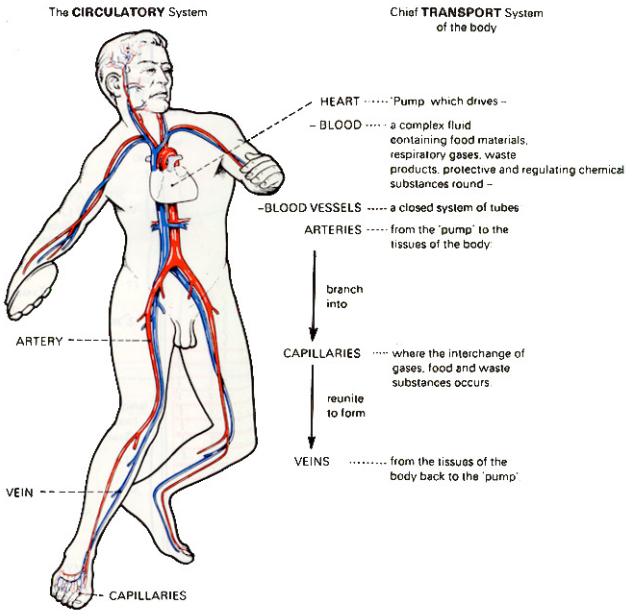
CARDIOVASCULAR SYSTEM

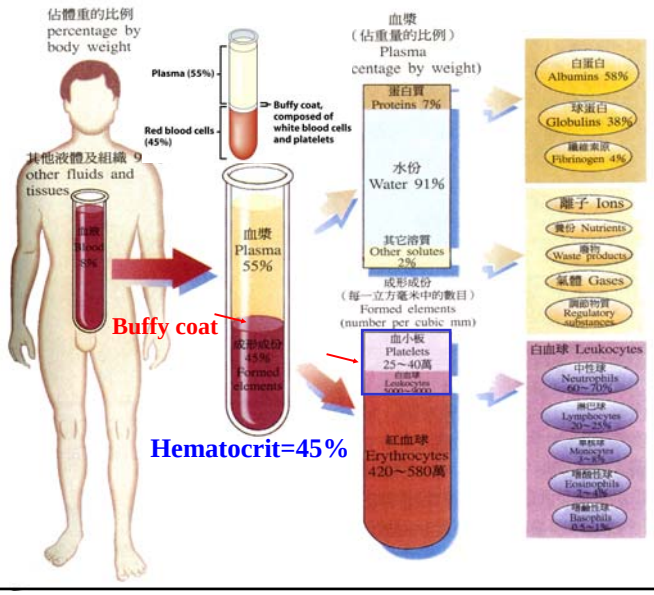


Functions of CVS

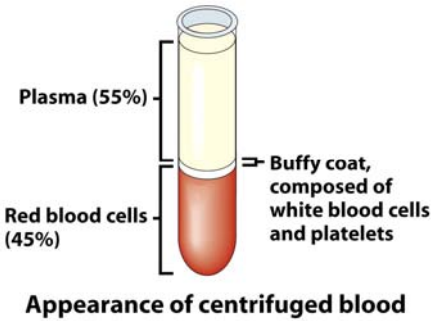
Table 12–1 The Cardiovascular System

Component	Function
Heart	
Atria	Chambers through which blood flows from veins to ventricles. Atrial contraction adds to ventricular filling but is not essential for it.
Ventricles	Chambers whose contractions produce the pressures that drive blood through the pulmonary and systemic vascular systems and back to the heart.
Vascular system	
Arteries	Low-resistance tubes conducting blood to the various organs with little loss in pressure. They also act as pressure reservoirs for maintaining blood flow during ventricular relaxation.
Arterioles	Major sites of resistance to flow; responsible for the pattern of blood flow distribution to the various organs; participate in the regulation of arterial blood pressure.
Capillaries	Major sites of nutrient, metabolic end product, and fluid exchange between blood and tissues.
Venules	Sites of nutrient, metabolic end product, and fluid exchange between blood and tissues.
Veins	Low-resistance conduits for blood flow back to the heart. Their capacity for blood is adjusted to facilitate this flow.
Blood	
Plasma	Liquid portion of blood that contains dissolved nutrients, ions, wastes, gases, and other substances. Its composition equilibrates with that of the interstitial fluid at the capillaries.
Cells	Includes erythrocytes that function mainly in gas transport, leukocytes that function in immune defenses, and platelets (cell fragments) for blood clotting.

Components of Blood



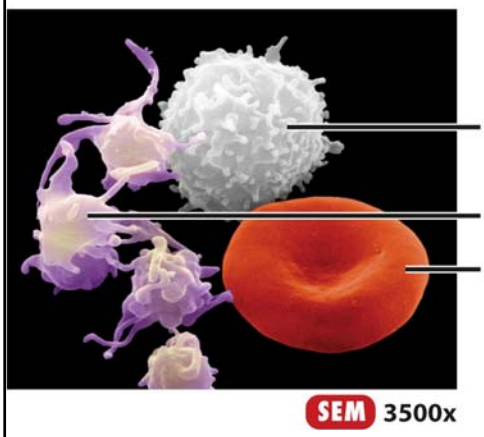
Blood Plasma



Appearance of centrifuged blood

- **Over 90% water**
- **7% plasma proteins**
  - created in liver
  - confined to bloodstream
  - albumin
    - maintain blood osmotic pressure
  - globulins (immunoglobulins)
    - antibodies bind to foreign substances called antigens
    - form antigen-antibody complexes
  - fibrinogen
    - for clotting
- **2% other substances**
  - electrolytes, nutrients, hormones, gases, waste products

Functions of Blood Cells



❖**Transportation**

O2, CO2, metabolic wastes, nutrients, heat & hormones

❖**Regulation**

helps regulate pH through buffers

helps regulate body temperature

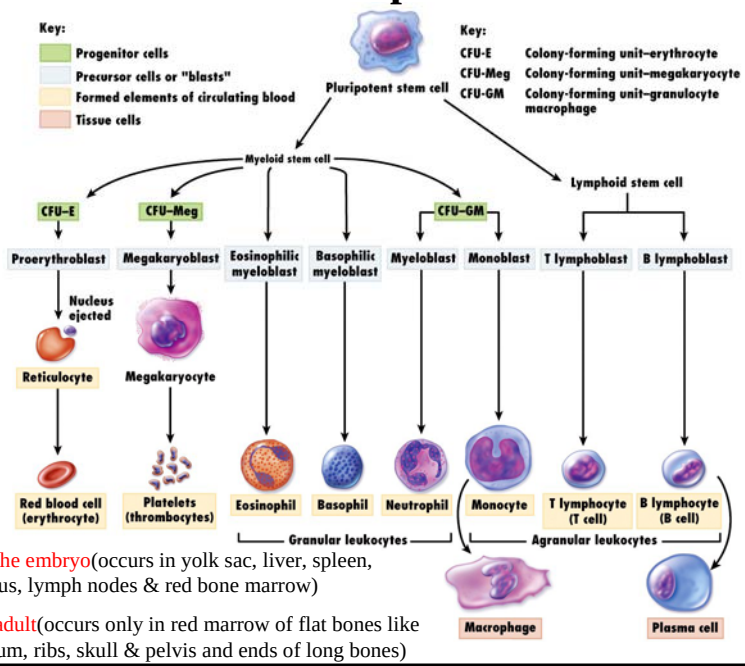
-coolant properties of water

-vasodilatation of surface vessels dump heat

helps regulate water content of cells by interactions with dissolved ions and proteins

❖**Protection** from disease & loss of blood

Hematopoiesis



➢In the embryo(occurs in yolk sac, liver, spleen, thymus, lymph nodes & red bone marrow)

➢In adult(occurs only in red marrow of flat bones like sternum, ribs, skull & pelvis and ends of long bones)

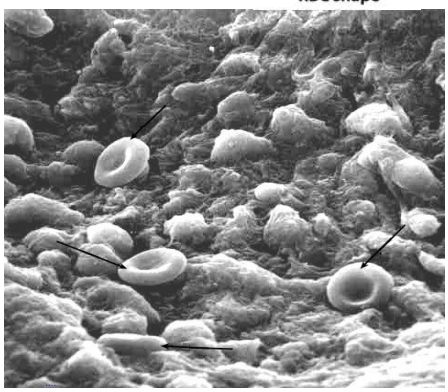
Stages of Blood Cell Formation

- **Pluripotent stem cells**
  - 1% of red marrow cells
  - replenish themselves as they differentiate into either myeloid or lymphoid stem cells
- **Myeloid stem cell line** of development continues:
  - progenitor cells(colony-forming units) no longer can divide and are specialized to form specific cell types
    - example: CFU-E develops eventually into only red blood cells
  - next generation is blast cells
    - have recognizable histological characteristics
    - develop within several divisions into mature cell types
- **Lymphoid stem cell line** of development
  - pre-B cells & prothymocytes finish their develop into B & T lymphocytes in the lymphatic tissue after leaving the red marrow

Hemopoietic Growth Factors

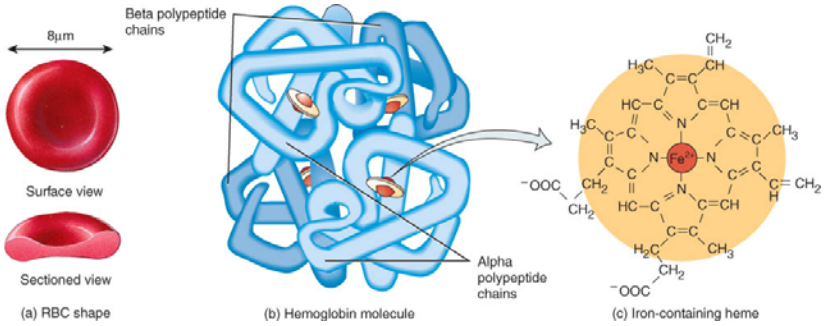
- Regulate differentiation & proliferation
- Erythropoietin (EPO)
  - produced by the kidneys increase RBC precursors
- Thrombopoietin (TPO)
  - hormone from liver stimulates platelet formation
- Cytokines are local hormones of bone marrow
  - produced by some marrow cells to stimulate proliferation in other marrow cells
  - colony-stimulating factor (CSF) & interleukin stimulate WBC production
- Available through recombinant DNA technology
  - recombinant erythropoietin (EPO) very effective in treating decreased RBC production of end-stage kidney disease
  - other products given to stimulate WBC formation in cancer patients receiving chemotherapy which kills bone marrow
    - granulocyte-macrophage colony-stimulating factor
    - granulocyte colony stimulating factor
  - thrombopoietin helps prevent platelet depletion during chemotherapy

Red Blood Cells or Erythrocytes



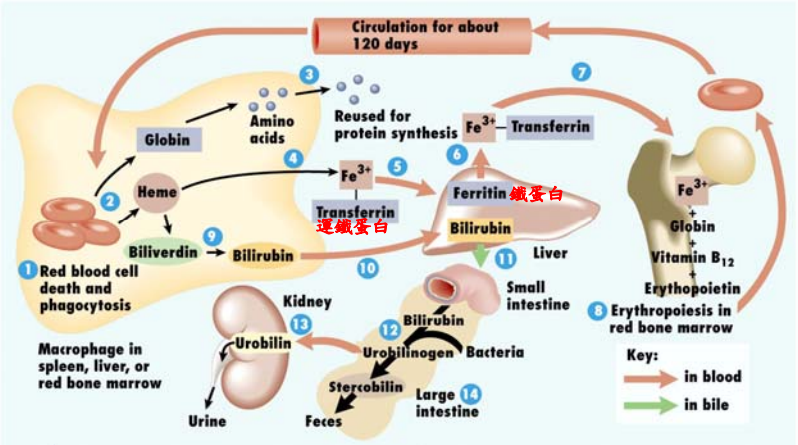
- Contain oxygen-carrying protein hemoglobin that gives blood its red color
  - –1/3 of cell's weight is hemoglobin
- Biconcave disk 8 microns in diameter
  - –increased surface area/volume ratio
  - –flexible shape for narrow passages
  - –no nucleus or other organelles
  - –no cell division or mitochondrial ATP formation
- Normal RBC count
  - –male 5.4 million/drop & female 4.8 million/drop
  - –new RBCs enter circulation at 2 million/second (life cycle 120 days)

Hemoglobin



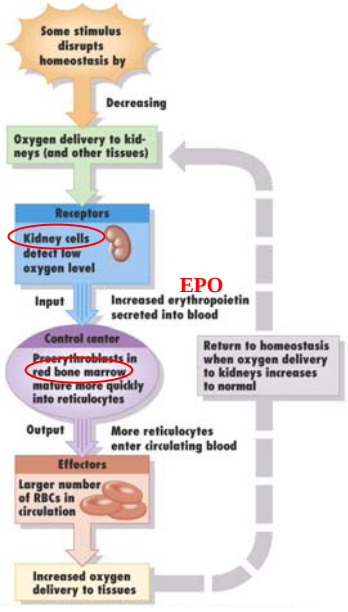
- Globin protein consisting of 4 polypeptide chains
- One heme pigment attached to each polypeptide chain
  - – each heme contains an iron ion (Fe+2) that can combine reversibly with one oxygen molecule

Recycling of Hemoglobin Components



- In macrophages of liver or spleen
  - –globin portion broken down into amino acids & recycled
  - –heme portion split into iron (Fe+3) and biliverdin (green pigment)
- Biliverdin (green) converted to bilirubin (yellow)
  - –bilirubin secreted by liver into bile

Feedback Control of RBC Production



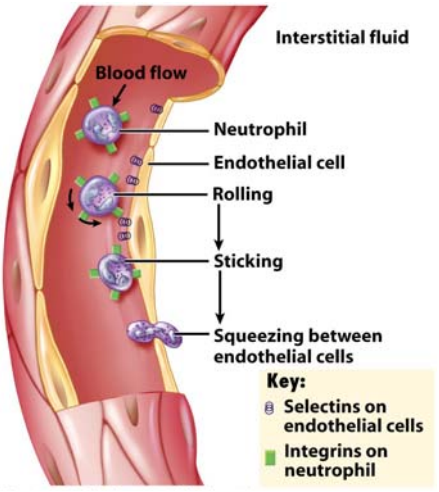
- Tissue hypoxia
  - – high altitude since air has less O2
  - – anemia
    - RBC production falls below RBC destruction
  - – circulatory problems
- Kidney response to hypoxia
  - – release erythropoietin
  - – speeds up development of proerythroblasts into reticulocytes

Types of Anemia

Type	Cause	Defect
Aplastic anemia	Toxic chemicals, radiation	Damaged bone marrow
Hemolytic anemia	Toxic chemicals	RBC destroyed
Iron deficiency anemia	Dietary lack of iron	Hemoglobin deficient
Pernicious anemia	Inability to absorb vitamin B_{12}	Excess of immature cells
Sickle cell disease	Defective gene	RBC abnormally shaped
Thalassemia	Defective gene	Hemoglobin deficient, RBC short-lived
Hemorrhagic	bleeding (ulcer)	loss of RBCs

➢The blood test, ***hemoglobin A1c(HbA1c糖化血色素)***, can be used to monitor blood glucose levels in diabetics

Function of WBCs(Leukocytes)



- WBCs leave the blood stream by ***emigration***.
- Some WBCs, particularly neutrophils and macrophages, are active in ***phagocytosis***.
- The chemical attraction of WBCs to a disease or injury site is termed ***chemotaxis***.

Differential WBC Count

- **Complete blood count(CBC)** is total RBC, WBC, platelet counts, differential WBC, hematocrit and hemoglobin measurements (screens for anemia and infection)
- **Differential WBC count** is detection of changes in numbers of circulating WBCs (percentages of each type)
  - indicates infection, poisoning, leukemia, chemotherapy, parasites or allergy reaction
- **Normal WBC counts**
  - neutrophils 60-70% (up if bacterial infection)
  - lymphocyte 20-25% (up if viral infection)
  - monocytes 3-8 % (up if fungal/viral infection)
  - eosinophil 2-4 % (up if parasite or allergy reaction)
  - basophil <1% (up if allergy reaction or hypothyroid)

Types of Blood Cells

Type	Describe	Number	Function
紅血球	雙凹圓盤狀無核，含有血紅素，可存活100到200天	4000000~~6000000/mm ^{3}	運輸氧和二氧化碳
白血球		5000~~10000/mm ^{3}	幫助防禦對抗微生物感染
I. 顆粒性細胞	大約是紅血球的兩倍大，細胞質中有顆粒存在，存活12小時到13天		
1. 嗜中性球	核分爲2到5葉，細胞質中的顆粒可被輕微的染上粉紅色	佔白血球的54%到62%	具吞噬細胞的功能，急性感染時，嗜中性球會大量增生
2. 嗜酸性球	核分爲2葉，細胞質中的顆粒在酸性染劑染成紅色	佔白血球的1%到3%	幫助將外來的物質解毒，分泌能溶解血塊的酵素，抵抗寄生蟲感染，與過敏反應有關
3. 嗜鹼性球	核分爲多葉，細胞質中的顆粒在蘇木素染劑中染成藍色	佔白血球的1% 以下	轉變成肥大細胞分泌肝素(抗凝劑) Histamine及5-HT(與過敏及發炎有關)

Types of Blood Cells

Type	Describe	Number	Function
II. 非顆粒性細胞	細胞質中沒有顆粒，存活100天到300天		
1. 單核球	比紅血球大2~~3倍，核的形狀多變化，有圓形的也有分葉的	佔白血球的3%到9%	轉變成巨噬細胞時，具吞噬細胞的功能
2. 淋巴球	只比紅血球大一點，核幾乎佔滿整個細胞	佔白血球的25%到33%	提供特定的免疫反應(包括抗體)
血小板	巨核細胞的碎片，存活5天到9天	250000~~450000/mm ^{3}	促進凝血，提供血管保護

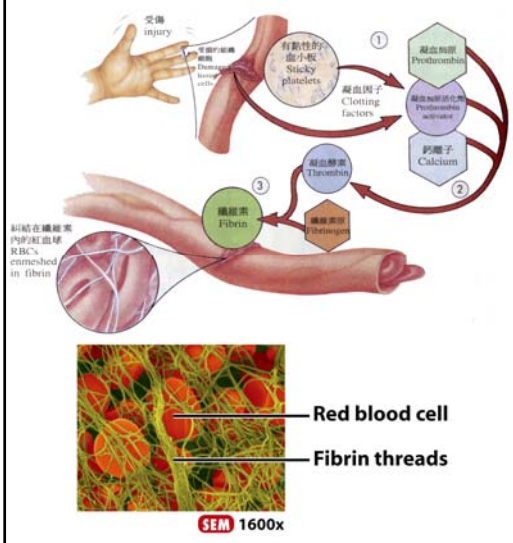
Normal Plasma Value

Test	Normal range
血液體積	80 – 85 ml/kg 體重
血液滲透值	280 – 296 mOsm
血液 pH 值	7.35 – 7.45
酵素	
肌酸磷酸酵素(CPK)	女性：10 – 79 U/L
	男性：17 – 148 U/L
乳酸去氫酵素(LDH)	40 – 90 U/L
磷酸酵素(phosphatase)	女性：0.01 – 0.56 Sigma U/ml
(酸性)(acid)	男性：0.13 – 0.63 Sigma U/ml
血液值	
血比溶	女性：37% – 48% 男性：45% – 52%
血紅素	女性：12 – 16 g/100 ml 男性：13 –18 g/100 ml
紅血球計數	4.2 – 5.9 million/mm^3
白血球計數	4300 – 10880 /mm^3

Normal Plasma Value

Test	Normal range
激素	
睪固酮	男性：300-1100 ng/100ml 女性：25-90 ng/100ml
腎上腺皮質刺激素(ACTH)	15-70 pg/ml
生長激素	小孩：高於10 ng/ml　成年男子：低於5 ng/ml
胰島素	6-26 μ U/ml (禁食)
離子	
重碳酸鹽	24-30 mmol/l
鈣	2.1-2.6 mmol/l
氯	100-106 mmol/l
鉀	3.5-5.0 mmol/l
鈉	135-145 mmol/l
有機分子(其它)	
膽固醇	120-220 mg/100ml
葡萄糖	70-110 mg/100ml(禁食)
乳酸	0.6-1.8 mmol/l
蛋白質(全部)	6.0-8.4 g/100ml
三酸甘油脂	40-150 mg/100ml
尿素氮	8-25 mg/100ml
尿酸	3-7 mg/100ml

Blood Clotting (Hemostasis)



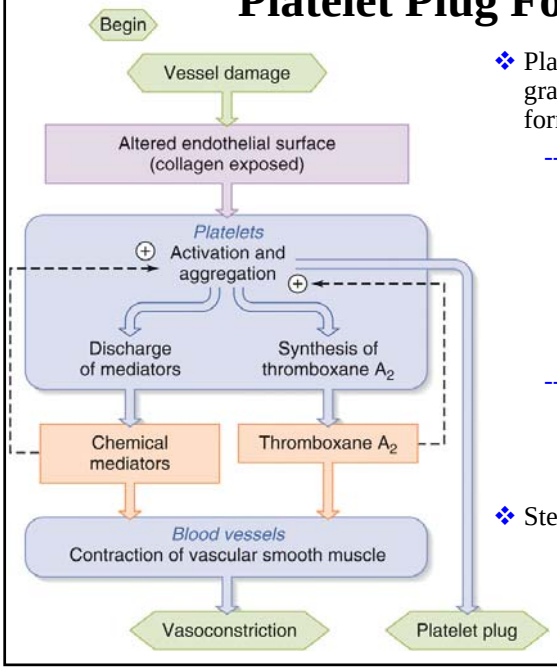
- A ***clot*** is a gel consisting of a network of insoluble protein fibers (fibrin) in which blood cells are trapped
- The chemicals involved in clotting are known as coagulation (clotting) factors; most are in blood plasma, some are released by platelets, and one is released from damaged tissue cells
- Blood clotting is a clotting cascade that may be divided into three stages:
  1. formation of prothrombinase (prothrombin activator)
  2. conversion of prothrombin into thrombin, and
  3. conversion of soluble fibrinogen into insoluble fibrin

Blood Clotting (Hemostasis)

- The clotting cascade can be initiated by either the extrinsic pathway or the intrinsic pathway.
- Normal coagulation requires vitamin K and also involves ***clot retraction*** (tightening of the clot) and ***fibrinolysis*** (dissolution of the clot).
- The fibrinolytic system dissolves small, inappropriate clots and clots at a site of damage once the damage is repaired.
- ***Plasmin*** (fibrinolysin) can dissolve a clot by digesting fibrin threads and inactivating substances such as fibrinogen, prothrombin, and factors V, VIII, and XII.
- Stoppage of bleeding in a quick & localized fashion when blood vessels are damaged
- Prevents hemorrhage (loss of a large amount of blood)

  Methods utilized
  - vascular spasm
  - platelet plug formation
  - blood clotting (coagulation = formation of fibrin threads)

Platelet Plug Formation



- Platelets store a lot of chemicals in granules needed for platelet plug formation

  --alpha granules
  - ✓clotting factors
  - ✓platelet-derived growth factor
    - –cause proliferation of vascular endothelial cells, smooth muscle & fibroblasts to repair damaged vessels

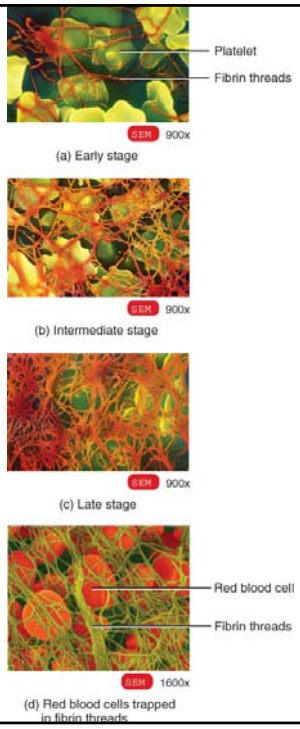
  --dense granules
  - ✓ADP, ATP, Ca^{+2}, serotonin, fibrin-stabilizing factor, & enzymes that produce TXA2

- Steps in the process

  (1) platelet adhesion

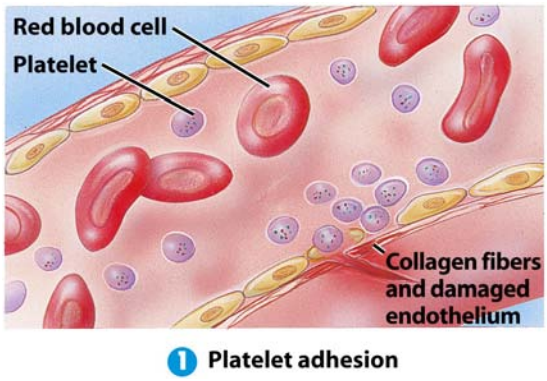
  (2) platelet release reaction

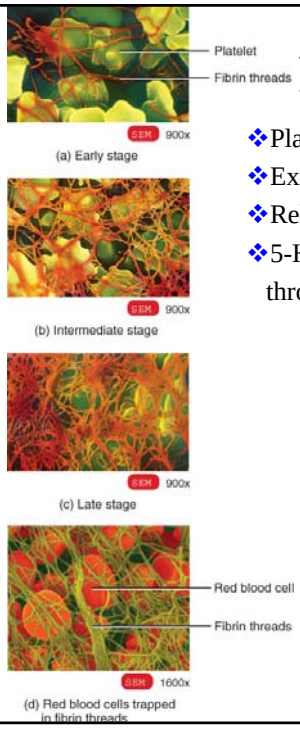
  (3) platelet aggregation



Platelet Adhesion

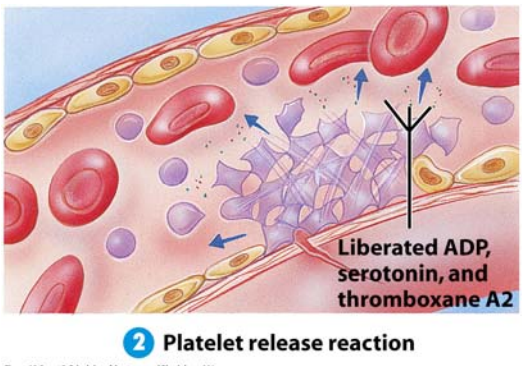
- Platelets stick to exposed collagen underlying damaged endothelial cells in vessel wall



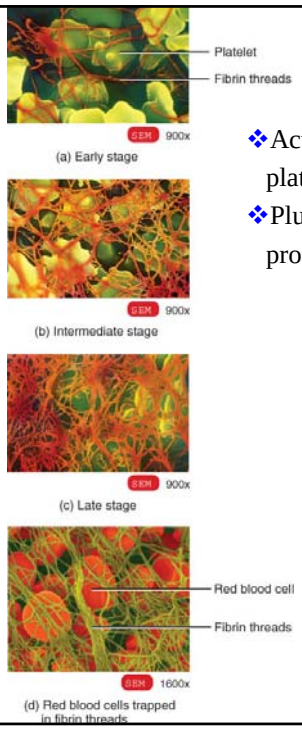


Platelet Release Reaction

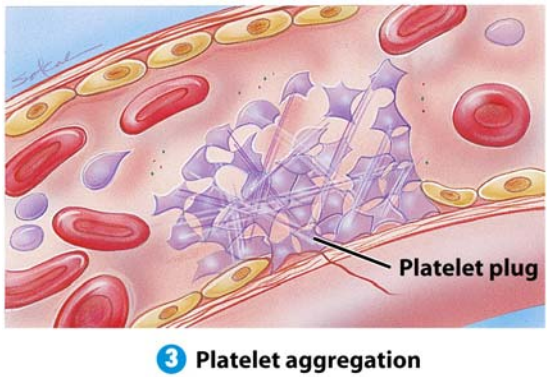
- Platelets activated by adhesion
- Extend projections to make contact with each other
- Release TXA2 & ADP activating other platelets
- 5-HT & TXA2 are vasoconstrictors decreasing blood flow through the injured vessel



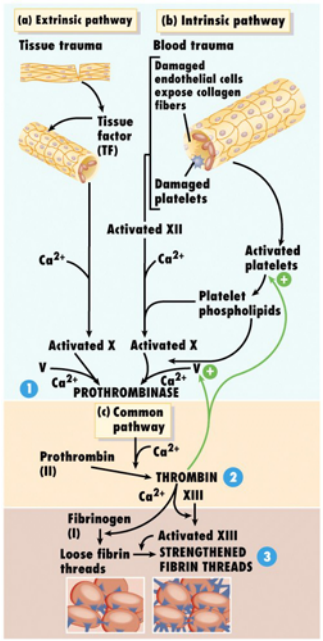
Platelet Aggregation



- Activated platelets stick together and activate new platelets to form a mass called a platelet plug
- Plug reinforced by fibrin threads formed during clotting process



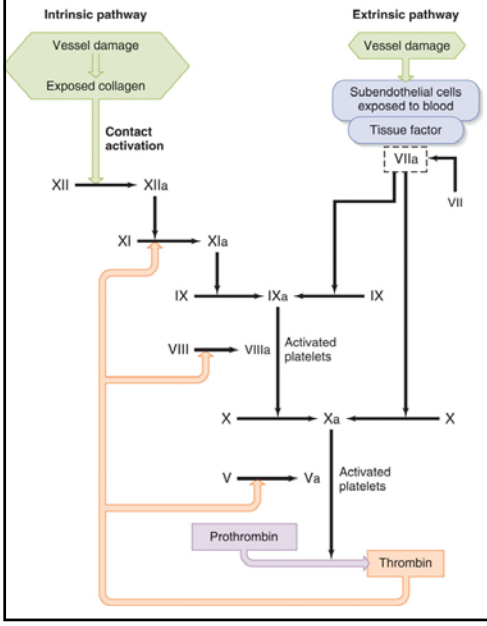
Clotting Cascade



- Prothrombinase is formed by either the intrinsic or extrinsic pathway
- Final common pathway produces fibrin threads

1. *Formation of prothrombinase (prothrombin activator)*
2. *Conversion of prothrombin (II) into thrombin (IIa), and*
3. *Conversion of soluble fibrinogen (I) into insoluble fibrin (Ia)*

Extrinsic & Intrinsic Pathway



- **Extrinsic pathway:**
- ✓ Damaged tissues leak tissue factor (thromboplastin) into bloodstream
- ✓ Prothrombinase forms in seconds
- ✓ In the presence of Ca+2, clotting factor X combines with V to form prothrombinase
- **Intrinsic pathway:**
- ✓ Activation occurs
  - --endothelium is damaged & platelets come in contact with collagen of blood vessel wall
  - --platelets damaged & release phospholipids
- ✓ Requires several minutes for reaction to occur
- ✓ Substances involved: Ca+2 and clotting factors XII, X and V

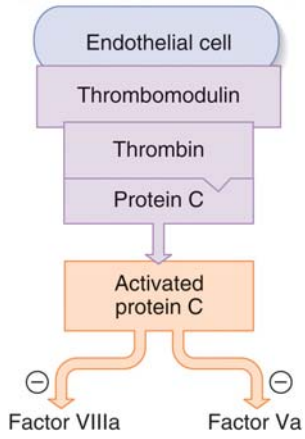
Clotting Factors

Table 12–13 Official Designations for Clotting Factors, Along with Synonyms More Commonly Used

Factor I (fibrinogen)
Factor Ia (fibrin)
Factor II (prothrombin)
Factor IIa (thrombin)
Factor III (tissue factor, tissue thromboplastin)
Factor IV (Ca^{2+})
Factors V, VII, VIII, IX, X, XI, XII, and XIII are the inactive forms of these factors; the active forms add an "a" (e.g., factor XIIa). There is no factor VI.
Platelet factor (PF)

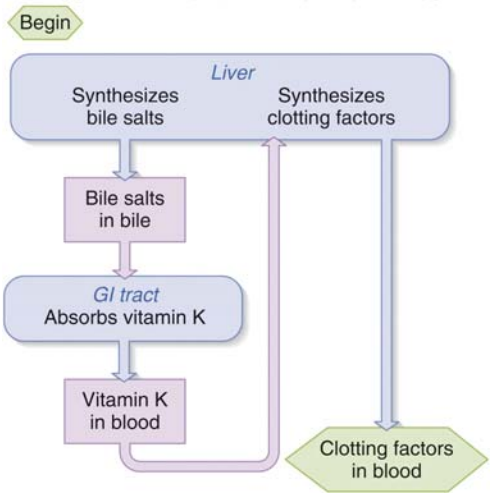
Table 12–14 Actions of Thrombin

Procoagulant	Cleaves fibrinogen to fibrin
	Activates clotting factors XI, VIII, V, and XIII
	Stimulates platelet activation
Anticoagulant	Activates protein C, which inactivates clotting factors VIIIa and Va



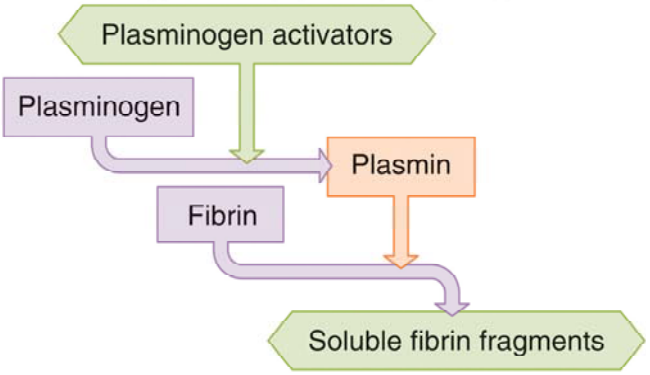
In an uninjured vessel, thrombin bound to thrombomodulin activates protein C, which blocks the clotting response

Role of Vitamin K in Clotting



- Normal clotting requires adequate vitamin K
  - --fat soluble vitamin absorbed if lipids are present
  - --absorption slowed if bile release is insufficient
- Required for synthesis of 4 clotting factors by hepatocytes
  - --factors II (prothrombin), VII, IX and X
- Produced by bacteria in large intestine

Fibrinolytic System (Hemostatic Control Mechanisms)



- Fibrinolysis is dissolution of a clot
- Inactive plasminogen is incorporated into the clot
  - --activation occurs because of factor XII and thrombin
  - --plasminogen becomes plasmin (fibrinolysin) which digests fibrin threads

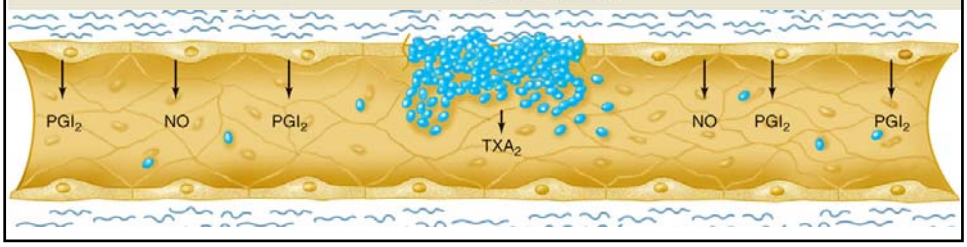
Plasminogen Activators

除了卡利克達(Kallikrein)外，一些其它胞漿素原活化者 (plasminogen activators)，在臨床上被使用來促進血塊溶解。令人興奮的是最近在基因工程技術方面的發展是一種內生性的化合物組織胞漿素原活化者(tissue plasminogen activators，簡稱t-PA)，已進入商業製造階段，TPA為安插到細菌中的人類基因的產物鏈球菌激酵素(streptokinase)，一種自然的細菌產物是一有效且更被廣泛使用的胞漿素原活化者。鏈球菌激胺和TPA也許被注射到一般的循環或特別注射到一被血栓(血塊)阻塞的冠狀動脈血管。

Anticlotting Roles of Endothelial Cells

Table 12–15 Anticlotting Roles of Endothelial Cells

Action	Result
Normally provide an intact barrier between the blood and subendothelial connective tissue	Platelet aggregation and the formation of tissue factor-factor VIIa complexes are not triggered.
Synthesize and release PGI_2 and nitric oxide	These inhibit platelet activation and aggregation.
Secrete tissue factor pathway inhibitor	This inhibits the ability of tissue factor-factor VIIa complexes to generate factor Xa.
Bind thrombin (via thrombomodulin), which then activates protein C	Active protein C inactivates clotting factors VIIIa and Va.
Display heparin molecules on the surfaces of their plasma membranes	Heparin binds antithrombin III, and this molecule then inactivates thrombin and several other clotting factors.
Secrete tissue plasminogen activator	Tissue plasminogen activator catalyzes the formation of plasmin, which dissolves clots.

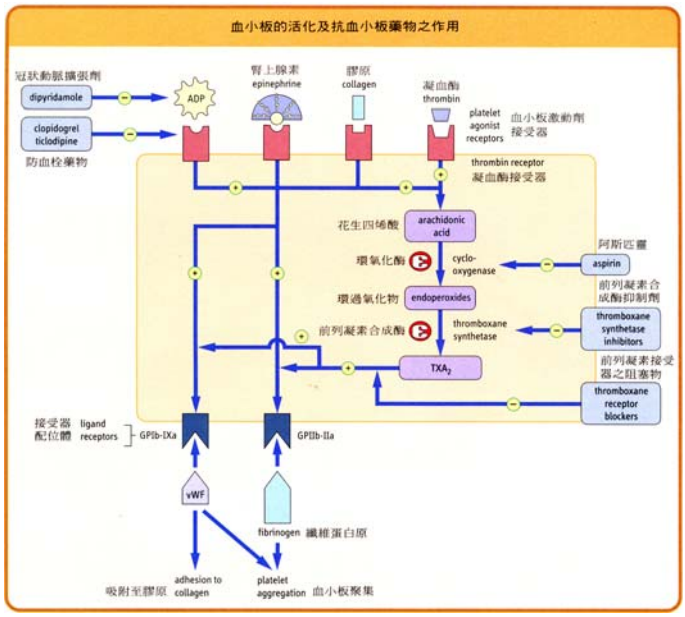


Intravascular Clotting

- **Thrombosis**
  - thrombus (clot) forming in an unbroken blood vessel
    - forms on rough inner lining of BV
    - if blood flows too slowly (stasis) allowing clotting factors to build up locally & cause coagulation
  - may dissolve spontaneously or dislodge & travel
- **Embolus**
  - clot, air bubble or fat from broken bone in the blood
    - pulmonary embolus is found in lungs
- **Low dose aspirin** blocks synthesis of TXA2 & reduces inappropriate clot formation
  - strokes, TIAs and myocardial infarctions

Anticoagulants and Thrombolytic Agents

- **Anticoagulants suppress or prevent blood clotting**
  - Heparin (present in blood)
    - binds antithrombin III (ATIII) and then inactivates thrombin
    - administered during hemodialysis and surgery
  - warfarin (Coumadin)
    - antagonist to vitamin K so blocks synthesis of clotting factors
    - slower than heparin
  - stored blood in blood banks treated with citrate phosphate dextrose (CPD) or EDTA that removes Ca^{+2}
- **Thrombolytic agents are injected to dissolve clots**
  - directly or indirectly activate plasminogen
  - streptokinase or tissue plasminogen activator (t-PA)



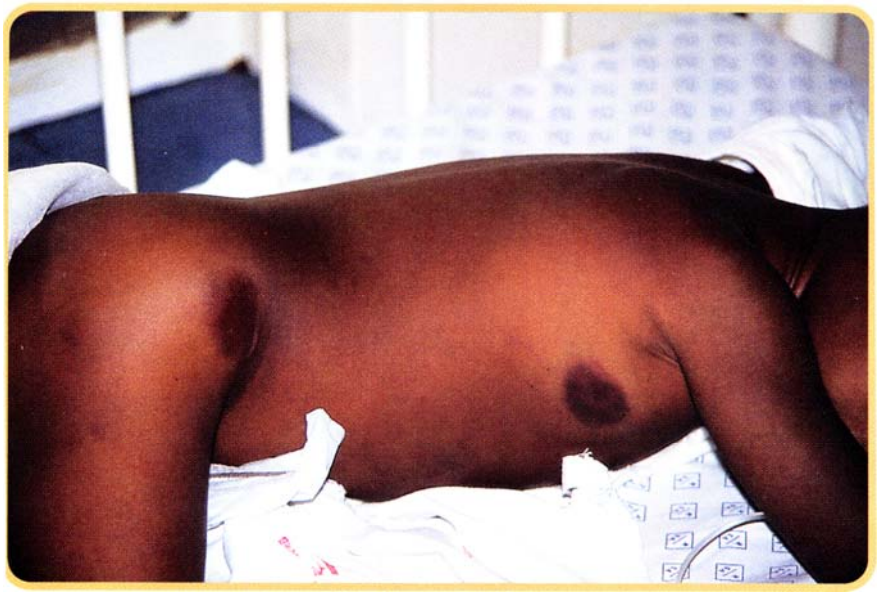
Clotting Disorders and Anticoagulants

種類	失調的原因	說明
後天凝血失調	缺乏維生素K	肝臟中prothrombin和其它凝血因子形成不 足
先天凝血失調	A型血友病 (缺陷的第八因子)	X染色體攜帶的隱性基因，導致纖維素的形成延緩。
	B型血友病 (缺陷的第九因子)，也稱為耶誕病	X染色體攜帶的隱性基因，導致纖維素的形成延緩。
抗凝血劑		
阿斯匹靈	抑制前列腺素的產生，導致血小板釋放反應不全。	
香豆素	與維生素K的作用競爭。	
肝素	抑制thrombin的活性。	
檸檬酸鹽	與鈣離子結合，因而抑制許多凝血因子的活性。	

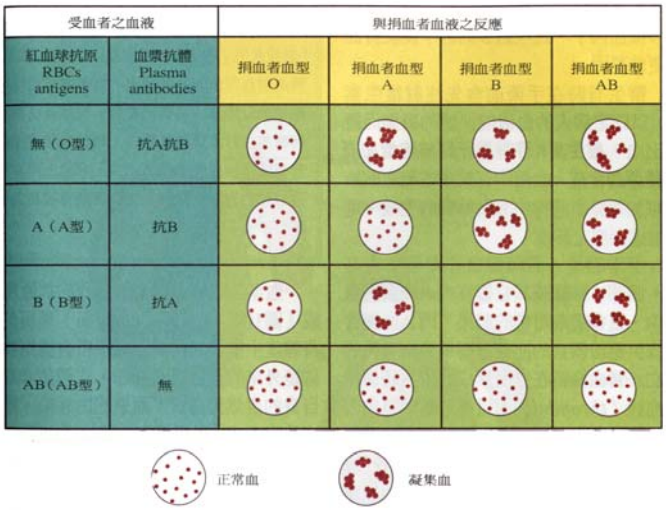
Hemophilia A

一些遺傳性疾病牽涉到凝血系統。遺傳性凝血失調的例子包括在第八因子兩個不同的基因缺陷。第八因子的其中一個次單位有缺陷，而使得第八因子無法參與內在凝血路徑，這個基因的疾病稱為A型血友病，是一個存在於X染色體上的隱性基因，在歐洲皇族是普通的。第八因子另一個次單位有缺陷導致Von Willebrand's disease 。在這種疾病當中，快速循環的血小板不能附著到膠原蛋白，所以血小板栓無法形成。

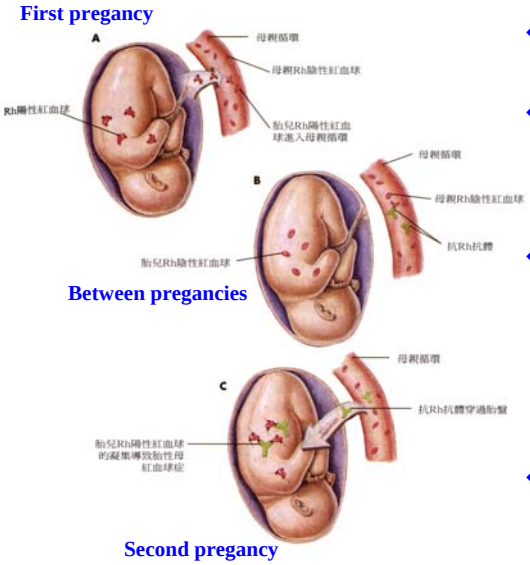
一位三歲大的血友病患，因輕微跌倒所造成之嚴重瘀傷



Blood Types



Erythroblastosis Fetalis



- Antigen was discovered in blood of *Rhesus* monkey (Rh blood group)
- People with Rh agglutinogens on RBC surface are Rh+. Normal plasma contains no anti-Rh antibodies
- Antibodies develop only in Rh- blood type & only with exposure to the antigen
  - –transfusion of positive blood
  - –during a pregnancy with a positive blood type fetus
- Transfusion reaction upon 2nd exposure to the antigen results in hemolysis of the RBCs in the donated blood

Acid-Base Balance of Blood

表 13.6 描述酸鹼平衡的名詞

名詞	定義
呼吸性酸中毒	CO_2 滯溜增加（由於換氣不足），會導致碳酸的累積，因而使血液 pH 值下降，低於正常。
代謝性酸中毒	非揮發酸如：乳酸、脂肪酸和酮體的產生增加，或血液重碳酸根(HCO_3^-)流失（如腹瀉時），導致血液 pH 值下降低於正常。
呼吸性鹼中毒	由於 CO_2 和碳酸流失（藉由換氣過度），而使血液 pH 值上升。
代謝性鹼中毒	由於非揮發性酸流失（如過度嘔吐）或由於過量累積重碳酸根(HCO_3^-)而造成血液 pH 值上升。
代償性酸中毒或鹼中毒	代謝性酸中毒或鹼中毒部份是由血液中碳酸濃度相對的改變（藉著通氣改變）來代償。 呼吸性酸中毒或鹼中毒部份是由增加保留重碳酸根或分泌於尿中來代償。

表 13.7 酸中毒和鹼中毒的代謝性和呼吸性組成的分類

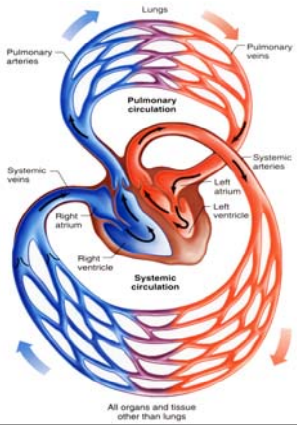
血漿 CO_2	血漿 HCO_3^-	情況	原因
正常	低	代謝性酸中毒	"非揮發性" 酸產生增加（如乳酸、酮體和其它），或腹瀉流失 HCO_3^-
正常	高	代謝性鹼中毒	嘔吐胃酸；低血鉀；過量服用類固醇
低	低	呼吸性鹼中毒	換氣過度
高	高	呼吸性酸中毒	換氣不足

❖血液pH值(7.35-7.45)是由二氧化碳和重碳酸根適當的比例來維持

肺臟－維持適當的二氧化碳濃度

腎臟－維持游離的重碳酸根濃度

Systemic & Pulmonary Circulations

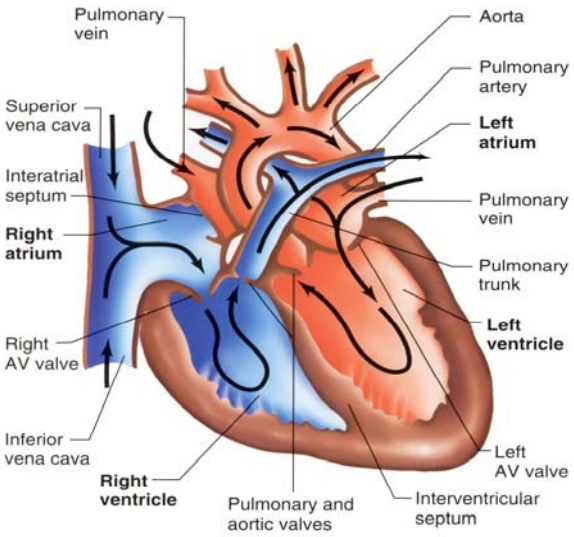


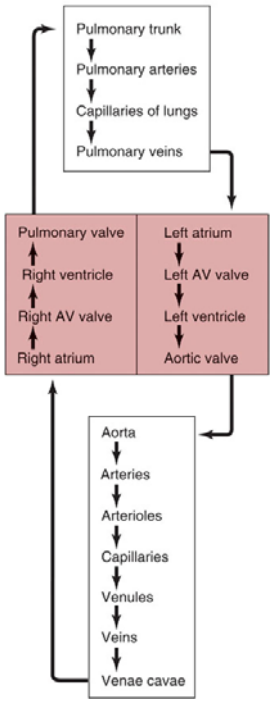
Organ	Flow at rest ml/min
Brain	650 (13%)
Heart	215 (4%)
Skeletal muscle	1030 (20%)
Skin	430 (9%)
Kidneys	950 (20%)
Abdominal organs	1200 (24%)
Other	525 (10%)
Total	5000 (100%)

	起源	動脈	動脈氧含量	靜脈	靜脈氧含量	終點
肺循環	右心室	肺動脈	低	肺靜脈	高	左心房
體循環	左心室	主動脈和它的分支	高	上、下腔靜脈和它的分支	低	右心房

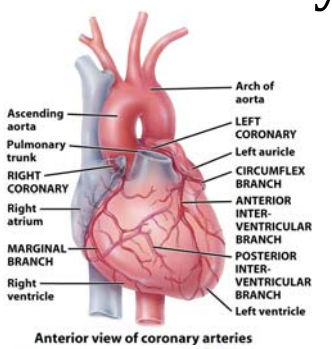
**冠狀動脈循環的血液不進入腔靜脈，而是直接由冠狀竇(coronary sinus)回到右心房*

Heart Circulation

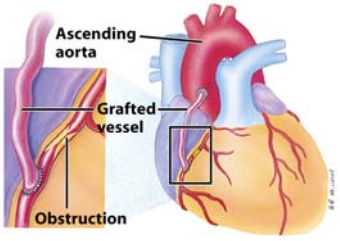




Coronary Circulation



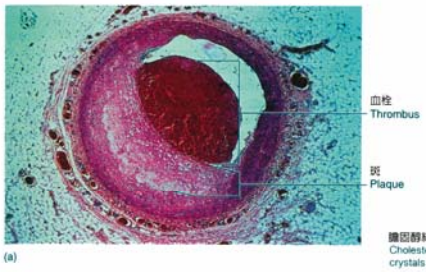
Anterior view of coronary arteries



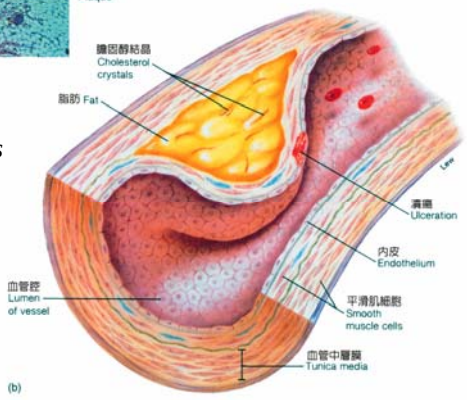
Coronary artery bypass grafting (CABG)

- Coronary arteries are branches off aorta above aortic semilunar valve
- Coronary circulation is blood supply to the heart (it delivers oxygenated blood and nutrients to and removes carbon dioxide and wastes from the myocardium)
- Heart as a very active muscle needs lots of O_2
- When the heart relaxes high pressure of blood in aorta pushes blood into coronary vessels
- Many anastomoses
  -- connections between arteries supplying blood to the same region, provide alternate routes if one artery becomes occluded

Coronary Artery Disease (CAD)

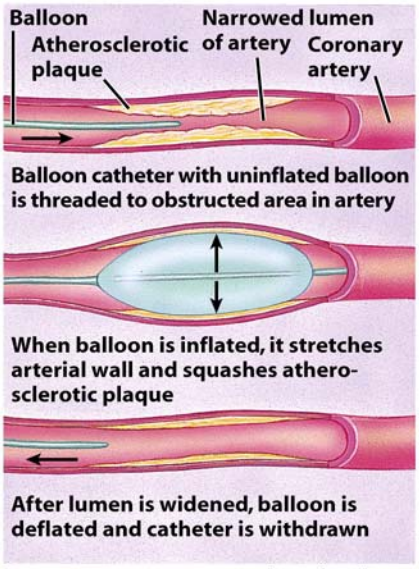


Atherosclerosis
coronary artery spasm,
or ***a clot*** *in a coronary artery*



Risk factors:

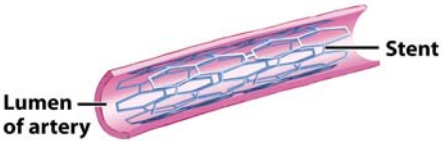
- ✓*high blood cholesterol levels*
- ✓*high blood pressure*
- ✓*cigarette smoking*
- ✓*obesity*
- ✓*diabetes*
- ✓*"type A" personality*
- ✓*sedentary lifestyle*



Percutaneous transluminal coronary angioplasty (PTCA)

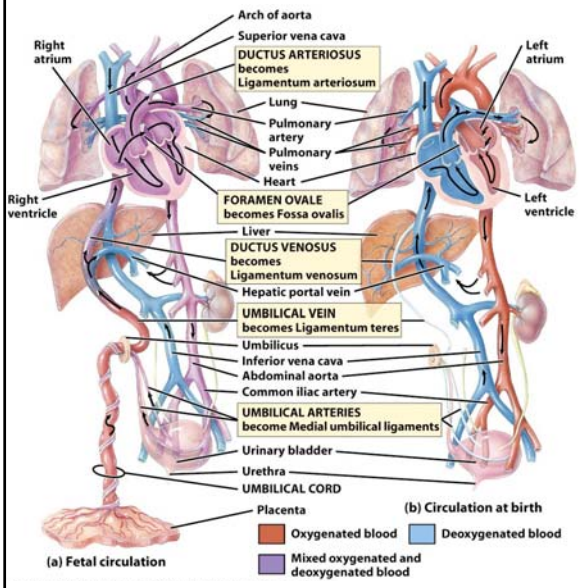
Treatment:

- ✓***Drugs***
- ✓***Angioplasty***
- ✓***Bypass graft***
- ✓***Stent***

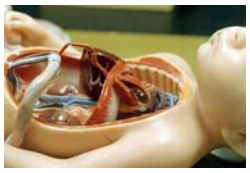


Angiogram showing a stent in the circumflex artery

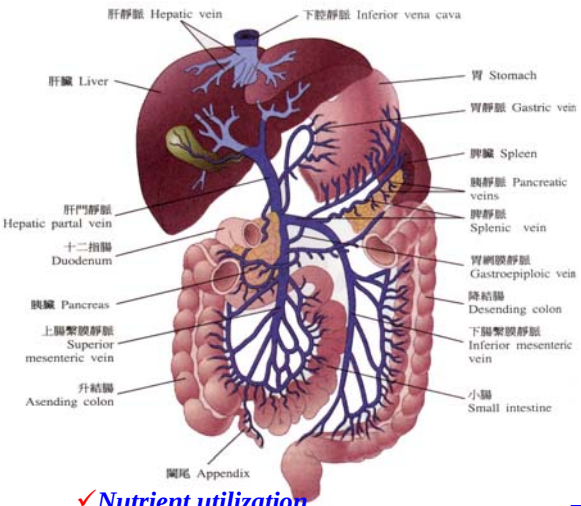
Fetal Circulation



PDA 血流通過一開放的動脈導管。正常狀況此導管於胎兒時開放，出生後則閉鎖，最後形成動脈韌帶。



Hepatic Portal Circulation



✓*Nutrient utilization*

✓*Blood detoxification by the liver*

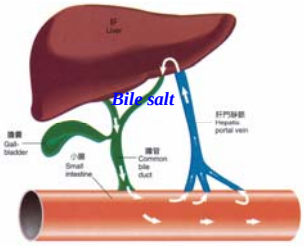
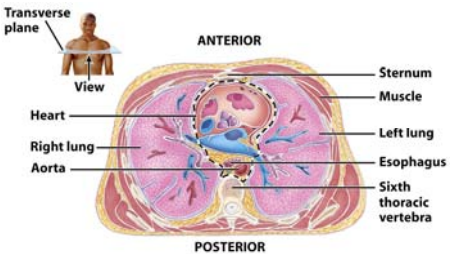


表 18.3 肝臟分泌至膽管中的化合物

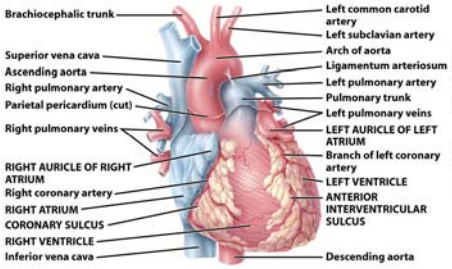
分類	化合物	說明
內在的（自然產生）	膽鹽	大部分被吸收且進入腸肝循環
	膽尿素原(urobilinogen)	
	膽固醇	
	卵磷脂(Lecithin)	小部分被吸收及進入腸肝循環
	膽紅素(Bilirubin)	無腸肝循環
外來的（藥物）	Ampicillin	大部分被吸收及進入腸肝循環
	streptomycin	
	tetracycline	
	Sulfonamides	小部分被吸收及進入腸肝循環
	penicillin	

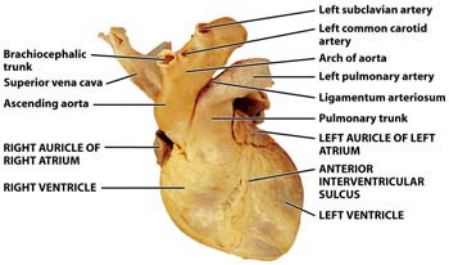
Enterohepatic Circulation

Heart Structure

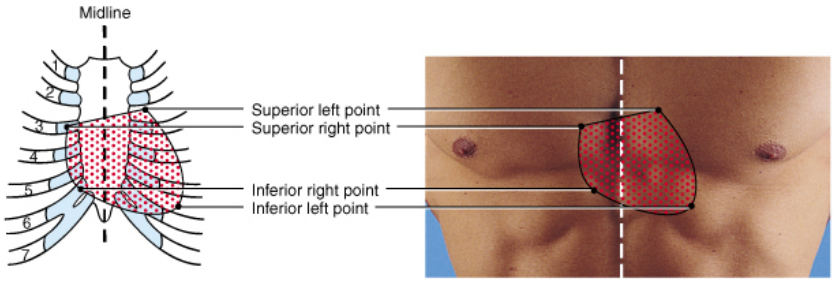


- The heart is situated between the lungs in the mediastinum with about two-thirds of its mass to the left of the midline
- Heart pumps over 1 million gallons per year (over 60,000 miles of blood vessels)



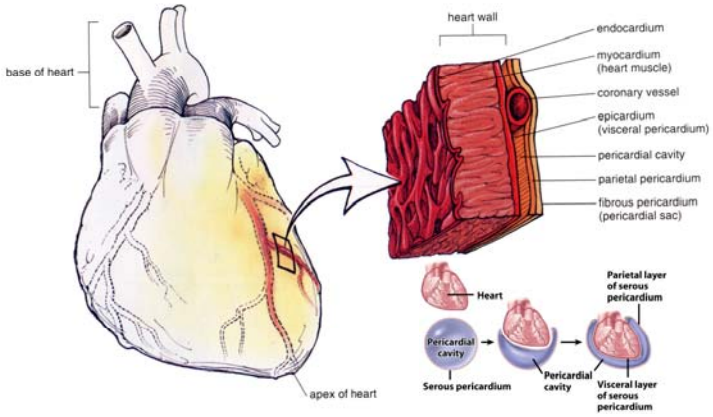


Surface Projection of the Heart



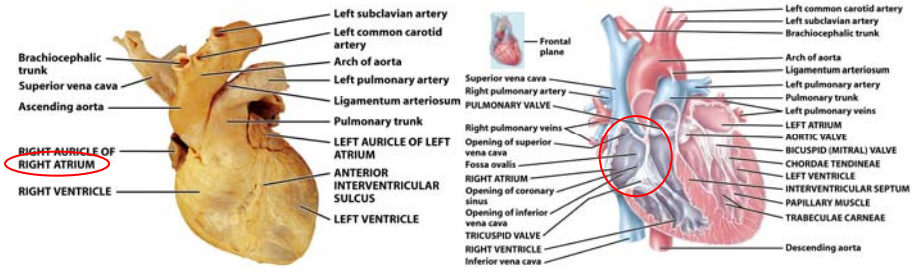
- Superior right point at the superior border of the 3rd right costal cartilage
- Superior left point at the inferior border of the 2nd left costal cartilage 3cm to the left of midline
- Inferior left point at the 5th intercostal space, 9 cm from the midline
- Inferior right point at superior border of the 6th right costal cartilage, 3 cm from the midline

Tissue Layers of Heart Wall



- The wall of the heart has three layers: ***periardium***, ***myocardium***, and ***endocardium***
- The epicardium consists of mesothelium and connective tissue, the myocardium is composed of cardiac muscle, and the endocardium consists of endothelium and connective tissue
- ***Myocarditis*** is an inflammation of the myocardium (***Pericarditis***:pericardium)
- ***Endocarditis*** in an inflammation of the endocardium (usually involves the heart valves)

Chambers of the Heart

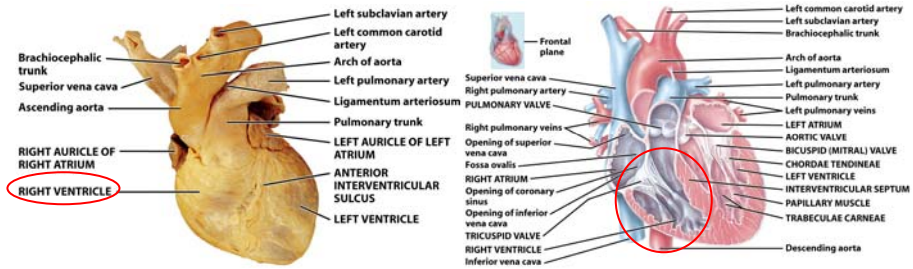


Four chambers (2 upper atria & 2 lower ventricles)

Right Atrium (RA)

- Receives blood from 3 sources
  --superior vena cava, inferior vena cava and coronary sinus
- Interatrial septum partitions the atria
- Fossa ovalis is a remnant of the fetal foramen ovale
- Tricuspid valve
  --Blood flows through into right ventricle
  --has three cusps composed of dense CT covered by endocardium

Chambers of the Heart

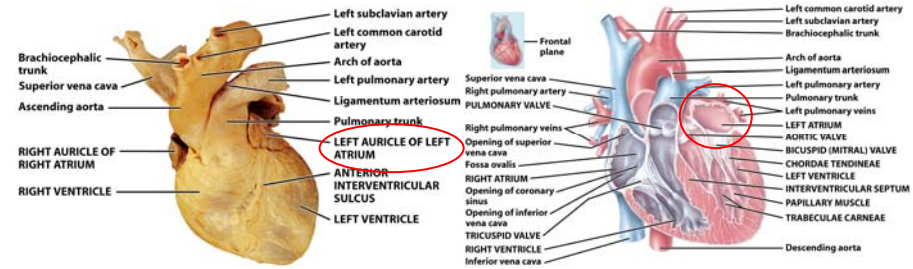


Four chambers (2 upper atria & 2 lower ventricles)

Right Ventricle (RV)

- Forms most of anterior surface of heart
- Papillary muscles are cone shaped trabeculae carneae (raised bundles of cardiac muscle)
- Chordae tendineae: cords between valve cusps and papillary muscles
- Interventricular septum: partitions ventricles
- Pulmonary semilunar valve: blood flows into pulmonary trunk

Chambers of the Heart

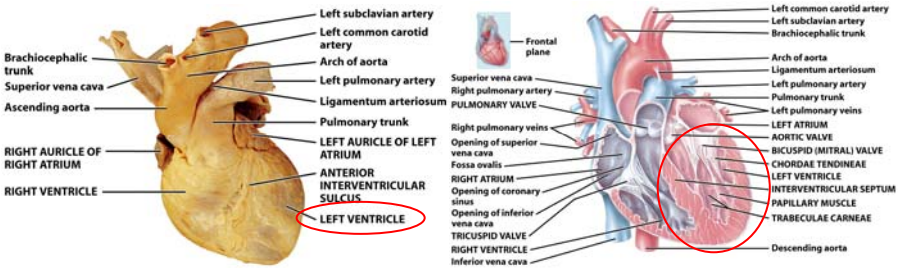


Four chambers (2 upper atria & 2 lower ventricles)

Left Atrium (LA)

- Forms most of the base of the heart
- Receives blood from lungs - 4 pulmonary veins (2 right + 2 left)
- Bicuspid valve: blood passes through into left ventricle
  --has two cusps
  --to remember names of this valve, try the pneumonic LAMB
  (Left Atrioventricular, Mitral, or Bicuspid valve)

Chambers of the Heart

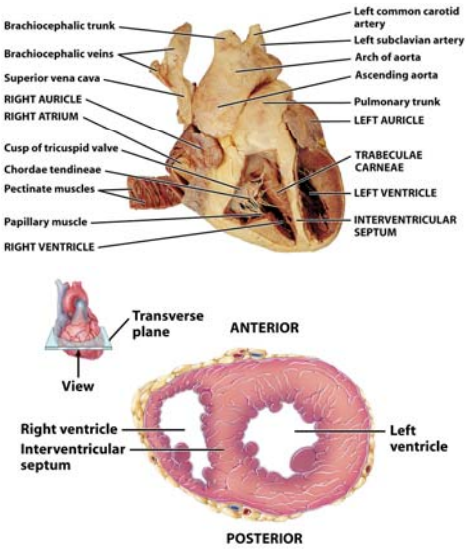


Four chambers (2 upper atria & 2 lower ventricles)

Left Ventricle (LV)

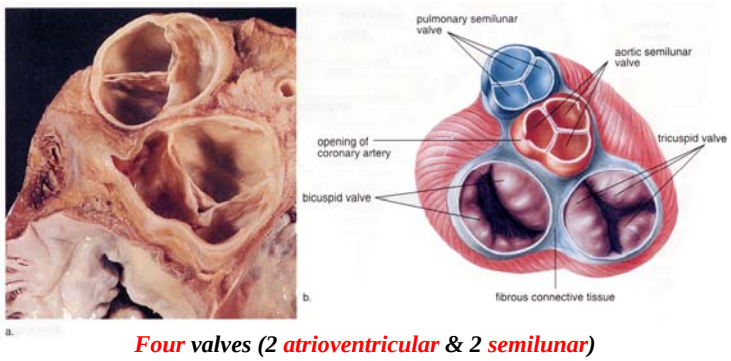
- Forms the apex of heart
- Chordae tendineae anchor bicuspid valve to papillary muscles (also has trabeculae carneae like right ventricle)
- Aortic semilunar valve:
  - --blood passes through valve into the ascending aorta
  - --just above valve are the openings to the coronary arteries

Myocardial Thickness and Function



- Thickness of myocardium varies according to the function of the chamber
- Atria are thin walled, deliver blood to adjacent ventricles
- Ventricle walls are much thicker and stronger
  - right ventricle supplies blood to the lungs (little flow resistance)
  - left ventricle wall is the thickest to supply systemic circulation`

Heart Valves

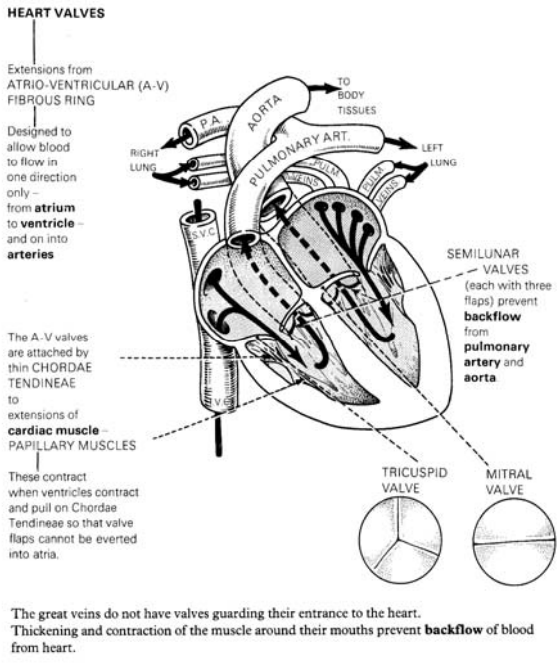


Four valves (2 atrioventricular & 2 semilunar)

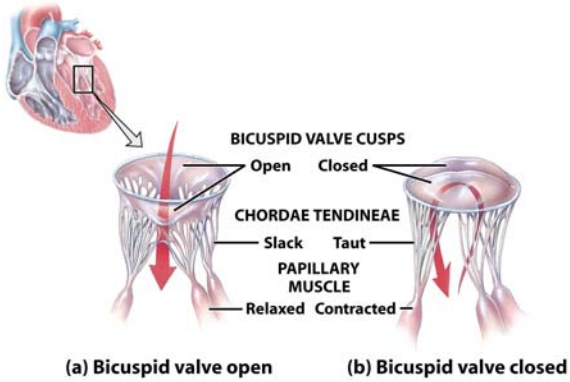
- Valves open and close in response to pressure changes as the heart contracts and relaxes

Heart valves disorders

- Stenosis is a narrowing of a heart valve which restricts blood flow
- Insufficiency or incompetence is a failure of a valve to close completely
- Stenosed valves may be repaired by balloon valvuloplasty, surgical repair, or valve replacement



The great veins do not have valves guarding their entrance to the heart. Thickening and contraction of the muscle around their mouths prevent **backflow** of blood from heart.



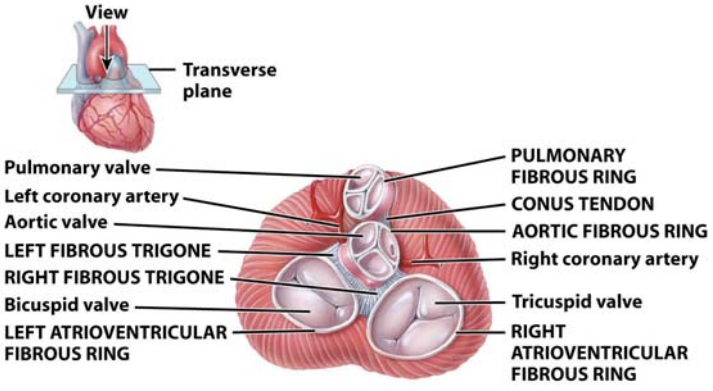
(a) Bicuspid valve open (b) Bicuspid valve closed

AV valves open

- AV valves open and allow blood to flow from atria into ventricles when ventricular pressure is lower than atrial pressure
  - -- occurs when ventricles are relaxed, chordae tendineae are slack and papillary muscles are relaxed

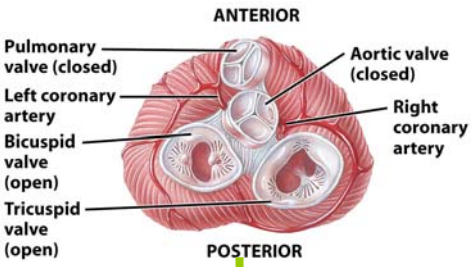
AV valves close

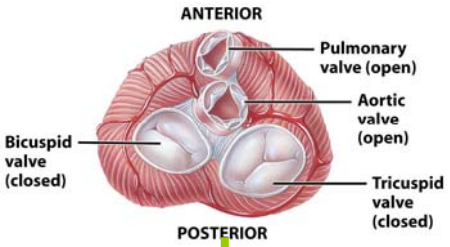
- AV valves close preventing backflow of blood into atria
  - -- occurs when ventricles contract, pushing valve cusps closed, chordae tendinae are pulled taut and papillary muscles contract to pull cords and prevent cusps from everting



Semilunar valves

- SL valves open with ventricular contraction
  - -- allow blood to flow into pulmonary trunk and aorta
- SL valves close with ventricular relaxation
  - -- prevents blood from returning to ventricles, blood fills valve cusps, tightly closing the SL valves

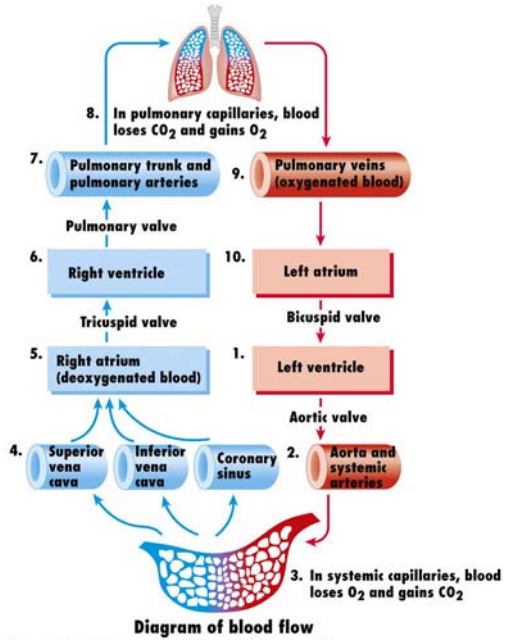


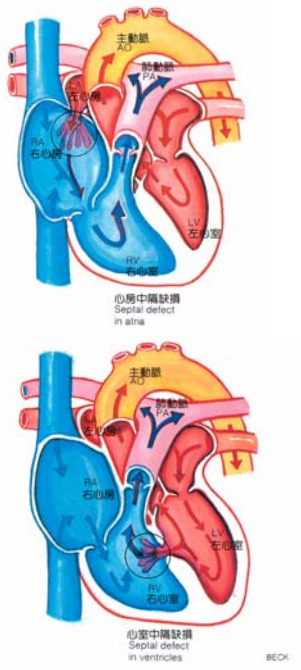


What are the ventricles doing?

Atria contract
blood fills ventricles through AV valves

Ventricles contract
blood pumped into aorta and pulmonary trunk through SL valves





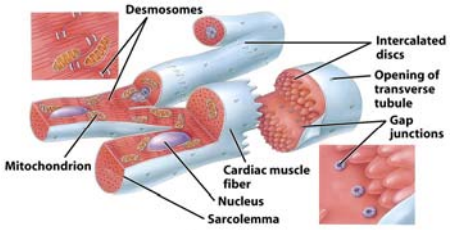
Heart Valves

table 12.1 Valves of the Heart

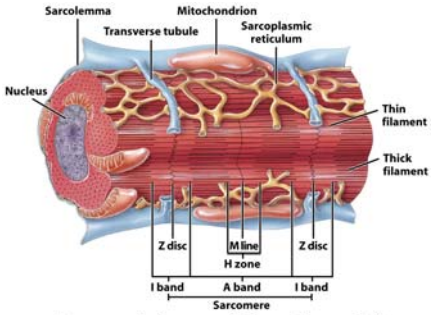
Right Side			Left Side		
Valve	Location	Function	Valve	Location	Function
Tricuspid valve	Right atrioventricular valve	Prevents blood from moving from right ventricle into right atrium during ventricular contraction	Bicuspid (mitral) valve	Left atrioventricular valve	Prevents blood from moving from left ventricle into left atrium
Pulmonary semilunar valve	Entrance to pulmonary trunk	Prevents blood from moving from pulmonary trunk into right ventricle during ventricular relaxation	Aortic semilunar valve	Entrance to aorta	Prevents blood from moving from aorta into left ventricle

Source: David Shier, et al., *Hole's Human Anatomy and Physiology*, 8th ed. Copyright © 1999 The McGraw-Hill Companies, Inc., Dubuque, Iowa.

Histology of Cardiac Muscle



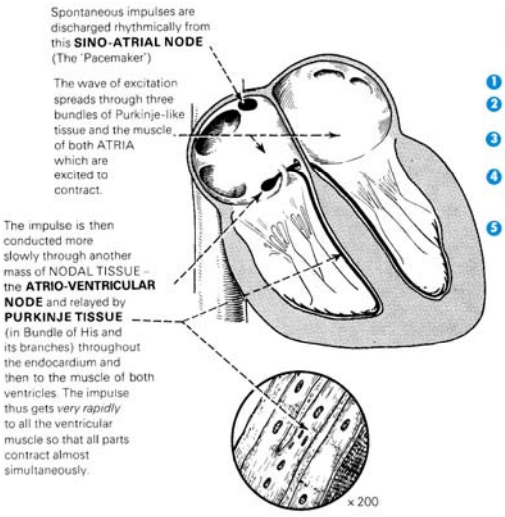
Cardiac muscle fibers

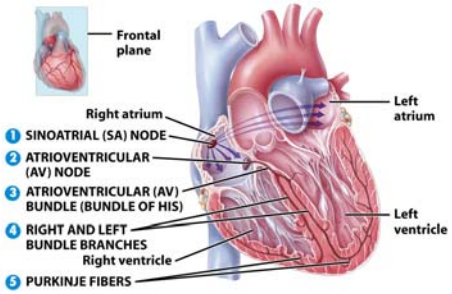


Arrangement of components in a cardiac muscle fiber

- Compared to skeletal muscle fibers, cardiac muscle fibers are shorter in length, larger in diameter, and squarish rather than circular in transverse section
- They also exhibit branching
- Fibers within the networks are connected by ***intercalated discs***, which consist of ***desmosomes*** and ***gap junctions***
- Cardiac muscles have the same arrangement of actin and myosin, and the same bands, zones, and Z discs as skeletal muscles
- They do have less sarcoplasmic reticulum than skeletal muscles and require Ca^{+2} from extracellular fluid for contraction

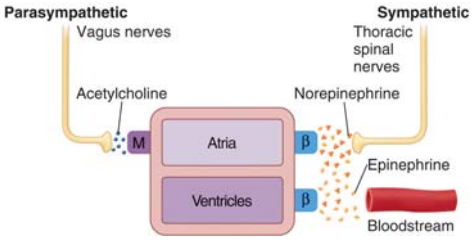
Conducting System of Heart





- Cardiac muscle cells are ***autorhythmic*** cells because they are self-excitable. They repeatedly generate spontaneous action potentials that then trigger heart contractions
- These cells act as a ***pacemaker*** to set the rhythm for the entire heart.
- They form the conduction system, the route for propagating action potential through the heart muscle.

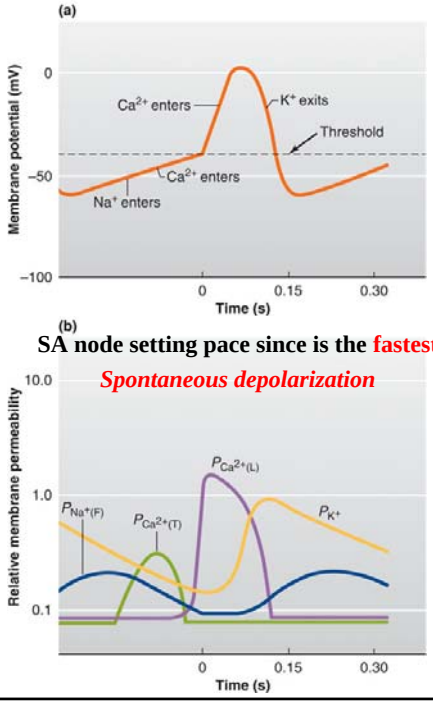
Rhythm of Conduction System



- Signals from the autonomic nervous system and hormones, such as epinephrine, do modify the heartbeat (in terms of rate and strength of contraction), but they do not establish the fundamental rhythm

- SA node fires spontaneously 90-100 times per minute
- AV node fires at 40-50 times per minute
- If both nodes are suppressed fibers in ventricles by themselves fire only 20-40 times per minute
- Artificial pacemaker needed if pace is too slow
- Extra beats forming at other sites are called ectopic pacemakers
  -- caffeine & nicotine increase activity

Pacemaker Potential & Action Potential in SA Node



SA node setting pace since is the fastest

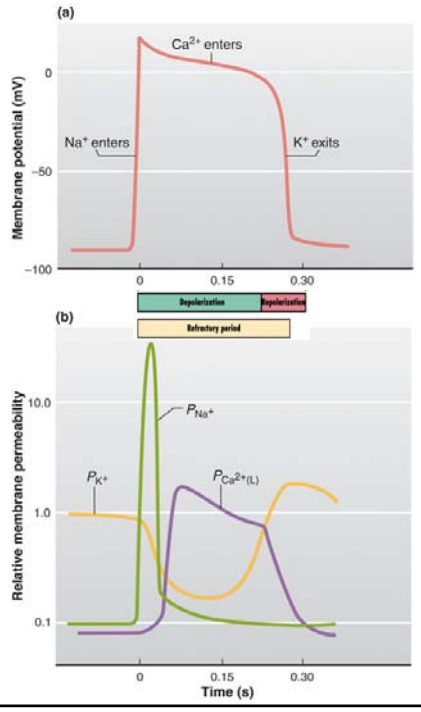
Spontaneous depolarization

Sodium ions "leaking" in through the F-type [funny] channels
PLUS
calcium ions moving in through the T [calcium] channels cause a threshold graded depolarization.

The rapid opening of voltage-gated calcium channels is responsible for the rapid depolarization phase.

Reopening of potassium channels
PLUS
closing of calcium channels are responsible for the repolarization phase.

Action Potential of Myocardial cell

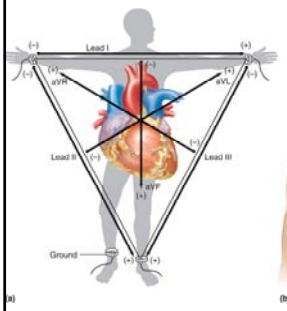


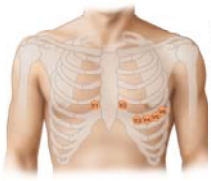
The rapid opening of voltage-gated sodium channels is responsible for the rapid depolarization phase.

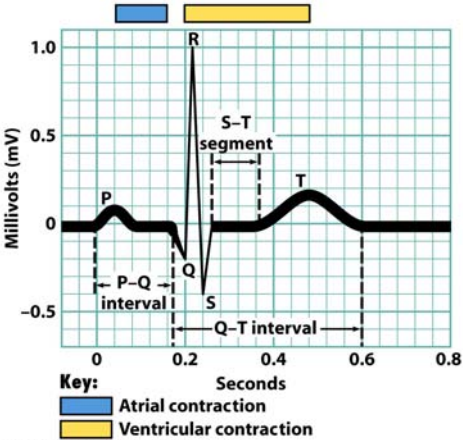
The prolonged "plateau" of depolarization is due to the slow but prolonged opening of voltage-gated calcium channels
PLUS
closure of potassium channels.

Opening of potassium channels results in the repolarization phase.

Electrocardiogram (ECG & EKG)



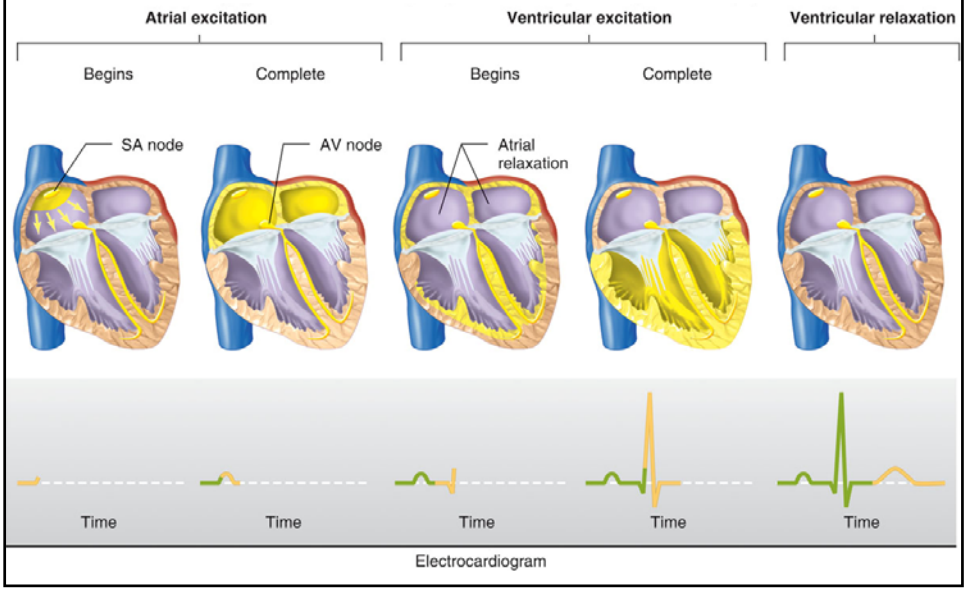


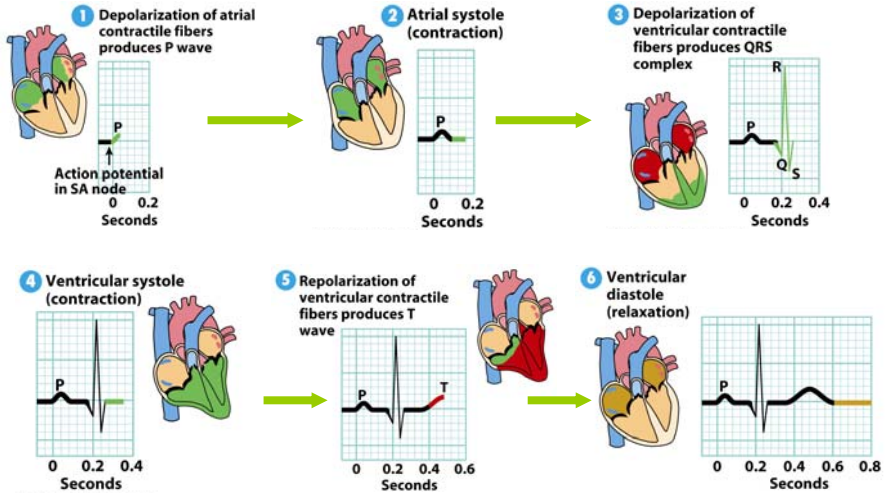


- Impulse conduction through the heart generates electrical currents that can be detected at the surface of the body. A recording of the electrical changes that accompany each cardiac cycle (heartbeat) is called an ***electrocardiogram* (*ECG* or *EKG*)**.
- The ECG helps to determine if the conduction pathway is abnormal, if the heart is enlarged, and if certain regions are damaged.

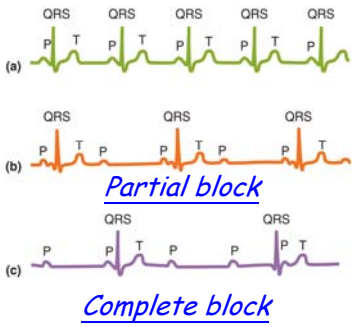
P wave-- ***atrial depolarization***
P-Q interval-- conduction time from ***atrial*** to ***ventricular excitation***
QRS complex-- ***ventricular depolarization***
T wave-- ***ventricular repolarization***

Sequence of Cardiac Excitation



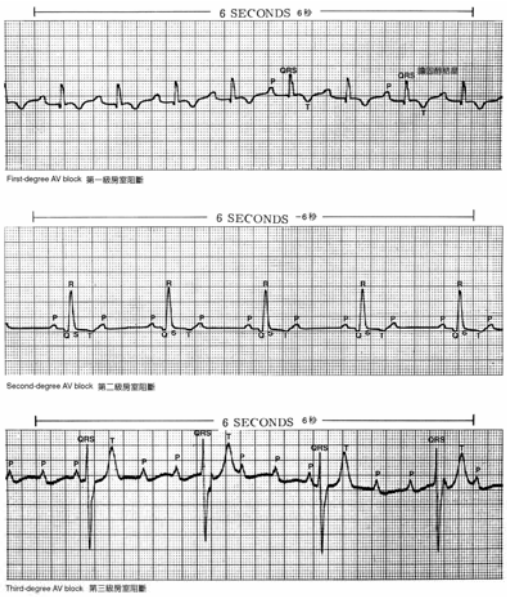


AV Block

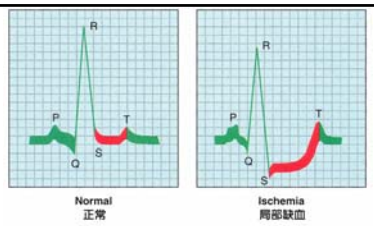


Partial block

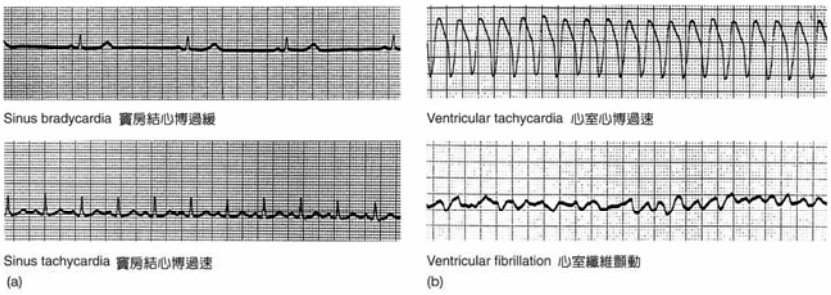
Complete block



■圖 13.31 **房室結阻斷**。在第一級阻斷，P-R 間期大於 0.20 秒（在本例當中，P-R 間期是 0.26~0.28 秒）。在第二級阻斷，可看見 QRS 波沒有伴隨著 P 波出現（在這個例子中，心房每分鐘跳 90 下（P 波所代表的），然而心室每分鐘跳 50 次（如 QRS 波所代表的）。第三級阻斷，心室依照一異位性節律之速率來跳動而獨立於心房跳動之外。因此在心電圖上心室的去極化(QRS)和再極化(T)相對於 P 波（心房去極化）就有不一定的位置。

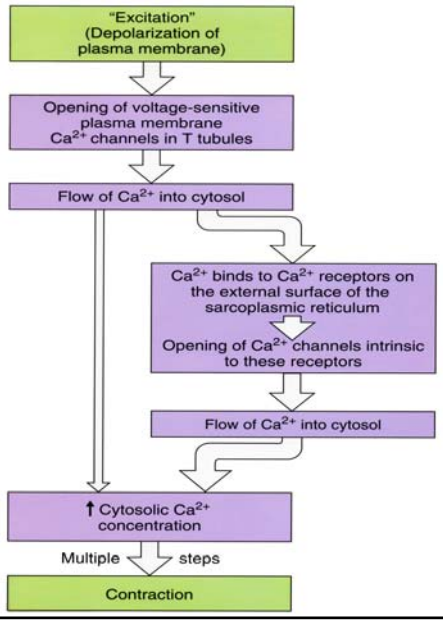


■圖　由於心肌局部缺血而使心電圖上 S-T 段下降。



■圖　**心電圖偵測心律不整**。在(a)心跳是由正常的節律點—竇房結來定速度的（稱為竇房結節律）。這可以是異常地慢（心搏過緩—在這個例子中每分鐘 42 下）或快速（心搏過速—在此例中為每分鐘 125 下）。比較在(a)中的心搏過速與在(b)中的心搏過速的型態。心室心搏過速是由在心室的異位性節律點產生的。這種危險的情況能很快導致心室纖維顫動，同樣如(b)所示。

EC Coupling of Cardiac Muscle

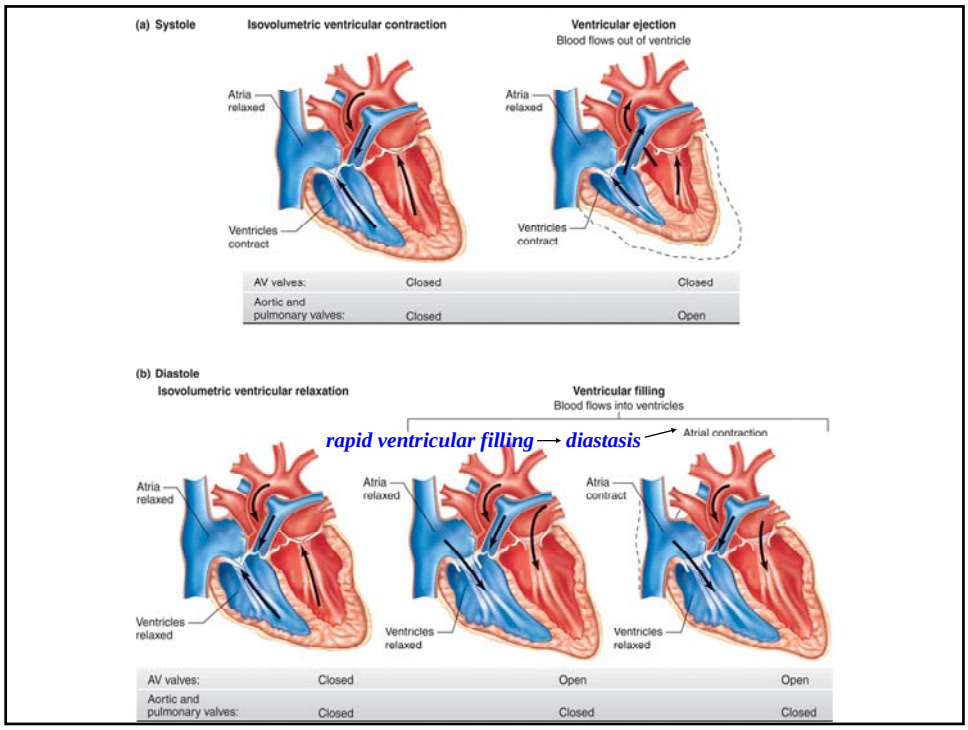


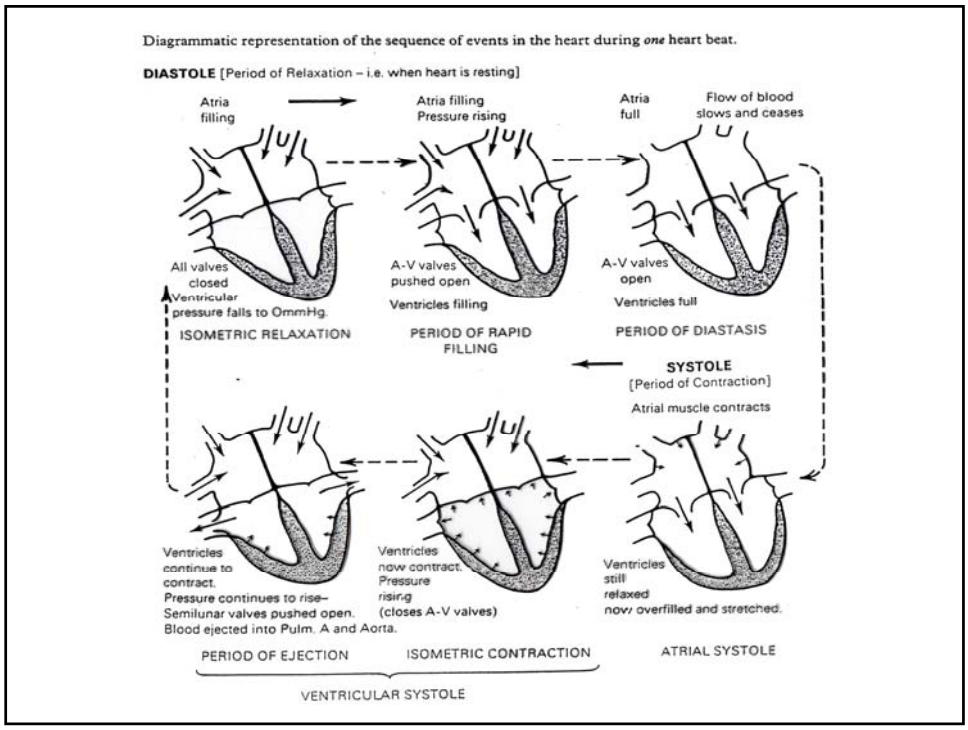
Cardiac Cycle

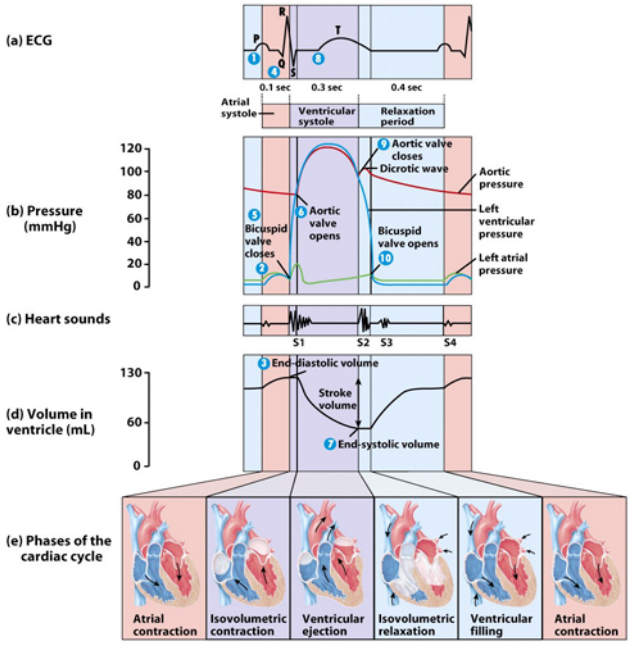
- A ***cardiac cycle*** = the systole (contraction) and diastole (relaxation) of both atria + the systole and diastole of both ventricles (at 75 bpm, one cycle requires 0.8 sec)
- Pressure and volume changes during the cardiac cycle
- End diastolic volume (EDV)
  -- volume in ventricle at end of diastole, about 130 ml
- End systolic volume (ESV)
  -- volume in ventricle at end of systole, about 60 ml
- Stroke volume (SV)
  -- the volume ejected per beat from each ventricle, about 70 ml
  SV = EDV - ESV

Phases of Cardiac Cycle

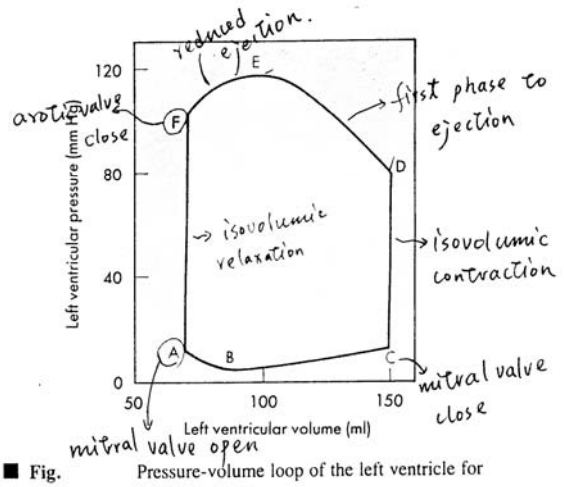
- Isovolumetric relaxation
  - brief period when volume in ventricles does not change--as ventricles relax, pressure drops and AV valves close
- Ventricular filling
  - rapid ventricular filling:as blood flows from full atria
  - diastasis: as blood flows from atria in smaller volume
  - atrial systole pushes final 20-25 ml blood into ventricle
- Ventricular systole
  - ventricular systole
  - isovolumetric contraction
    - brief period, AV valves close before SL valves open
  - ventricular ejection: as SL valves open and blood is ejected


(a) Systole
Isovolumetric ventricular contraction
Ventricular ejection
Blood flows out of ventricle
Atria relaxed
Ventricles contract
Atria relaxed
Ventricles contract
AV valves: Closed Closed
Aortic and pulmonary valves: Closed Open
(b) Diastole
Isovolumetric ventricular relaxation
Ventricular filling
Blood flows into ventricles
rapid ventricular filling
diastasis
Atrial contraction
Atria relaxed
Ventricles relaxed
Atria relaxed
Ventricles relaxed
Atria contract
Ventricles relaxed
AV valves: Closed Open Open
Aortic and pulmonary valves: Closed Closed Closed


Diagrammatic representation of the sequence of events in the heart during one heart beat.
DIASTOLE [Period of Relaxation – i.e. when heart is resting]
Atria filling
Atria filling Pressure rising
Atria full
Flow of blood slows and ceases
All valves closed Ventricular pressure falls to 0mmHg.
ISOMETRIC RELAXATION
A-V valves pushed open
Ventricles filling
PERIOD OF RAPID FILLING
A-V valves open
Ventricles full
PERIOD OF DIASTASIS
SYSTOLE
[Period of Contraction]
Atrial muscle contracts
Ventricles continue to contract. Pressure continues to rise– Semilunar valves pushed open. Blood ejected into Pulm. A and Aorta.
Ventricles now contract. Pressure rising (closes A-V valves)
Ventricles still relaxed now overfilled and stretched.
PERIOD OF EJECTION
ISOMETRIC CONTRACTION
ATRIAL SYSTOLE
VENTRICULAR SYSTOLE



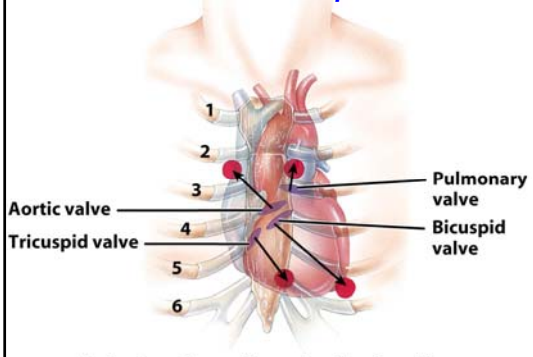
Pressure-Volume Loop



■ **Fig.** Pressure-volume loop of the left ventricle for a single cardiac cycle *(ABCDEF)*.

Heart Sounds

Where to listen on chest wall for heart sounds ?



Anterior view of heart valve locations and auscultation sites

- The sound of a heartbeat comes primarily from the turbulence in blood flow caused by the **closure of the valves**, not from the contraction of the heart muscle.
- The **first** heart sound (***lubb***) is created by blood turbulence associated with the closing of the **atrioventricular** valves soon after ventricular systole begins.
- The **second** heart sound (***dupp***) represents the closing of the **semilunar** valves close to the end of the ventricular systole.

Heart Sounds

第一心音或許可以更進一步分為三尖瓣和僧帽瓣，特別是在吸氣時。三尖瓣的關閉在第五肋間區 (在肋骨之間) 聽得最清楚，恰在胸骨的左邊；僧帽瓣的關閉在左邊第五肋間區間、心臟的尖端聽得最清楚。第二心音在特定情況下也可再細分。肺動脈和主動脈半月瓣的關閉分別在左邊第二肋間區和右邊第二肋間區聽得最清楚。

Murmurs

- A ***heart murmur*** is an abnormal sound that consists of a flow noise that is heard before, between, or after the lubb-dupp or that may mask the normal sounds entirely.
- Some murmurs are caused by turbulent blood flow around valves due to abnormal anatomy or increased volume of flow.
- Not all murmurs are abnormal or symptomatic, but most indicate a valve disorder.

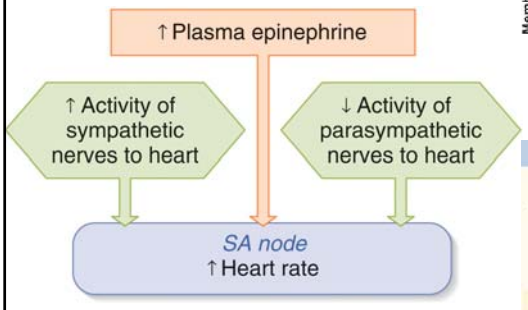
Heart Disease

- **Risk factors:**
  - ✓ ***high blood cholesterol level***
  - ✓ ***high blood pressure***
  - ✓ ***cigarette smoking***
  - ✓ ***obesity***
  - ✓ ***lack of regular exercise***
- **Other factors include:**
  - ✓ ***diabetes mellitus***
  - ✓ ***genetic predisposition***
  - ✓ ***male gender***
  - ✓ ***high blood levels of fibrinogen***
  - ✓ ***left ventricular hypertrophy***

- Risk factor for developing heart disease is high blood cholesterol level.
  - ✓ promotes growth of fatty plaques
  - ✓ Most lipids are transported as lipoproteins
    - -- **HDLs** remove excess cholesterol from circulation
    - -- **LDLs** are associated with the formation of fatty plaques
    - -- **VLDLs** contribute to increased fatty plaque formation
- There are two sources of cholesterol in the body:
  - ✓ in foods we ingest & formed by liver

Cardiac Output(CO) = Heart Rate(HR) × Stroke Volume(SV)

- at 70 ml stroke volume & 72 beat/min-- 5 L/min
- entire blood supply passes through circulatory system every minute



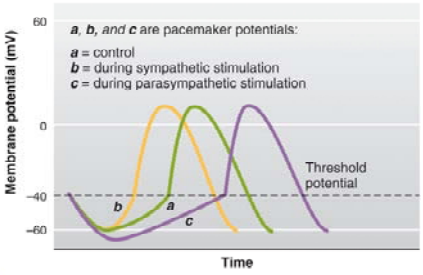
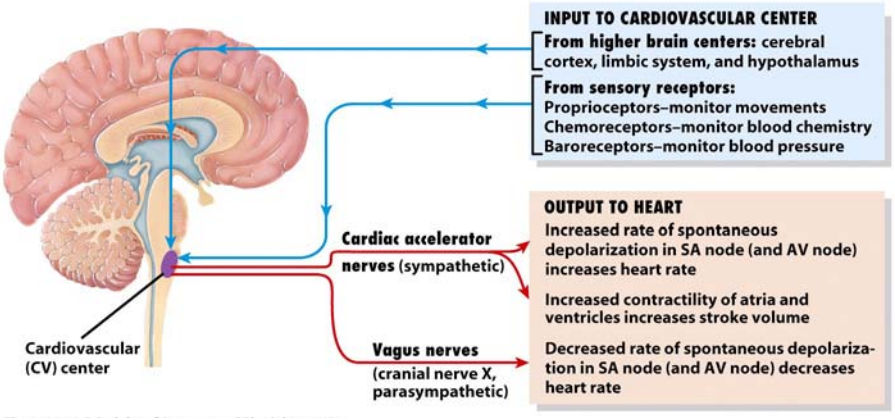


表 14.1 自主神經活動對心臟的影響

受影響區域	交感神經效應	副交感神經效應
竇房結	增加舒張期去極化速率：增加心跳速率	降低舒張期去極化速率：降低心跳速率
房室結	增加傳導速率	降低傳導速率
心房肌	增加收縮強度	降低收縮強度
心室肌	增加收縮強度	沒有顯著的影響

Influences on Heart Rate

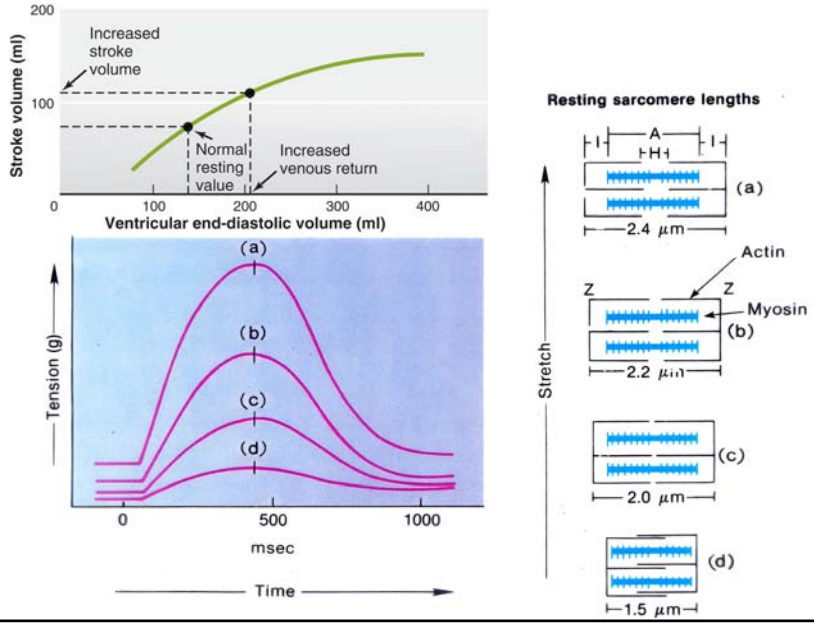


- Nervous control from the cardiovascular center in the medulla
  --Sympathetic, parasympathetic impulses & broreceptors (pressure receptors)
- HR is also affected by hormones
  --epinephrine, norepinephrine, thyroid hormones
  --ions (Na+, K+, Ca2+)
  --age, gender, physical fitness, and temperature

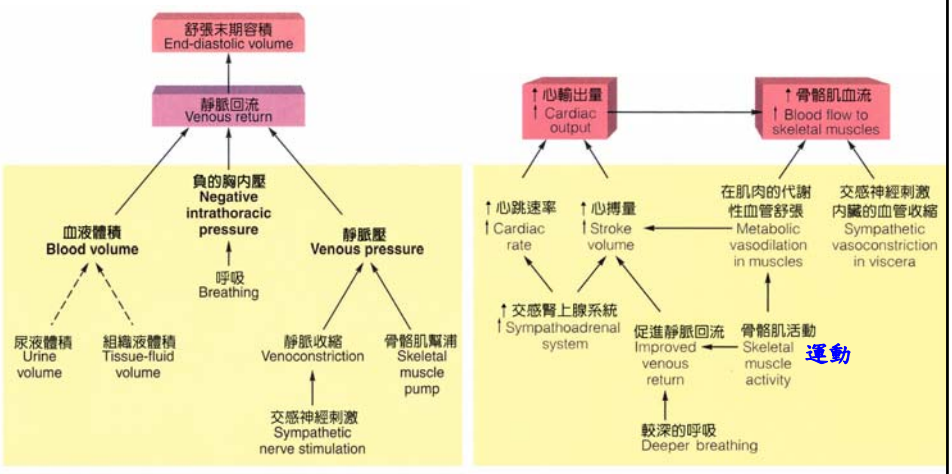
Influences on Stroke Volume

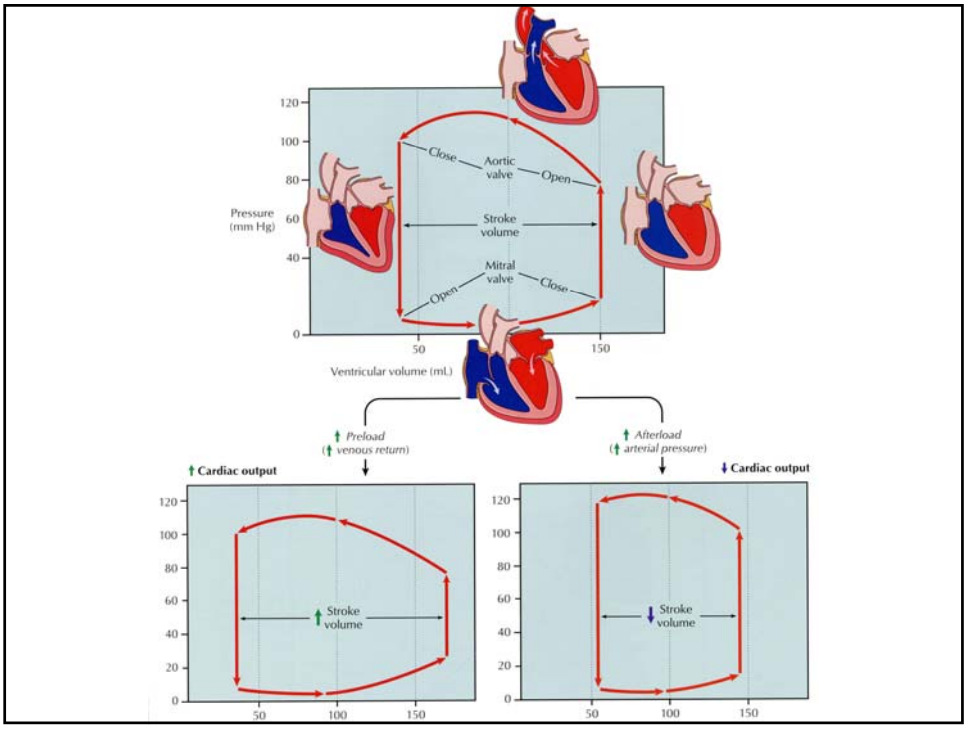
- **Preload=EDV** (affect of stretching)
  - --*Frank-Starling* Law of Heart (EDV is determined by length of ventricular diastole and **venous return**)
  - --more muscle is stretched, greater force of contraction
  - --more blood more force of contraction results
- **Contractility**
  - --autonomic nerves, hormones, Ca^{+2} or K^{+} levels
  - -- is affected by *positive* and *negative inotropic agents*
    - Positive inotropic agents increase contractility
    - Negative inotropic agents decrease contractility
- **Afterload**
  - --amount of **arterial pressure** created by the blood in the way
  - --high blood pressure creates high afterload

Frank-Starling Law

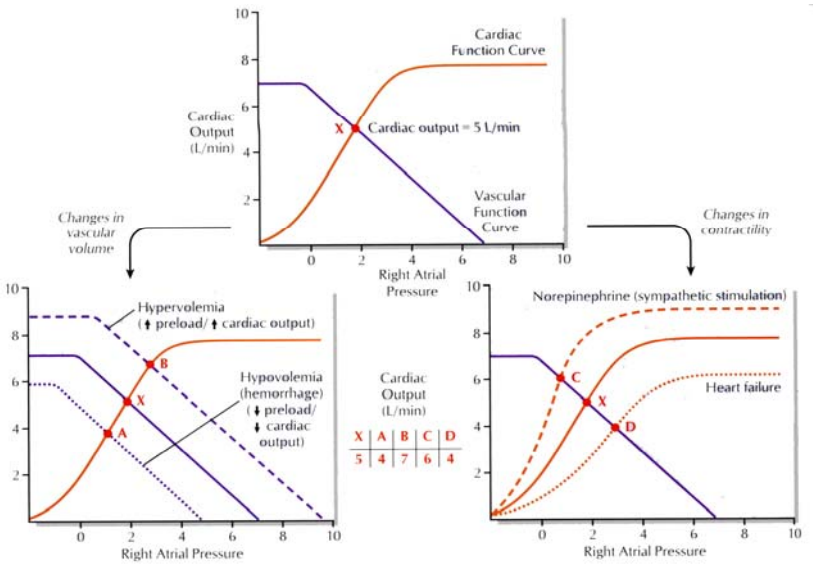


EDV & Venous Return

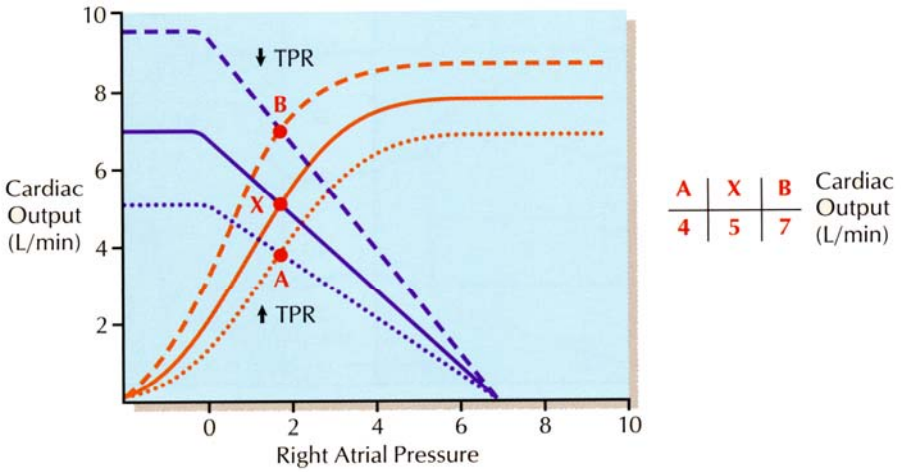




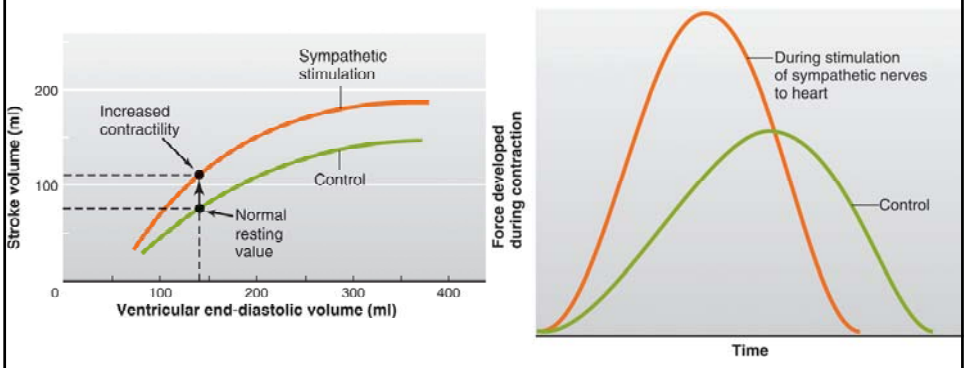
Cardiac & Vascular Function Curves

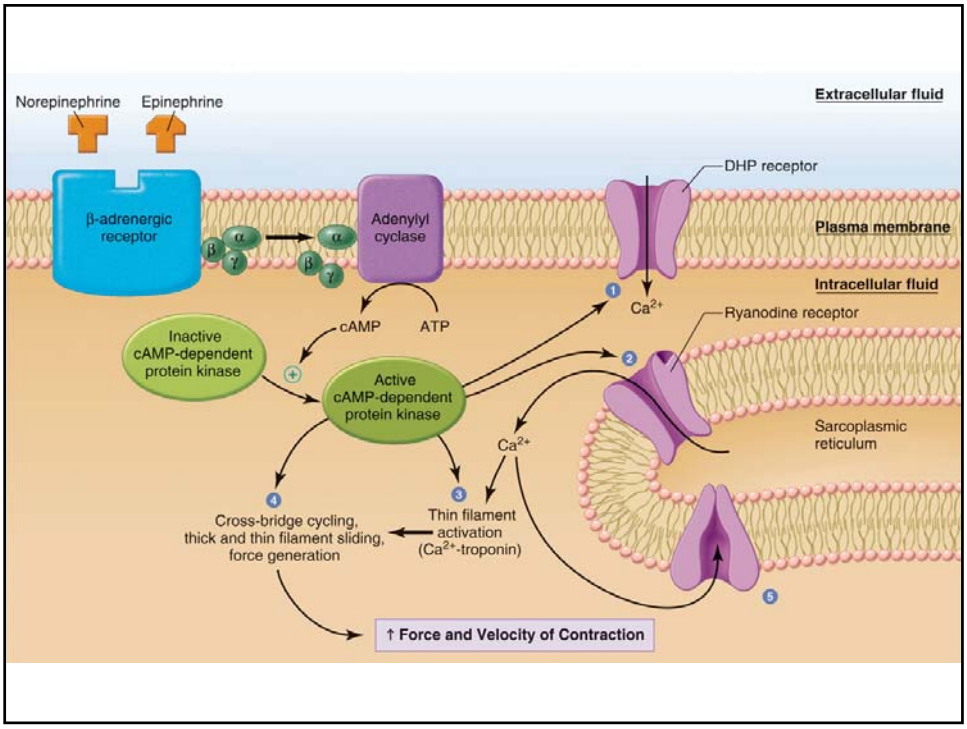


Cardiac & Vascular Function Curves



Sympathetic & Contractility





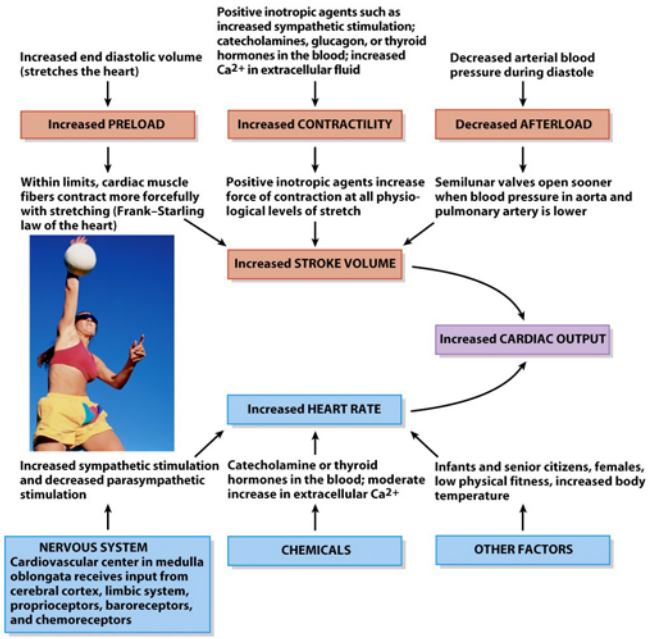
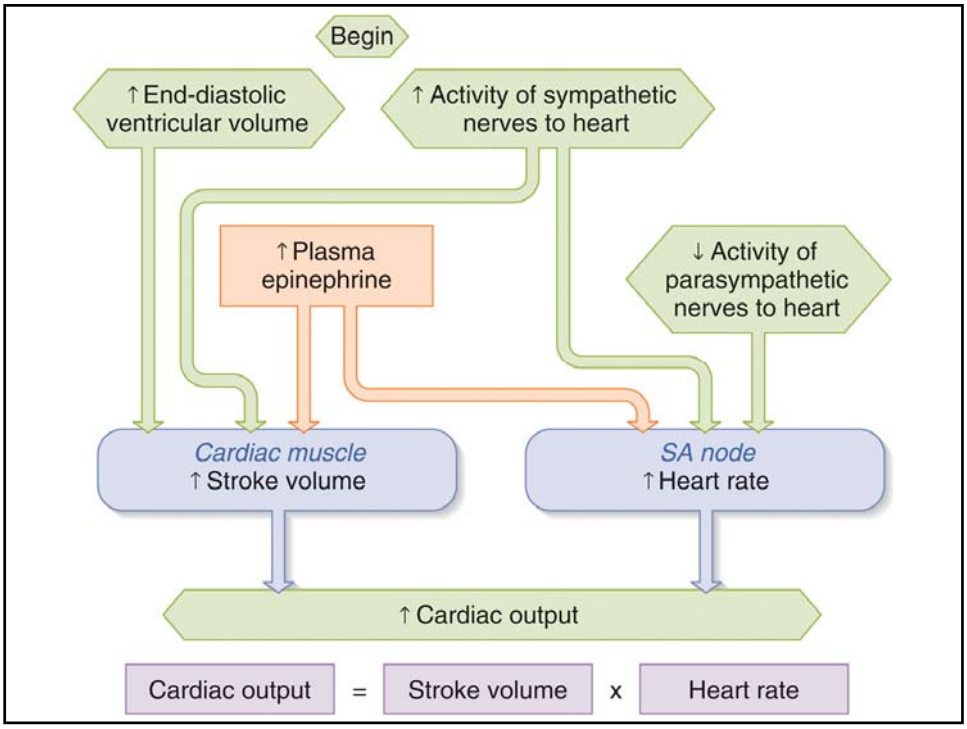


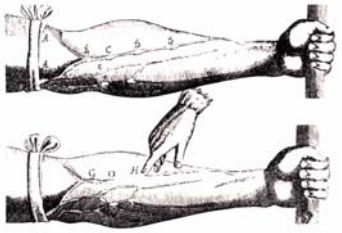
Figure 20-17 Principles of Anatomy and Physiology, 11/e



Structure and Function of Blood Vessels

(William Harvey，1578 - 1657)

- ***Blood vessels*** form a **closed system** of tubes that carry blood away from the heart, transport it to the tissues of the body, and then return it to the heart (***one-way***)
  - *Arteries* carry blood from the heart to the tissues
  - *Arterioles* are small arteries that connect to capillaries
  - *Capillaries* are the site of substance exchange between the blood and body tissues
  - *Venules* connect capillaries to larger veins
  - *Veins* convey blood from the tissues back to the heart



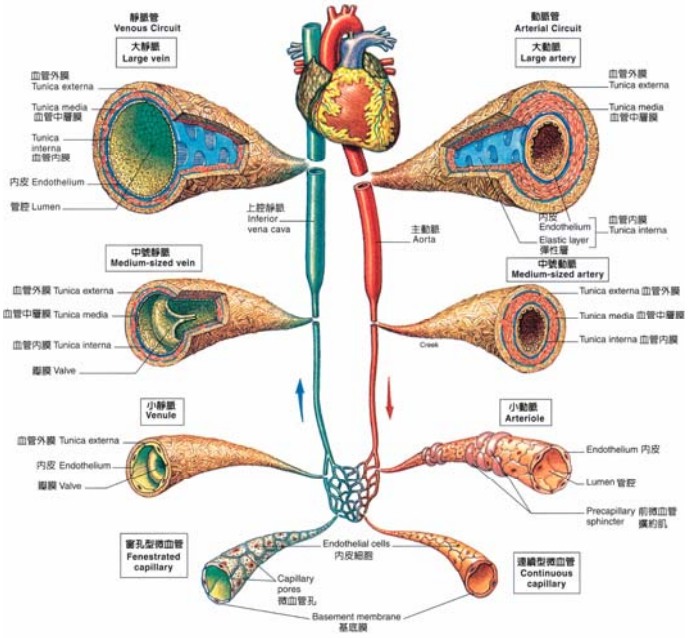
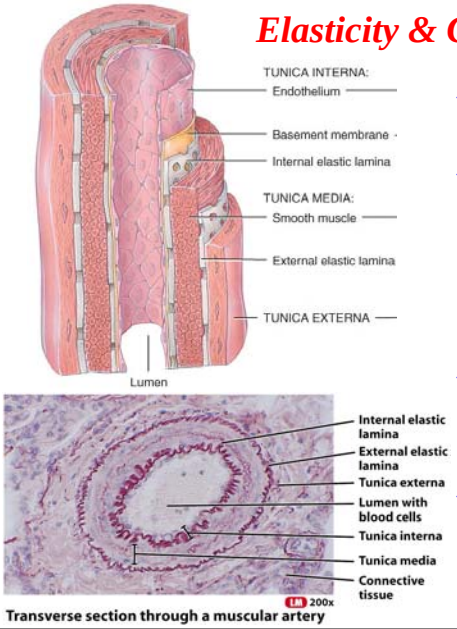


TABLE 21.1 Distinguishing Features of Blood Vessels

	Diameter	Tunica Interna	Tunica Media	Tunica Externa	Function
Elastic arteries	Greater than 1 cm.	Endothelium, basement membrane, and incomplete internal elastic lamina.	Smooth muscle and higher proportion of elastic fibers and thin external elastic lamina.	Collagen and elastic fibers.	Conduct blood from the heart to muscular arteries.
Muscular arteries	0.1–10 mm	Endothelium, basement membrane, and thin internal elastic lamina.	Higher proportion of smooth muscle, fewer elastic fibers, and prominent external elastic lamina.	Collagen and elastic fibers.	Distribute blood to arterioles.
Arterioles (near arteries from which they branch)	10–100 μm.	Endothelium, basement membrane, and internal elastic lamina.	Smooth muscle and very few elastic fibers.	Collagen and elastic fibers.	Deliver blood to capillaries and help regulate blood flow.
Capillaries	4–10 μm.	Endothelium and basement membrane.	None.	None.	Permit exchange of nutrients and wastes between blood and interstitial fluid.
Venules (closer to convergence with veins)	10–100 μm.	Endothelium and basement membrane.	Smooth muscle.	Collagen and elastic fibers.	Collect blood from capillaries and pass it on to veins.
Veins	0.1mm–greater than 1 mm.	Endothelium and basement membrane; contains valves.	Smooth muscle and elastic fibers.	Collagen and elastic fibers.	Return blood to the heart, facilitated by valves in veins in limbs.

Arteries

Elasticity & Contractility



Transverse section through a muscular artery

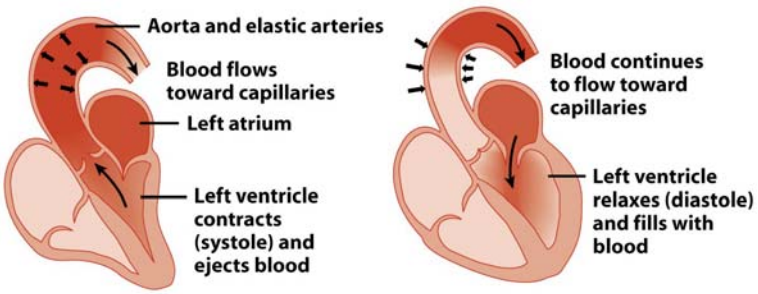
- The wall of an artery consists of three major layers
- **Tunica interna (intima)**
  - --simple squamous epithelium known as endothelium
  - --basement membrane
  - --internal elastic lamina
- **Tunica media**
  - --circular smooth muscle & elastic fibers
- **Tunica externa**
  - --elastic & collagen fibers

Sympathetic Innervation

- **Vascular smooth muscle** is innervated by sympathetic nervous system
  - increase in stimulation causes muscle contraction or vasoconstriction
    - decreases diameter of vessel
  - injury to artery or arteriole causes muscle contraction reducing blood loss (vasospasm)
  - decrease in stimulation or presence of certain chemicals causes vasodilation
    - increases diameter of vessel
    - nitric oxide, K+, H+ and lactic acid cause vasodilation

Elastic Arteries

- **Large arteries** with more elastic fibers and less smooth muscle are called ***elastic arteries*** and are able to receive blood under pressure and propel it onward
- They are also called ***conducting arteries*** because they conduct blood from the heart to medium sized muscular arteries
- They function as a **pressure reservoir**



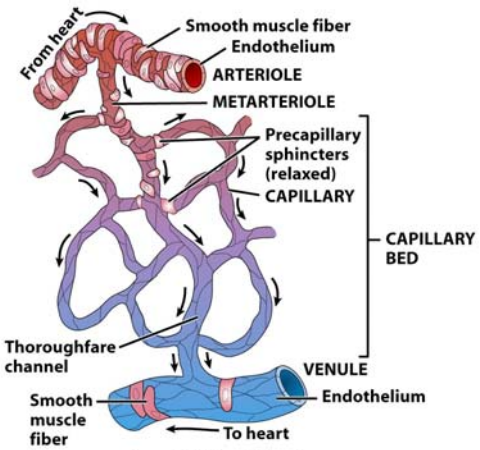
(a) Elastic aorta and arteries stretch during ventricular contraction

(b) Elastic aorta and arteries recoil during ventricular relaxation

Muscular Arteries

- ***Medium-sized arteries*** with more muscle than elastic fibers in tunica media
- Capable of greater vasoconstriction and vasodilation to adjust rate of flow
  - --walls are relatively thick
  - --called ***distributing arteries*** because they direct blood flow

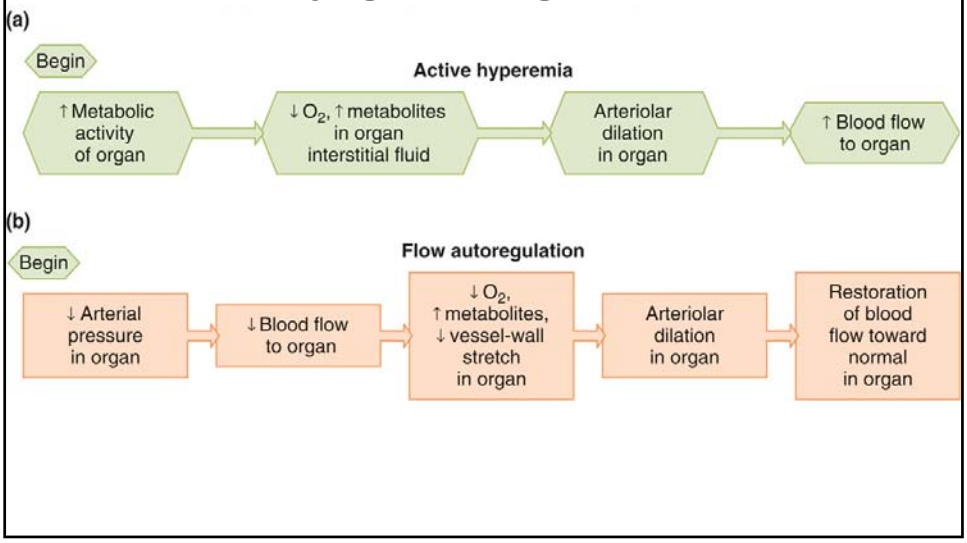
Arterioles



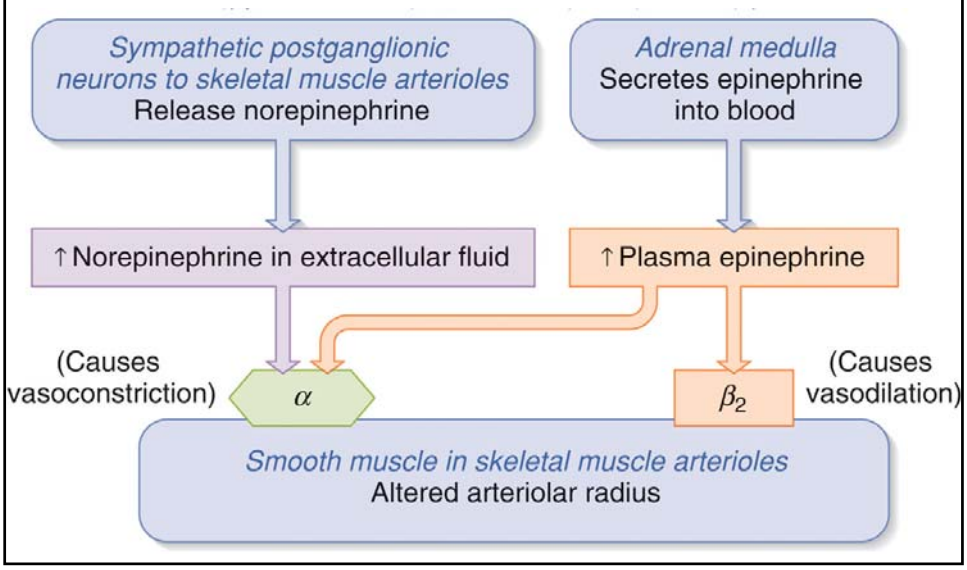
Sphincters relaxed: blood flowing through capillary bed

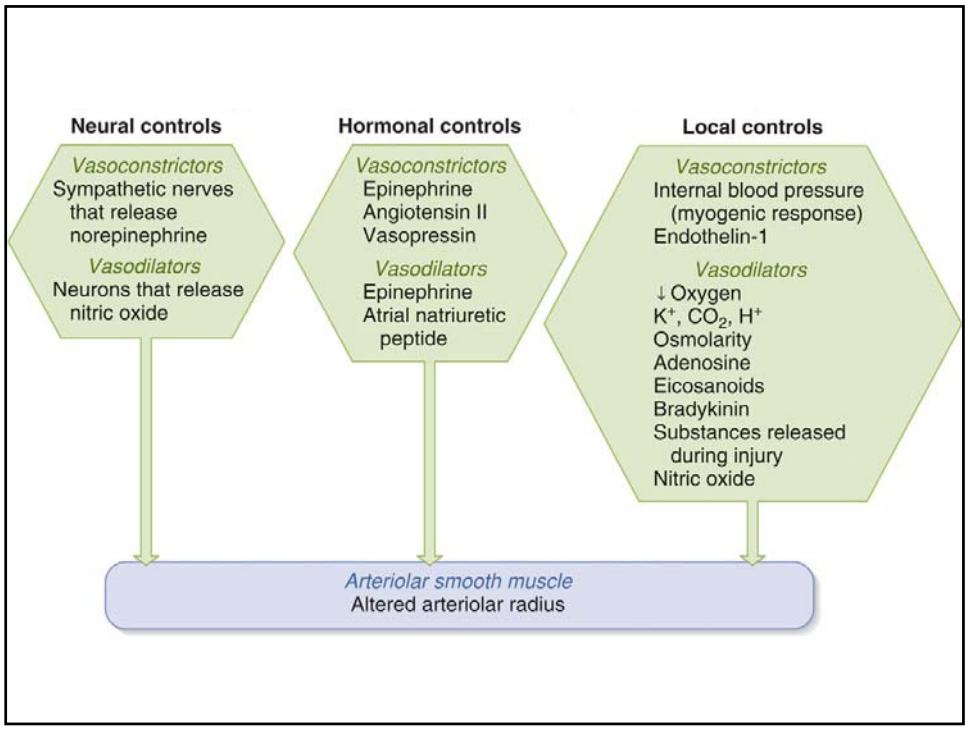
- ***Arterioles*** ***(resistance arteries)*** are very small, almost microscopic, arteries that deliver blood to capillaries
- Through *vasoconstriction* and *vasodilation*, arterioles assume a key role in regulating blood flow from arteries into capillaries and in **altering arterial blood pressure**
- Small arteries delivering blood to capillaries
  - --tunica media containing few layers of muscle
- Metarterioles form branches into capillary bed
  - --to bypass capillary bed, precapillary sphincters close & blood flows out of bed in thoroughfare channel
  - --vasomotion is intermittent contraction & relaxation of sphincters that allow filling of capillary bed 5-10 times/minute

Metabolic Regulation & Myogenic Regulation



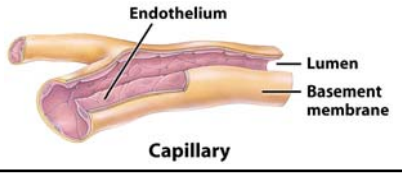
Adrenergic Receptor & Arteriolar Radius

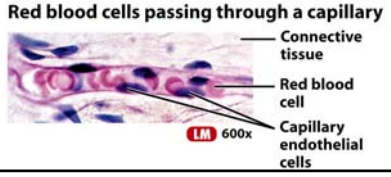




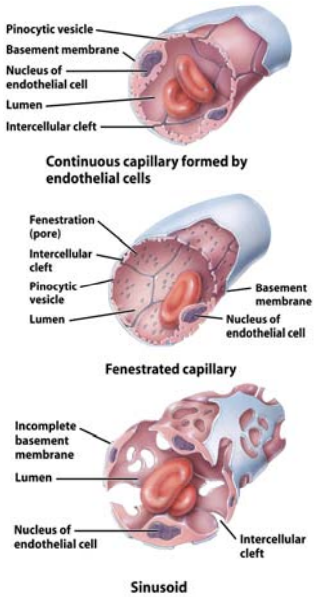
Capillaries form Microcirculation

- **Microscopic vessels** that connect arterioles to venules
- Found near every cell in the body but more extensive in highly active tissue (muscles, liver, kidneys & brain)
  - --entire capillary bed fills with blood when tissue is active
  - --lacking in epithelia, cornea and lens of eye & cartilage
- Function is exchange of nutrients & wastes between blood and tissue fluid
- Capillary walls are composed of only a single layer of cells (endothelium) and a basement membrane



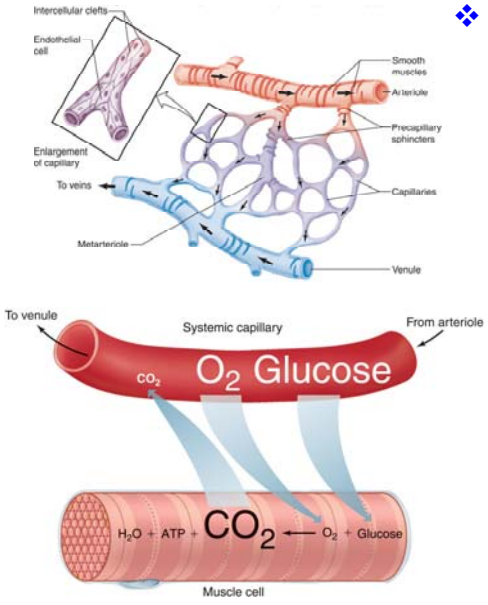


Types of Capillaries



- **Continuous capillaries**
  - --intercellular clefts are gaps between neighboring cells
  - --skeletal & smooth, connective tissue and lungs
- **Fenestrated capillaries**
  - --plasma membranes have many holes
  - --kidneys, small intestine, choroid plexuses, ciliary process & endocrine glands
- **Sinusoids**
  - --very large fenestrations
  - --incomplete basement membrane
  - --liver, bone marrow, spleen, anterior pituitary, & parathyroid gland

Capillary Exchange



- Movement of materials in & out of a capillary
  - **Diffusion** (most important method)
    - Substances such as O2, CO2, glucose, amino acids, hormones, and others diffuse down their concentration gradients.
    - all plasma solutes except large proteins pass freely across
      - through lipid bilayer, fenestrations or intercellular clefts
      - blood brain barrier does not allow diffusion of water-soluble materials (nonfenestrated epithelium with tight junctions)
  - **Transcytosis**
    - passage of material across endothelium in tiny vesicles by endocytosis and exocytosis
      - large, lipid-insoluble molecules such as insulin or maternal antibodies passing through placental circulation to fetus
  - **Bulk flow**

Bulk Flow: Filtration & Reabsorption

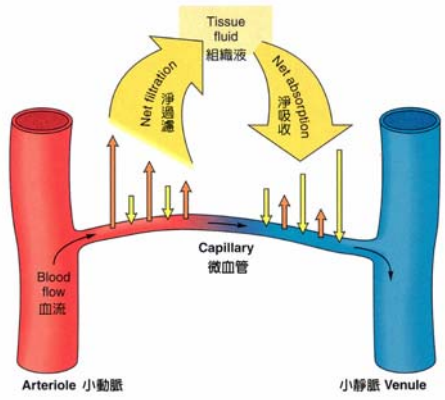
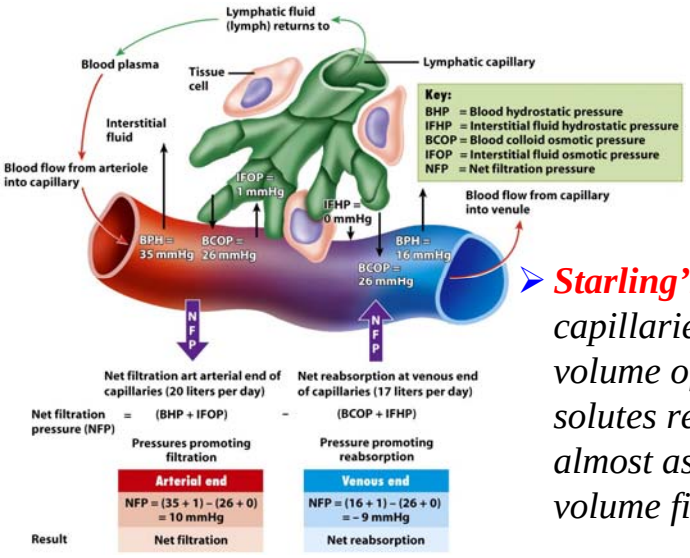


圖 14.8 液體進出微血管的分佈圖。組織（間）液是由微血管動脈端的血壓迫使血液過濾形成的，並藉由血漿蛋白的膠體滲透壓（黃色箭頭）而回到微血管的靜脈端。

- Movement of large amount of dissolved or suspended material in same direction
  - move in response to pressure
    - from area of high pressure to area of low
  - faster rate of movement than diffusion or osmosis
- Most important for regulation of relative volumes of blood & interstitial fluid
  - **Filtration** is movement of material into interstitial fluid
    - promoted by blood hydrostatic pressure & interstitial fluid osmotic pressure
  - **Reabsorption** is movement from interstitial fluid into capillaries
    - promoted by blood colloid osmotic pressure
  - balance of these pressures is net filtration pressure

Dynamics of Capillary Exchange



➢ ***Starling's law*** *of the capillaries is that the volume of fluid & solutes reabsorbed is almost as large as the volume filtered*

Edema

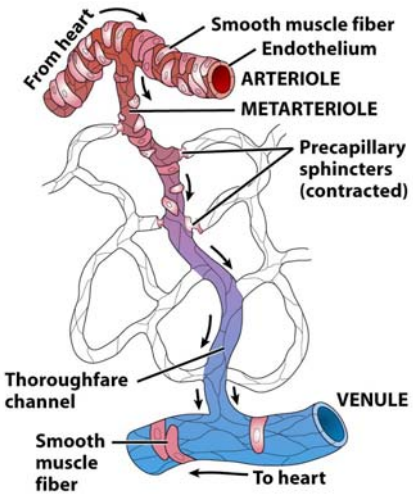
An abnormal increase in interstitial fluid
(Filtration > Reabsorption)

水腫的原因

原因	註解
血壓增加或靜脈阻塞	增加微血管過濾壓，所以有較多的組織液在微血管動脈端形成
組織蛋白濃度增加	降低水分滲透進入微血管靜脈端。通常局部組織水腫是由於在發炎和過敏反應時血漿蛋白經由微血管漏出所致。甲狀腺功能低下造成的黏液水腫也是屬於這一類
血漿蛋白濃度降低	降低水分滲透進入微血管靜脈端。可能是由肝臟疾病（其與血漿蛋白製造不足有關）、腎臟病（由於血漿蛋白滲漏進尿液中）、或蛋白質營養失調引起的
淋巴管阻塞	由特殊種類的蚊子傳染而感染絲蟲蛔蟲(filaria roundworms)（線蟲類），其阻斷淋巴流動，引起水腫及感染區域巨大的腫脹

- **Excess filtration**
  - increased blood pressure (hypertension)
  - increased permeability of capillaries allows plasma proteins to escape
- **Inadequate reabsorption**
  - decreased concentration of plasma proteins lowers blood colloid osmotic pressure
    - inadequate synthesis or loss from liver disease, burns, malnutrition or kidney disease blockage of lymphatic vessels postoperatively or due to filarial worm infection

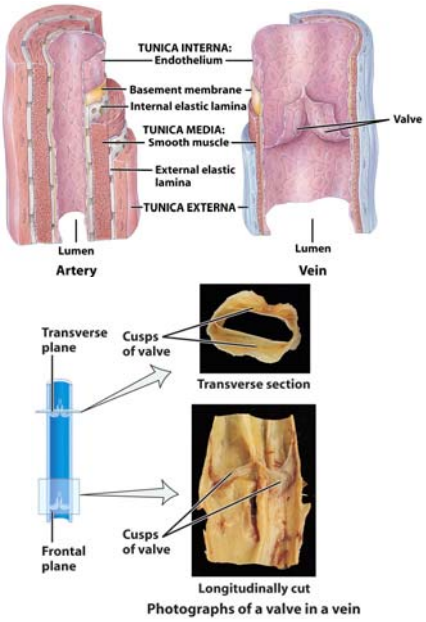
Venules



Sphincters contracted: blood flowing through thoroughfare channel

- **Small veins** collecting blood from capillaries
- Tunica media contains only a few smooth muscle cells & scattered fibroblasts
  --very porous endothelium allows for escape of many phagocytic white blood cells
- Venules that approach size of veins more closely resemble structure of vein

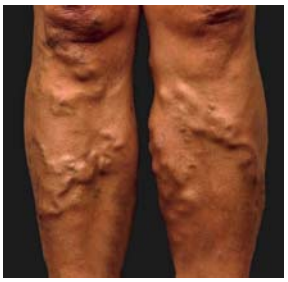
Veins

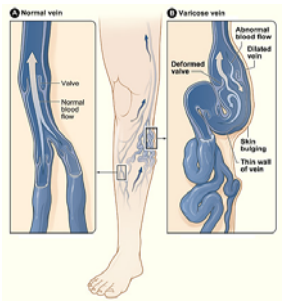


Photographs of a valve in a vein

- ***Veins*** consist of the same three tunics as arteries but have a thinner tunica interna and media and a thicker tunica externa
  - --less elastic tissue and smooth muscle
  - --thinner-walled than arteries
  - --contain ***valves*** to prevent the backflow of blood
- Still adaptable to variations in volume & pressure
- ***Vascular (venous) sinuses*** are veins with very thin walls with no smooth muscle to alter their diameters. Examples are the brain's superior sagittal sinus and the coronary sinus of the heart

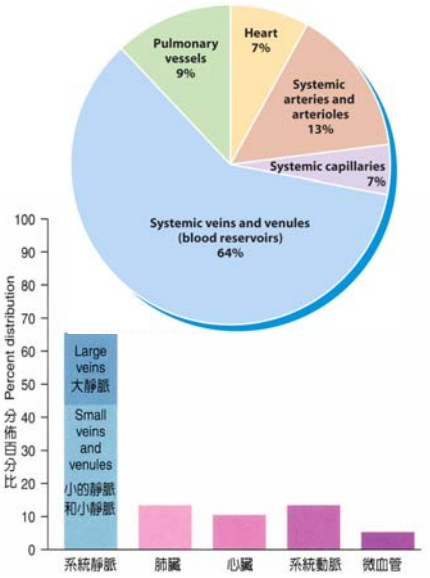
Varicose Veins





- Twisted, dilated superficial veins
  - caused by **leaky venous valves**
    - congenital or mechanically stressed from prolonged standing or pregnancy
  - allow backflow and pooling of blood
    - extra pressure forces fluids into surrounding tissues
    - nearby tissue is inflamed and tender
- The most common sites for varicose veins are in the esophagus, superficial veins of the lower limbs, and veins in the anal canal (hemorrhoids). Deeper veins not susceptible because of support of surrounding muscles
- The treatments for varicose veins in the lower limbs include: *sclerotherapy, radiofrequency endovenous occlusion, laser occlusion,* and *surgical stripping*

Blood Distribution

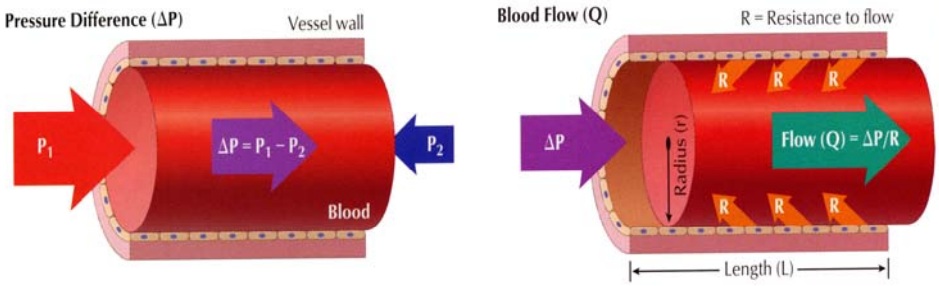


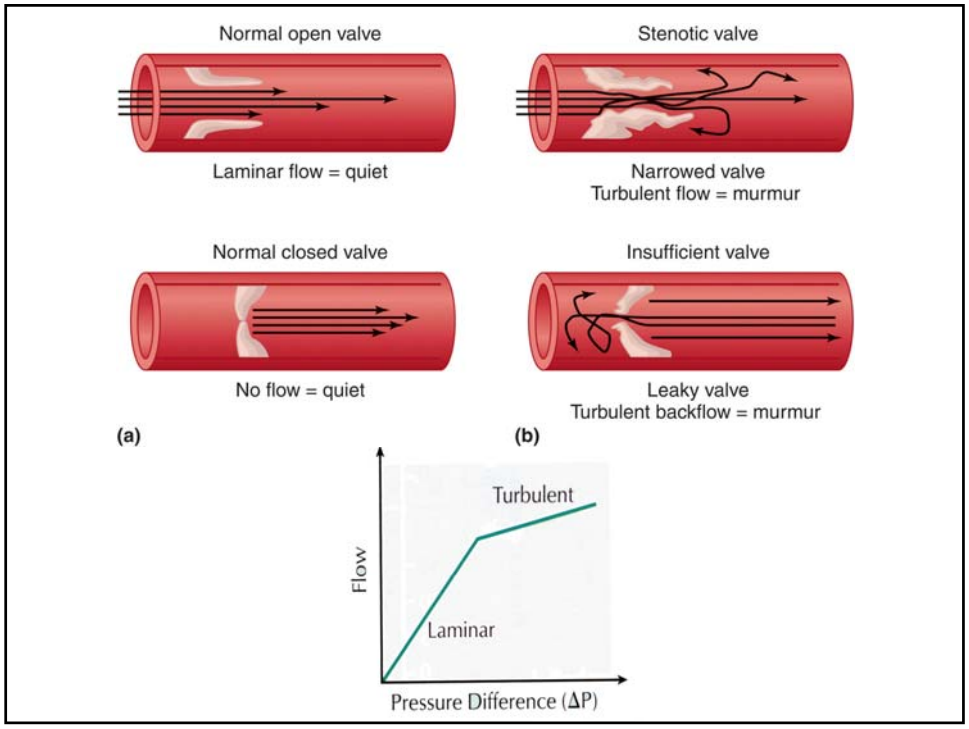
- **64%** of blood volume at rest is in systemic veins and venules
  - function as blood reservoir
    - veins of skin & abdominal organs (liver and spleen)
  - blood is diverted from it in times of need
    - increased muscular activity produces venoconstriction
    - hemorrhage causes venoconstriction to help maintain blood pressure
- **13%** of blood volume in arteries & arterioles

Hemodynamics: Factors Affecting Blood Flow

- The distribution of cardiac output to various tissues depends on the interplay of the **pressure difference** (△P) that drives the blood flow and the **resistance** (R) to blood flow.
- ***Blood pressure*** (BP) is the pressure exerted on the walls of a blood vessel; in clinical use, BP refers to pressure in arteries.
- Cardiac output (CO) equals **mean arterial pressure** (MAP) divided by total resistance (R).
- Factors that affect blood pressure (**MAP=CO × R**) include cardiac output, blood volume, viscosity, resistance, and elasticity of arteries.

Hemodynamic: Pressure Difference





Hemodynamics: Resistance

Resistance to Flow (R)

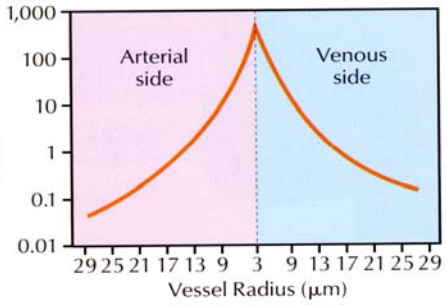
Poiseuille's Law

$$R = \frac{\eta \times L \times 8}{\pi r^4}$$

η = viscosity
L = vessel length
r = vessel radius

Resistance (R) per unit length

$$\left(\frac{\text{mm Hg}}{(\text{mm}^3/\text{sec})/\mu\text{m}}\right)$$



➢***Resistance*** refers to the opposition to blood flow as a result of friction between blood and the walls of the blood vessels.
➢Vascular resistance depends on the ***diameter of the blood vessel***, ***blood viscosity***, and ***total blood vessel length***.
➢***Systemic vascular resistance*** (also known as ***total peripheral resistance=TPR***) refers to all of the vascular resistances offered by systemic blood vessels; most resistance is in arterioles, capillaries, and venules due to their small diameters.

Systemic Vascular Resistance (SVR)

✓***Neural Controls***
✓***Hormone Controls***
✓***Local Controls***

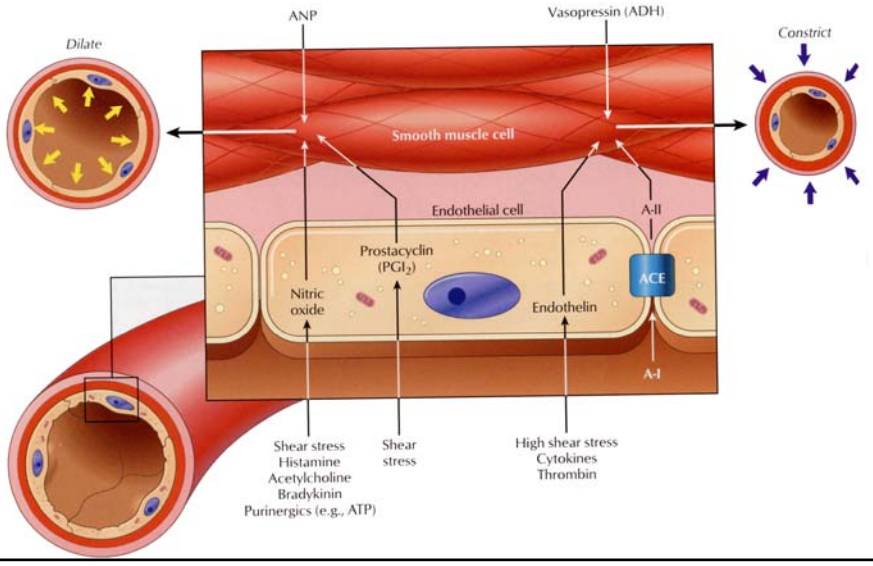
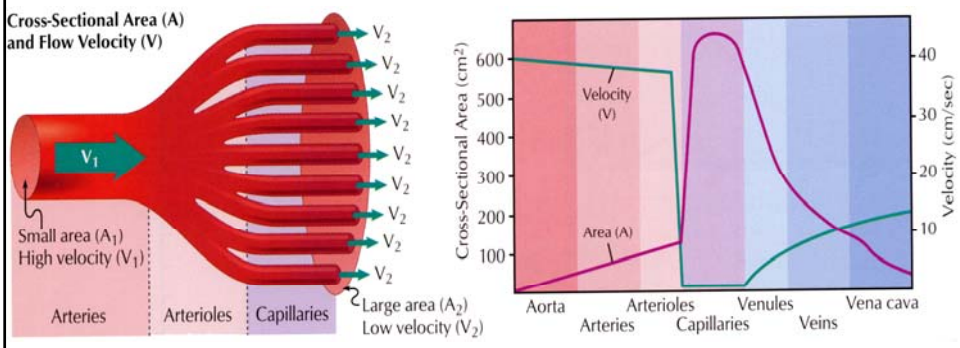


表 14.4　血管阻力和血流的外在控制

外在因子	效 應	註 解
交感神經		
·作用在 α 受器－腎上腺激導性的	血管舒張	血管收縮是交感神經刺激血管系統的主要效應，且是全身性的。
·作用在 β 受器－腎上腺激導性的	血管收縮	其對骨骼肌的小動脈和冠狀動脈的生理影響不明顯，因其效應常被主導的 α－受器調節的收縮所掩蓋了。
·膽鹼激導性的	血管舒張	效應局限於骨骼肌的小動脈，並且只有在警戒戰鬥反應時才會產生。
副交感神經	血管舒張	效應主要限於胃腸道、外生殖器和唾液腺，並對末稍總阻力有微小的影響。
血管緊縮素 II	血管收縮	是一種有力的血管收縮劑。它是由腎臟腎素的分泌而產生的因子，當系統血流和血壓降低時，它能幫助腎臟維持適當的過濾壓。
抗利尿激素（血管加壓素）	血管收縮	雖然已很清楚這個激素對於麻醉中動物的血管阻力和血壓的效應，但對清醒狀態下的人類，這些效應仍有爭議性。
組織胺	血管舒張	在發炎或過敏反應時，組織胺促進局部的血管舒張。
緩激肽	血管舒張	緩激肽是內皮和汗腺分泌的多胜肽，能促進局部的血管舒張。
前列腺素	血管舒張或血管收縮	前列腺素是環狀的脂肪酸，能由大部份的組織產生，包括血管壁。前列腺素 I_2 是一個血管舒張因子，然而凝血脂素 A_2 是一個血管收縮因子。但這些效應的生理意義目前仍在爭論中。

Hemodynamics: Cross-Sectional Area

$$V = Q/A$$

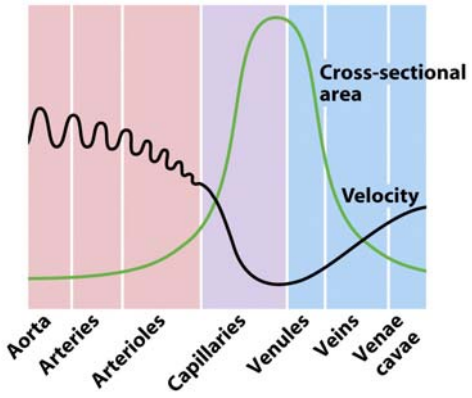


The velocity of blood flow is inversely related to the cross-sectional area of blood vessels

Hemodynamics

- Factors affecting circulation
  - **Pressure differences** that drive the blood flow
    - ***Velocity of blood flow***
    - ***Volume of blood flow (CO=SV x HR)***
      - ***--venous return***
    - ***Blood pressure***
  - **Resistance to flow**
- An interplay of forces result in blood flow

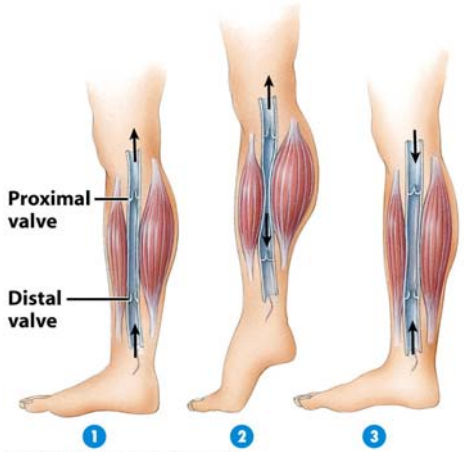
Velocity of Blood Flow



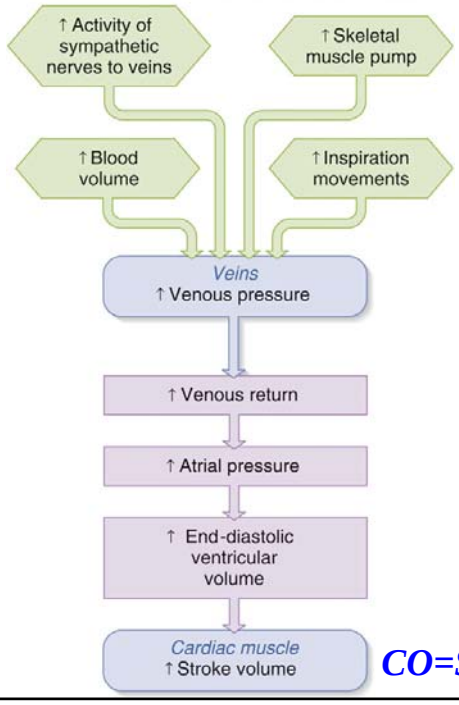
- Speed of blood flow in cm/sec is inversely related to cross-sectional area
  - blood flow is slower in the arterial branches
    - flow in aorta is 40 cm/sec while flow in capillaries is .1 cm/sec
    - slow rate in capillaries allows for exchange
- Blood flow becomes faster when vessels merge to form veins
- Blood flow decreases from the aorta to arteries to capillaries and increases as it returns to the heart

Volume of Blood Flow

Venous Return

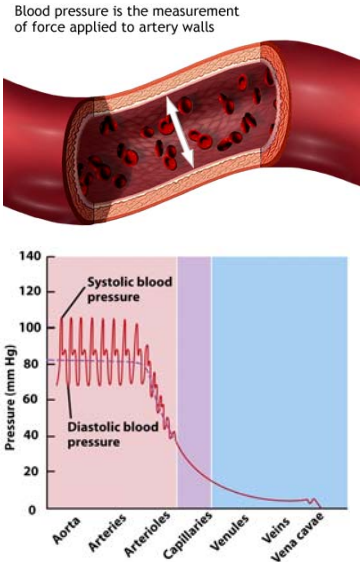


- Volume of blood flowing back to the heart from the systemic veins
  - depends on pressure difference from venules (16 mm Hg) to right atrium (0 mm Hg)
  - tricuspid valve leaky and buildup of blood on venous side of circulation
- **Skeletal muscle pump**
  - contraction of muscles & presence of valves
- **Respiratory pump**
  - decreased thoracic pressure and increased abdominal pressure during inhalation, moves blood into thoracic veins and the right atrium



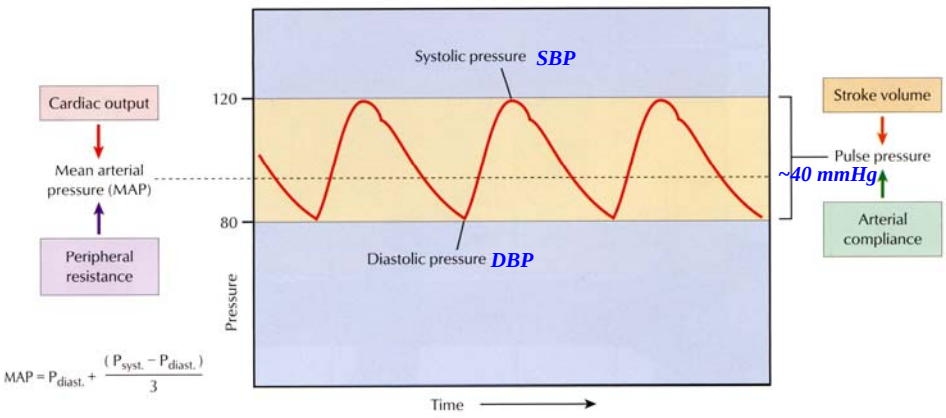
CO=SV x HR

Blood Pressure

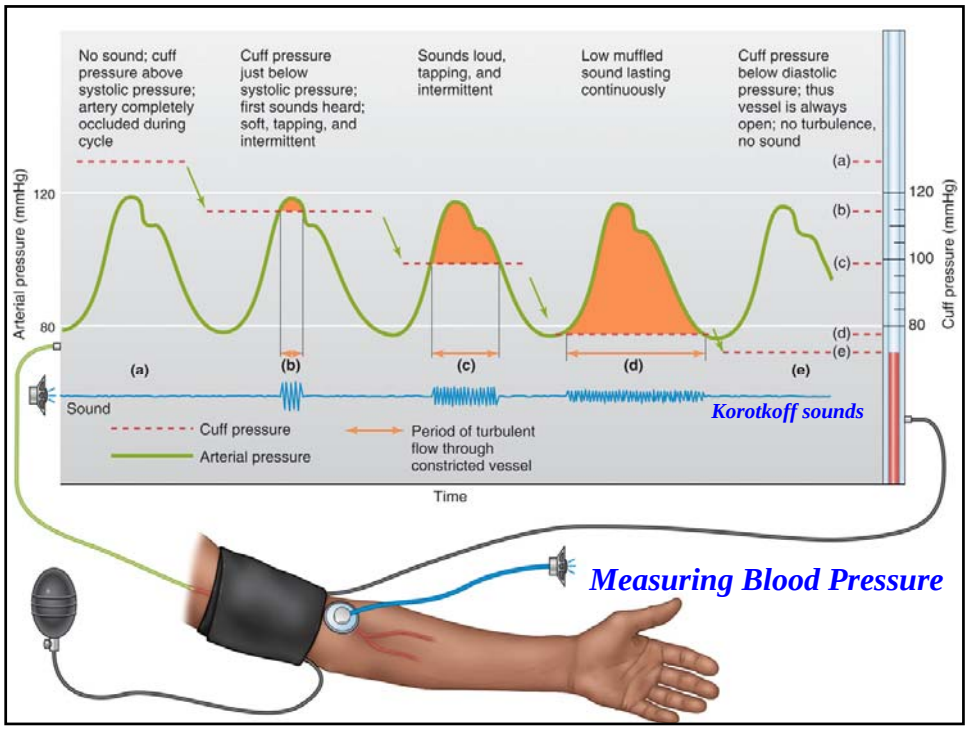


- Pressure exerted by blood on walls of a vessel
  - caused by contraction of the ventricles
  - highest in aorta
    - 120 mm Hg during systole & 80 during diastole
- If heart rate increases cardiac output, BP rises (MAP=CO×TPR)
- Pressure falls steadily in systemic circulation with distance from left ventricle
  - 35 mm Hg entering the capillaries
  - 0 mm Hg entering the right atrium
- If decrease in blood volume is over 10%, BP drops
- Water retention increases blood pressure

Arterial Pressure



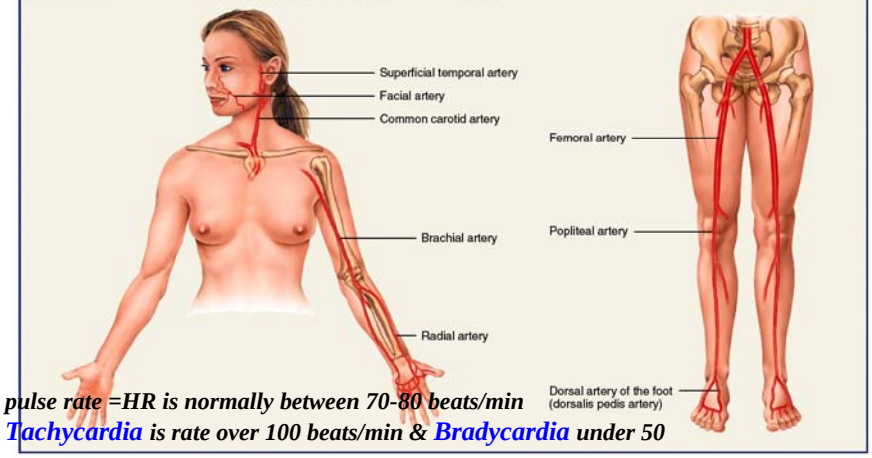
SBP:DBP:PP= 3:2:1



Pulse ***is a pressure wave that alternate expansion & recoil of elastic artery after each systole of the left ventricle***

TABLE 21.3 Pulse Points

Structure	Location	Structure	Location
Superficial temporal artery	Lateral to orbit of eye.	Femoral artery	Inferior to inguinal ligament.
Facial artery	Mandible (lower jawbone) on a line with the corners of the mouth.	Popliteal artery	Posterior to knee.
Common carotid artery	Lateral to larynx (voice box).	Radial artery	Distal aspect of wrist.
Brachial artery	Medial side of biceps brachii muscle.	Dorsal artery of the foot (dorsalis pedis artery)	Superior to instep of foot.



pulse rate =HR is normally between 70-80 beats/min

Tachycardia ***is rate over 100 beats/min &*** ***Bradycardia*** ***under 50***

Cardiovascular Adaptation to Exercise

表 14.5　在安靜和運動情況下骨骼肌血流的改變

情 況	血 流（毫升／分鐘）	機 制
安靜時	1,000	腎上腺性的交感神經刺激血管 α －受器，引起血管收縮
開始運動時	增加	由於膽鹼素性交感神經的活性和腎上腺激素刺激 β －腎上腺性接受器而使骨骼肌中的小動脈舒張
劇烈運動	20,000	(1) 腎上腺性的活性降低 (2) 膽鹼素性的交感神經活性增加 (3) 運動肌肉的代謝率增加，產生內在影響的血管舒張

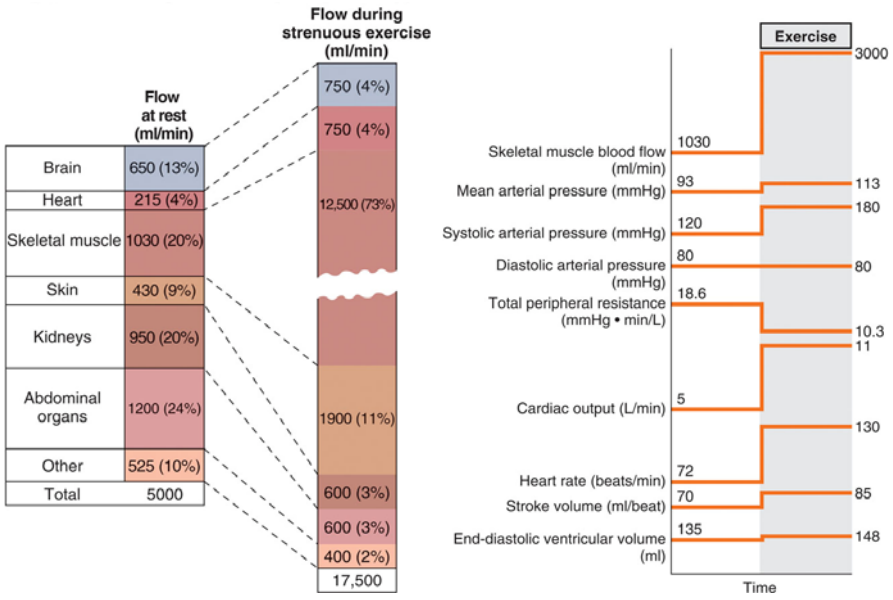
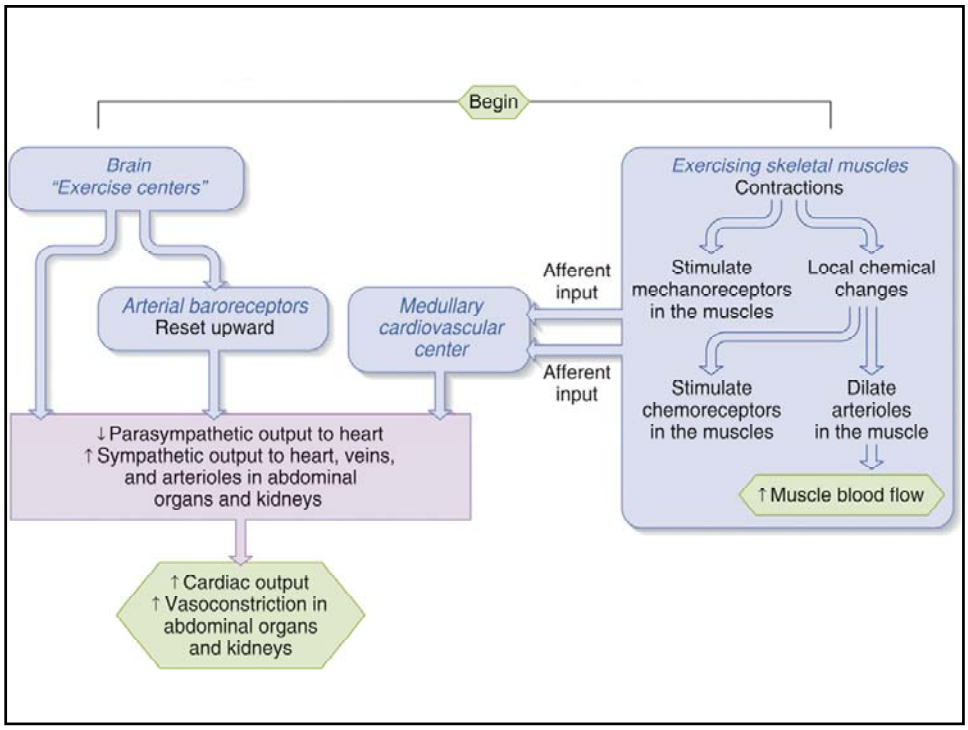
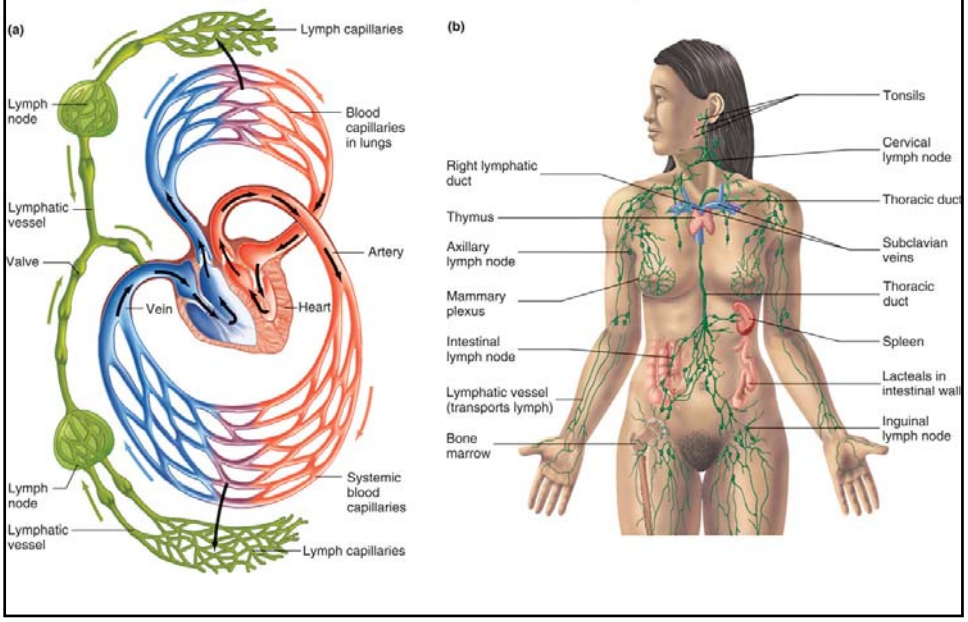


Table 12–7 Cardiovascular Changes During Moderate Exercise

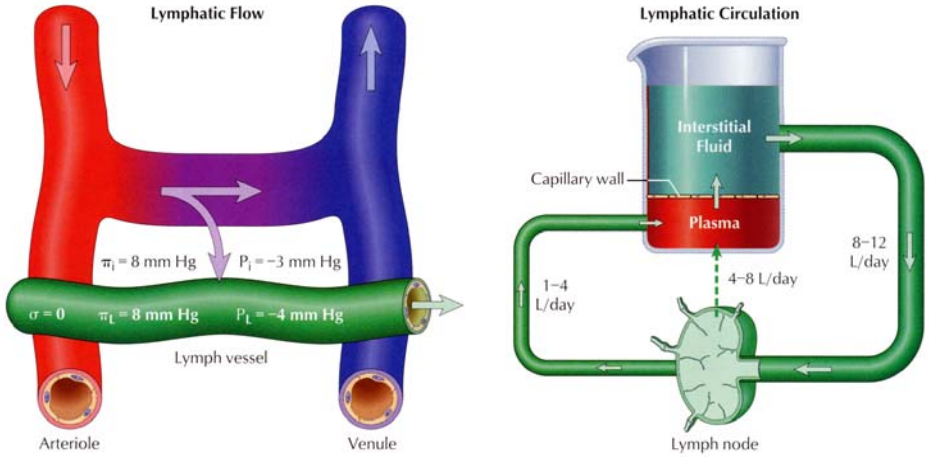
Variable	Change	Explanation
Cardiac output	Increases	Heart rate and stroke volume both increase, the former to a much greater extent.
Heart rate	Increases	Sympathetic nerve activity to the SA node increases, and parasympathetic nerve activity decreases.
Stroke volume	Increases	Contractility increases due to increased sympathetic nerve activity to the ventricular myocardium; increased ventricular end-diastolic volume also contributes to increased stroke volume by the Frank-Starling mechanism.
Total peripheral resistance	Decreases	Resistance in heart and skeletal muscles decreases more than resistance in other vascular beds increases.
Mean arterial pressure	Increases	Cardiac output increases more than total peripheral resistance decreases.
Pulse pressure	Increases	Stroke volume and velocity of ejection of the stroke volume increase.
End-diastolic volume	Increases	Filling time is decreased by the high heart rate, but the factors favoring venous return—venoconstriction, skeletal muscle pump, and increased inspiratory movements—more than compensate for it.
Blood flow to heart and skeletal muscle	Increases	Active hyperemia occurs in both vascular beds, mediated by local metabolic factors.
Blood flow to skin	Increases	Sympathetic nerves to skin vessels are inhibited reflexly by the increase in body temperature.
Blood flow to viscera	Decreases	Sympathetic nerves to the blood vessels in the abdominal organs and kidneys are stimulated.
Blood flow to brain	Increases slightly	Autoregulation of brain arterioles maintains constant flow despite the increased mean arterial pressure.



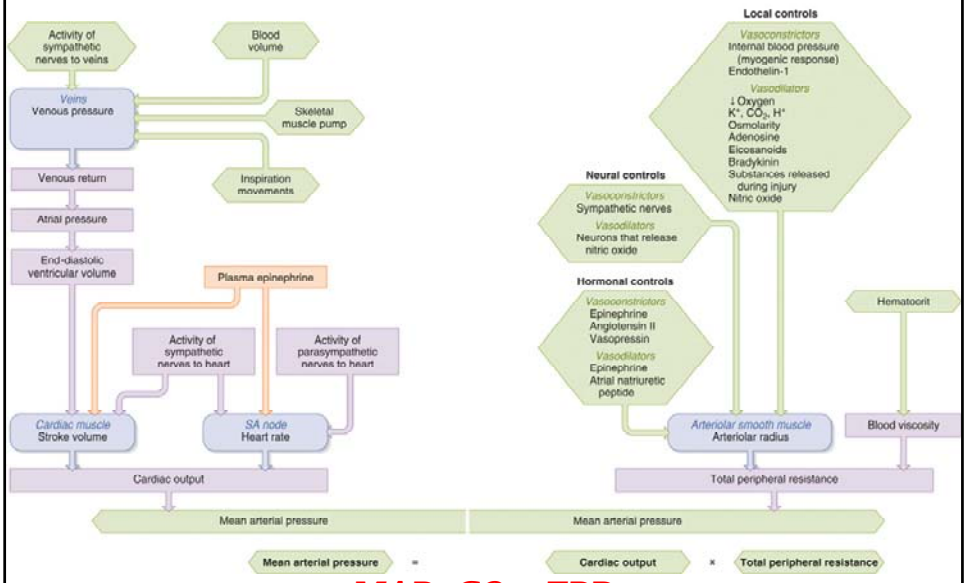
Lymphatic System



Lymphatic Circulation



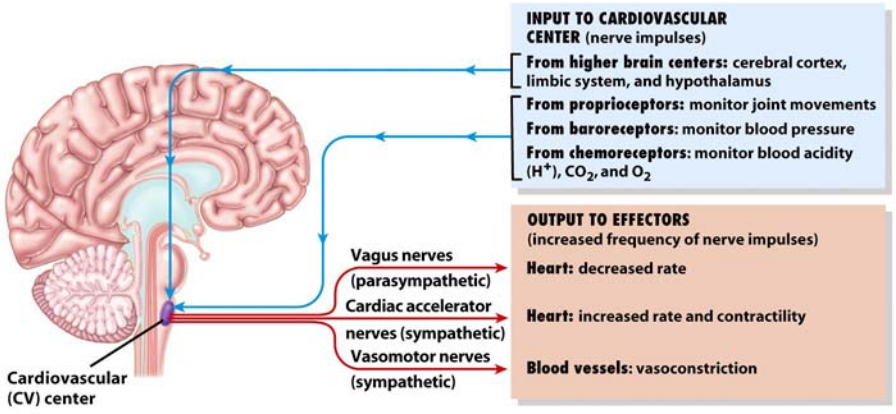
Control of Blood Pressure



MAP=CO ⨉ TPR

Control of Blood Pressure

- Role of **cardiovascular center**
  - help regulate heart rate & stroke volume
  - specific neurons regulate blood vessel diameter



Cardiovascular Center

- The ***cardiovascular center* (*CV*)** is a group of neurons in the medulla that regulates heart rate, contractility, and blood vessel diameter.
  - input from higher brain regions and sensory receptors (baroreceptors and chemoreceptors).
  - output from the CV flows along sympathetic and parasympathetic fibers.
  - Sympathetic impulses along cardioaccelerator nerves increase heart rate and contractility.
  - Parasympathetic impulses along vagus nerves decrease heart rate.
- The sympathetic division also continually sends impulses to smooth muscle in blood vessel walls via vasomotor nerves. The result is a moderate state of tonic contraction or vasoconstriction, called **vasomotor tone**.

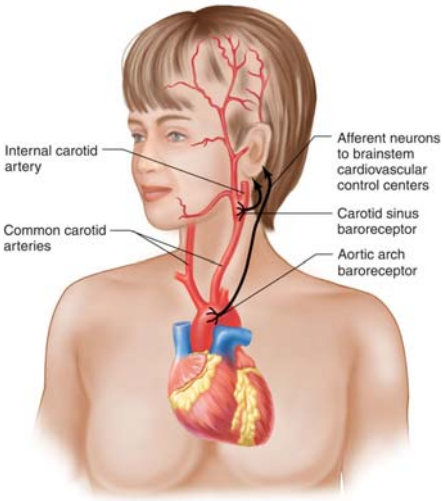
Input to CV Center

- **Higher brain centers** such as cerebral cortex, limbic system & hypothalamus
  - anticipation of competition
  - increase in body temperature
- **Proprioceptors**
  - input during physical activity
- **Baroreceptors**
  - changes in pressure within blood vessels
- **Chemoreceptors**
  - monitor concentration of chemicals in the blood

Output from CV Center

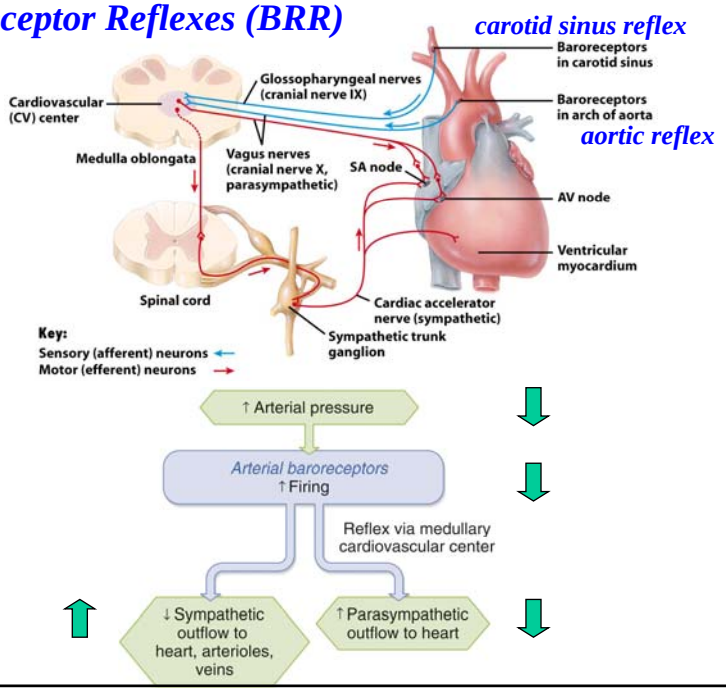
- **Heart**
  - *parasympathetic (vagus nerve)*
    - decrease heart rate
  - *sympathetic (cardiac accelerator nerves)*
    - cause increase or decrease in contractility & rate
- **Blood vessels**
  - *sympathetic vasomotor nerves*
    - continual stimulation to arterioles in skin & abdominal viscera producing vasoconstriction (vasomotor tone)
    - increased stimulation produces constriction & increased BP

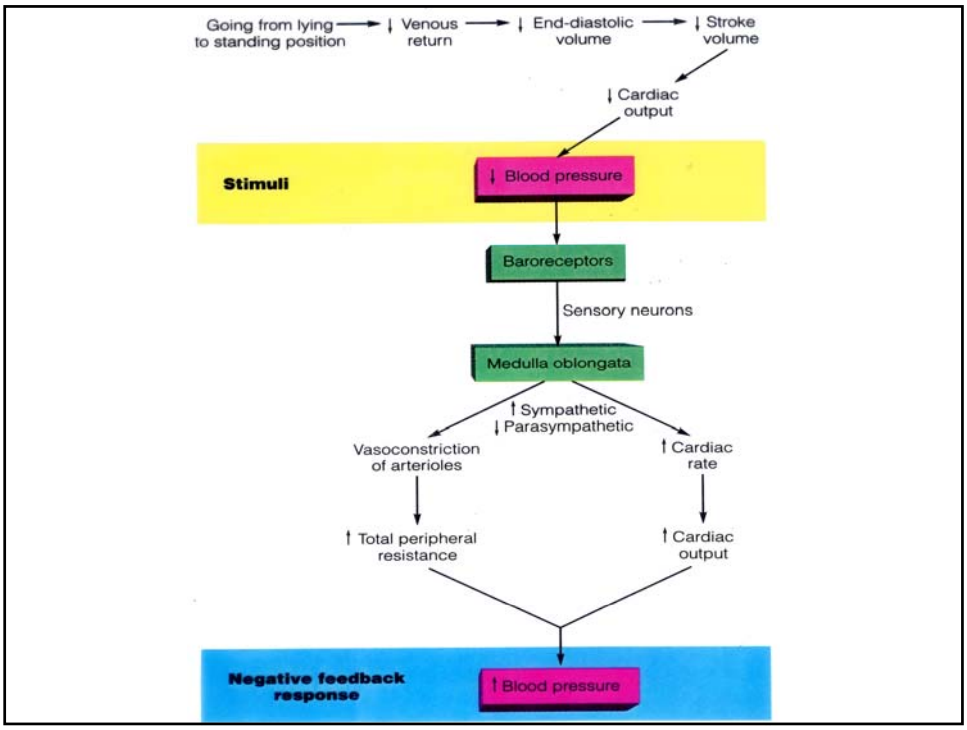
Neural Regulation of Blood Pressure



- ***Baroreceptors*** are important pressure-sensitive sensory neurons that monitor stretching of the walls of blood vessels and the atria.
  - The *cardiac sinus reflex* is concerned with maintaining normal blood pressure in the brain and is initiated by baroreceptors in the wall of the carotid sinus.
  - The *aortic reflex* is concerned with general systemic blood pressure and is initiated by baroreceptors in the wall of the arch of the aorta or attached to the arch.
- If blood pressure falls, the baroreceptor reflexes accelerate heart rate, increase force of contraction, and promote vasoconstriction

Baroreceptor Reflexes (BRR)

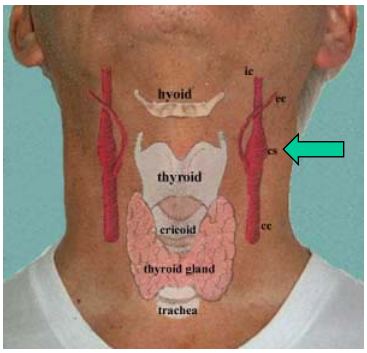




Orthostatic Hypotension

活化感壓反射需數秒的時間。故若站起來的速度太快，會造成許多人頭暈而分不清方向。如果感壓受器的敏感性異常降低，或由於動脈粥狀瘤硬化所引起，在站起來時會發生無法補償的血壓下降。這種情形－稱為**姿勢性**的(postural)，或**直立性**(orthostatic)的低血壓 (hypotension) --能使一個人感覺極度頭暈，或由於腦部血流不足而甚至昏厥。

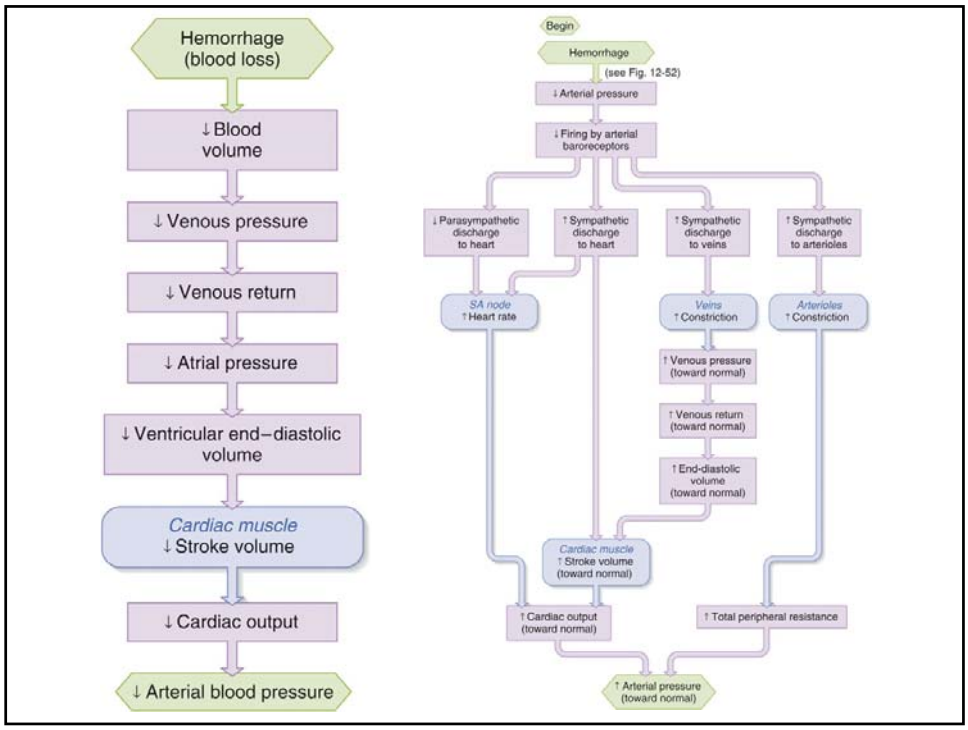
Carotid Sinus Massage & Syncope

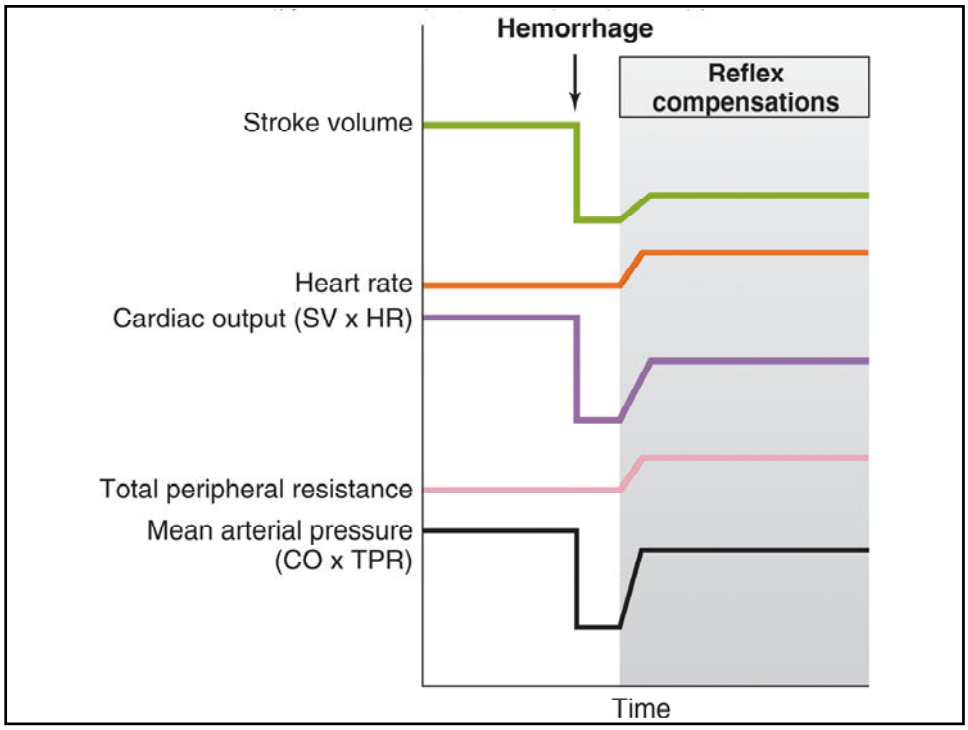


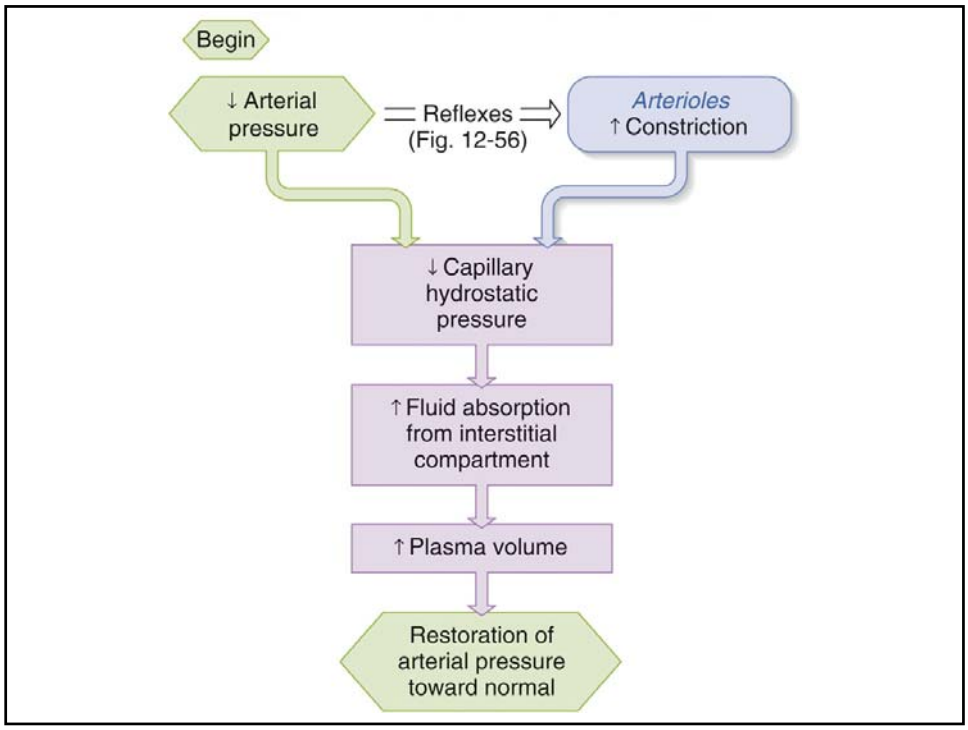
- **Carotid sinus massage** can slow heart rate in paroxysmal superventricular tachycardia
- Stimulation (careful neck massage) over the carotid sinus lowers heart rate
  - paroxysmal superventricular tachycardia (SVT)
    - tachycardia originating from the atria
- Anything that puts pressure on carotid sinus
  - tight collar or hyperextension of the neck
  - may slow heart rate & cause carotid sinus syncope or fainting

Syncope

- **Fainting** or a sudden, temporary loss of consciousness not due to trauma
  - due to cerebral ischemia or lack of blood flow to the brain
- **Causes**
  - **vasodepressor syncope** = sudden emotional stress
  - **situational syncope** = pressure stress of coughing, defecation, or urination
  - **drug-induced syncope** = antihypertensives, diuretics, vasodilators and tranquilizers
  - **orthostatic hypotension** = decrease in BP upon standing


Hemorrhage (blood loss)
↓ Blood volume
↓ Venous pressure
↓ Venous return
↓ Atrial pressure
↓ Ventricular end–diastolic volume
Cardiac muscle
↓ Stroke volume
↓ Cardiac output
↓ Arterial blood pressure
Begin
Hemorrhage
(see Fig. 12-52)
↓ Arterial pressure
↓ Firing by arterial baroreceptors
↓ Parasympathetic discharge to heart
↑ Sympathetic discharge to heart
↑ Sympathetic discharge to veins
↑ Sympathetic discharge to arterioles
SA node
↑ Heart rate
Veins
↑ Constriction
Arterioles
↑ Constriction
↑ Venous pressure (toward normal)
↑ Venous return (toward normal)
↑ End-diastolic volume (toward normal)
Cardiac muscle
↑ Stroke volume (toward normal)
↑ Cardiac output (toward normal)
↑ Total peripheral resistance
↑ Arterial pressure (toward normal)


Hemorrhage
Reflex compensations
Stroke volume
Heart rate
Cardiac output (SV x HR)
Total peripheral resistance
Mean arterial pressure (CO x TPR)
Time



Hormonal Regulation of Blood Pressure

TABLE 21.2 Blood Pressure Regulation by Hormones

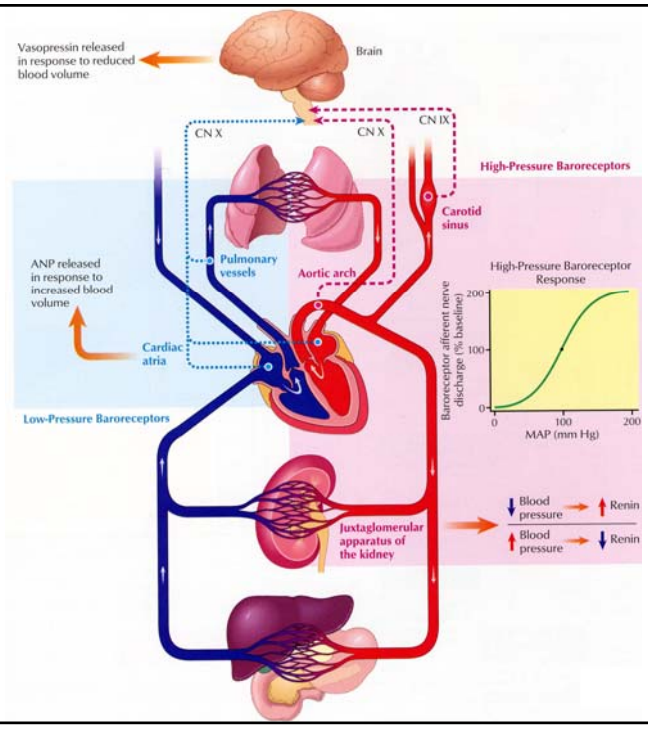
Factor Influencing Blood Pressure	Hormone	Effect on Blood Pressure
Cardiac Output		
Increased heart rate and contractility	Norepinephrine Epinephrine	Increase
Systemic Vascular Resistance		
Vasoconstriction	Angiotensin II	Increase
	Antidiuretic hormone (vasopressin)	
	Norepinephrine*	
	Epinephrine*	
Vasodilation	Atrial natriuretic peptide	Decrease
	Epinephrine†	
	Nitric oxide	
Blood Volume		
Blood volume increase	Aldosterone Antidiuretic hormone	Increase
Blood volume decrease	Atrial natriuretic peptide	Decrease

*Acts at α_1 receptors in arterioles of abdomen and skin.
†Acts at β_2 receptors in arterioles of cardiac and skeletal muscle; norepinephrine has a much smaller vasodilating effect.

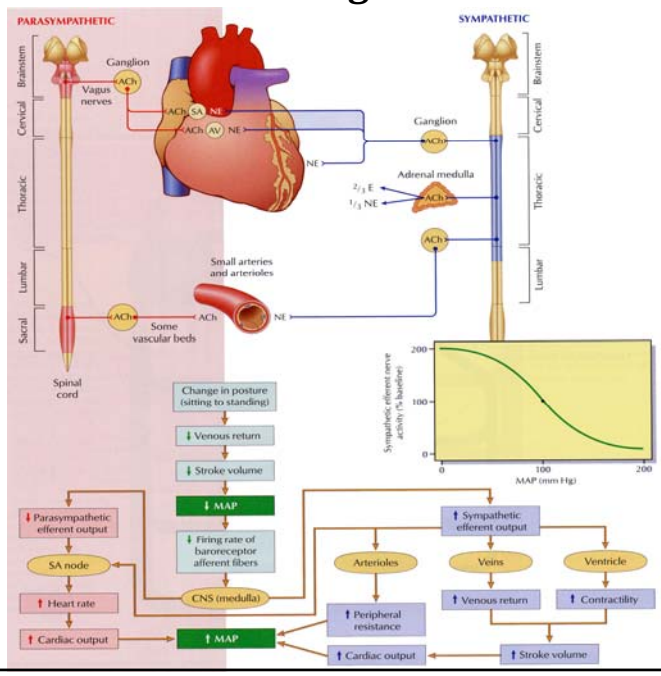
- **Renin-angiotensin-aldosterone (RAA) system**
  - decrease in BP or decreased blood flow to kidney
  - release of renin/results in formation angiotensin II
    - systemic vasoconstriction
    - causes release aldosterone (H2O & Na+ reabsorption)
- **Epinephrine & norepinephrine**
  - increases heart rate & force of contraction
  - causes vasoconstriction in skin & abdominal organs
  - vasodilation in cardiac & skeletal muscle
- **ADH** causes vasoconstriction
- **ANP** (atrial natriuretic peptide) lowers BP
  - causes vasodilation & loss of salt and water in the urine

Local Regulation of Blood Pressure

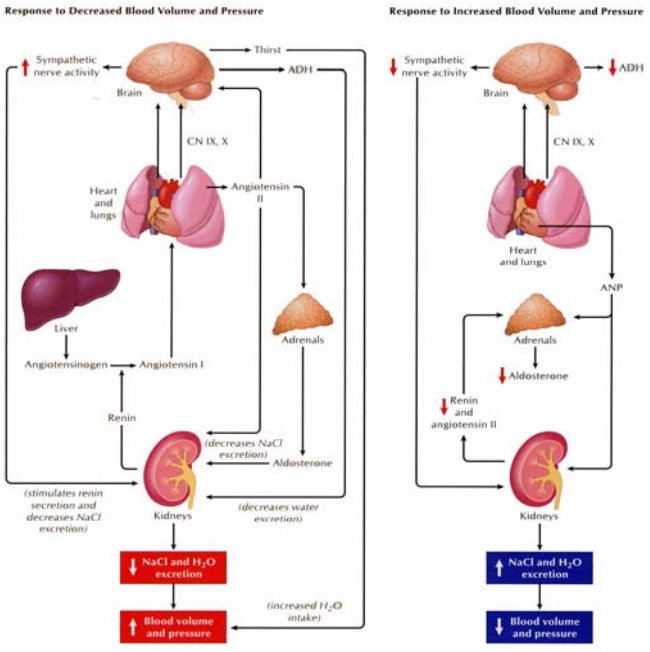
- The ability of a tissue to automatically adjust its own blood flow to match its metabolic demand for supply of O_2 and nutrients and removal of wastes is called ***autoregulation***.
- **Local factors** cause changes in each capillary bed
  - important for tissues that have major increases in activity (brain, cardiac & skeletal muscle)
- Local changes in response to **physical changes**
  - warming & decrease in vascular stretching promotes vasodilation
- **Vasoactive substances** released from cells alter vessel diameter (K+, H+, lactic acid, nitric oxide)
  - systemic vessels dilate in response to low levels of O2
  - pulmonary vessels constrict in response to low levels of O2



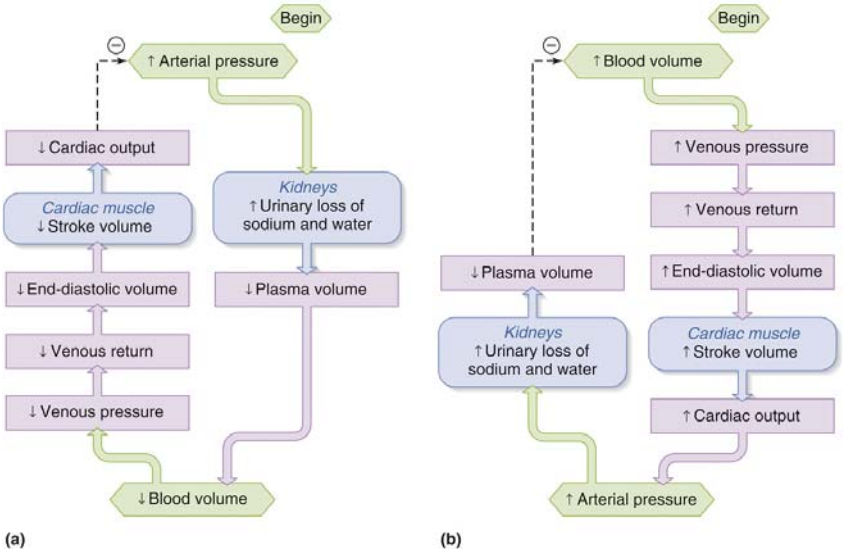
Short-Term Regulation of BP



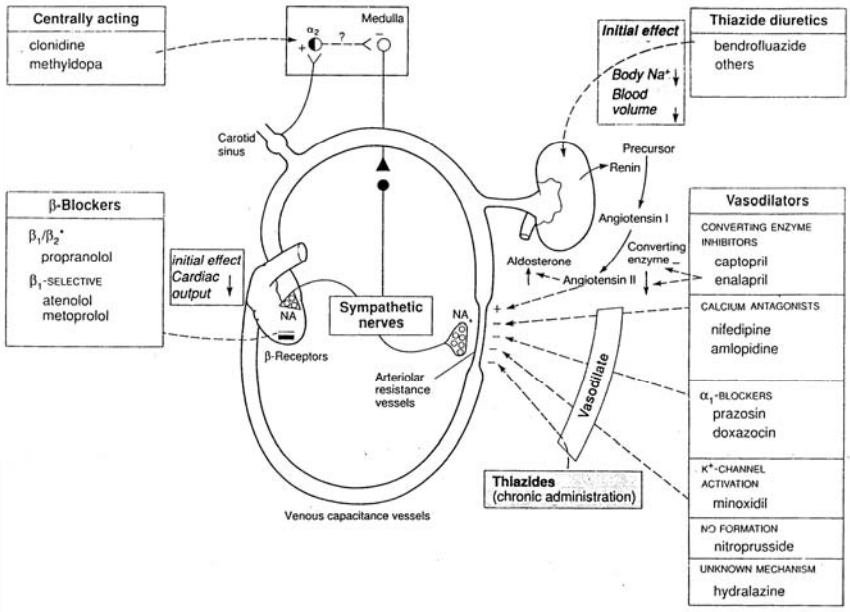
Long-Term Regulation of BP



Blood Volume & Long-Term Regulation of BP



Drugs used in hypertension



藥物的種類	例子	機制
減少細胞外液體積	Thiazide diuretics	增加尿液排泄的體積，因此降低血液體積。
交感腎上腺系統抑制劑	Clonidine；α-methyldopa	藉著與腦中α_2-受器結合的作用，而降低交感腎上腺刺激。
	Guanethidine；reserpine	消耗盡交感神經末梢釋放的正腎上腺素。
	Propranolol；atenolol	阻斷β-受器，降低心輸出量和/或腎素分泌。
	Phentolamine	阻斷α-受器，降低交感神經刺激血管收縮。
直接血管舒張劑	Hydralazine；minoxidil Sodium nitroprusside	藉著直接作用在血管平滑肌，而引起血管舒張。
鈣通道阻斷劑	Verapamil；diltiazem	抑制鈣離子擴散進入血管平滑肌細胞，引起血管舒張和降低週邊阻力。
血管收縮素轉換酵素抑制劑(ACEI)	Captopril；benazepril	抑制血管收縮素I轉換成血管收縮素II。

Shock and Homeostasis

- ***Shock*** is an inadequate cardiac output that results in failure of the cardiovascular system to deliver adequate amounts of oxygen and nutrients to meet the metabolic needs of body cells. As a result, cellular membranes dysfunction, cellular metabolism is abnormal, and cellular death may eventually occur without proper treatment.

- ✓***Inadequate perfusion***
- ✓***Cells forced to switch to anaerobic respiration***
- ✓***Lactic acid builds up***
- ✓***Cells and tissues become damaged & die***

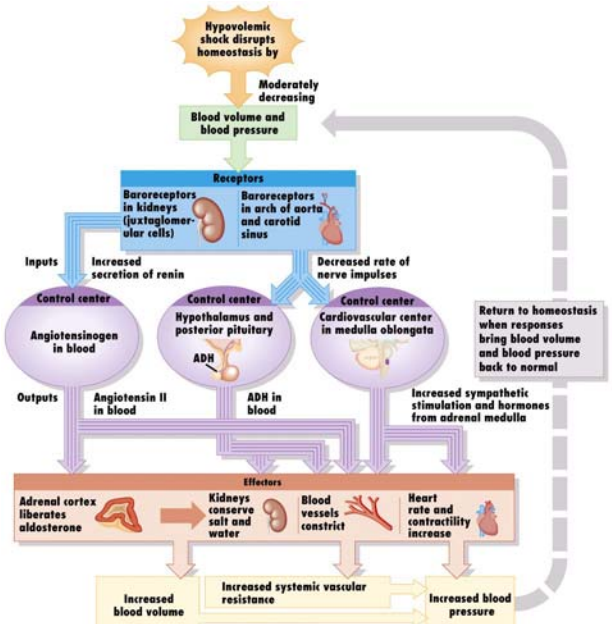
Types of Shock

- ***Hypovolemic shock*** is due to loss of blood or body fluids (hemorrhage, sweating, diarrhea).
- venous return to heart declines & output decreases
- ***Cardiogenic shock*** is caused by damage to pumping action of the heart (MI, ischemia, valve problems or arrhythmias).
- ***Vascular shock*** causing drop inappropriate vasodilation -- anaphylatic shock, septic shock or neurogenic shock (head trauma).
- ***Obstructive shock*** caused by blockage of circulation (pulmonary embolism).
- **Homeostatic responses** to shock include activation of the RAA system, secretion of ADH, activation of the sympathetic division of the ANS, and release of local vasodilators.
- **Signs and symptoms** of shock include clammy, cool, pale skin; tachycardia; weak, rapid pulse; sweating; hypotension (systemic pressure < 90 mm HG); altered mental status; decreased urinary output; thirst; and acidosis.

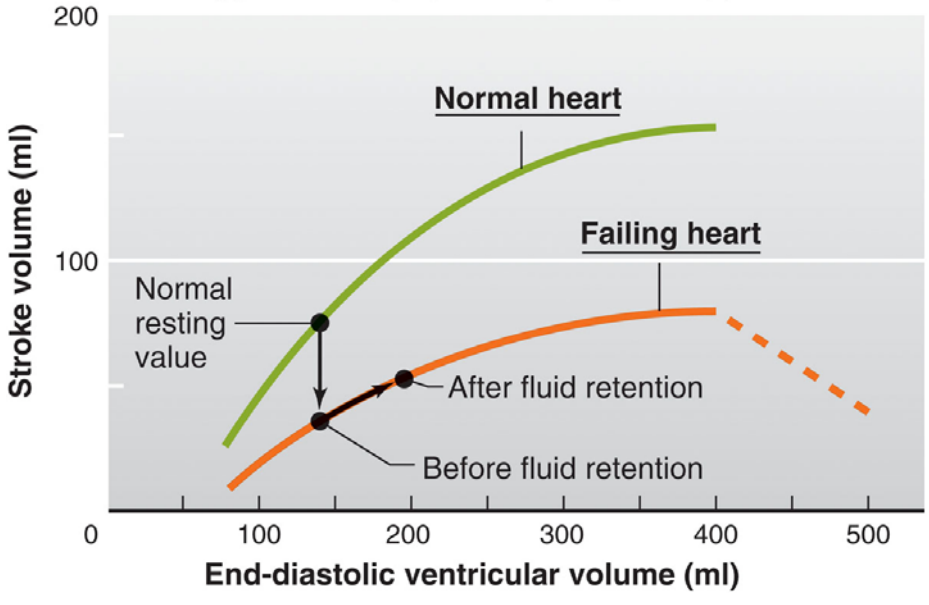
Homeostatic Responses to Shock

- **Mechanisms of compensation** in shock attempt to return cardiac output & BP to normal
  - ***activation of renin-angiotensin-aldosterone***
  - ***secretion of antidiuretic hormone***
  - ***activation of sympathetic nervous system***
  - ***release of local vasodilators***
- If blood volume drops by **10-20%** or if BP does not rise sufficiently, perfusion may be inadequate -- cells start to die

Restoring BP during Hypovolemic Shock



Heart Failure



Congestive Heart Failure

患有充血性心衰竭的人通常用毛地黄(digitalis) 來治療。毛地黄是結合並阻斷細胞膜上Na^+ / K^+幫蒲的作用，造成細胞內鈉離子濃度上升。鈉離子濃度增加，接著刺激膜上另一個運輸攜帶體的活性，以細胞外鈣離子交換細胞內鈉離子。結果，細胞內鈣離子濃度增加，來加強心臟的收縮。

Table 12–9 Types of Drugs Used to Treat Heart Failure

1. ***Diuretics:*** Drugs that increase urinary excretion of sodium and water (Chapter 14). These drugs eliminate the excessive fluid accumulation contributing to edema and/or worsening myocardial function.
2. ***Cardiac inotropic drugs:*** Drugs such as ***digitalis*** that increase ventricular contractility by increasing cytosolic calcium concentration in the myocardial cell. The use of these drugs is currently controversial, however, because although they clearly improve the symptoms of heart failure, they do not prolong life and, in some studies, seem to have shortened it.
3. ***Vasodilator drugs:*** Drugs that lower total peripheral resistance and thus the arterial blood pressure (afterload) the failing heart must pump against. Some inhibit a component of the sympathetic nervous pathway to the arterioles, whereas others [angiotensin-converting enzyme (ACE) inhibitors] block the formation of angiotensin II (see Chapter 14). In addition, the ACE inhibitors prevent or reverse the maladaptive remodeling of the myocardium that is mediated by the elevated plasma concentration of angiotensin II in heart failure.
4. ***Beta-adrenergic receptor blockers:*** Drugs that block the major adrenergic receptors in the myocardium. The mechanism by which this action improves heart failure is unknown (indeed, you might have predicted that such an action, by blocking sympathetically induced increases in cardiac contractility, would be counterproductive). One hypothesis is that excess sympathetic stimulation of the heart reflexly produced by the decreased cardiac output of heart failure may cause an excessive elevation of cytosolic calcium concentration, which would lead to cell apoptosis and necrosis; beta-adrenergic receptor blockers would prevent this.

Preeclampsia

初期子癇(Preeclampsia)是懷孕時產生高血壓以及蛋白尿(尿液中出現蛋白)特徵的情形。正常只有微量的蛋白質會出現在尿液中，而血漿蛋白流失在尿液中會引起水腫。初期子癇的危險是它會很快惡化成一個稱為子癇的狀態，此時就會發作。這可能會危及生命，所以女人患有初期子癇應立即治療她的症狀並且應盡快將胎兒生出來。

Arrhythmias

心臟異常型態的電傳導會產生異常的心動週期並嚴重連累心臟功能。這些節律不整 (arrhythmias) 或許可以用各種不同的藥物來治療，如抑制特定方面的心臟動作電位並以這種方式抑制脈衝沿著異常路徑產生或傳導。使用來治療節律不整的藥物可能為(1)阻斷快速鈉離子孔道 (如: quinidine、procainamide、lidocaine) ；(2) 阻斷慢速鈉離子孔道 (如: verapmil) ；或 (3)阻斷 β - 腎上腺素性接受器(propranolol、atenolol)因為兒茶酚胺會刺激脈衝產生和傳導的速率。