

# Heart 2

## Fox Chapter 13 part 2

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### Arrhythmias and the ECG

Sinus bradycardia & tachycardia: changes in heart rate due to changes in SA Node pacemaker, e.g. by sympathetic stimulation of HCN channels -> tachycardia during "fight or flight"

**Ectopic pacemakers** outside of the SA node, e.g. ectopic pacemakers in ventricles -> ventricular tachycardia -> ventricular fibrillation

**Circus rhythms:** continuous recycling of AP around ventricles when refractory periods of myocardial cells become desynchronized. Circus rhythms can arise after damage to heart leading to disconnected portions of ventricle, or by electrical shock in middle of T wave.

**Defibrillator:** electrical shock depolarizes all of the myocardial cells at the same time, and synchronize in refractory state so SA node can restart contraction.

**AV node block:** damage to AV node slows or blocks atrial pacemaker signal. Can observe P-waves (of atrial contraction) without QRS wave (of ventricular contraction).

bradycardia = slow heart beat; tachycardia = rapid heart beat  
fibrillation = "quivering" of myocardium; uncoordinated contraction  
arrhythmia = loss of rhythm

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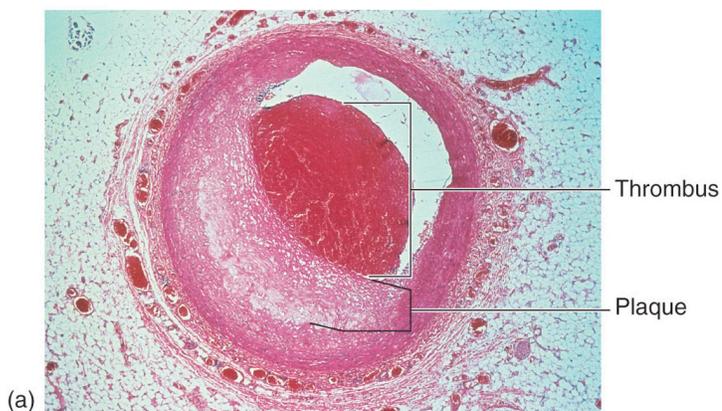
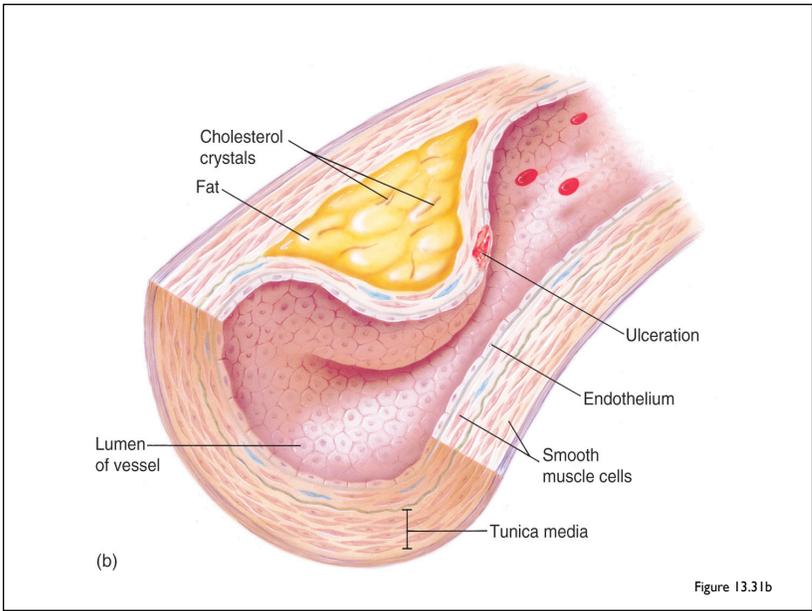


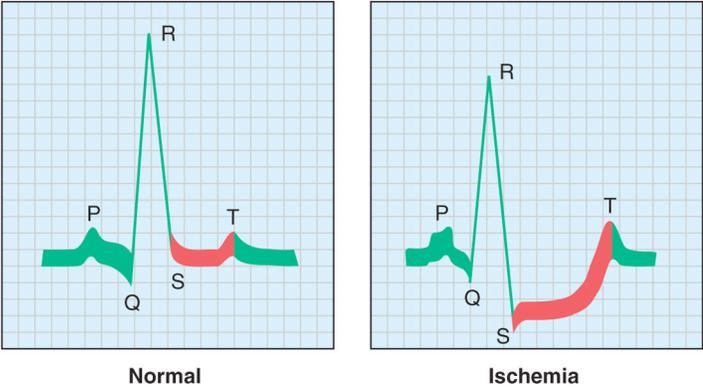
Figure 13.31a

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**Depression of ST interval = damage to myocardium, intracellular accumulation of Ca<sup>++</sup>**



ischemia = loss of oxygen due to reduced blood flow -> cell damage & death (infarction)

Figure 13.33

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bradycardia = slow heart beat  
 tachycardia = rapid heart beat  
 fibrillation = "quivering" of myocardium; uncoordinated contraction  
 arrhythmia = loss of rhythm

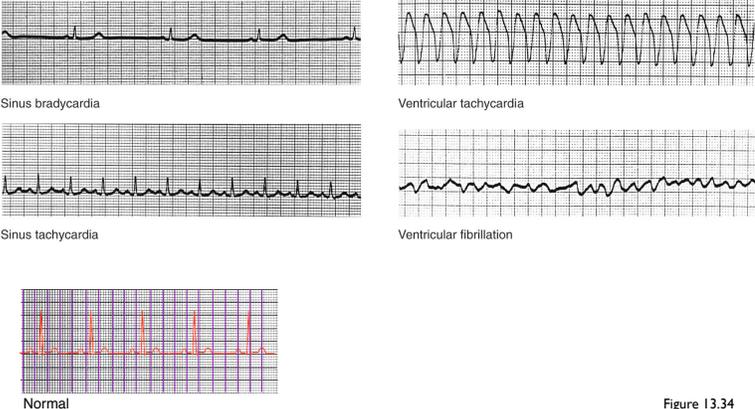
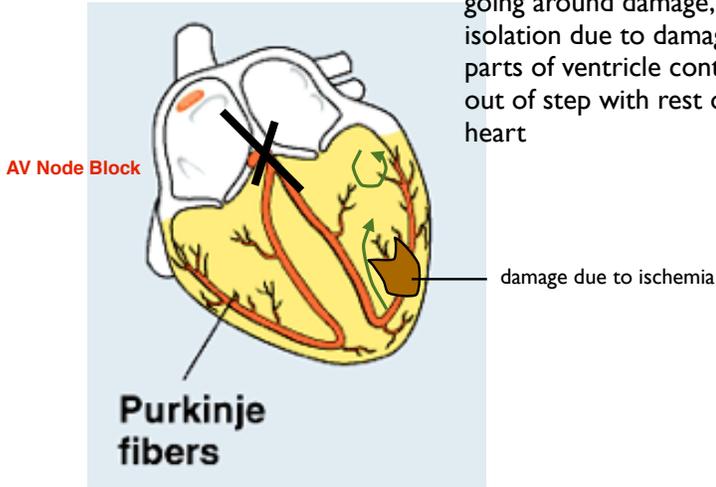


Figure 13.34

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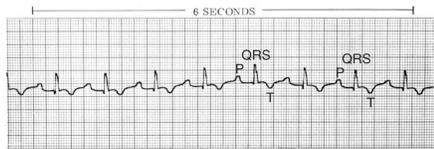
## Circus Rhythms:

because of delay of AP going around damage, or isolation due to damage, parts of ventricle contract out of step with rest of heart

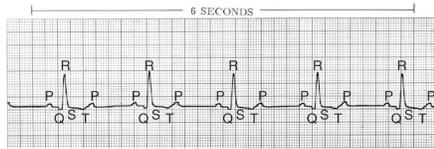


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P-R interval > 0.2 sec  
(but P still drives QRS)



P waves without  
QRS waves



P waves without QRS;  
spontaneous QRS waves  
produced by  
ectopic pacemaker

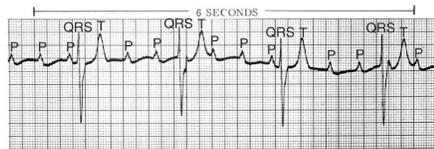


Figure 13.35

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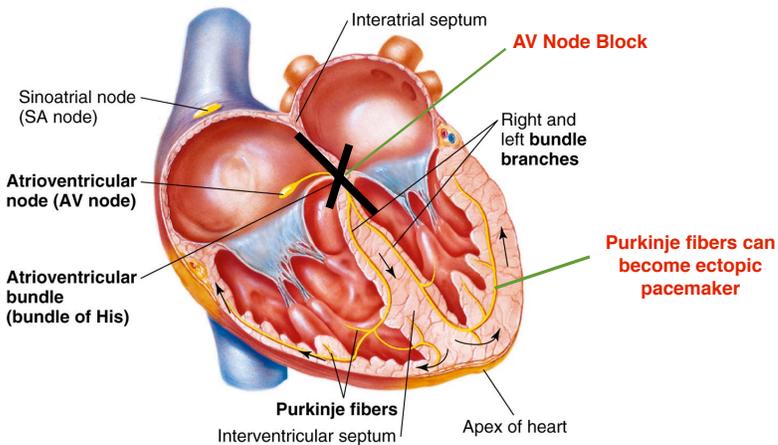


Figure 13.20

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# Pharmacological Regulation of Heart Rate

## Autonomic Nervous System:

### Sympathetic NS raises HR.

Sympathetic chain ganglia -> norepinephrine release onto pacemaker cells -> beta-adrenergic receptors -> increased cAMP -> open HCN channels, open Ca<sup>++</sup> channels.

### Parasympathetic NS slows HR.

Vagus nerve -> acetylcholine release onto pacemaker cells -> muscarinic receptors -> decreased cAMP -> close HCN channels, open K<sup>+</sup> channels

### Drugs to treat Elevated Heart Rate (tachycardia)

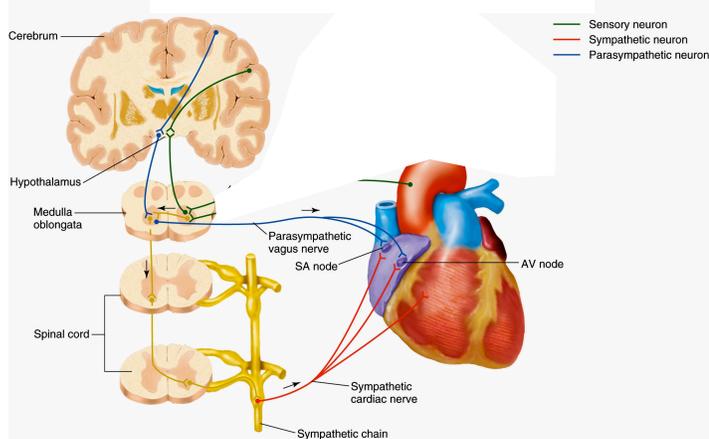
Lidocaine - blocks voltage-gated Na<sup>+</sup> channels

Propranolol - "beta blocker": blocks norepi from binding beta-adrenergic receptors

Verapamil - blocks the voltage-gated Ca<sup>++</sup> channels

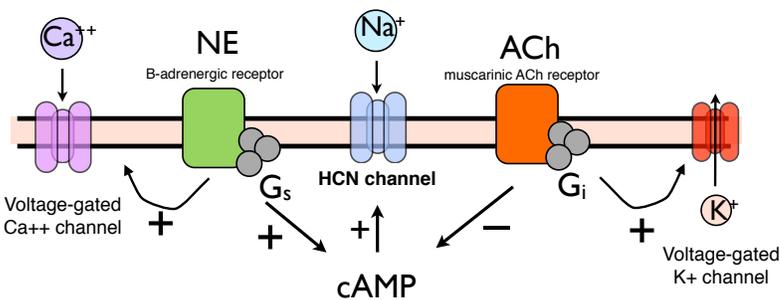
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## Autonomic Nervous System & Heart Rate



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## Autonomic Nervous System & Heart Rate



What would the effects of NE and ACh agonists & antagonists be on heart rate?

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### Effect of Norepinephrine on Pacemaker Cells

HCN channels open faster & Ca<sup>++</sup> channels open faster -> faster beat

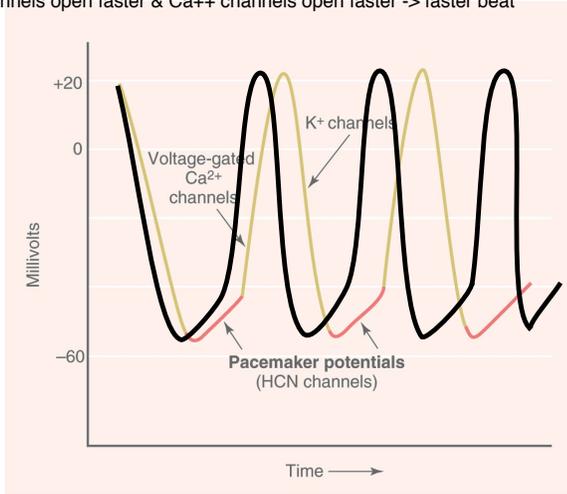


Figure 13.18

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### Effect of Acetylcholine on Pacemaker Cells

HCN channels open slower, more K<sup>+</sup> channels open -> slower beat

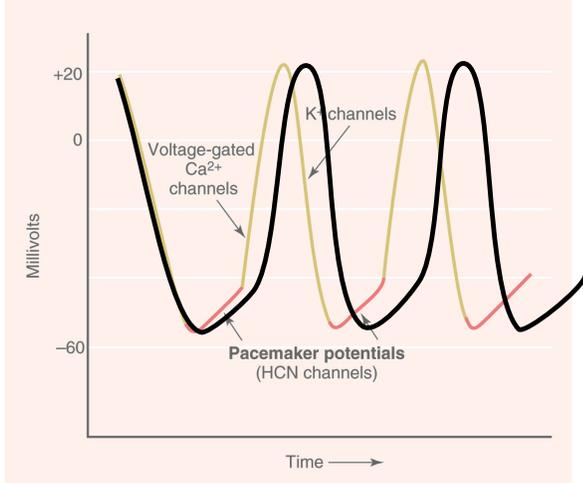
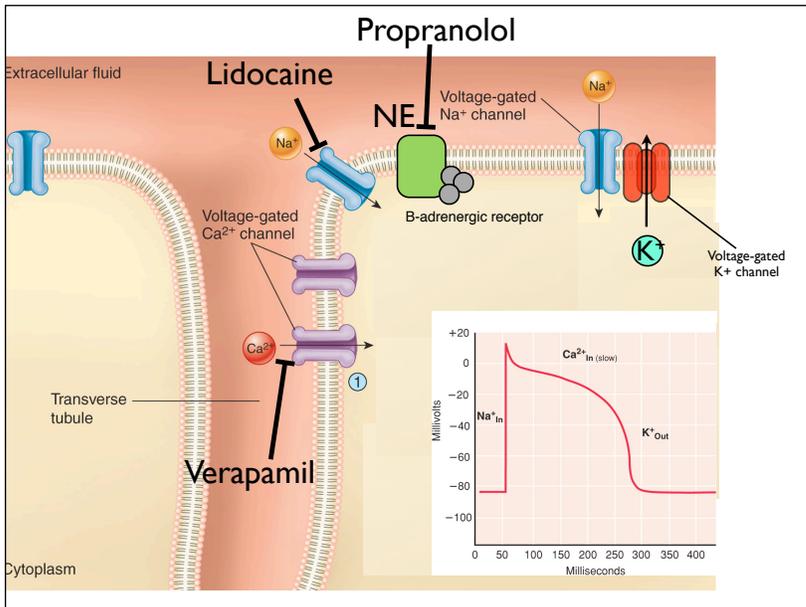


Figure 13.18

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# Blood Vessels

## Arteries (arterial blood)

vessels carrying blood from heart towards the capillaries. Thick muscular walls to keep pressure up. High in oxygen (except for pulmonary arteries).

## Veins (venous blood)

vessels carrying blood from capillaries back to heart. Very thin flabby walls with low pressure, but have one-way valves to prevent blood from backing up. Low in oxygen (except for pulmonary veins).

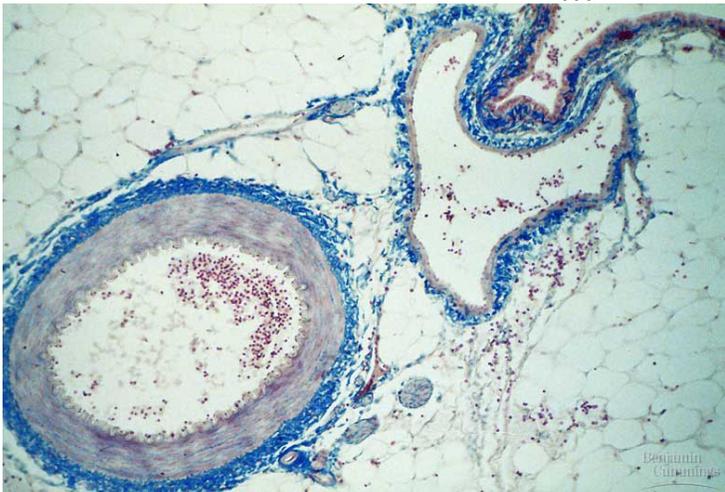
## Capillaries

very small vessels (1 blood cell wide, with endothelium 1 cell thick) that perfuse all the tissues. Most capillaries are **fenestrated**, or have channels, or have discontinuous endothelium so that dissolved molecules can easily pass from blood to interstitial fluid & tissues. (Except for **blood brain barrier** formed by tight junctions of the capillary endothelium in brain.)

**Precapillary Sphincters** can regulate blood flow to capillaries or bypass thru shunt.

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Vein with thin floppy wall

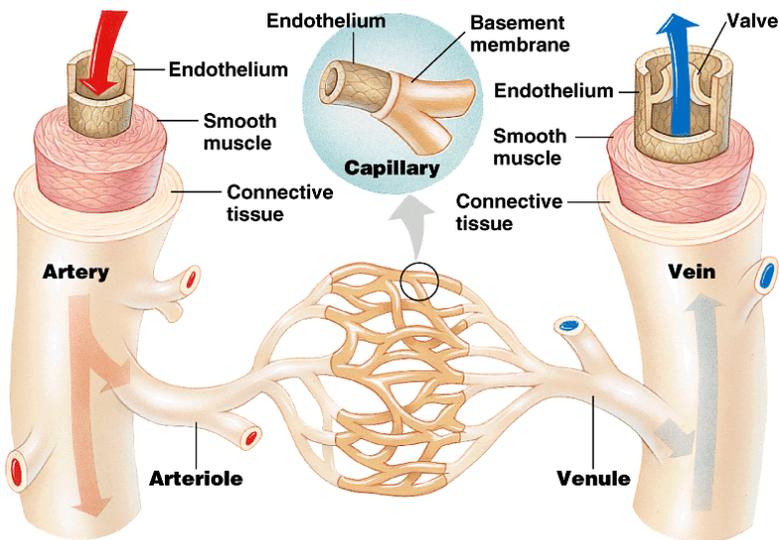


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Artery with thick, muscular elastic wall

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Figure 42.8 The structure of blood vessels



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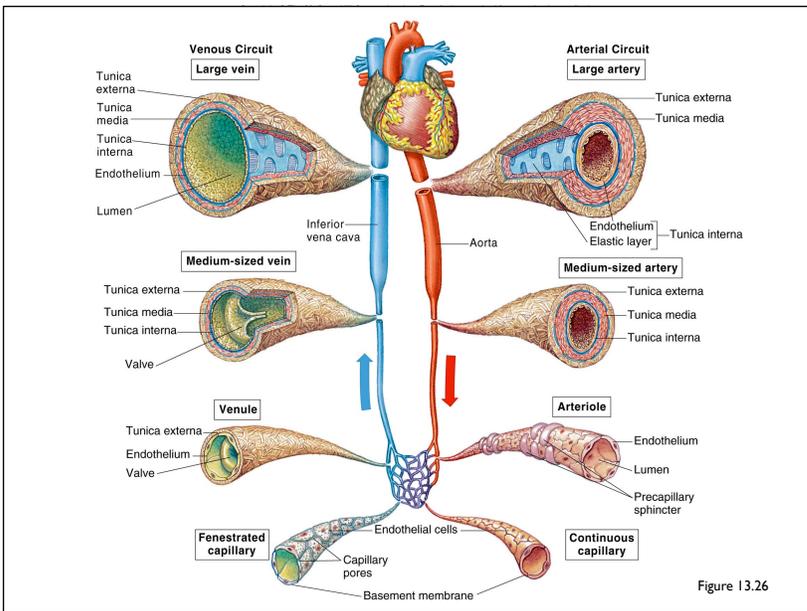


Figure 13.26

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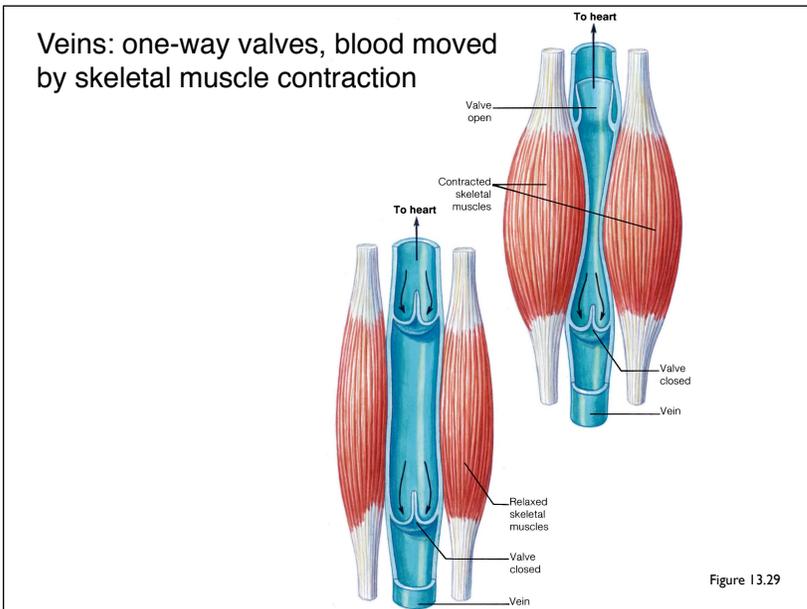
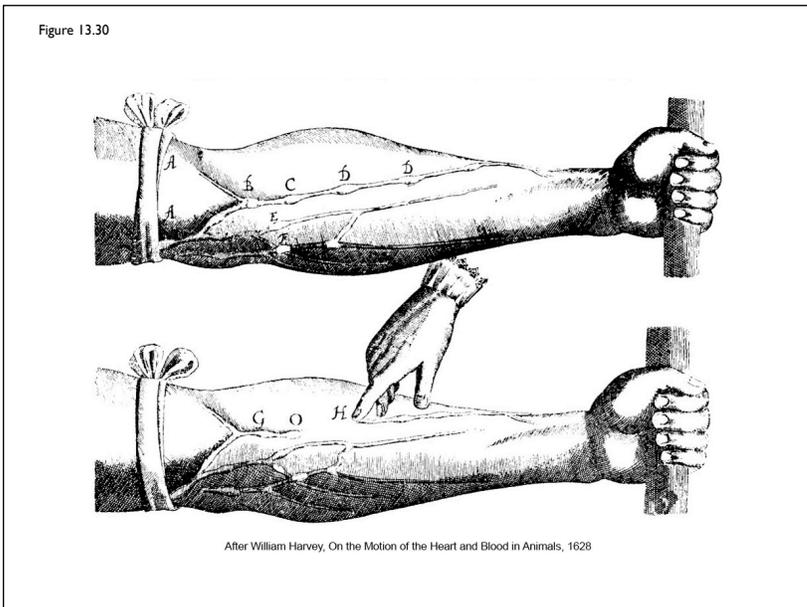
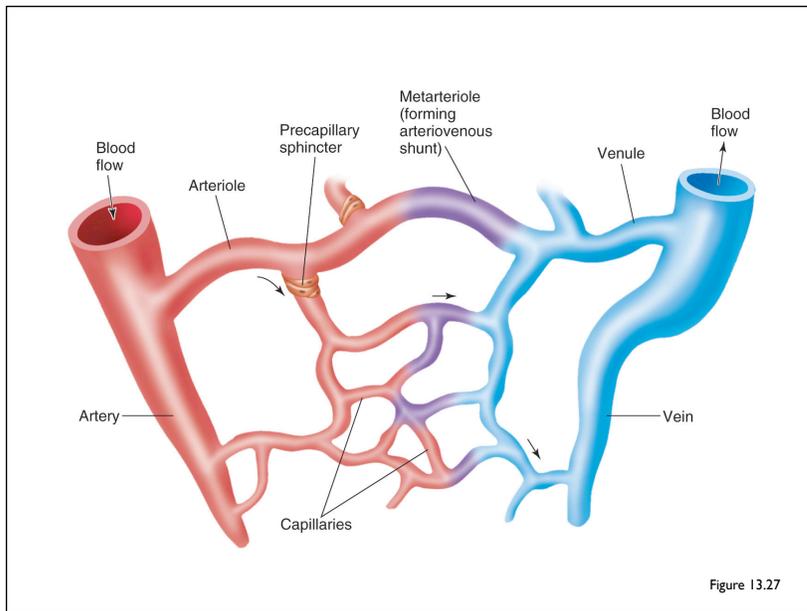


Figure 13.29

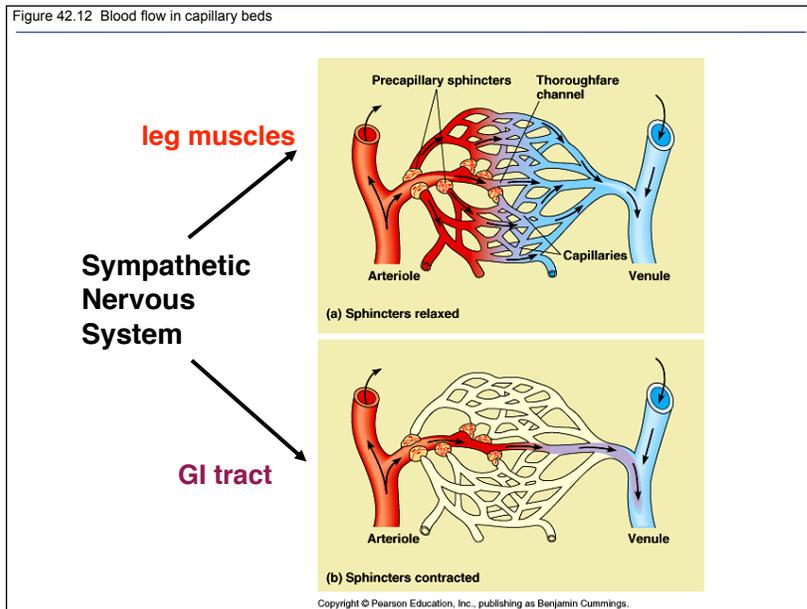
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**Table 13.8 | Characteristics of the Vascular Supply to the Mesenteries in a Dog**

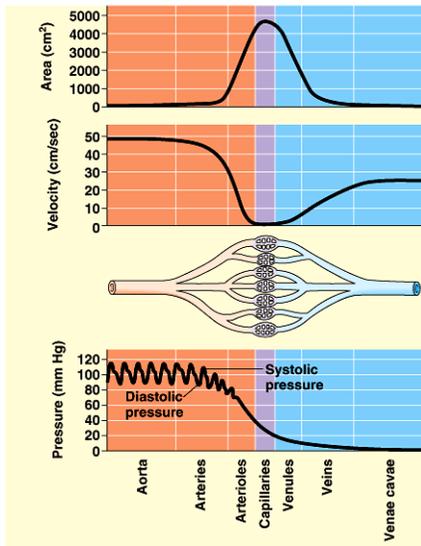
Kind of Vessels	Diameter (mm)	Number	Total Cross-Sectional Area (cm <sup>2</sup> )	Length (cm)	Total Volume (cm <sup>3</sup> )
Aorta	10	1	0.8	40	30
Large arteries	3	40	3.0	20	60
Main artery branches	1	600	5.0	10	50
Terminal branches	.06	1,800	5.0	1	25
Arterioles	0.02	40,000,000	125	0.2	25
Capillaries	0.008	1,200,000,000	600	0.1	60
Venules	0.03	80,000,000	570	0.2	110
Terminal veins	1.5	1,800	30	1	30
Main venous branches	2.4	600	27	10	270
Large veins	6.0	40	11	20	220
Vena cava	12.5	1	1.2	40	50
					930

Note: The pattern of vascular supply is similar in dogs and humans.  
Source: *Animal Physiology*, 4th ed. by Gordon et al., © 1982. Adapted by permission of Prentice-Hall, Inc., Upper Saddle River, NJ.

Table 13.8

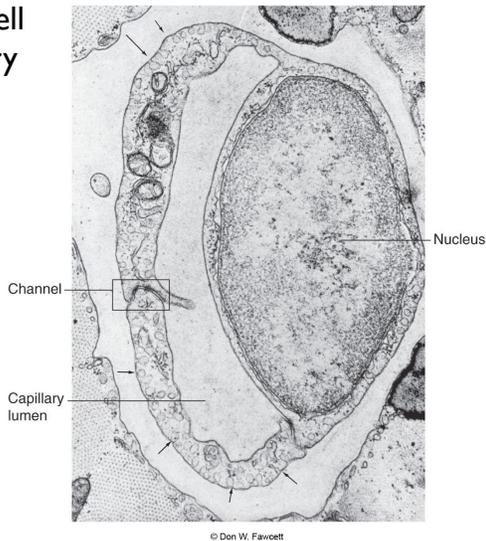
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Figure 42.10 The interrelationship of blood flow velocity, cross-sectional area of blood vessels, and blood pressure



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### Endothelial cell lining capillary

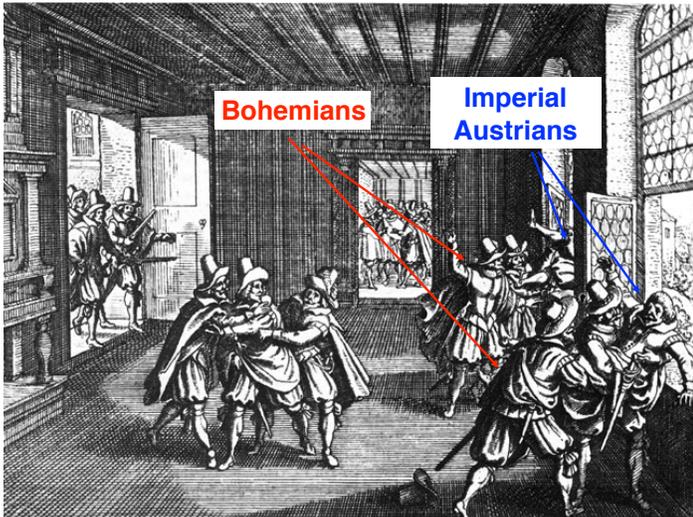


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Figure 13.28

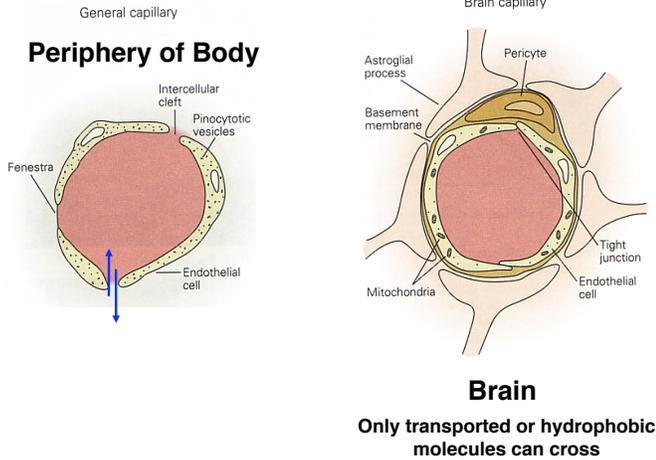
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### Defenestration of Prague in 1618: started 30-years war



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## Fenestrated Capillaries vs. Blood Brain Barrier



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## Composition of Blood

### Red Blood Cells

**Biconcave discoids. Contain hemoglobin, which binds O<sub>2</sub> and helps transport CO<sub>2</sub>. 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.**

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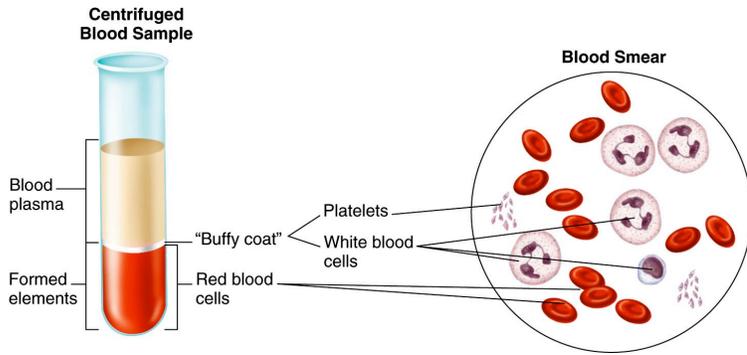
Table 13.2

**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 <sup>3</sup>	Transports oxygen and carbon dioxide
Leukocytes (white blood cells)		5,000 to 10,000 / mm <sup>3</sup>	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 <sup>3</sup>	Enables clotting; releases serotonin, which causes vasoconstriction

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Figure 13.1



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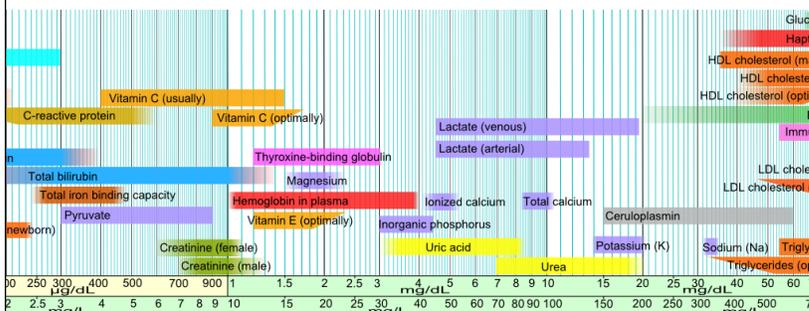
**Table 13.1 | Representative Normal Plasma Values**

Measurement	Normal Range
Blood volume	80–85 ml/kg body weight
Blood osmolality	285–295 mOsm
Blood pH	7.38–7.44
<b>Enzymes</b>	
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
<b>Hematology Values</b>	
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 <sup>3</sup>
White blood cell count	4,500–11,000/mm <sup>3</sup>
<b>Hormones</b>	
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 $\mu$ U/ml (fasting)

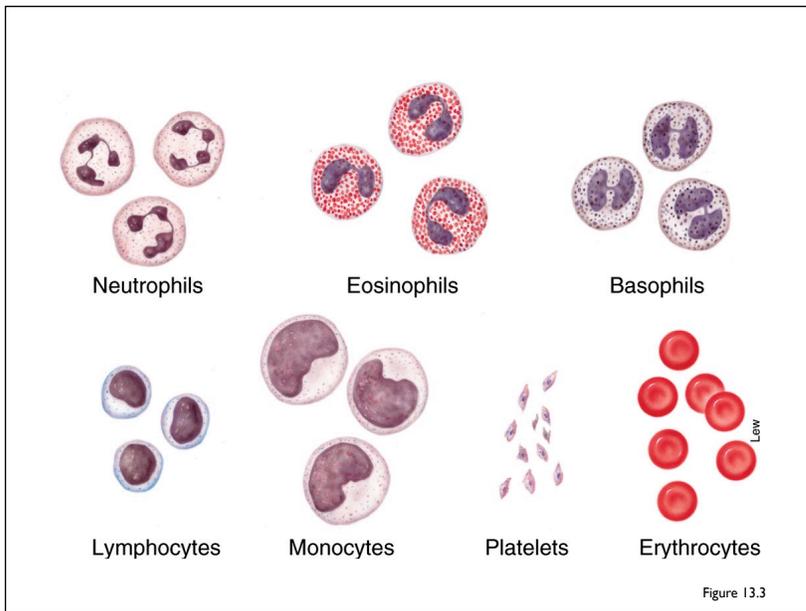
[http://en.wikipedia.org/wiki/Reference\\_ranges\\_for\\_blood\\_tests](http://en.wikipedia.org/wiki/Reference_ranges_for_blood_tests)

Table 13.1

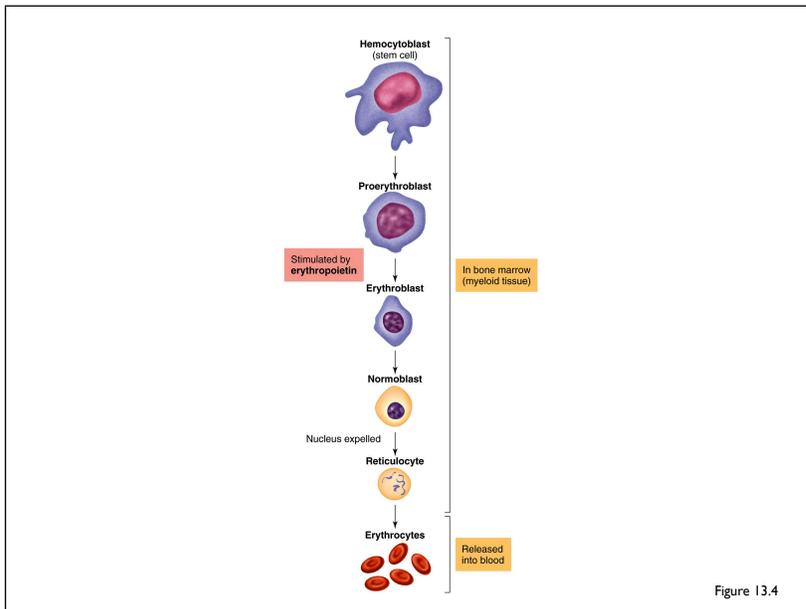
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## Blood Clotting (hemostasis)

**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)

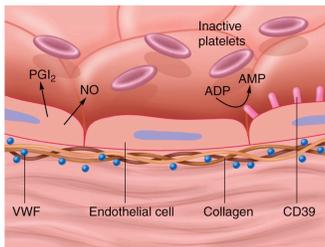
2) Platelets release secretory granules (platelet release reaction):  
ADP & thromboxane A → recruit more platelets to plug  
serotonin causes **vasoconstriction** (aspirin inhibits prostaglandin production)

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

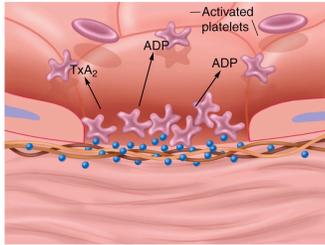
*hemo-* related to blood  
*hemostasis-* preventing blood loss (i.e. stop bleeding)  
*hemorrhage-* bleeding

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

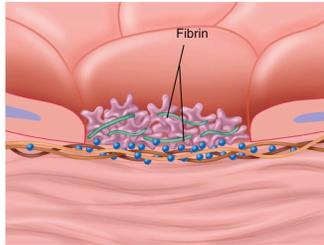
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(a)



(b)



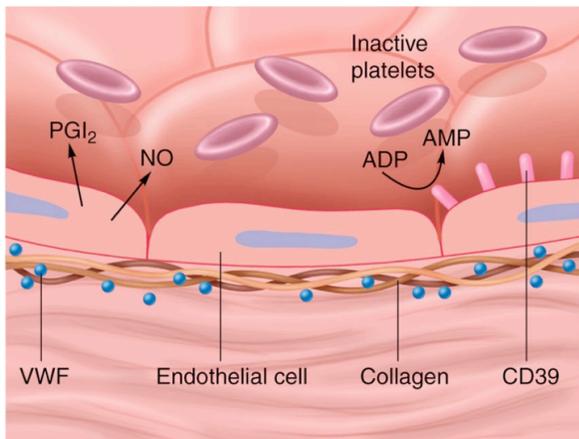
(c)

Figure 13.7

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**Intact Blood Vessel:**

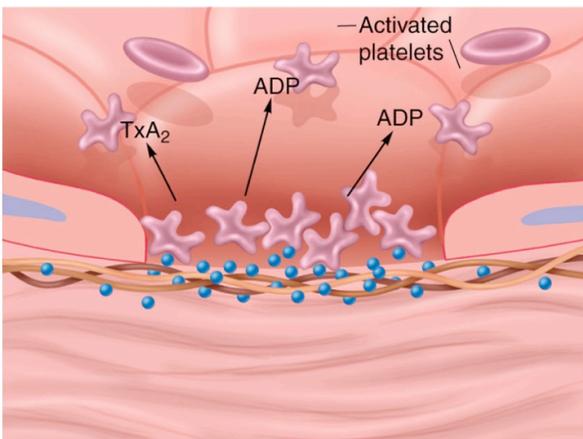
Prostaglandin & NO keep vessel dilated; ADP levels low, so platelets inactive



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**Damaged Blood Vessel:**

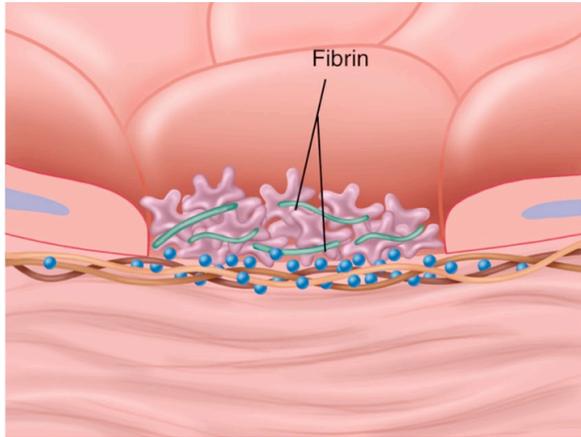
Prostaglandin TxA2, high levels of ADP activate platelets. Activated platelets bind to collagen and von Willebrand's factor



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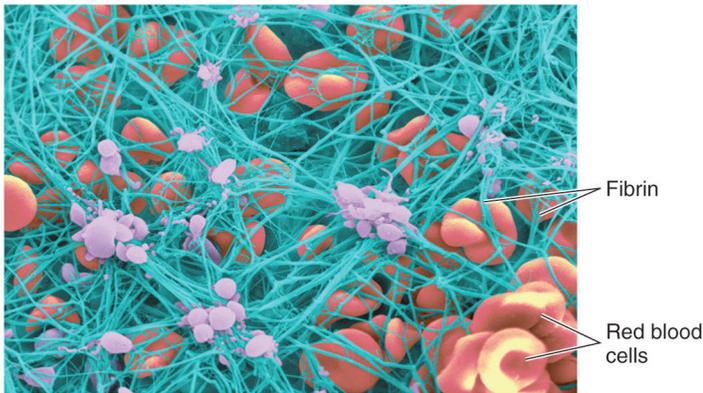
## Clot Formation:

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



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Figure 13.8



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

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## 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)

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Table 13.4

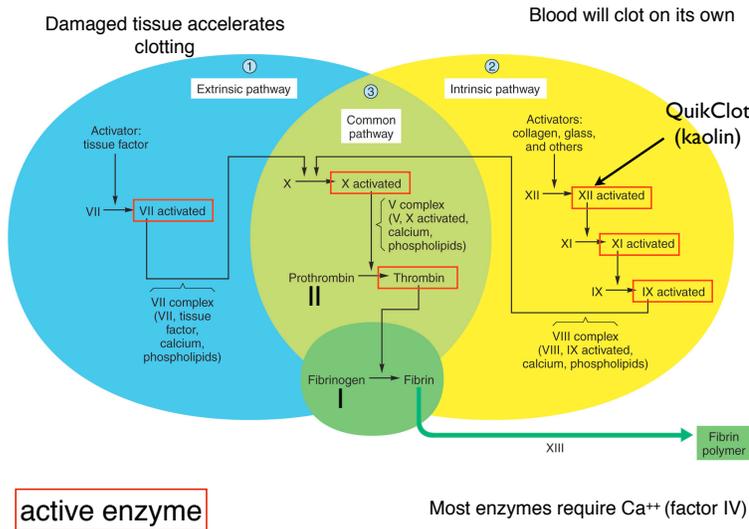
**Table 13.4 | The Plasma Clotting Factors**

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 <sup>2+</sup> )	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.

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Figure 13.9



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Table 13.5

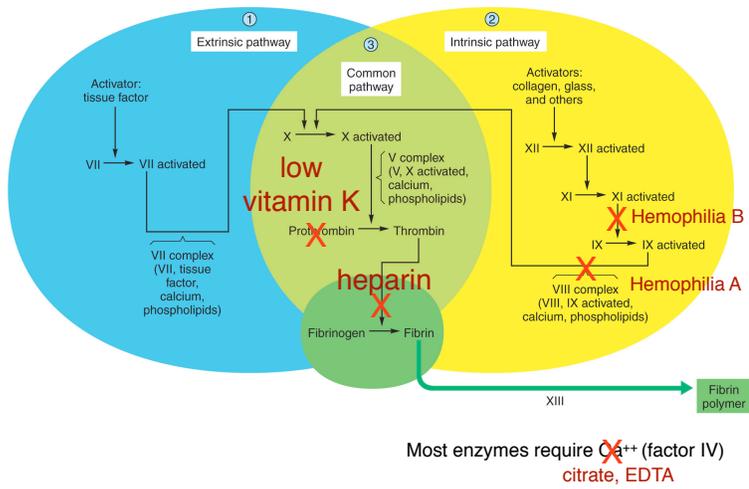
**Table 13.5 | Some Acquired and Inherited Clotting Disorders and a Listing of Anticoagulant Drugs**

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 <sub>AHP</sub> )	Recessive trait carried on X chromosome; results in delayed formation of fibrin
	Von Willebrand's disease (defective factor VIII <sub>VWD</sub> )	Dominant trait carried on autosomal chromosome; impaired ability of platelets to adhere to collagen subendothelial connective tissue
	Hemophilia B (defective factor IX); also called Christmas disease	Recessive trait carried on X chromosome; results in delayed formation of fibrin
<b>Anticoagulants</b>		
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 <sup>2+</sup> , and thus inhibits the activity of many clotting factors	

hemophilia - "love to bleed"

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Figure 13.9



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### Hemophilia A & B are X-linked recessive disease

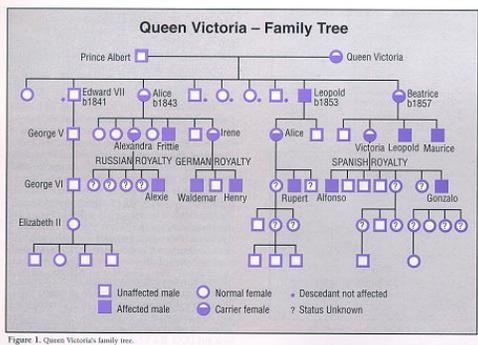
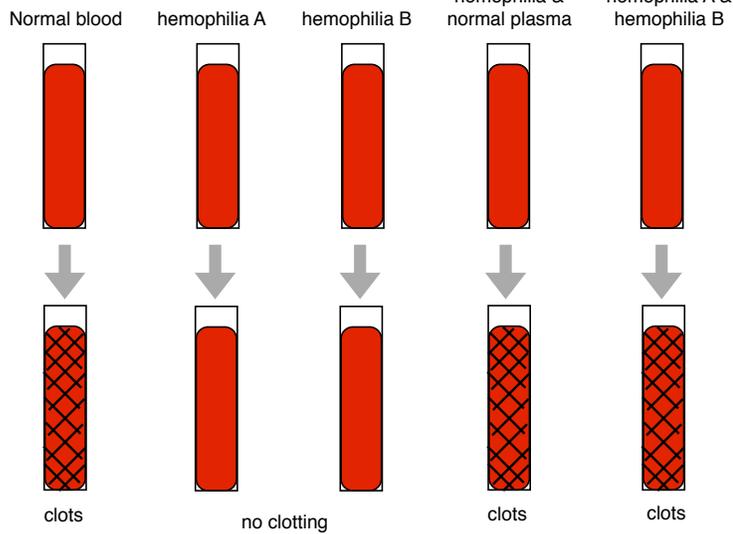


Figure 1. Queen Victoria's family tree.

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### Mixing blood for hemophilia



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