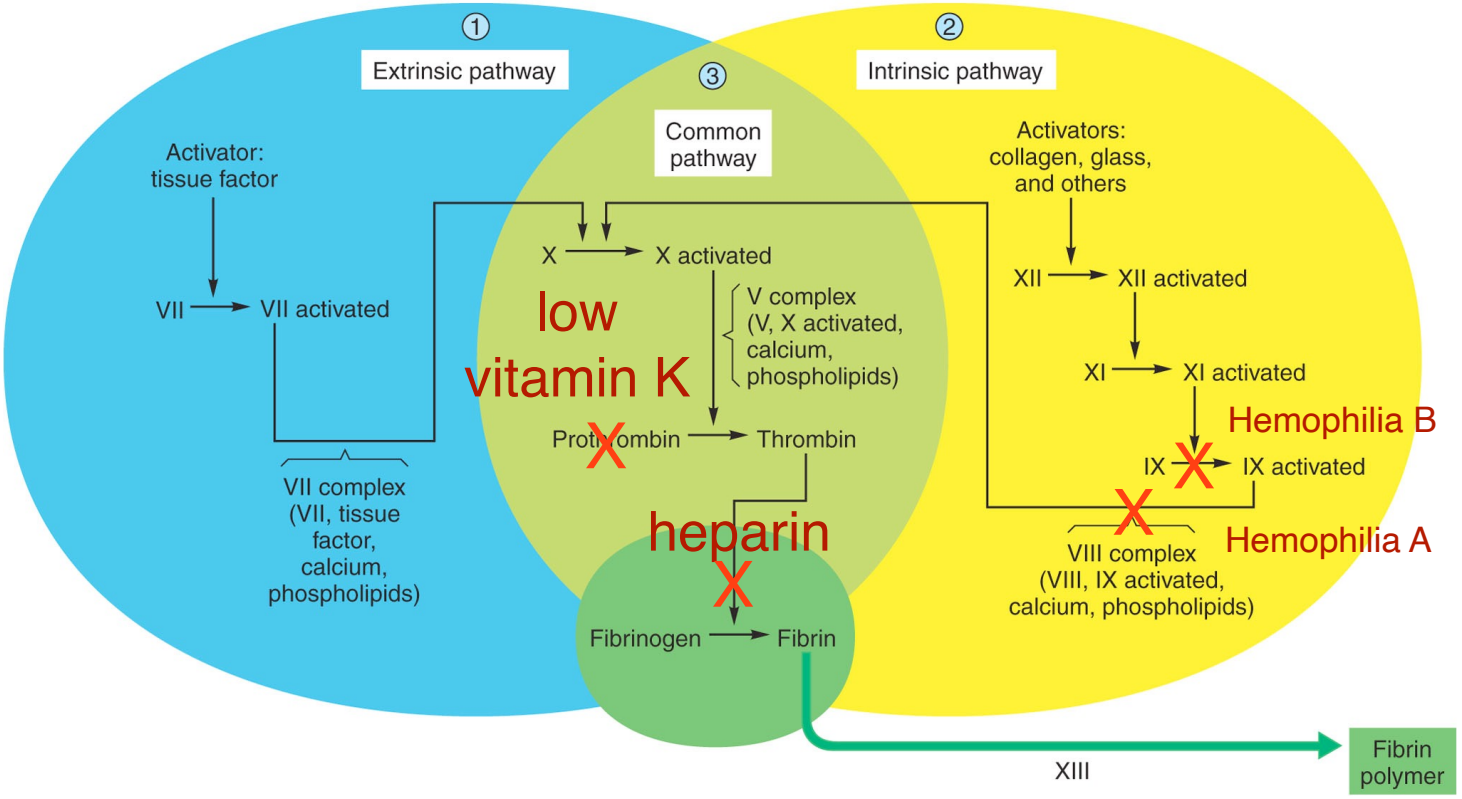
Table 13.5

Table 13.5 | Some Acquired and Inherited Clotting Disorders and a Listing of Anticoagulant Drugs

Category	Cause of Disorder	Comments
Acquired clotting disorders	Vitamin K deficiency	Inadequate formation of prothrombin and other clotting factors in the liver
Inherited clotting disorders	Hemophilia A (defective factor $VIII_{AHF}$)	Recessive trait carried on X chromosome; results in delayed formation of fibrin
	Von Willebrand's disease (defective factor $VIII_{VWF}$)	Dominant trait carried on autosomal chromosome; impaired ability of platelets to adhere to collagen in subendothelial connective tissue
	Hemophilia B (defective factor IX); also called Christmas disease	Recessive trait carried on X chromosome; results in delayed formation of fibrin
Anticoagulants		
Aspirin	Inhibits prostaglandin production, resulting in a defective platelet release reaction	
Coumarin	Inhibits activation of vitamin K	
Heparin	Inhibits activity of thrombin	
Citrate	Combines with Ca^{2+}, and thus inhibits the activity of many clotting factors	

hemophilia - "love to bleed"

Figure 13.9



Most enzymes require Ca^{++} (factor IV)

citrate, EDTA

Hemophilia A & B are X-linked recessive disease

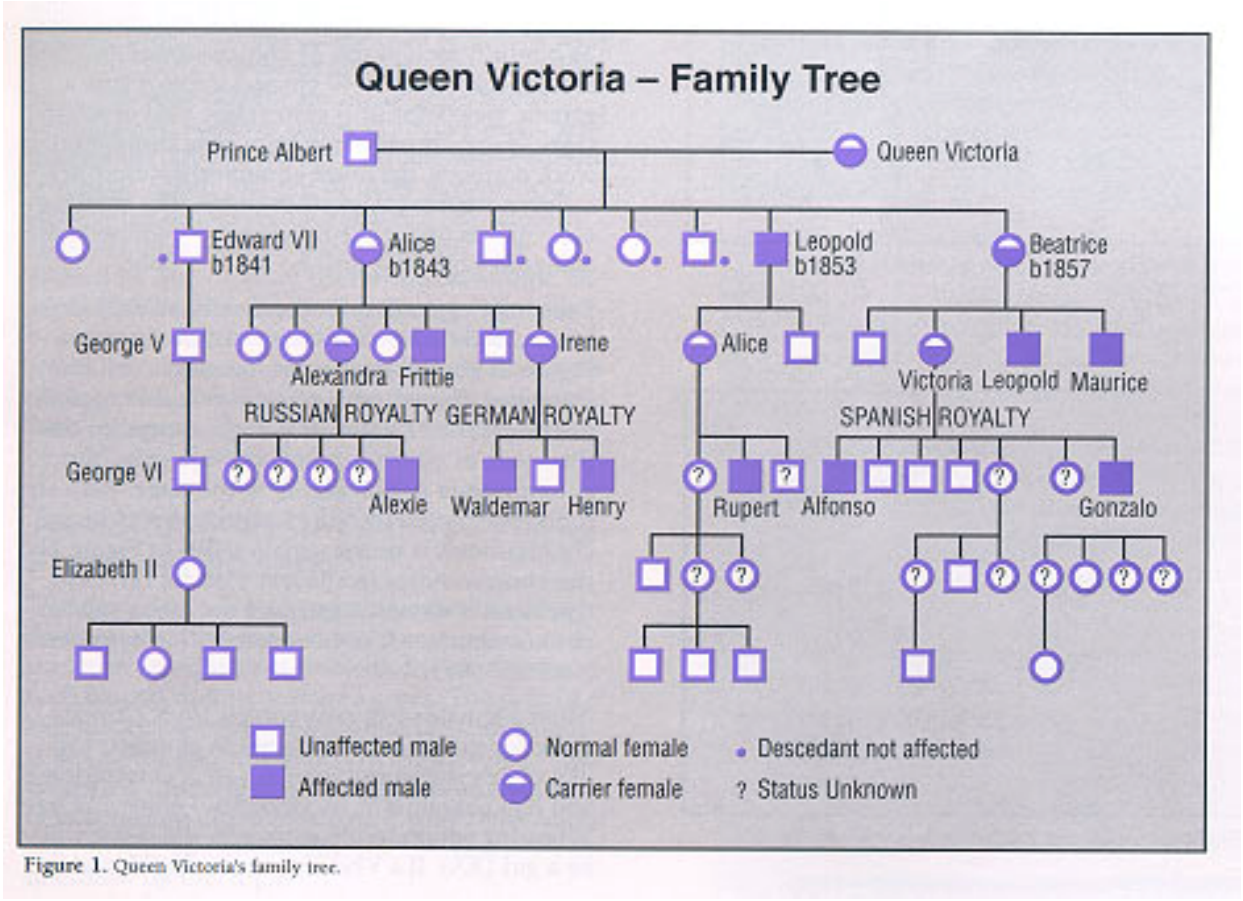
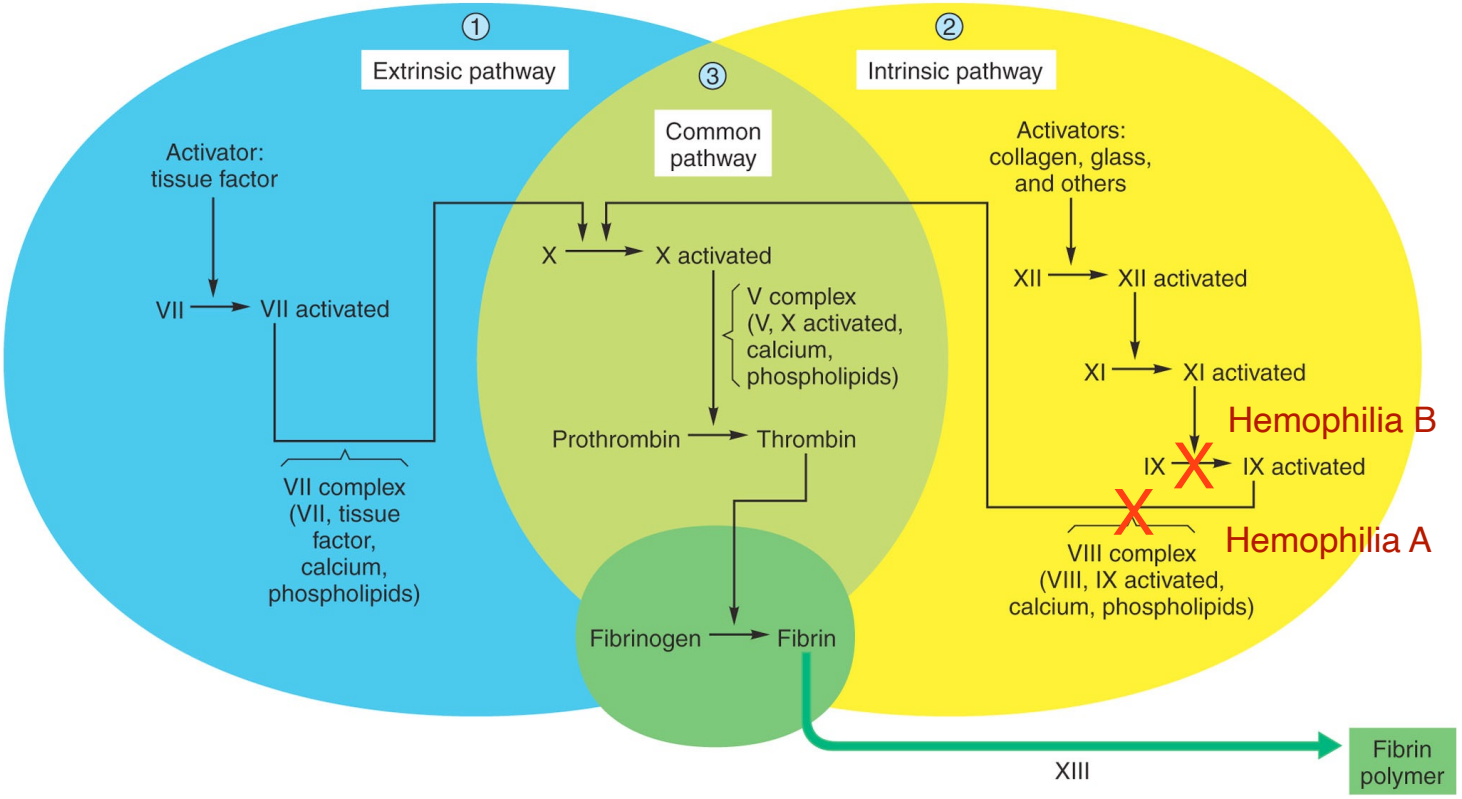


Figure 1. Queen Victoria's family tree.

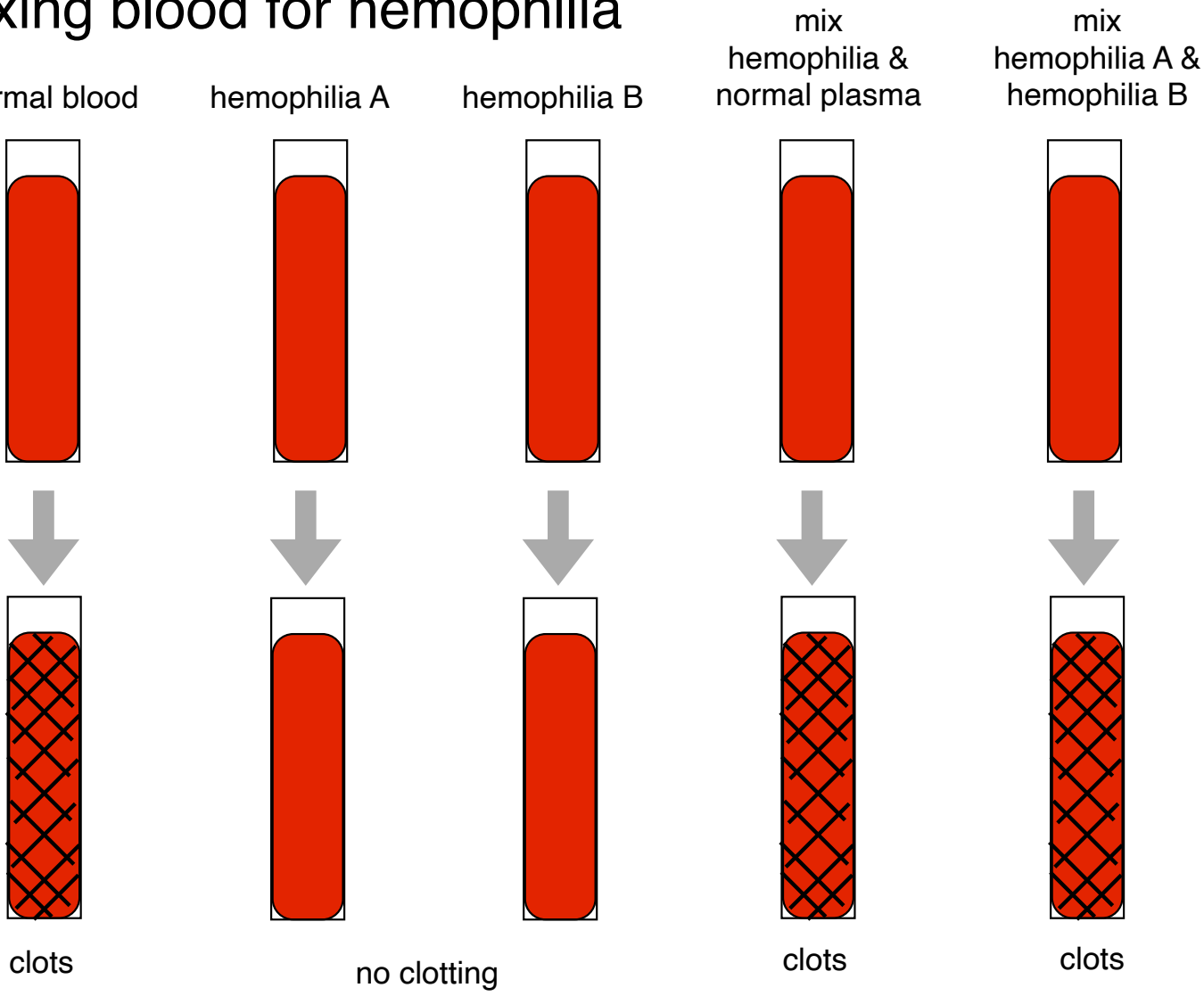
Figure 13.9

Top Hat



Most enzymes require Ca^{++} (factor IV)

Mixing blood for hemophilia



The main treatment for hemophilia is called replacement therapy. Concentrates of clotting factor VIII (for hemophilia A) or clotting factor IX (for hemophilia B) are slowly dripped or injected into a vein. These infusions help replace the clotting factor that's missing or low.