Chapter 11 心血管系統

11-1 心 臟

11-2 血 管

11-3 血流、血壓與阻力

11-4 血液容積

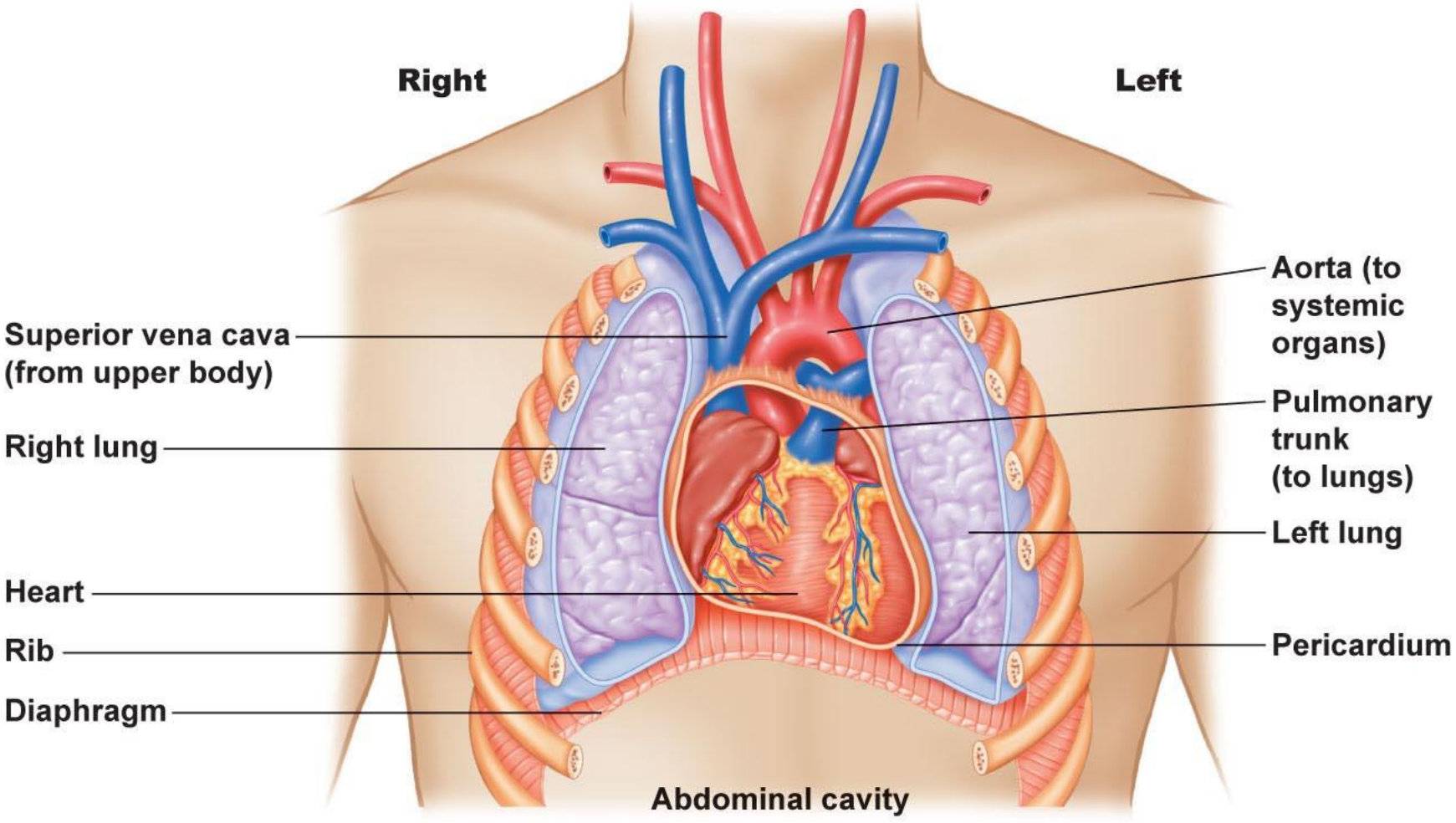
11-5 循環路徑

Circulatory System Components

- **Cardiovascular system**
  - --**Blood:** a fluid that circulates around the body through blood vessels
  - --**Heart:** four-chambered pump
  - --**Blood vessels:** arteries, arterioles, capillaries, venules, and veins
- **Lymphatic system**
  - --Lymphatic vessels, lymphoid tissues, lymphatic organs (spleen, thymus, tonsils, lymph nodes)

Heart Location

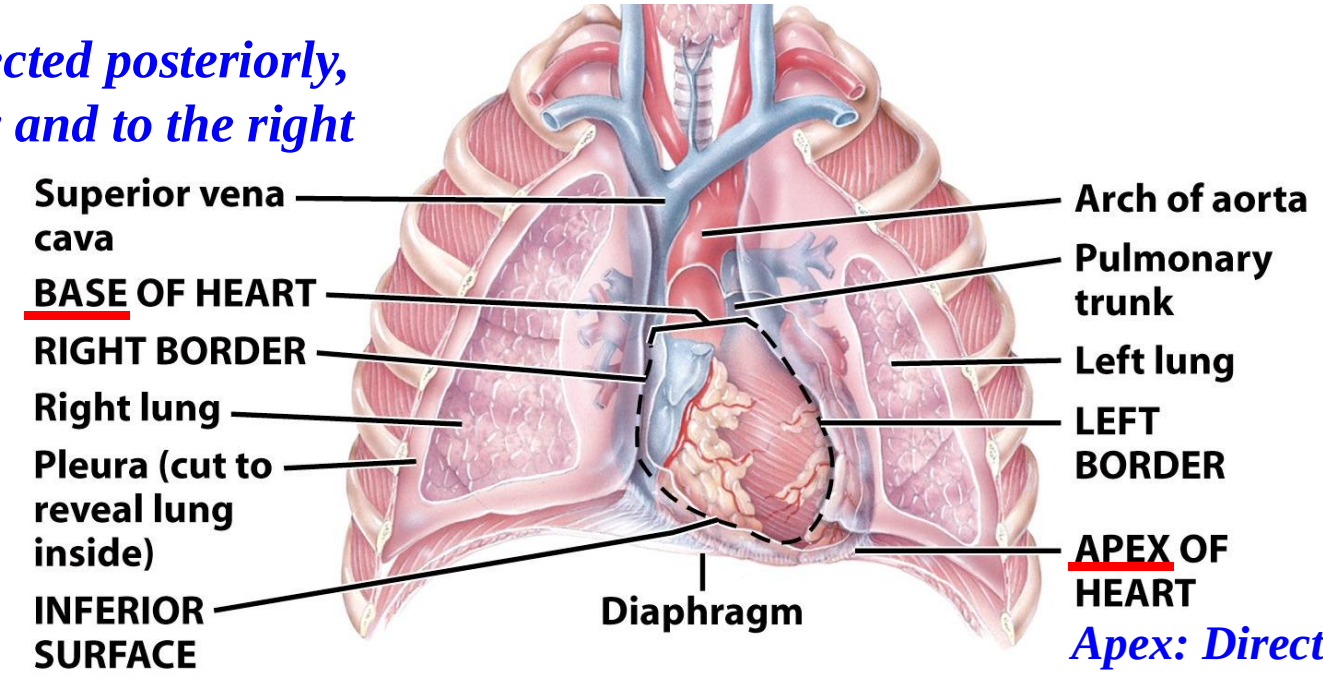
- Located in thoracic cavity (between the lungs in the mediastinum) just above the diaphragm
- Size of fist, weighs approximately 250–350 g (0.5% of BW), and surrounded by pericardium



Heart Orientation

Heart has 2 surfaces: Anterior and Inferior
2 borders: Right and Left

Base: directed posteriorly, superiorly and to the right

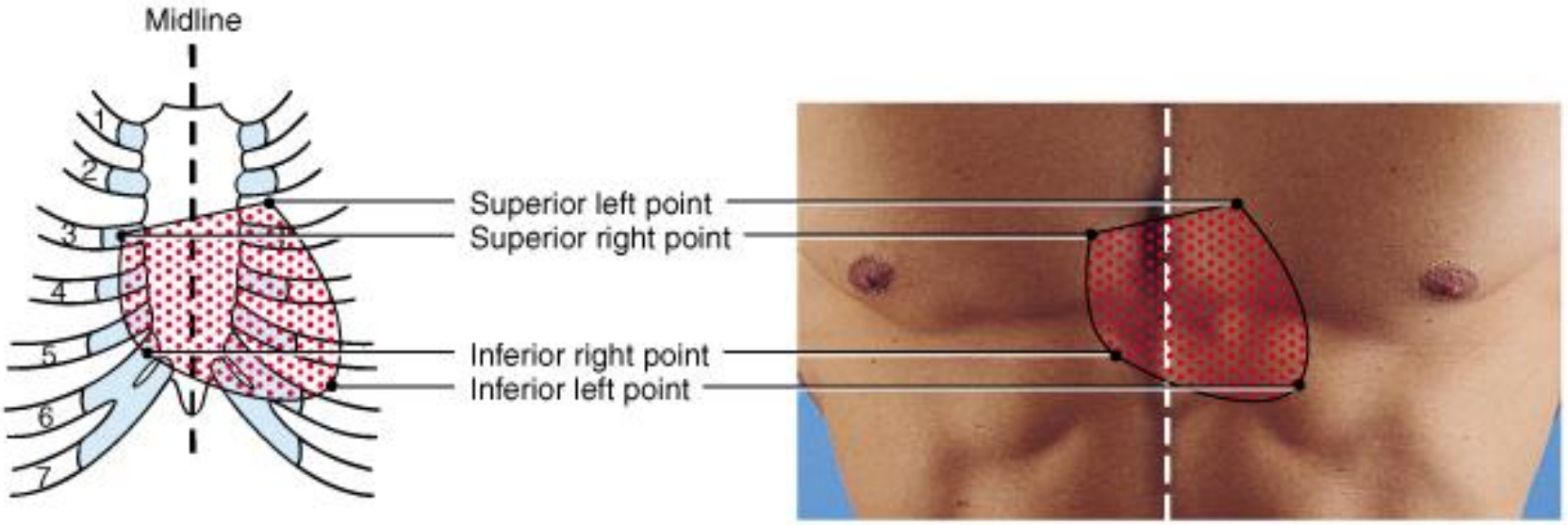


Apex: Directed anteriorly, inferiorly and to the left

- **Anterior surface** deep to sternum and ribs
- **Inferior surface** between apex and right border
- **Right border** faces right lung
- **Left border** (pulmonary border) faces left lung

Surface Projection of the Heart

~ 2/3 of mass to the left of the midline



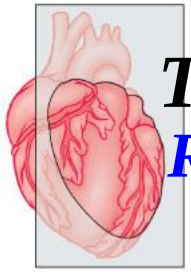
- **Superior right point** at the superior border of the 3rd right costal cartilage
- **Superior left point** at the inferior border of the 2nd left costal cartilage, 3 cm to the left of midline
- **Inferior left point** at the 5th intercostal space, 9 cm from the midline
- **Inferior right point** at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

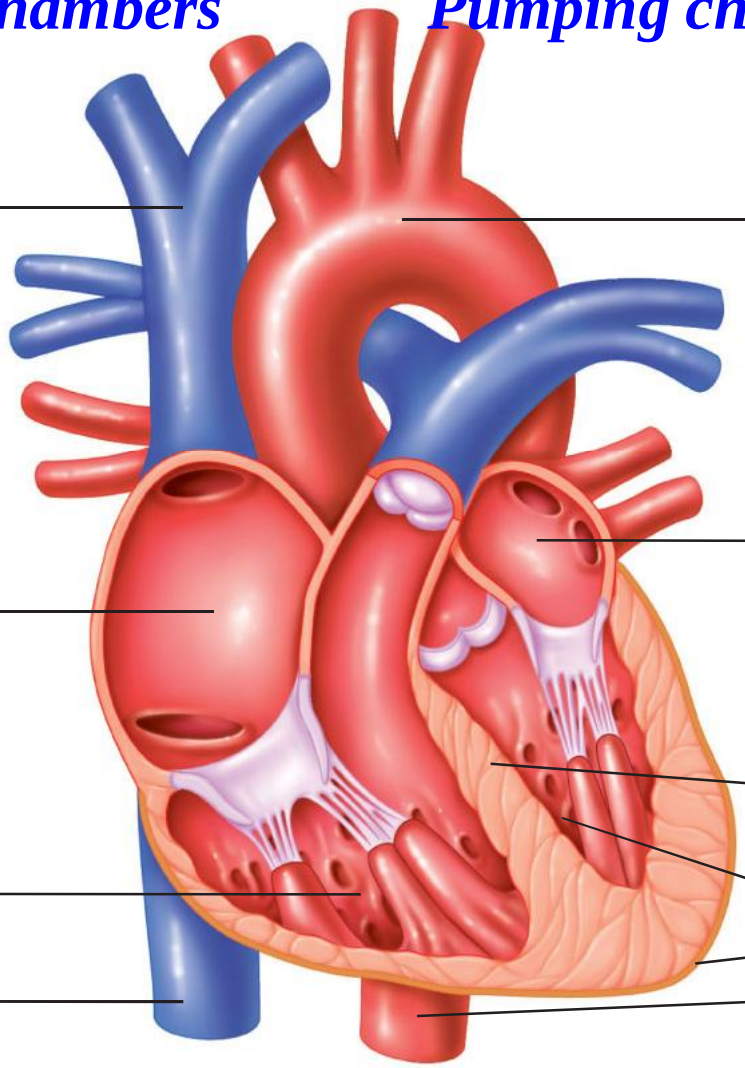
Heart Structure

Four Chambers:

Two upper (atria) + Two lower (ventricles)

Receiving chambers *Pumping chambers*





Superior vena cava
(from upper body)

Aorta (to systemic organs)

Left atrium

Right atrium

Interventricular septum

Right ventricle

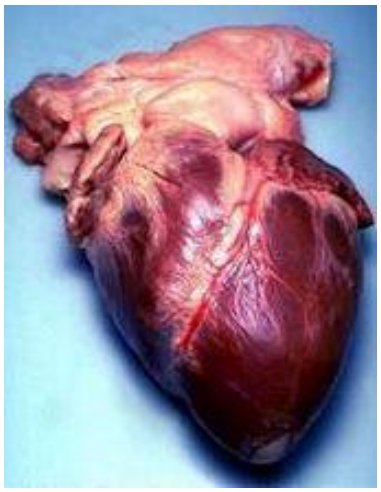
Left ventricle

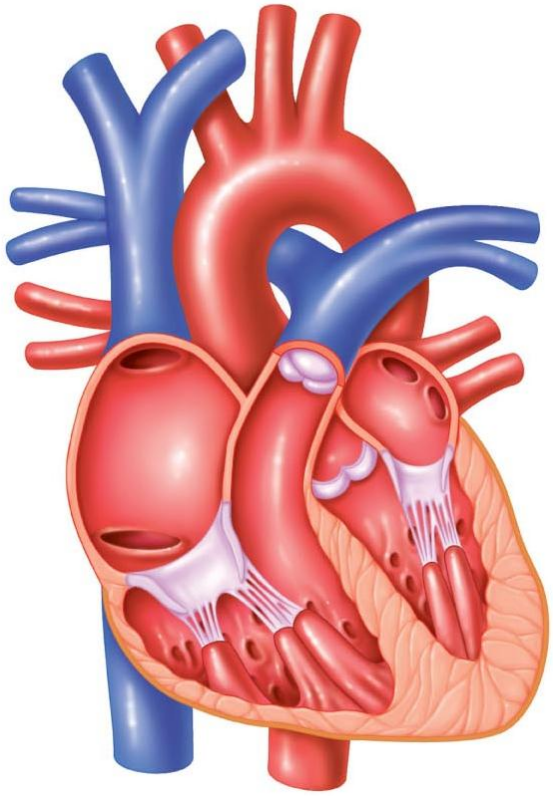
Apex of heart

Inferior vena cava
(from lower body)

Descending aorta
(to lower body)

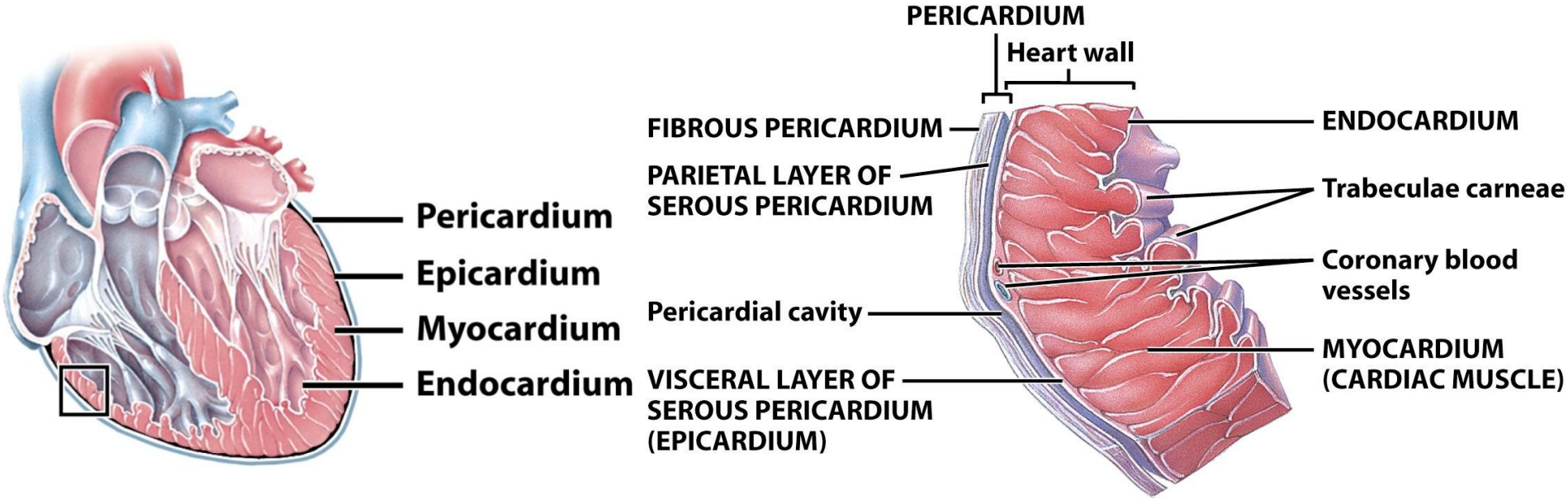
Heart Structure





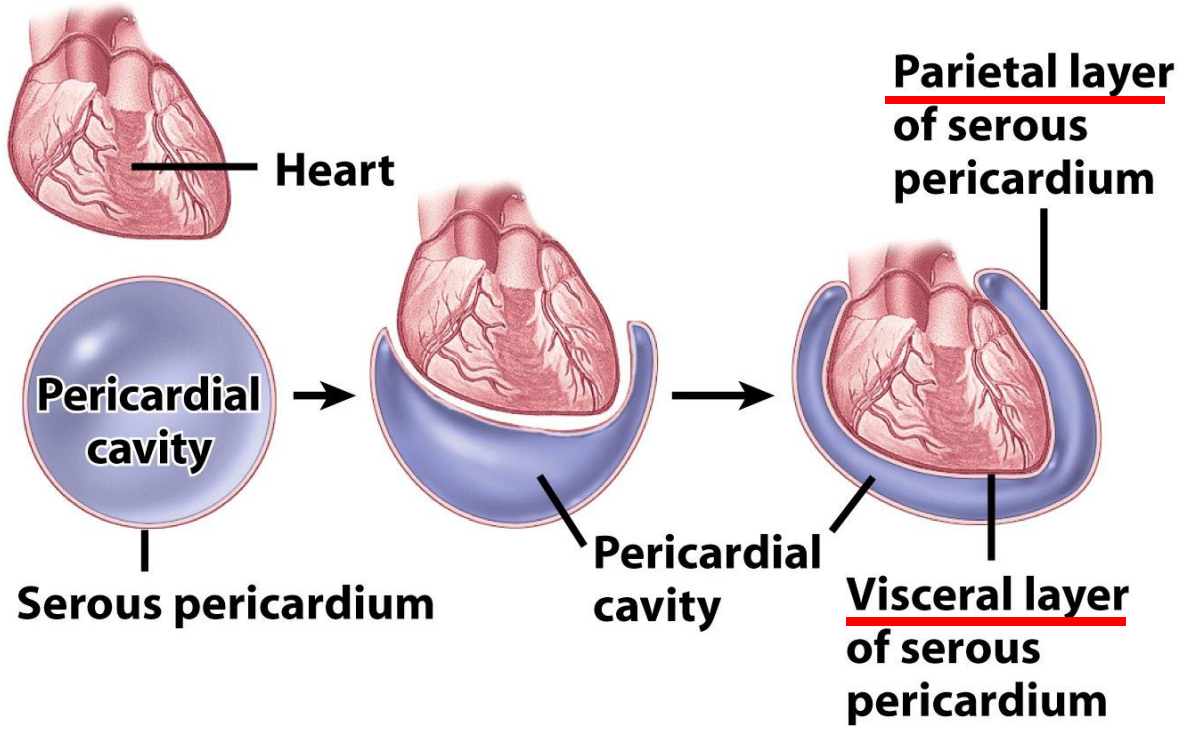
- **Functional heart**
  - --**Left heart:** atrium and ventricle in the left side of heart
  - --**Right heart:** atrium and ventricle in the right side of heart
- **Septum:** left heart and right heart are separated by a wall
  - --**Interatrial septum**
  - --**Interventricular septum**
- **Base:** wider upper pole (end) of heart (top)
- **Apex:** narrower lower pole (bottom)

Tissue Layers of Heart Wall

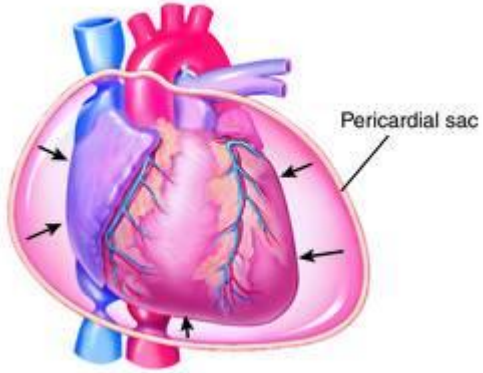


- **The wall of the heart has three layers: *Epicardium*, *Myocardium (95%)*,** and ***Endocardium***
- **Pericardium 2 main parts: *Fibrous* and *Serous pericardium***
  - **--Fibrous pericardium:** tough, inelastic, dense irregular connective tissue – prevents overstretching, protection, anchorage
  - **--Serous pericardium:** thinner, more delicate membrane – double layer (parietal layer fused to fibrous pericardium, visceral layer also called epicardium)
  - --Pericardial fluid reduces friction – secreted into pericardial cavity

Pericardium and Heart Wall

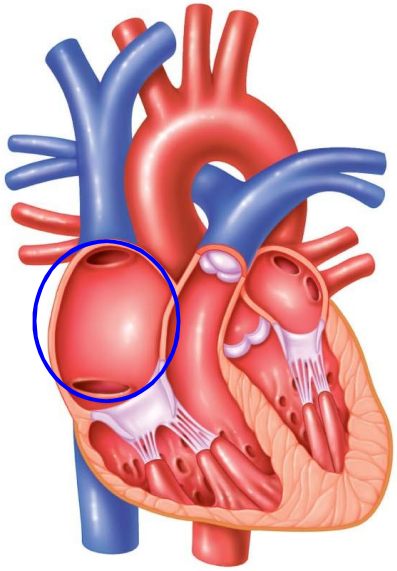


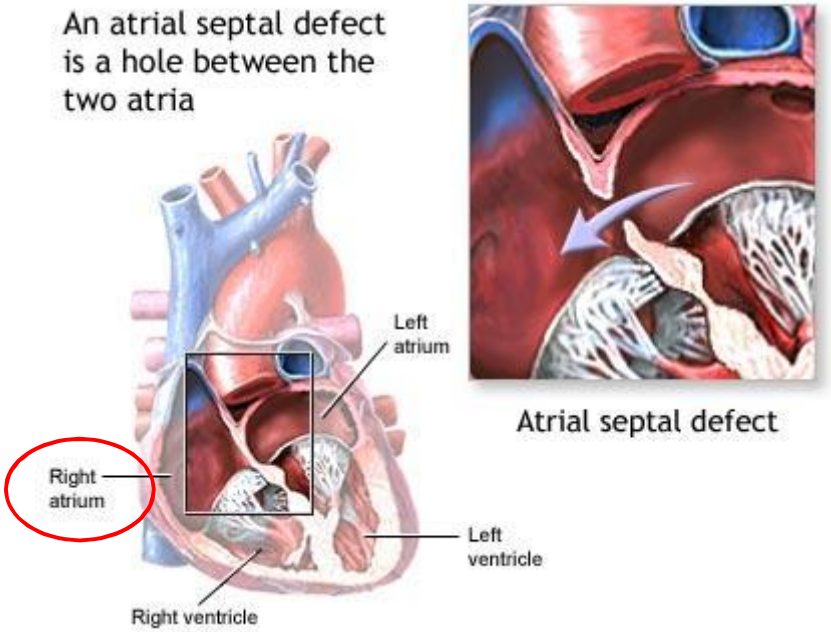
Cardiac Tamponade
心包填塞



- ***Pericarditis*** is an inflammation of the pericardium
- ***Endocarditis*** is an inflammation of the endocardium (usually involves the heart valves)
- Associated bleeding into the pericardial cavity compresses the heart (***cardiac tamponade***) and is potentially lethal

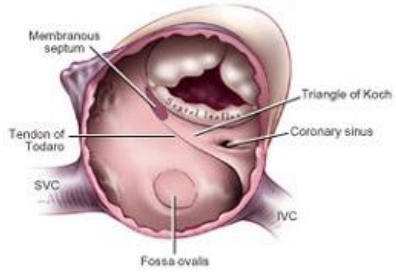
Chambers of the Heart



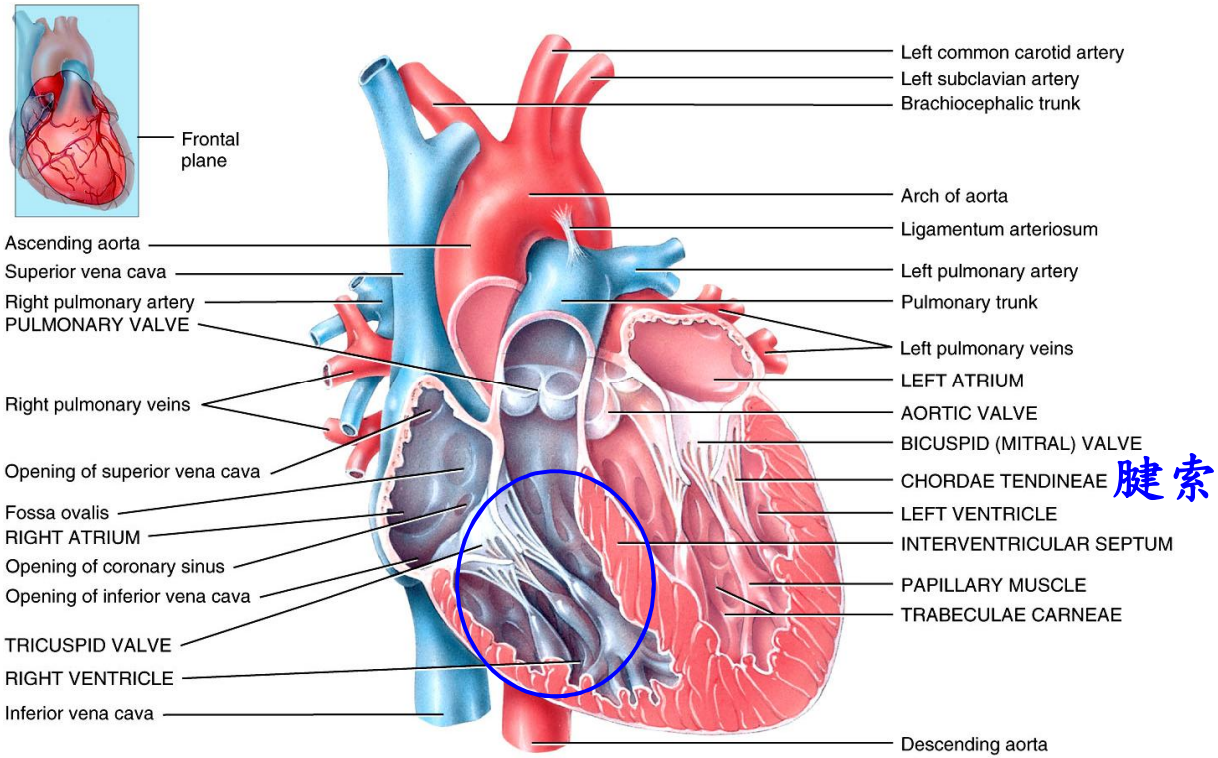


Right Atrium (RA)

- Receives blood from **3 sources**
  --Superior vena cava, inferior vena cava and coronary sinus
- **Interatrial septum** has **Fossa ovalis**
  --A remnant of the fetal **foramen ovale**
- **Tricuspid valve (right atrioventricular valve)**
  --Blood flows through into right ventricle
  --Three cusps composed of dense CT covered by endocardium



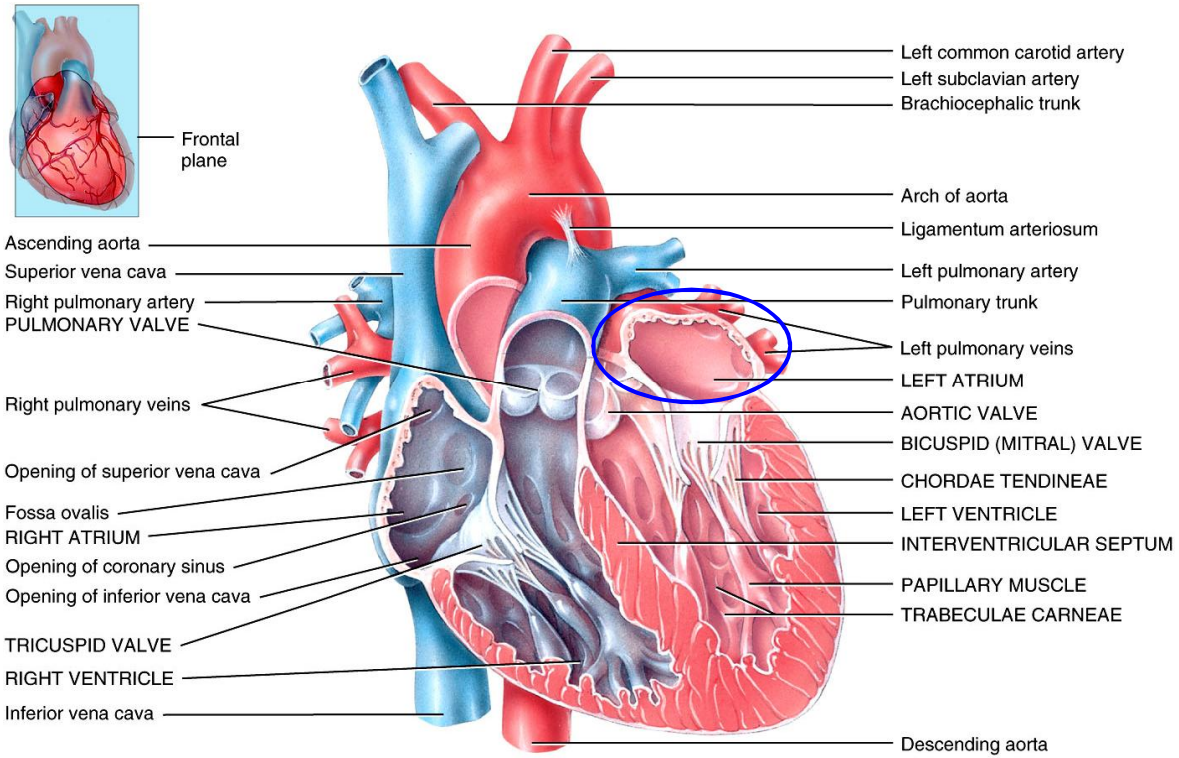
Chambers of the Heart



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

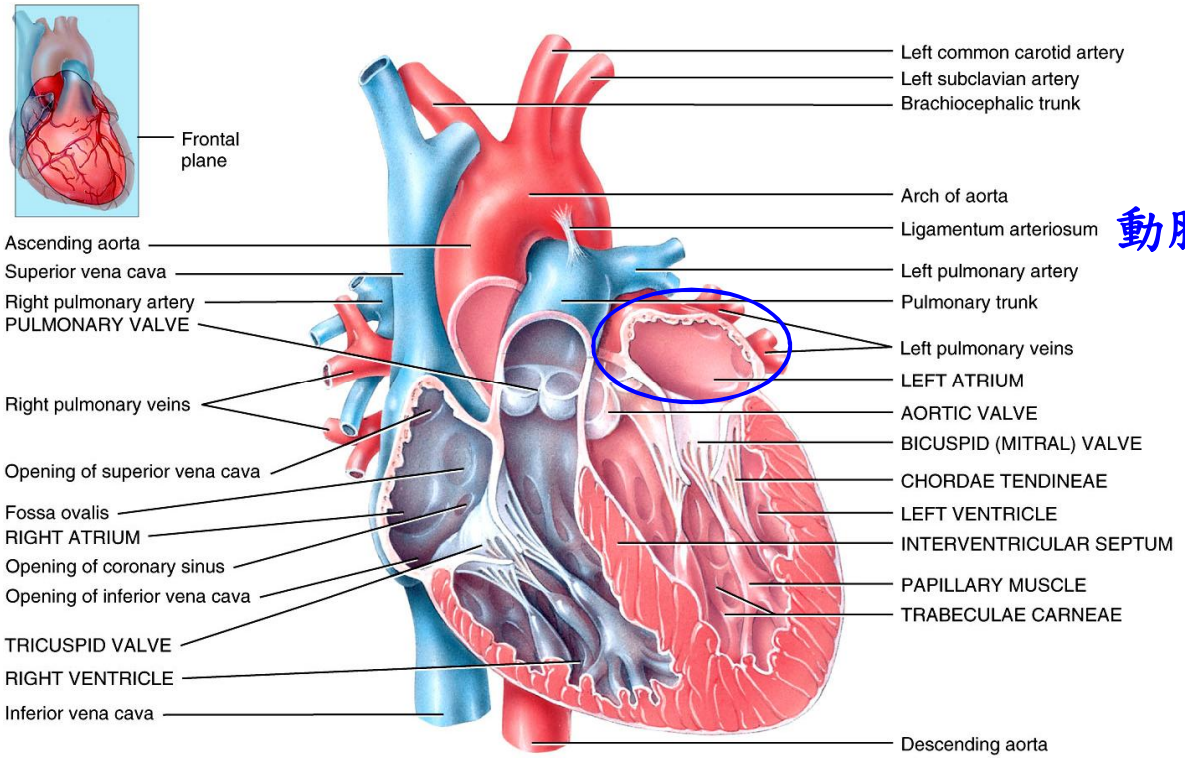
Chambers of the Heart



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
  --Two cusps= **Mitral valve= Left Atrioventricular valve**

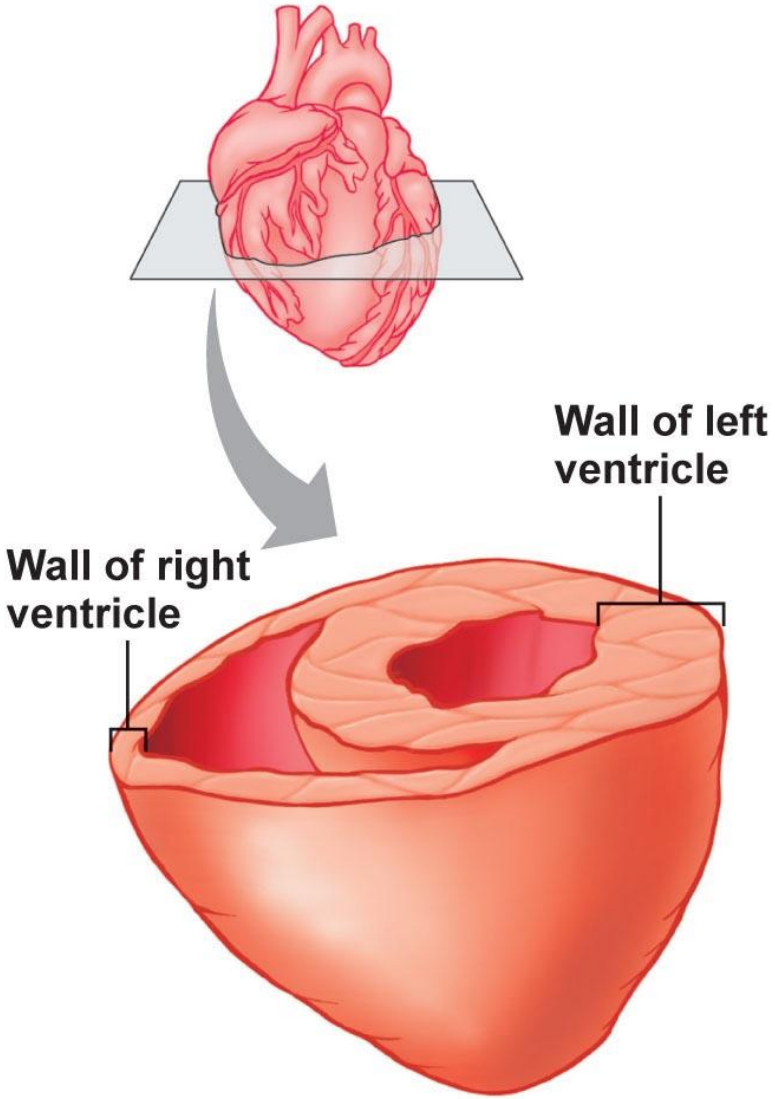
Chambers of the Heart



Left Ventricle (LV)

- Forms the **apex** of heart (**thickest chamber**)
- **Chordae tendineae** anchor bicuspid valve to papillary muscles
- Blood passes through **aortic valve** (**aortic semilunar valve**) into ascending aorta; some blood flows into **coronary arteries**, remainder to body
- During fetal life **ductus arteriosus** shunts blood from pulmonary trunk to aorta (lung bypass) closes after birth with remnant called **ligamentum arteriosum**

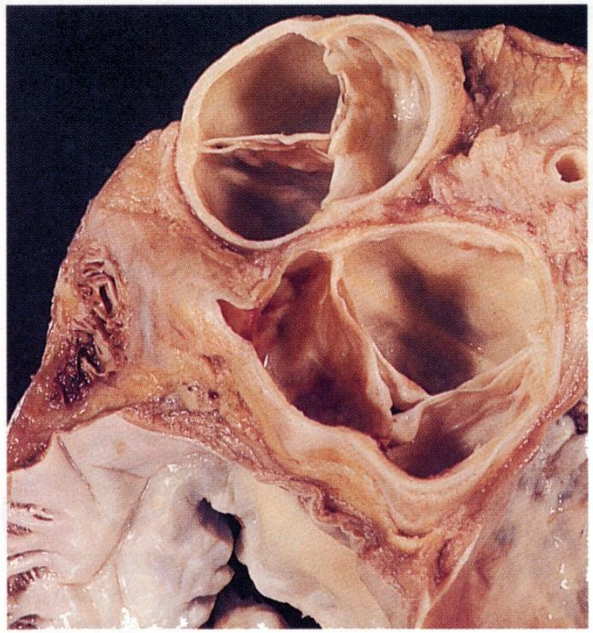
Myocardial Thickness and Function



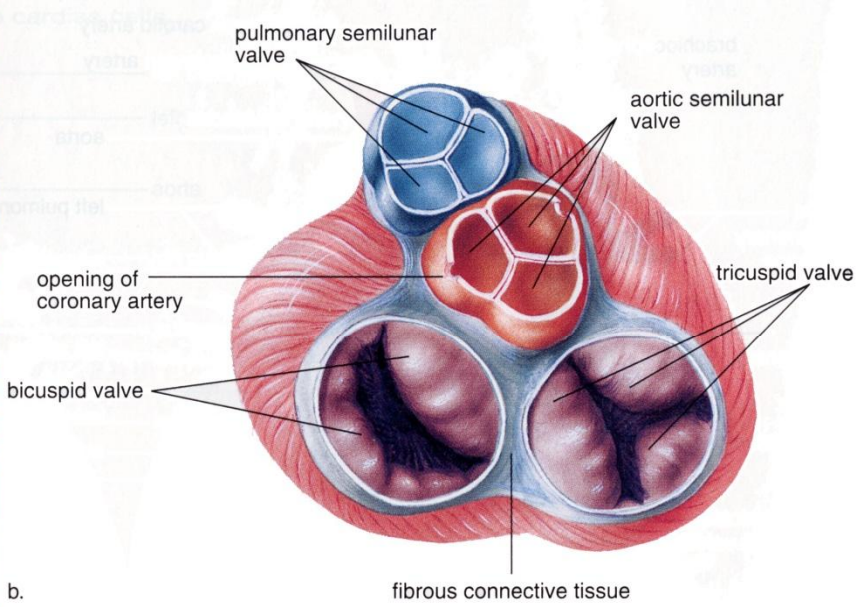
Right ventricle < Left ventricle

- Thickness of myocardium varies according to the **function of the chamber**
- **Atria** are **thin** walled, deliver blood to adjacent ventricles
- **Ventricle** walls are **thicker** because they pump blood greater distances
  - **--Right ventricle** supplies blood to the lungs (little flow resistance)
  - **--Left ventricle** wall is the thickest to supply systemic circulation

Heart Valves



a.



b.

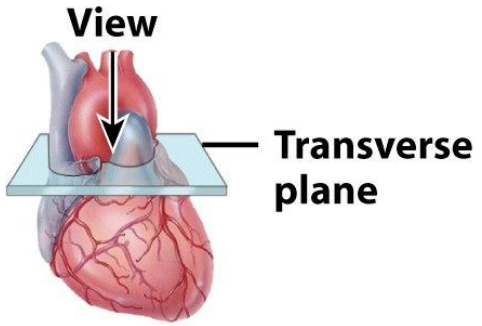
***Four* valves (2 *atrioventricular* & 2 *semilunar*)**

- Valves open and close in response to **pressure changes** as the heart contracts and relaxes (valves **prevent backward flow of blood**)

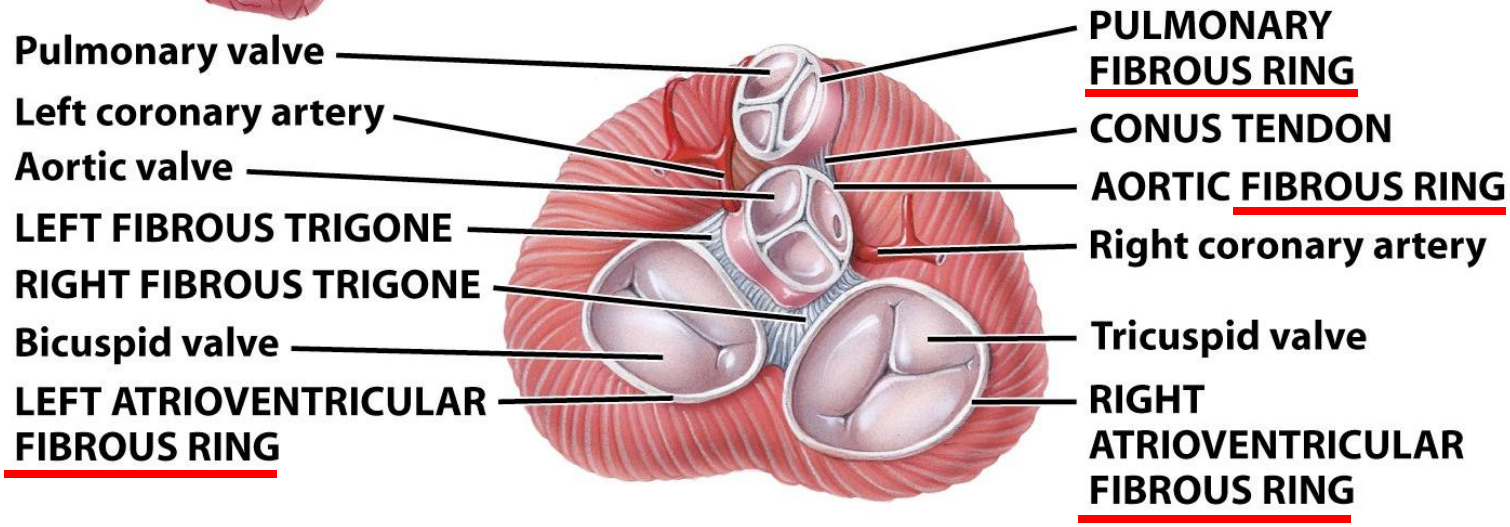
Heart valves disorders

- **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

Fibrous Skeleton of Heart



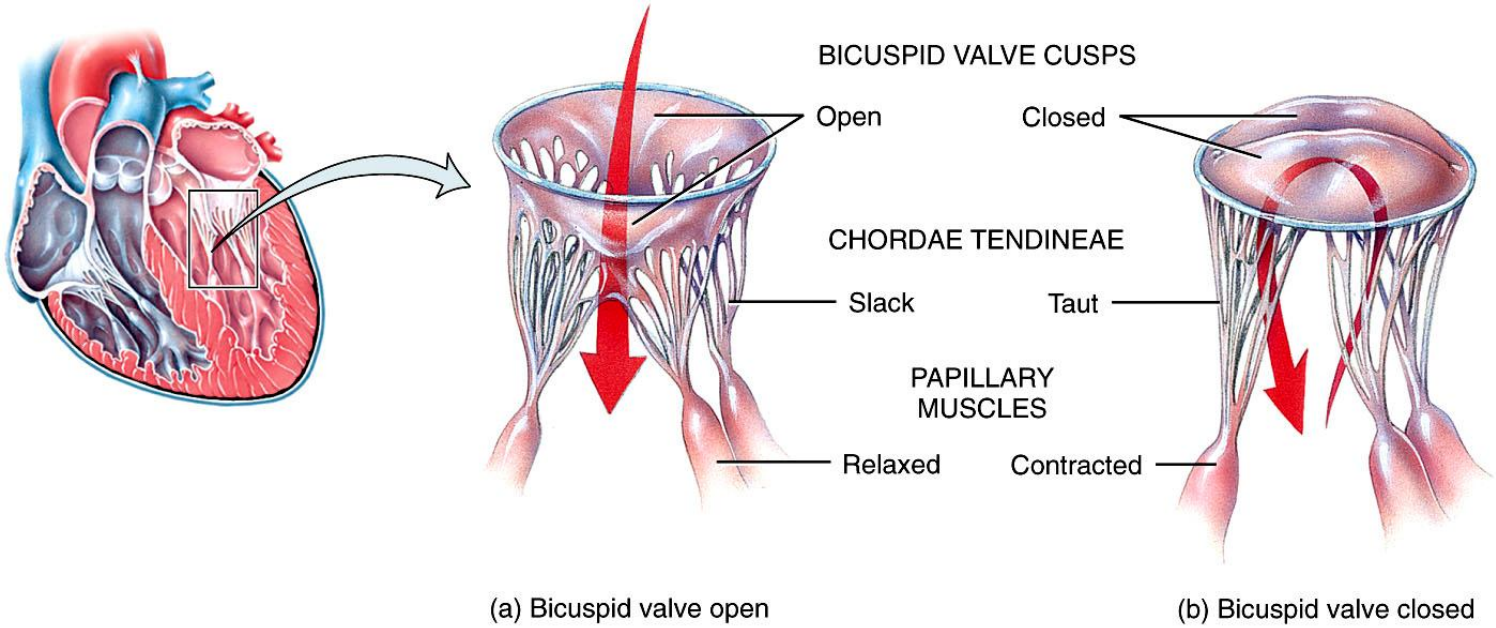
***Dense CT rings** surround the valves of the heart, fuse and merge with the interventricular septum*



- **Support structure** for heart valves
- **Insertion point** for cardiac muscle bundles
- **Electrical insulator** between atria and ventricles

  --prevents direct propagation of AP's to ventricles

Action of AV Valve



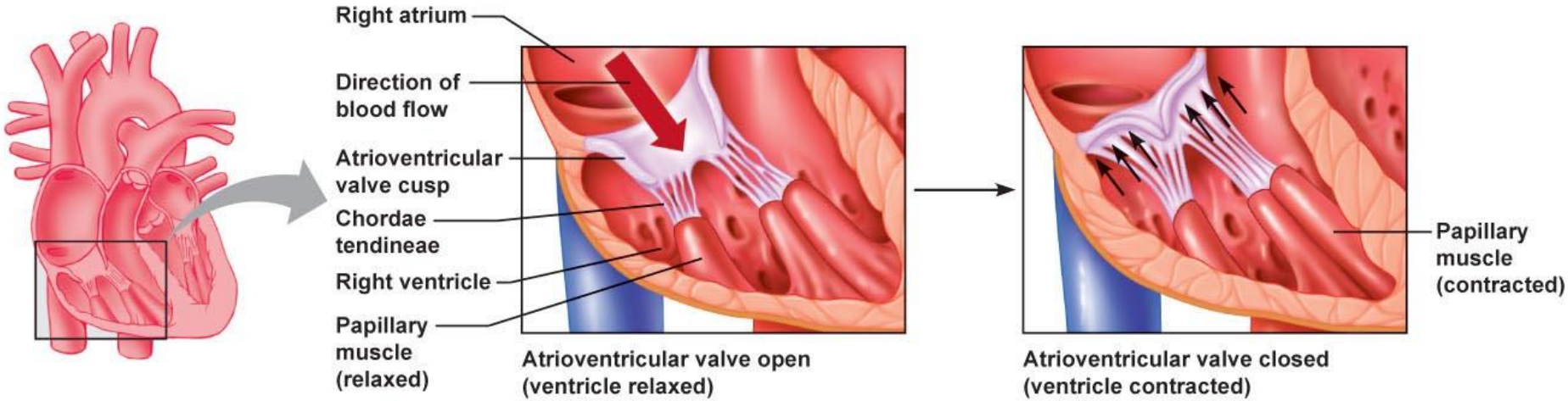
AV valves open

- **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 prevents regurgitation

Action of AV Valve

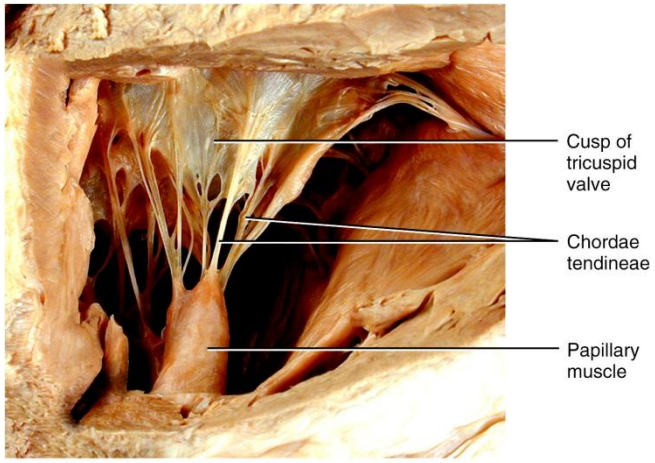


(a) When the ventricles are relaxed, blood enters the atria, pushing the atrioventricular valve cusps down into the ventricles, opening the valves.

- ***Atria Contracts***
- ***Ventricle Relaxed***

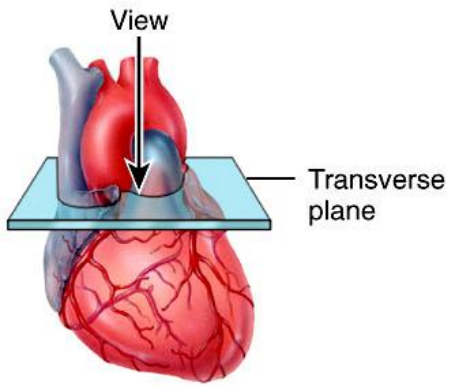
(b) When the ventricles contract, blood presses up against the atrioventricular valve cusps, forcing the valves closed. Contraction of the papillary muscles tightens the chordae tendineae, preventing the valve cusps from being pushed into the atria.

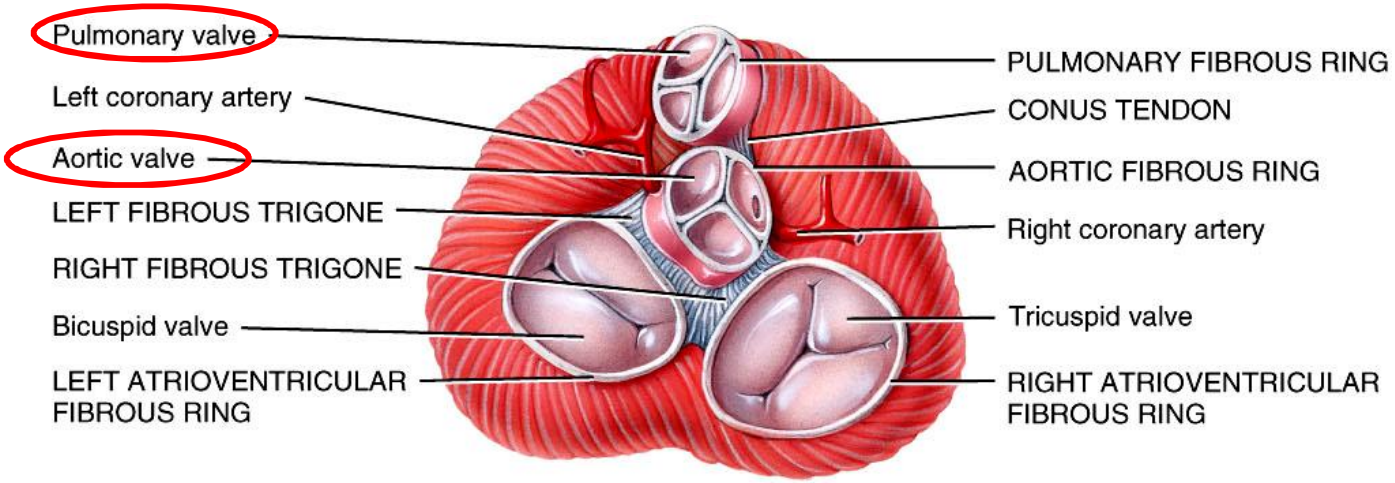
- ***Atria Relaxed***
- ***Ventricle Contracts***



(c) Tricuspid valve open

Action of Semilunar Valve



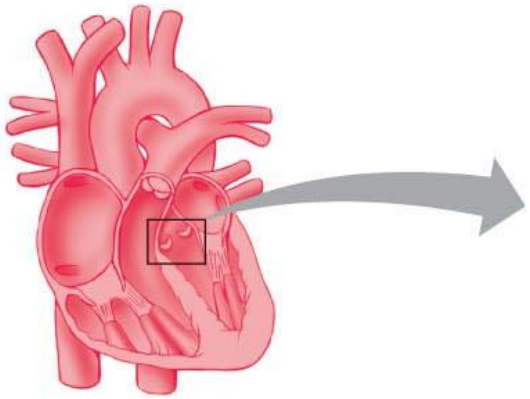


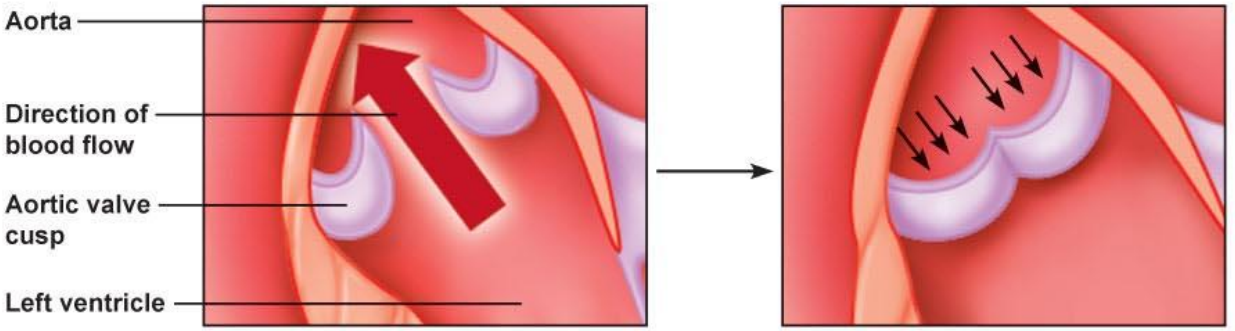
Superior view (the atria have been removed)

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

Action of Semilunar Valve





Aortic semilunar valve open (ventricle contracted)

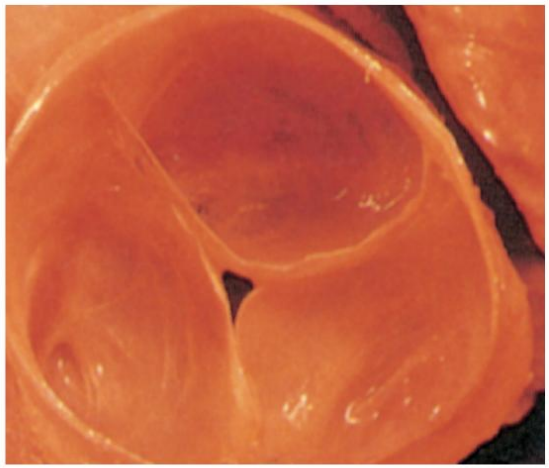
Aortic semilunar valve closed (ventricle relaxed)

(a) When the ventricles contract, blood presses up against the semilunar valve cusps, forcing the valves open and allowing blood to flow into the aorta and pulmonary artery.

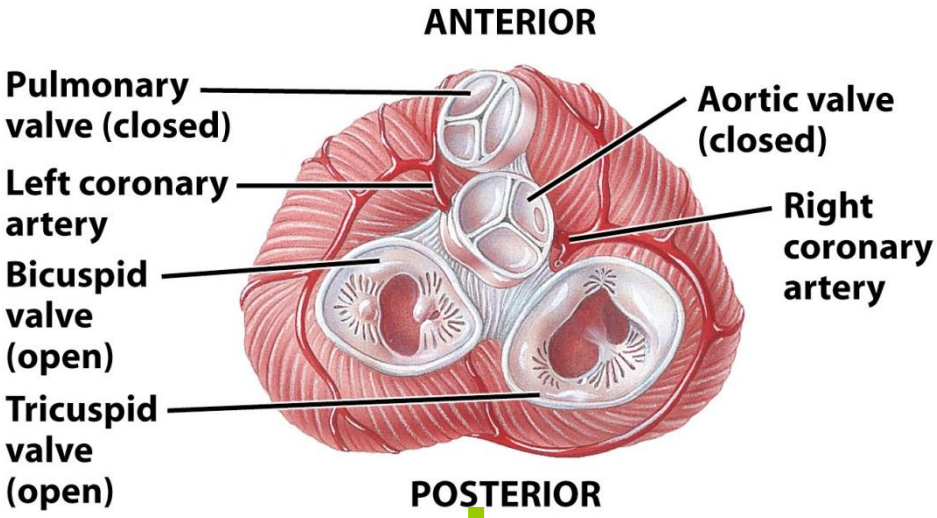
➢ ***Ventricle Contracts***

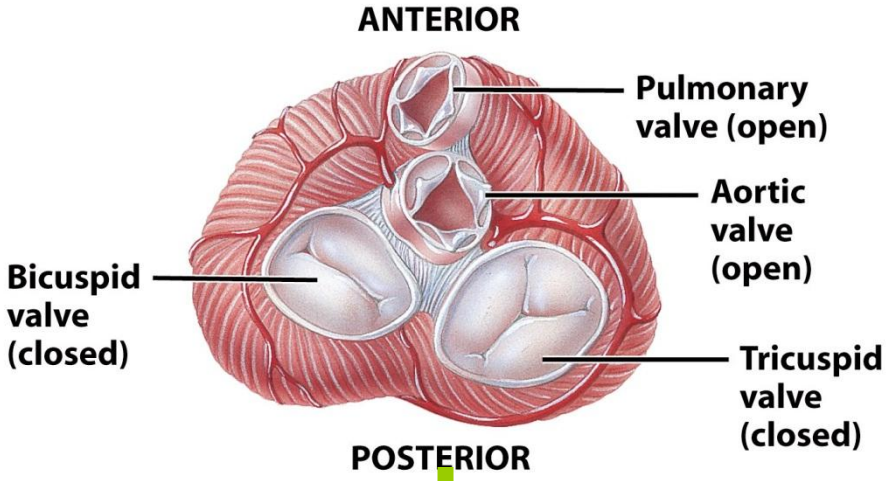
(b) When the ventricles relax, blood in the aorta and pulmonary artery presses down against the valve cusps, forcing them to close.

➢ ***Ventricle Relaxed***



Valve almost completely closed





What are the ventricles doing?

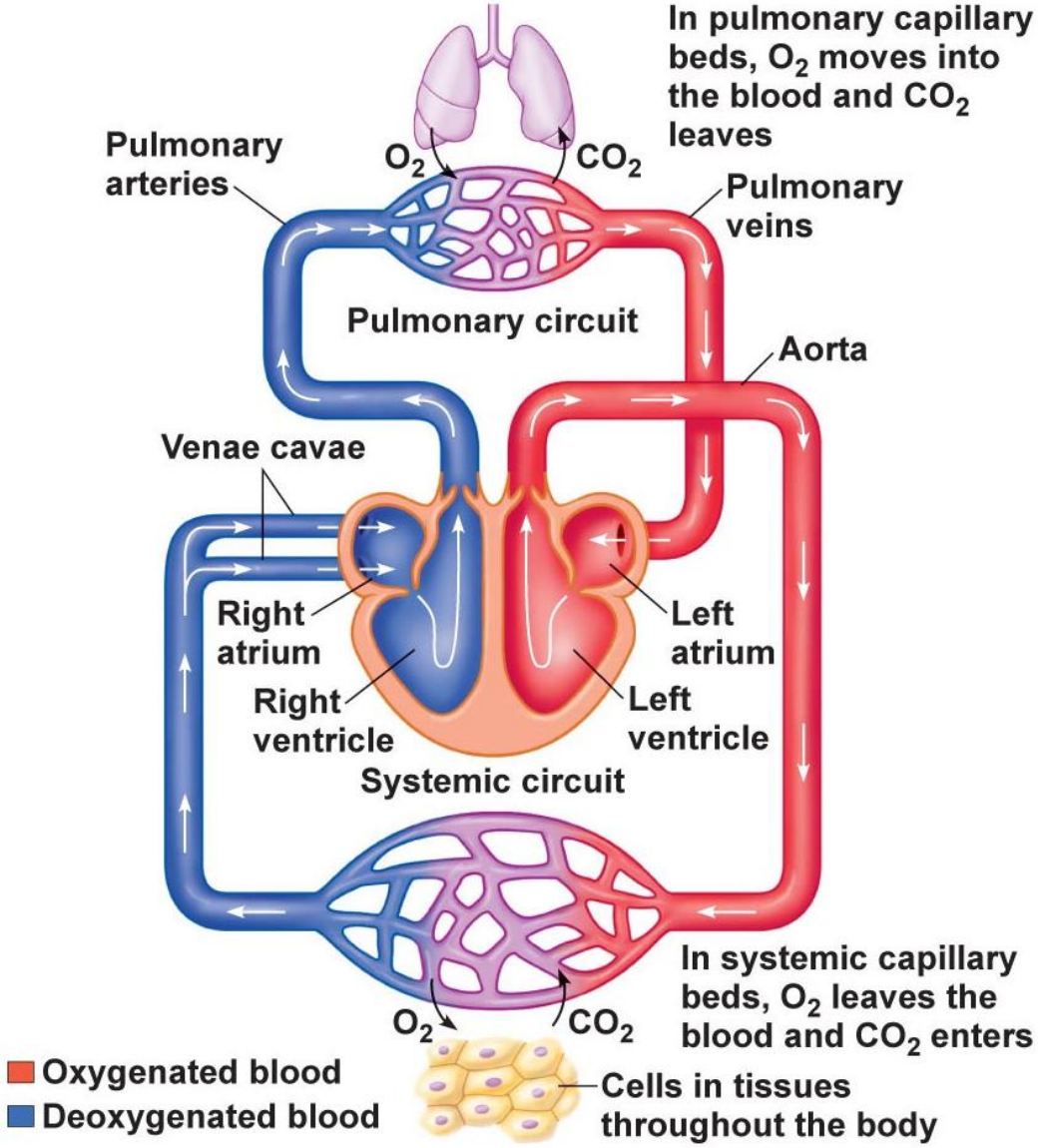
Atria contract
blood fills ventricles through AV valves

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

Heart Valves

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

Pathway of Blood Flow



- Cardiovascular system = **closed system**
- Flow through **systemic** and **pulmonary circuits** is in series
- ***Left ventricle → aorta → systemic circuit → vena cava → right atrium → right ventricle → pulmonary artery → pulmonary circuit → pulmonary veins → left atrium → left ventricle***

Pulmonary Circulation

Heart Circulation

Systemic Circulations

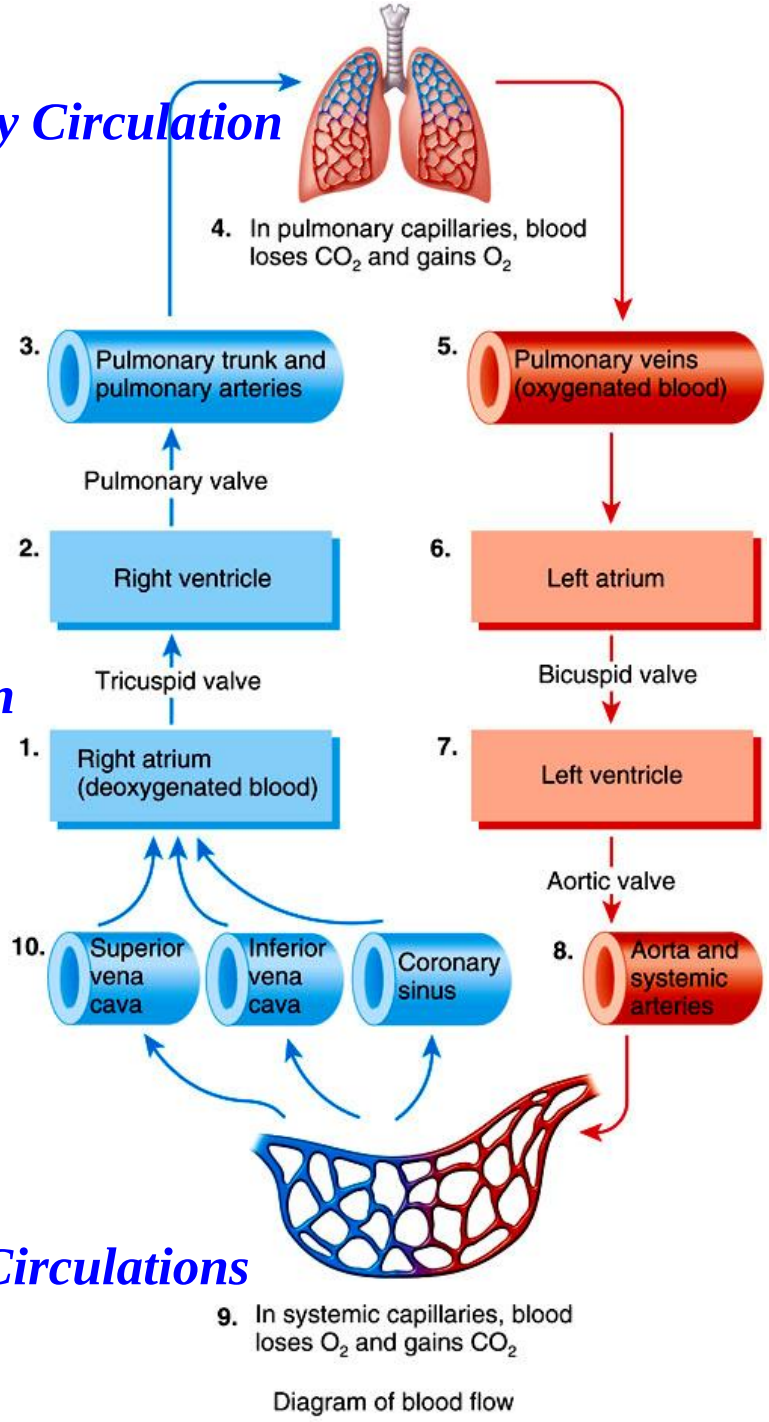
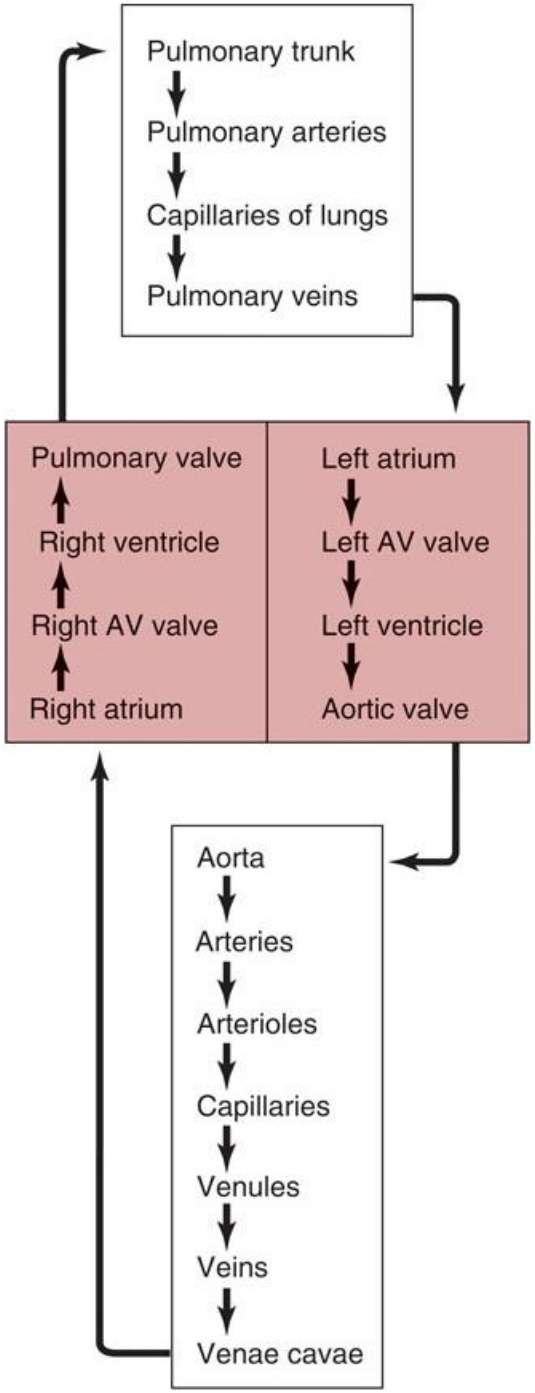
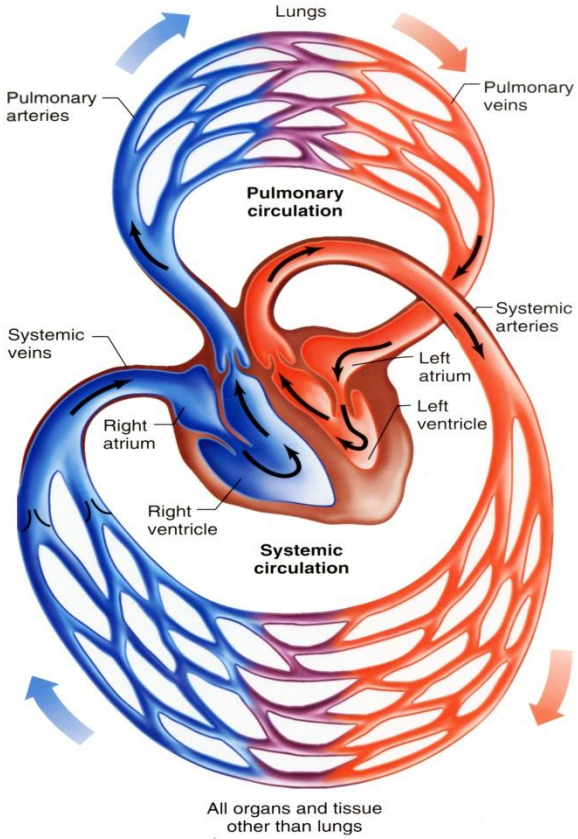


Diagram of blood flow



Systemic & Pulmonary Circulations

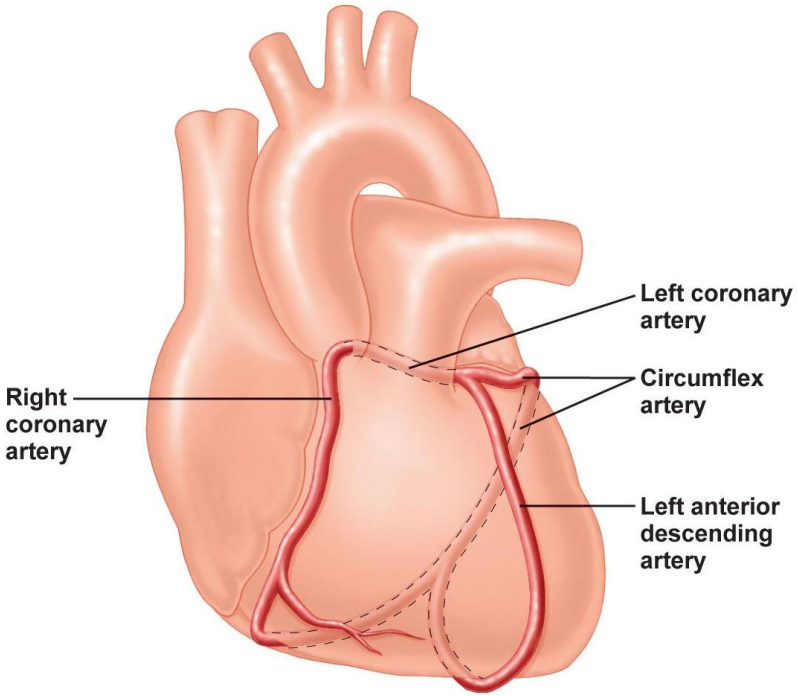


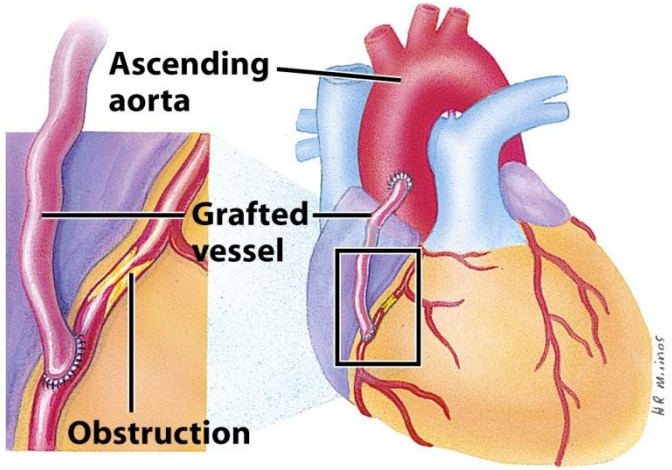
Organ	Flow at rest ml/min
Brain	650 (13%)
Heart	215 (4%)
Skeletal muscle	1030 (20%)
Skin	430 (9%)
Kidneys	950 (20%)
Abdominal organs	1200 (24%)
Other	525 (10%)
Total	5000 (100%)

	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

Coronary Circulation



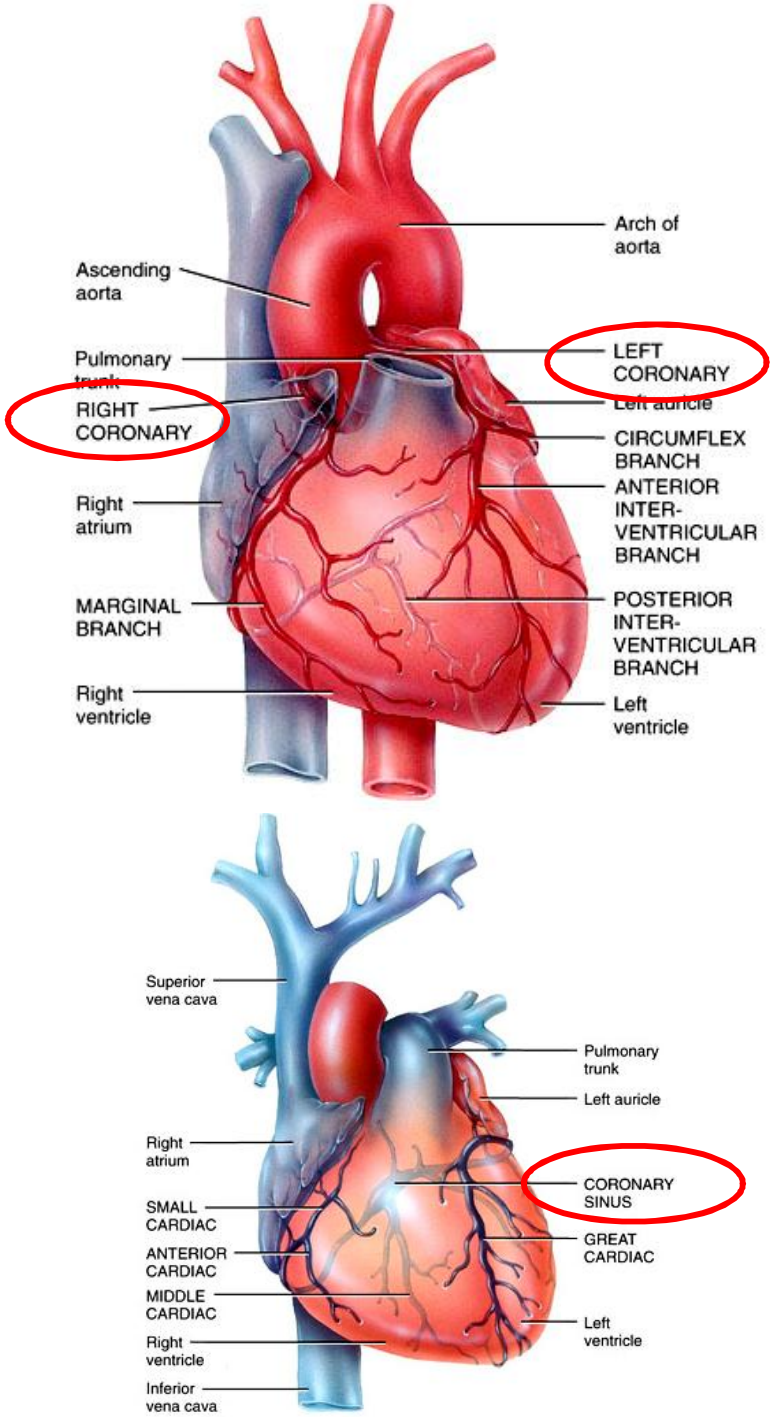


Coronary artery bypass grafting (CABG)

Blood flow: 4-5% of cardiac output (200-250 ml/min)

- **Myocardium has its own network of blood vessels** (blood in chambers does not supply nutrients to cardiac cells)
- **Coronary arteries branch from ascending aorta**
  - --**Anastomoses** provide alternate routes or collateral circuits
  - --Allows heart muscle to receive sufficient oxygen even if an artery is partially blocked
- **Coronary capillaries**
- **Coronary veins**
  - --Collects in **coronary sinus**
  - --Empties into **right atrium**

Coronary Artery



- **Branches off aorta above aortic semilunar valve**
- **Left coronary artery**
  - --***Circumflex branch***

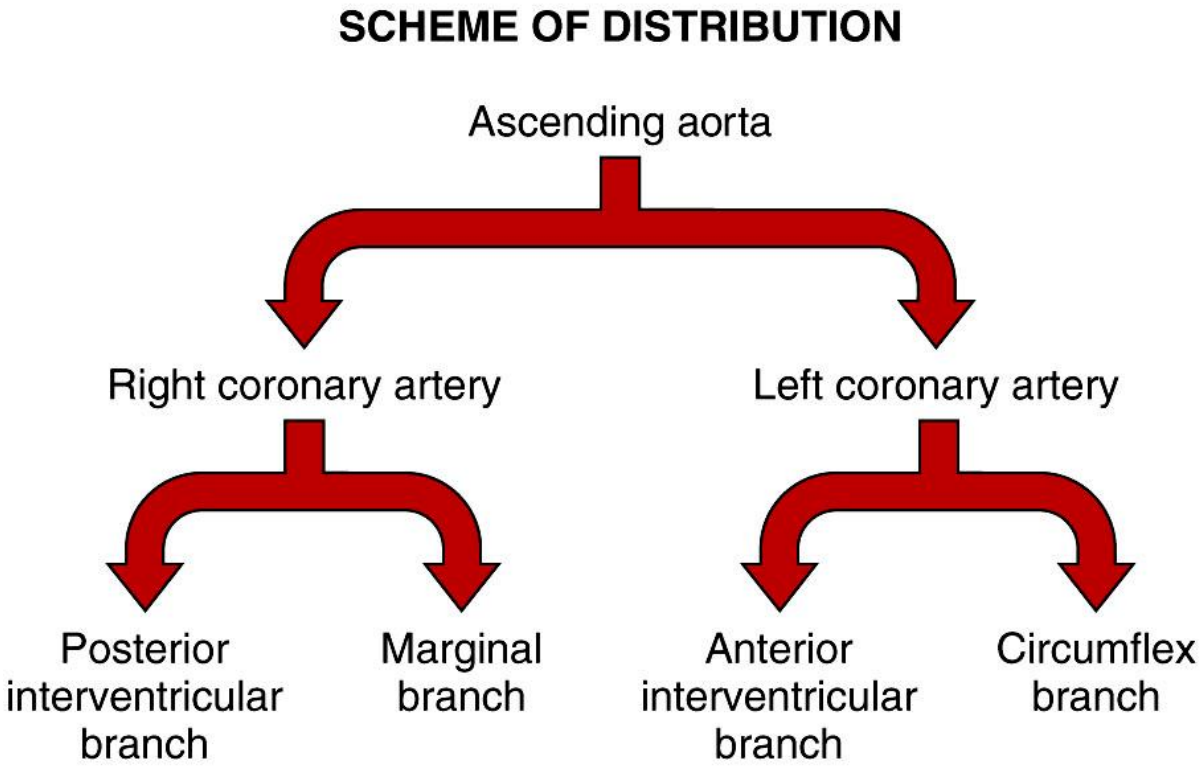
    In coronary sulcus, supplies left atrium and left ventricle
  - --***Anterior interventricular art.***

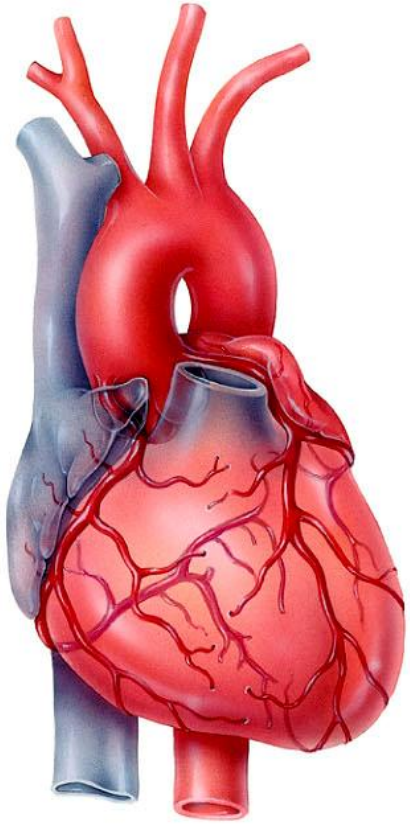
    Supplies both ventricles
- **Right coronary artery**
  - --***Marginal branch***

    In coronary sulcus, supplies right ventricle
  - --***Posterior interventricular art.***

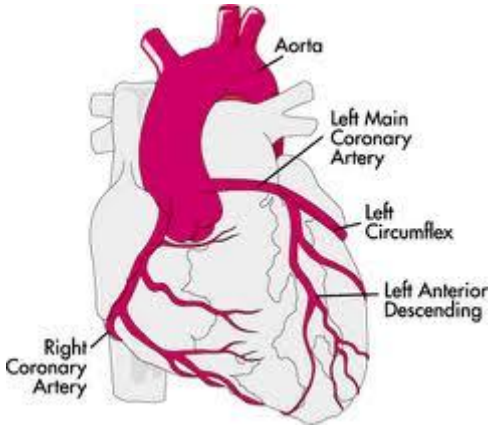
    Supplies both ventricles

Coronary Artery





Characteristics of Coronary Circulation



- The path is ***shorter*** and ***faster*** blood flow
- ***High*** blood pressure and blood volume
- ***High*** arteriovenous oxygenated blood difference and oxygen uptake rate
- Blood supply mainly in ***diastolic period***

Blood Flow Regulation of Coronary Circulation

1. Myocardial metabolism

--心肌收縮的能量主要來源於有氧代謝，心肌耗氧量大，安靜時每百克心肌的耗氧量為 **7~9 ml/min**。

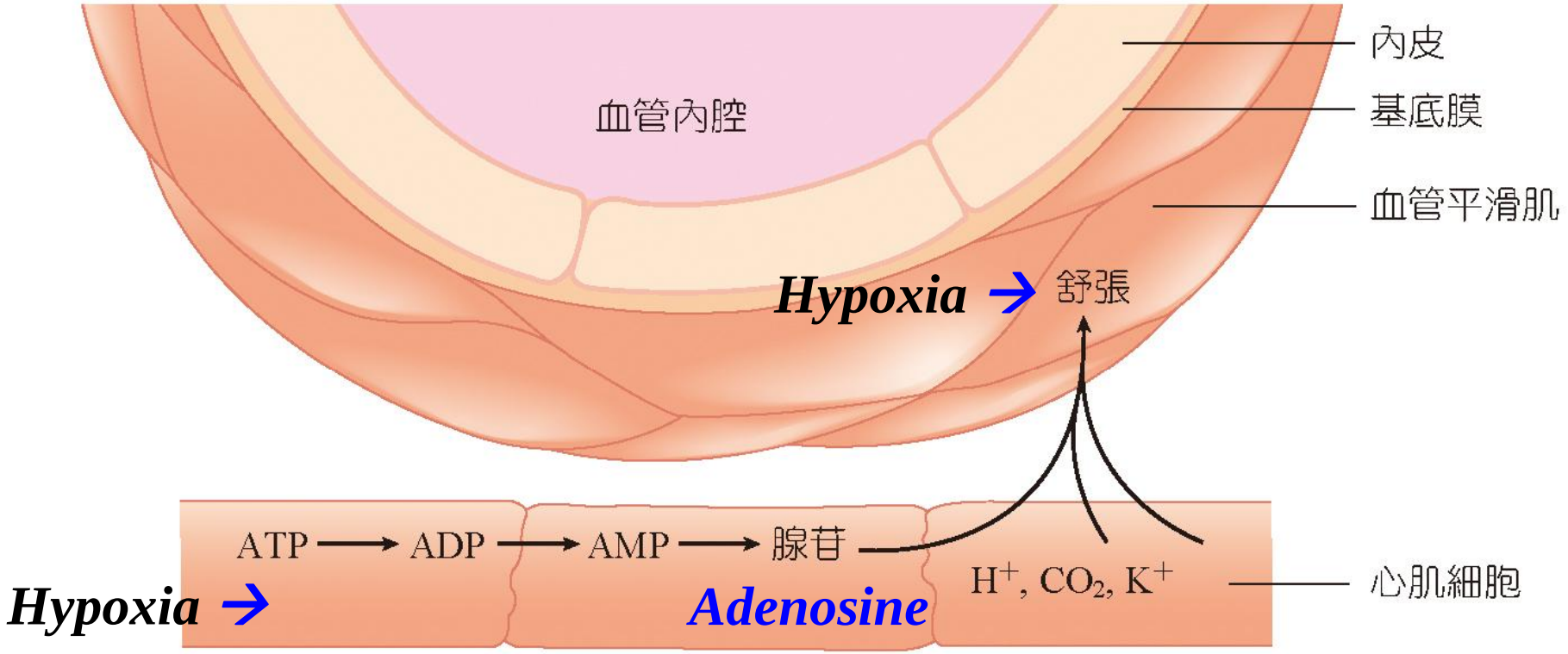
--在運動或精神緊張等情況下，心肌自身代謝明顯增加，耗氧量增加，冠狀血管舒張，冠狀血管流量增加，增至原來血流量的 **5 倍 (Autoregulation)**。

--擴張冠狀血管的主要物質是心肌代謝產物， 其中最重要物質是**腺苷(adenosine)**。

--當心肌代謝增強和局部缺氧時，心肌細胞中的 ATP 分解供能，其產物 AMP 在**5'-nucleotidase**作用下生成adenosine。

Blood Flow Regulation of Coronary Circulation

1. Myocardial Metabolism



• 圖 11-4　體液因素舒張冠狀動脈的機制。

Blood Flow Regulation of Coronary Circulation

2. Neuronal Regulation

--冠狀動脈受交感神經和迷走神經雙重支配。

--刺激交感神經，可使冠狀動脈先**收縮(α-receptor)**後**舒張(β-receptor)**，使心肌活動加強、耗氧量增加、代謝加速、代謝產物增多造成的繼發性反應。

--血管收縮作用往往被強大的繼發性血管舒張作用所掩蓋，因此交感神經興奮常引起**冠狀動脈舒張**。

--迷走神經對冠狀動脈的直接作用是**舒張冠狀動脈**，給予冠狀動脈內灌注 ACh 會使冠狀動脈舒張。

Blood Flow Regulation of Coronary Circulation

3. Humoral Regulation

--**Epinephrine**和**norepinephrine**可透過增強心肌代謝活動和耗氧量使冠狀血管血流量增加。

--直接作用於冠狀血管的**α-**或**β-receptor**，引起冠狀血管收縮或舒張。

--**Thyroxine**增多時，心肌代謝加強，耗氧量增加，冠狀動脈舒張，冠狀血管血流量增加。

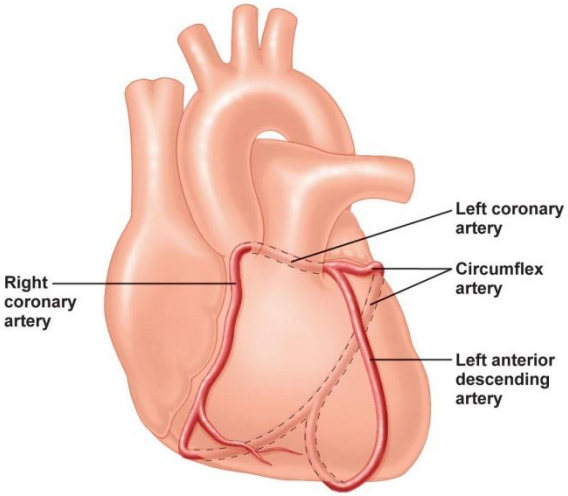
--**Vasopressin**和**angiotensin II** 能使冠狀動脈收縮，冠狀血管血流量減少。

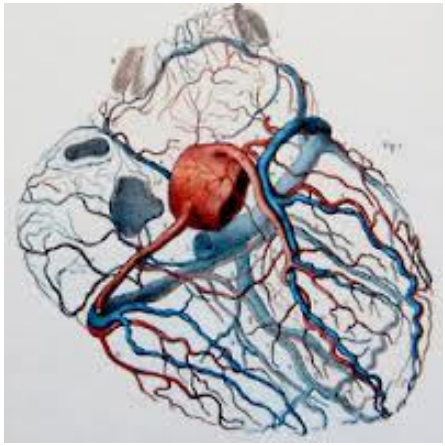
Blood Flow Regulation of Coronary Circulation

4. Vascular Endothelium

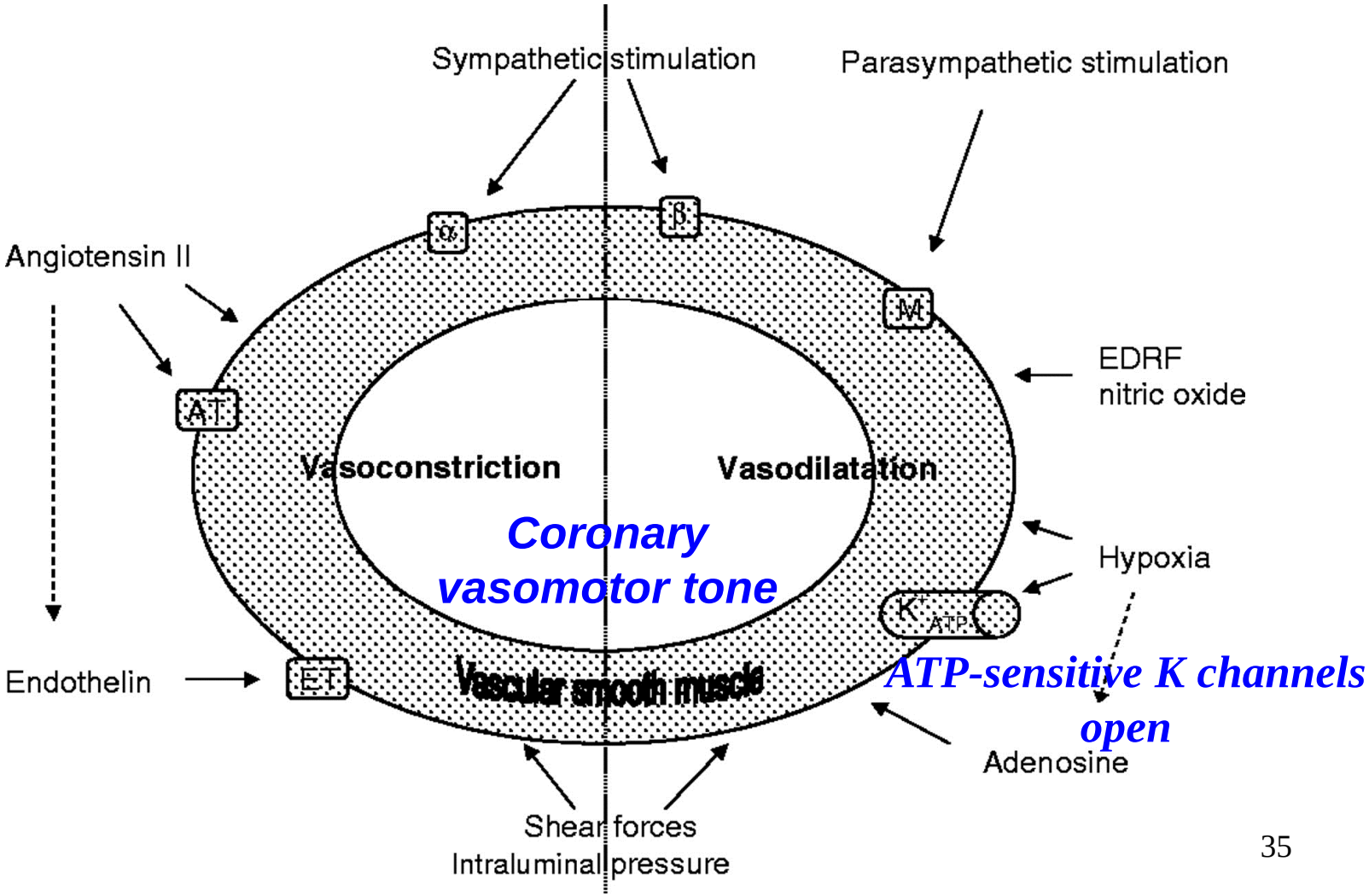
--**Vasorelaxants:** nitric oxide, prostacyclin and bradykinin.

--**Vasoconstrictors:** endothelin and thromboxane A2

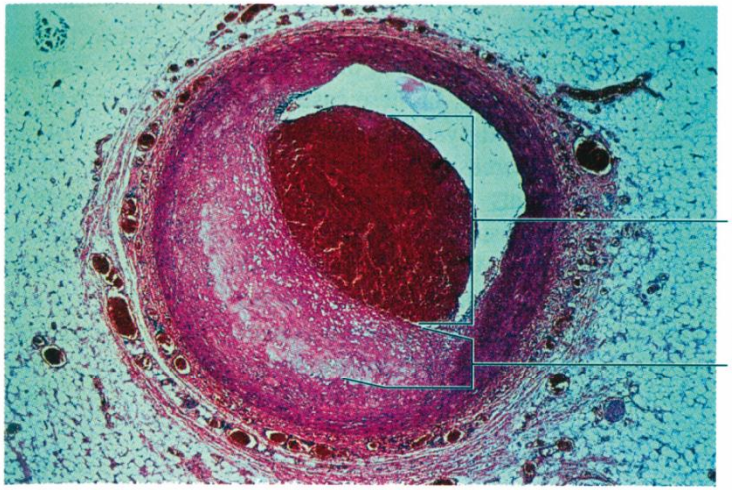




Blood Flow Regulation of Coronary Circulation



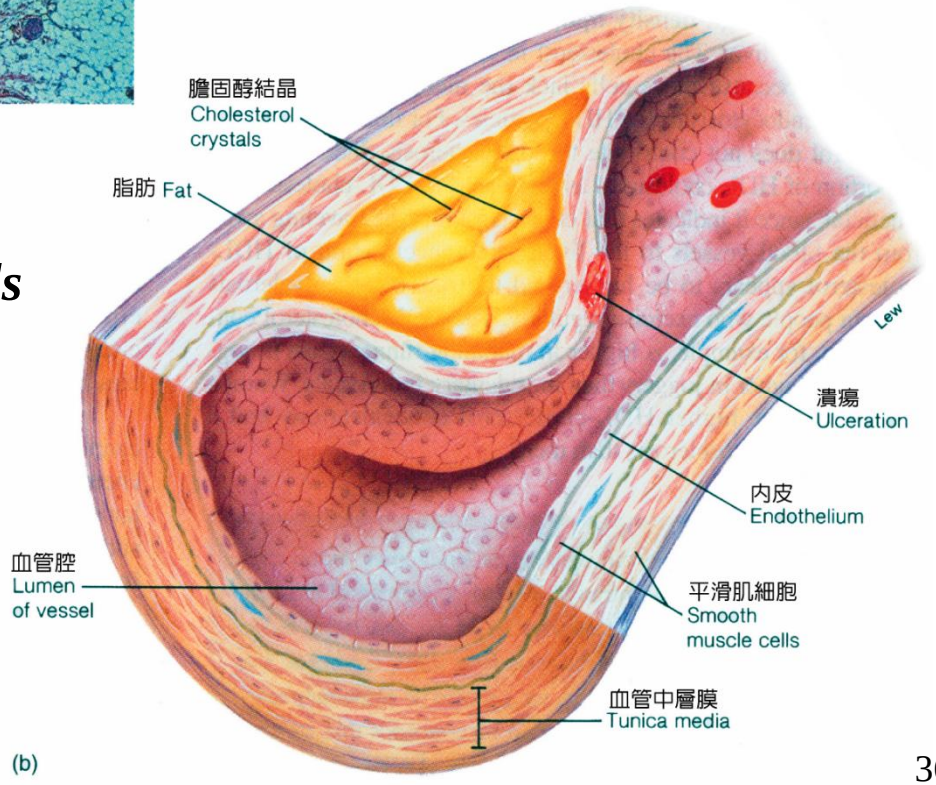
Coronary Artery Disease (CAD)



Atherosclerosis

Coronary artery spasm, *or*

A clot *in a coronary artery*

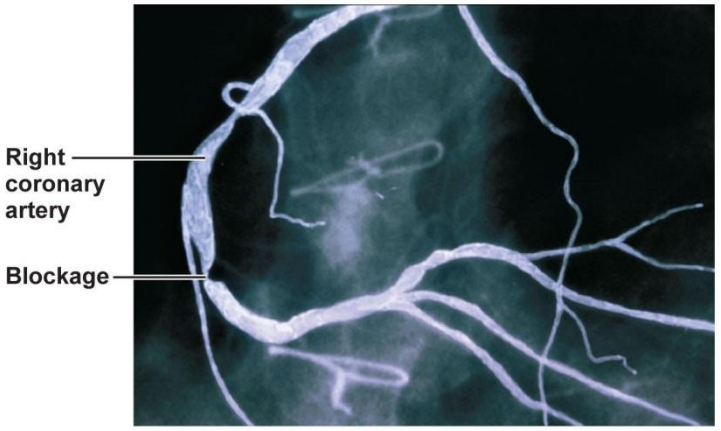


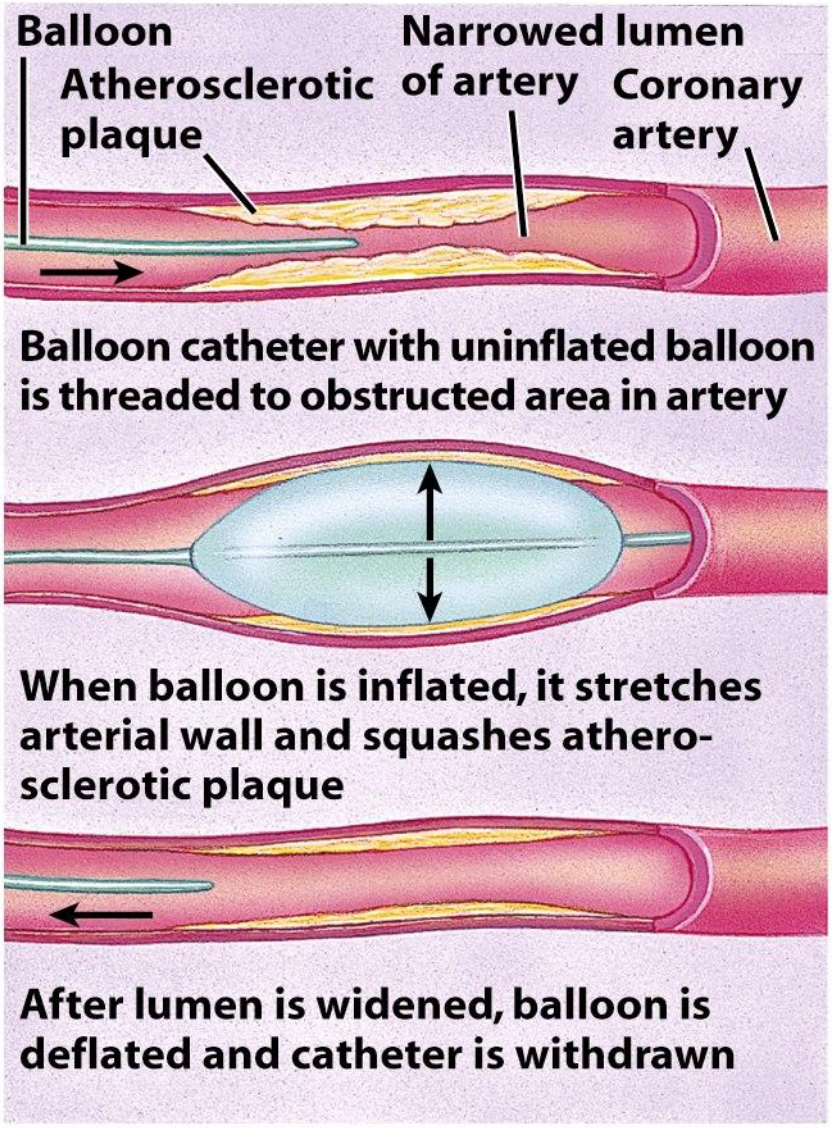
Risk factors:

- ✓ ***High blood cholesterol levels***
- ✓ ***High blood pressure***
- ✓ ***Diabetes***
- ✓ ***Obesity***
- ✓ ***Cigarette smoking***
- ✓ ***"Type A" personality***
- ✓ ***Sedentary lifestyle***

Myocardial Ischemia and Infarction (MI)

- Reduced blood flow through coronary arteries may cause **ischemia**. Ischemia causes **hypoxia** and may weaken the myocardial cells.
- Ischemia is often manifested through **angina pectoris**.
  --A complete obstruction of flow in a coronary artery may cause **myocardial infarction (heart attack).**
  --Tissue distal to the obstruction dies and is replaced by scar tissue.
  --Treatment may involve injection of **thrombolytic agents**, **coronary angioplasty**, or **coronary artery bypass grafts**.

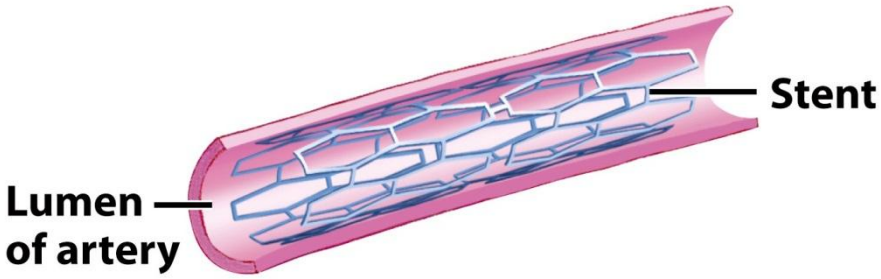


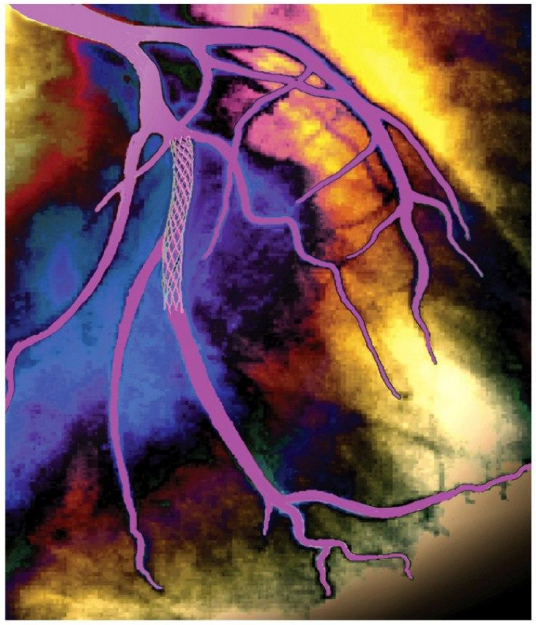


Percutaneous transluminal coronary angioplasty (PTCA)

Treatment:

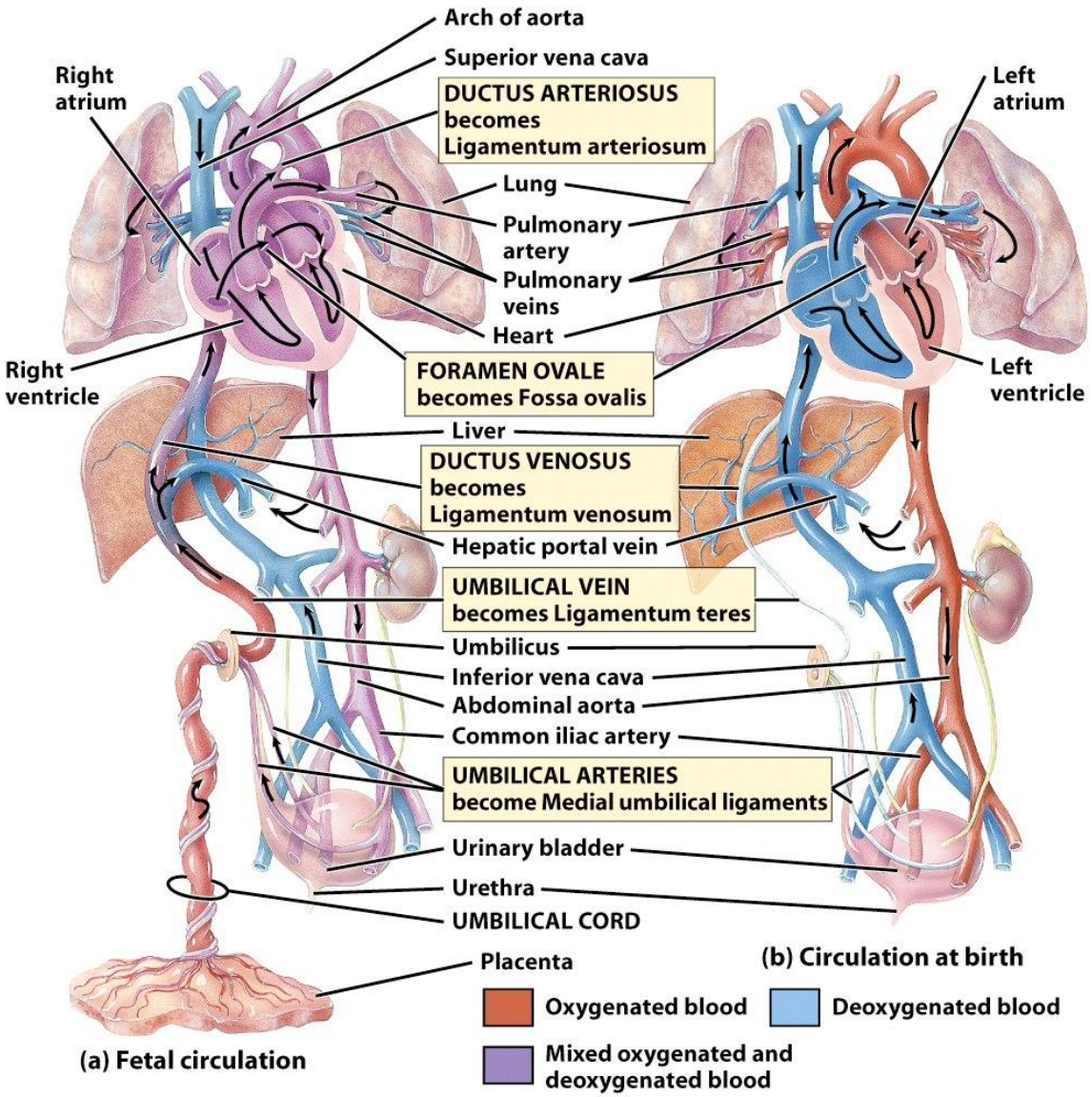
- ✓ *Drugs*
- ✓ *Angioplasty*
- ✓ *Bypass graft*
- ✓ *Stent*



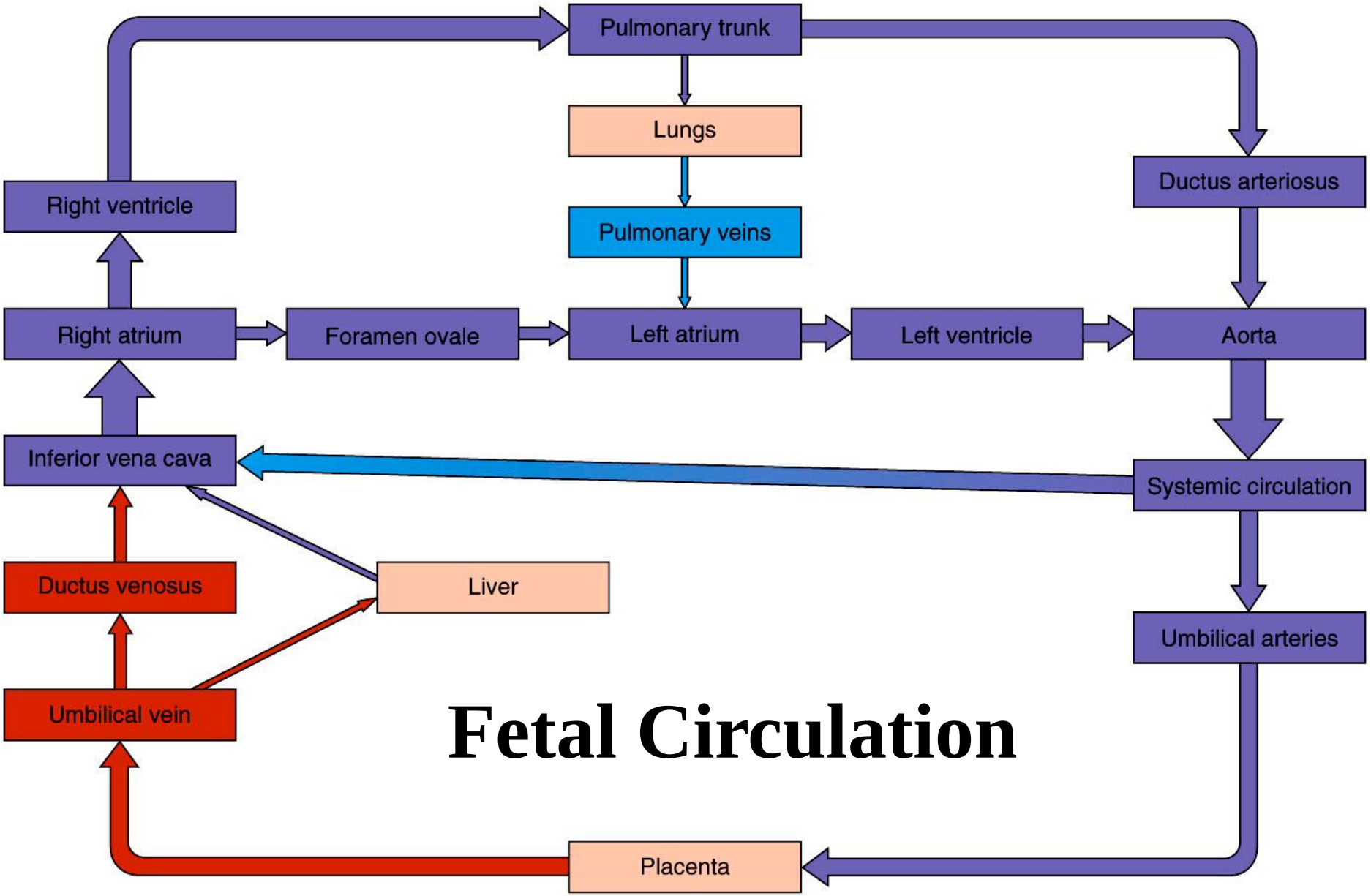


Angiogram showing a stent in the circumflex artery

Fetal Circulation



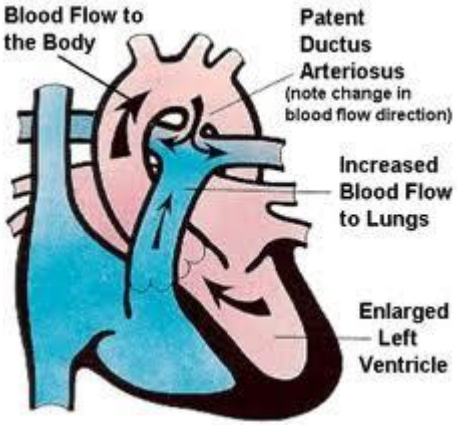
- 胎盤(充氧血)—臍靜脈—肝門脈入肝&肝靜脈出肝/或(約一半血量)經由**靜脈導管**—匯入下腔靜脈(與缺氧血混合)—右心房
  1. **卵圓孔**—左心房—左心室—主動脈
  2. 右心室—肺動脈—供給胎兒肺臟/或經**動脈導管**進入主動脈共應全身
- 回胎盤之路線為：下大動脈—總跨動脈(CIA)—內跨動脈(IIA)—臍動脈

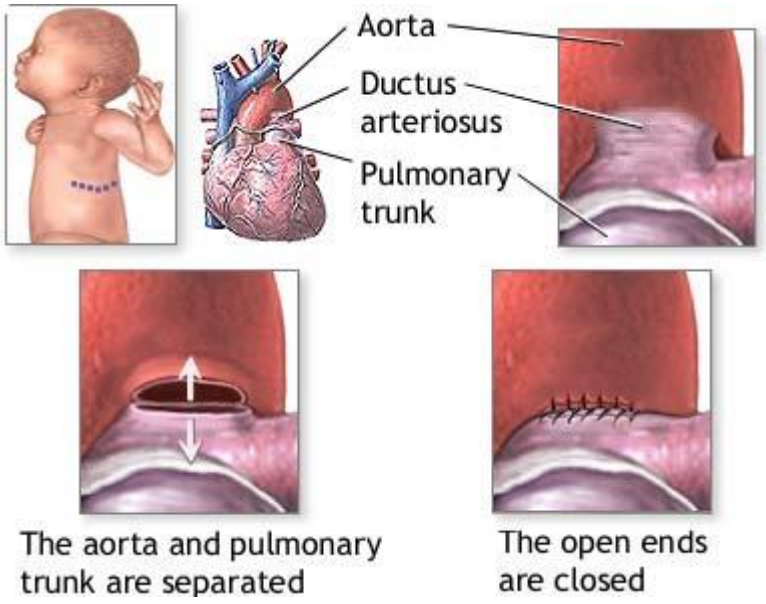


Fetal Circulation

Clinical Application: Patent Ductus Arteriosus

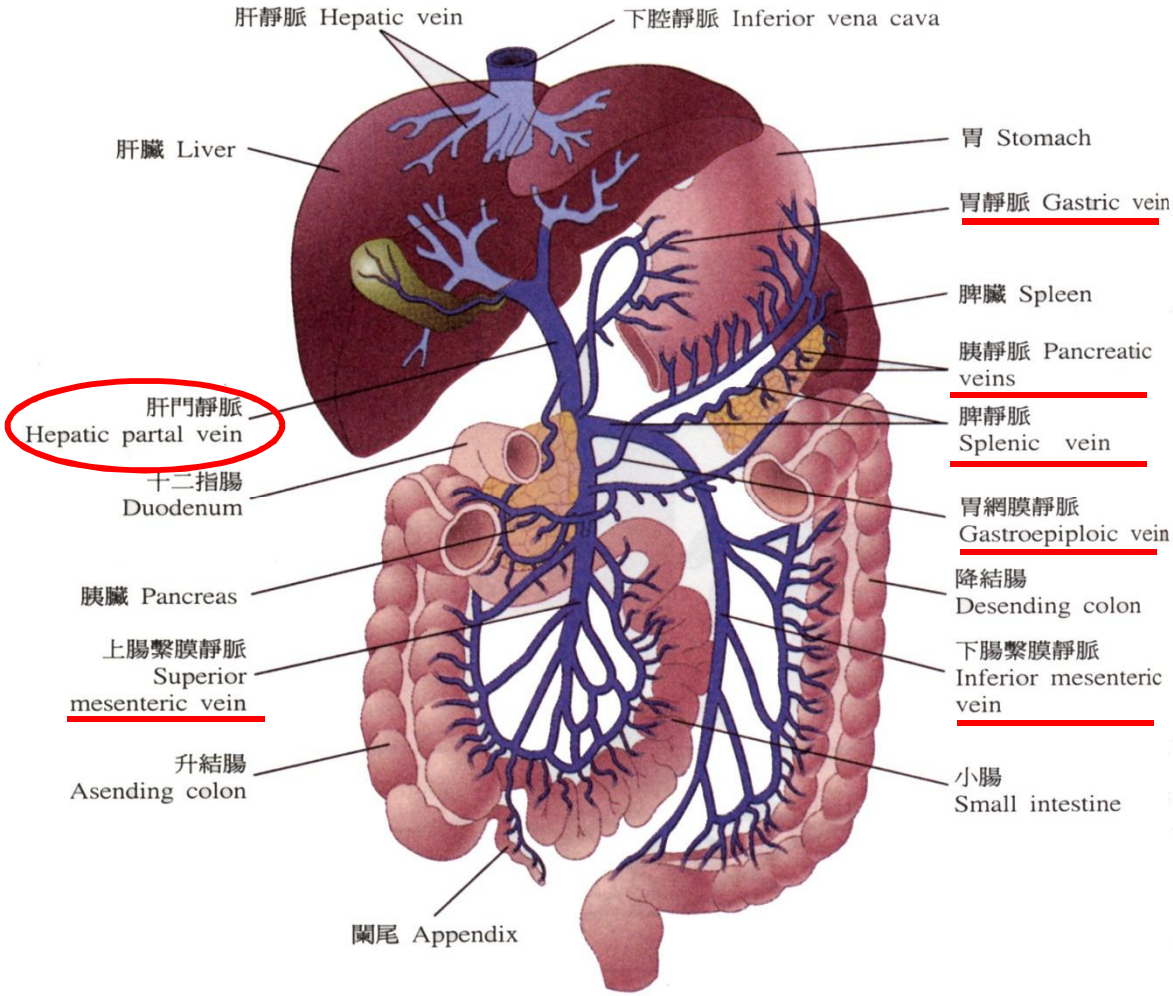
- 出生時在動脈導管方面首先出現暫時的血液逆流，接著降低**前列腺素**濃度誘使其管壁平滑肌收縮(出生後**4到10天內**閉合)。
- 若動脈導管未在出生後閉合，產生**開放性動脈導管(patent ductus arteriosus, PDA)**。因左右心岔道會導致充氧血(主動脈)與缺氧血(肺動脈)混合，造成肺循環高血壓、心雜音、低血氧飽和度及心律不整等症。
- 過高前列腺素濃度是PDA可能成因之一。據統計唐氏兒中有PDA情形者約佔40%。
- 處理方式可由內科注射藥物**Indomethacin (NSAID)**、導管動脈栓塞術(TAE)或外科手術結紮等。





Hepatic Portal Circulation

Hepatic Portal System= Portal Venous System



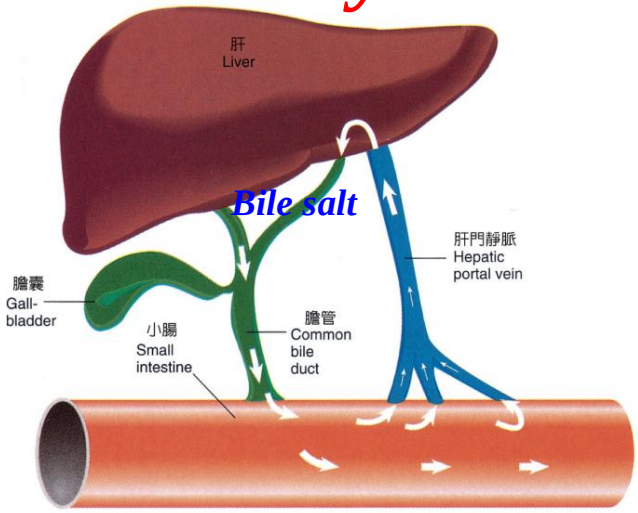


表 18.3 肝臟分泌至膽管中的化合物

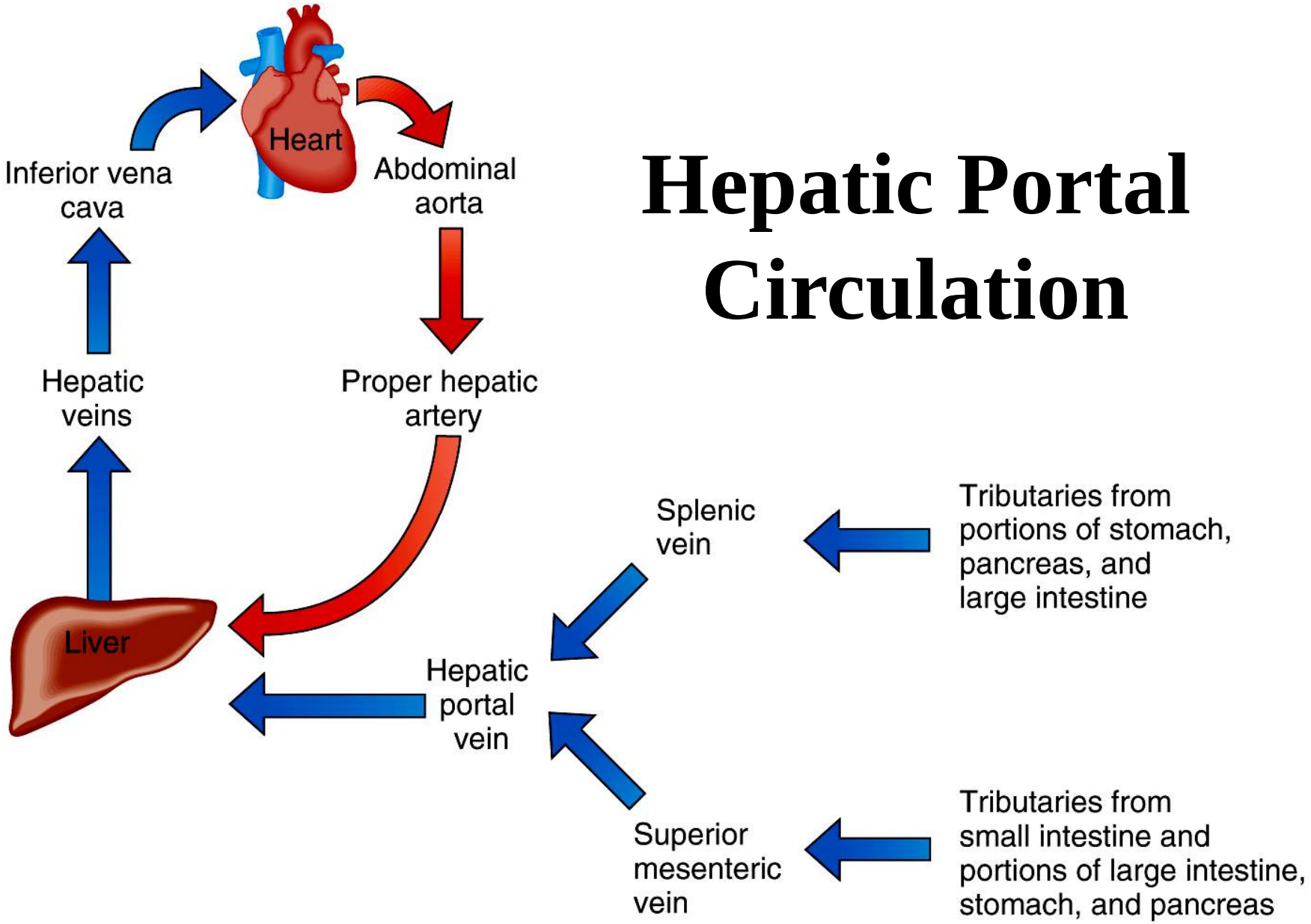
分類	化合物	說明
內在的（自然產生）	膽鹽	大部分被吸收且進入腸肝循環
	膽尿素原(urobilinogen)	
	膽固醇	
	卵磷脂(Lecithin)	小部分被吸收及進入腸肝循環
	膽紅素(Bilirubin)	無腸肝循環
外來的（藥物）	Ampicillin	大部分被吸收及進入腸肝循環
	streptomycin	
	tetracycline	
	Sulfonamides	小部分被吸收及進入腸肝循環
	penicillin	

✓*Nutrient utilization*

✓*Blood detoxification by the liver*

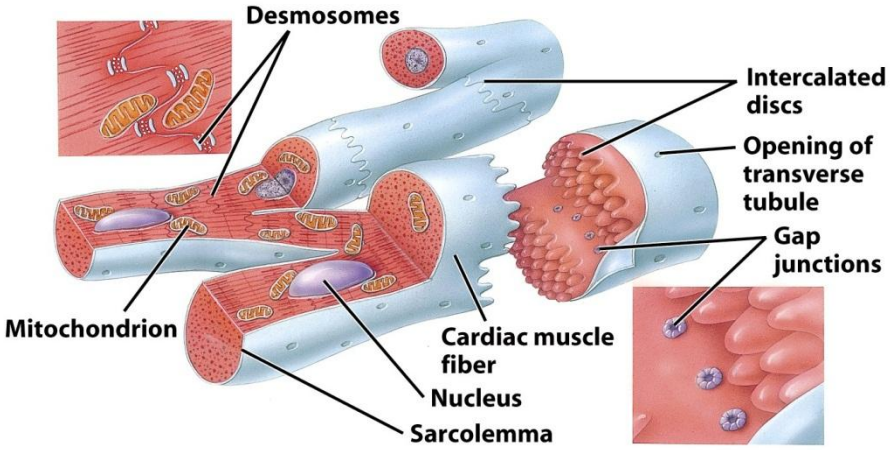
Enterohepatic Circulation

Hepatic Portal Circulation

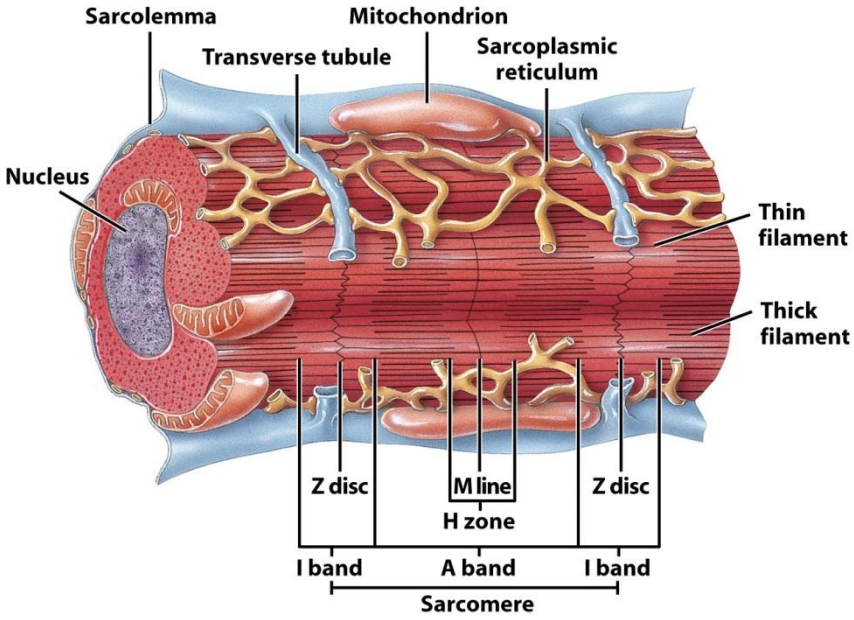


(b) Scheme of principal blood vessels of hepatic portal circulation and arterial supply and venous drainage of liver

Histology of Cardiac Muscle



Cardiac muscle fibers

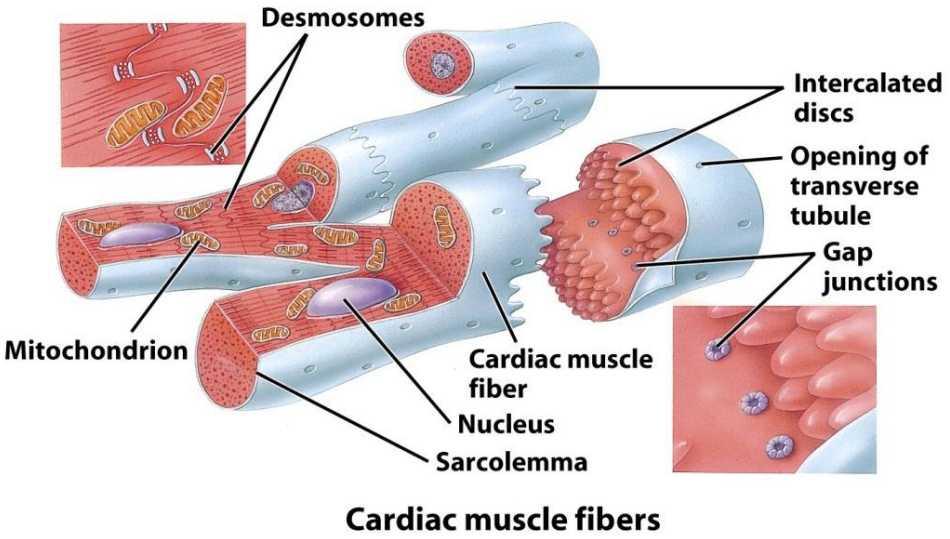


Arrangement of components in a cardiac muscle fiber

- 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 and usually one centrally located nucleus
- Fibers within the networks are connected by ***intercalated discs: desmosomes*** (hold fibers together)+ ***gap junctions*** (action potential)
- The same arrangement of actin and myosin as skeletal muscles
- They do have less sarcoplasmic reticulum than skeletal muscles and require Ca^{+2} from **ECF** for contraction

Properties of Cardiac Muscle

- **Intercalated disks**
  - --Gap junctions (***cause heart to contract as a unit***)
  - --Desmosomes (***resist stress***)
- **Atria and ventricles**
  - --Separate units
- **Aerobic muscle**
- **No cell division** after infancy—growth by ***hypertrophy***



Cardiac muscle fibers

1. ***99% Contractile cells (for pumping)***
2. ***1% Autorhythmic cells (set pace)***

Cardiac Muscle Cell

比較項目 ＼ 心肌細胞		工作細胞 *Contractile cells*	自律性細胞 *Autorhythmic cells*
組織細胞		心室肌 心房肌	竇房結（節律點細胞、過渡細胞）→ 房室結（房結區、結區、結希區）→ 房室束→左、右束分支→浦金氏纖維
生理學特性	興奮性	有	有
	自律性	無	有（結區、過渡細胞除外）
	傳導性	有	有
	收縮性	有	無
組織學特徵	肌原纖維	豐富	缺少或無
	屬 性	心肌細胞	節律點細胞、浦金氏細胞

Autorhythmic Cells

- **Autorhythmicity** is the ability to generate own rhythm
- **Autorhythmic cells**: provide a pathway for spreading excitation through the heart (***conduction system= electrical activity***)

  --***Specialized cardiac muscle fibers***

  --***Self-excitable***

  --***Repeatedly generate action potentials that trigger heart contractions***

  --***2 important functions***

  1.Act as ***pacemaker***

  2.Form ***conduction system***

- Recording the electrical activity of the heart with an **electrocardiogram (ECG)**

Conducting System of Heart

- **Two types of autorhythmic cells**

1. Pacemaker cells

--Spontaneously depolarizing membrane potentials to generate action potentials

--Coordinate and provide heart rhythm

--***Sinoatrial node (Pacemaker)+Atrioventricular node***

2. Conduction fibers

--Rapidly conduct action potentials initiated by pacemaker cells to myocardium

--Conduction velocity = 4 meters/second

--Ordinary muscle fibers, CV = 0.4 meter/second

--***Internodal pathways+Bundle of His+Purkinje fibers***

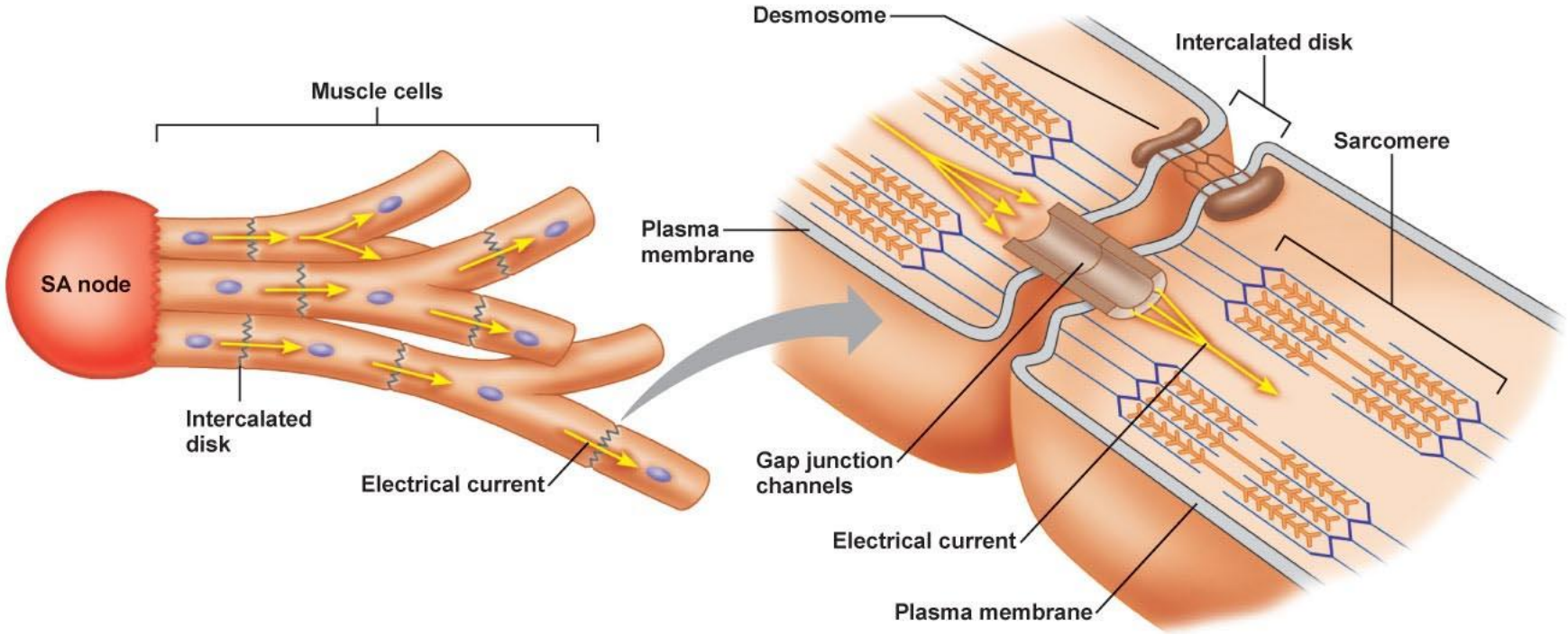
Autorhythmic Cells

Location	Firing Rate at Rest
SA node	**70–80 APs/min***
AV node	**40–60 APs/min**
Bundle of His	**20–40 APs/min**
Purkinje fibers	**20–40 APs/min**

- Cardiac cells are linked by **gap junctions**
- **Fastest depolarizing cells** control other cells
- **Fastest cells = pacemaker = set rate for rest of heart**

* Action potentials per minute

Cardiac Electrical Connections



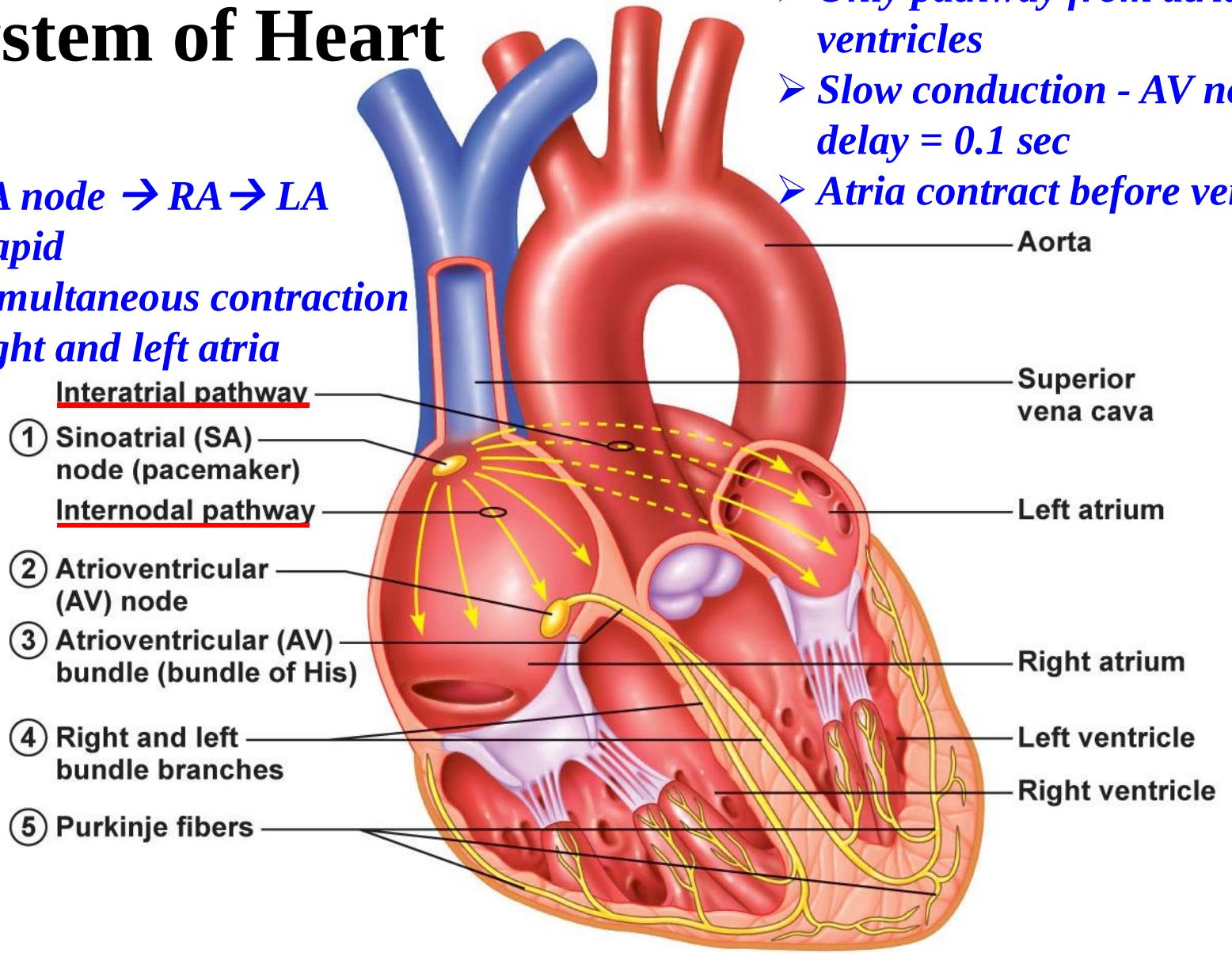
- **Atria contract**, then followed by **ventricles**
- Coordination due to presence of ***gap junctions*** and ***conduction pathways***
- **Intercalated disks (**Junctions between adjacent myocardial cells): ***Desmosomes*** to resist mechanical stress + ***Gap junctions*** for electrical coupling

Conducting System of Heart

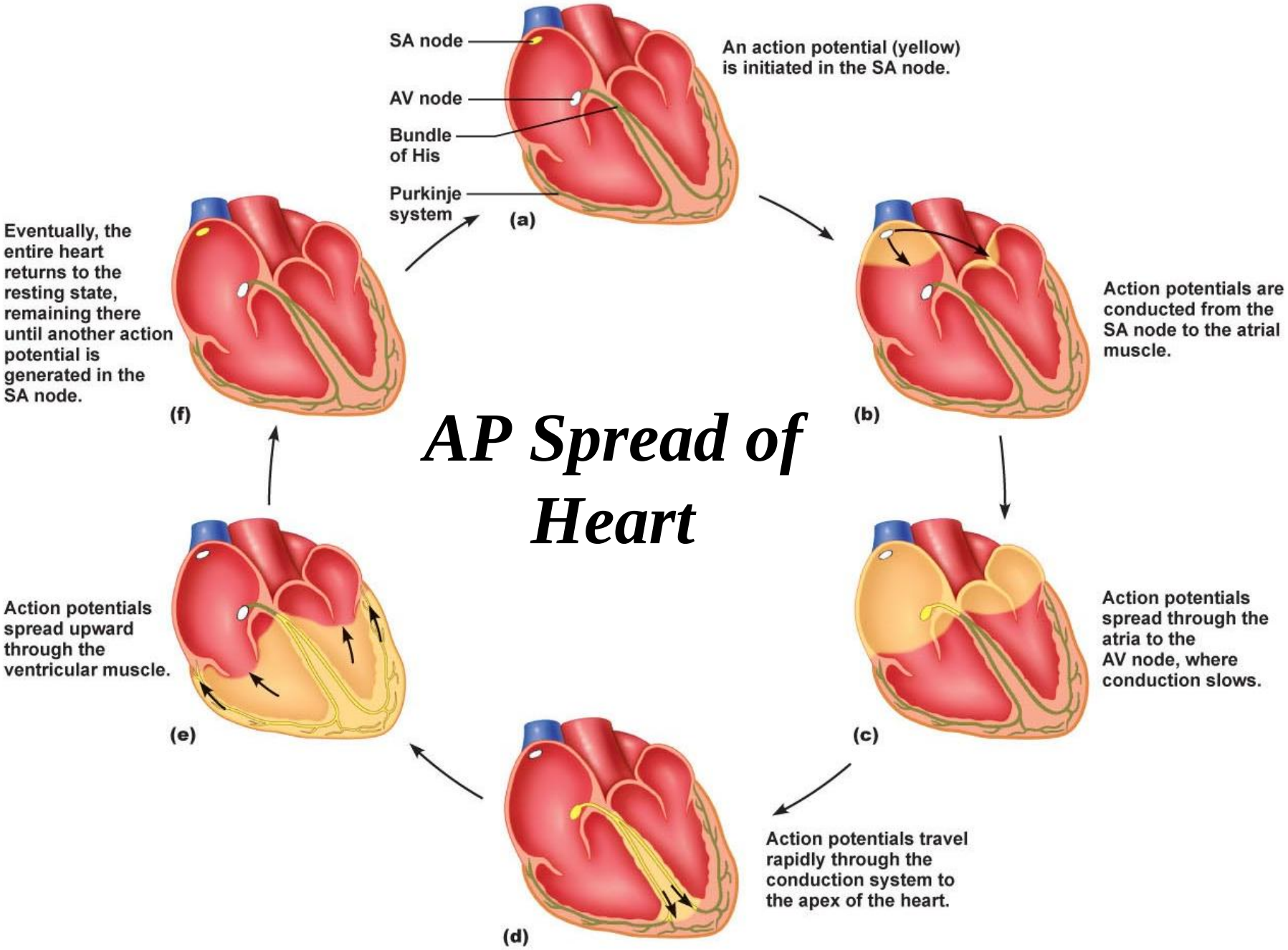
- *SA node → RA → LA*
- *Rapid*
- *Simultaneous contraction right and left atria*

AV node transmission

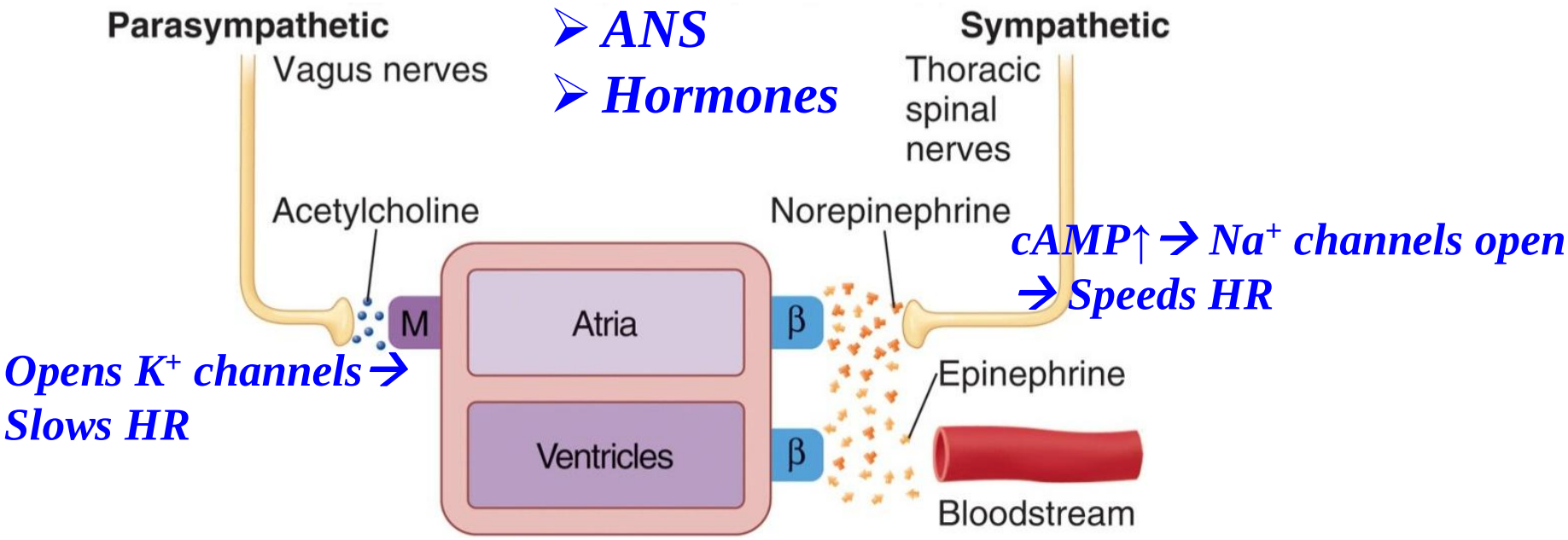
- *Only pathway from atria to ventricles*
- *Slow conduction - AV nodal delay = 0.1 sec*
- *Atria contract before ventricles*



AP Spread of Heart



Rhythm of Conduction System



➢ ***ANS***

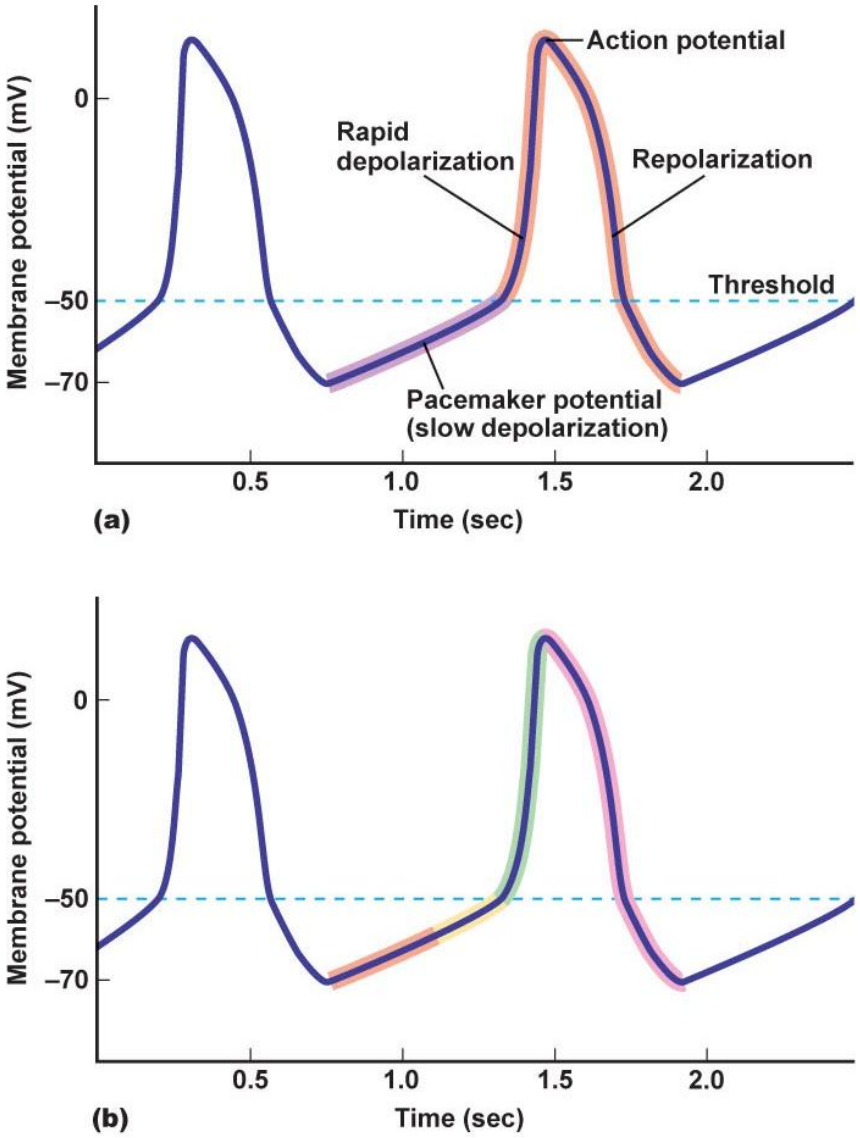
➢ ***Hormones***

cAMP↑ → Na^+ channels open
→ Speeds HR

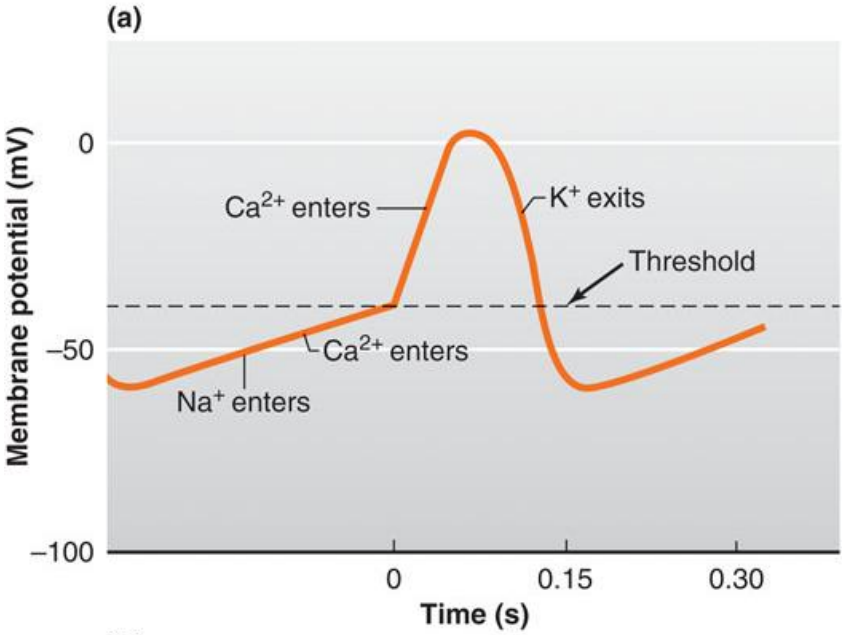
Opens K^+ channels →
Slows HR

- SA node fires spontaneously 90-100 times per minute
- AV node fires at 40-50 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

Ionic Basis of Electrical Activity in Pacemaker Cell



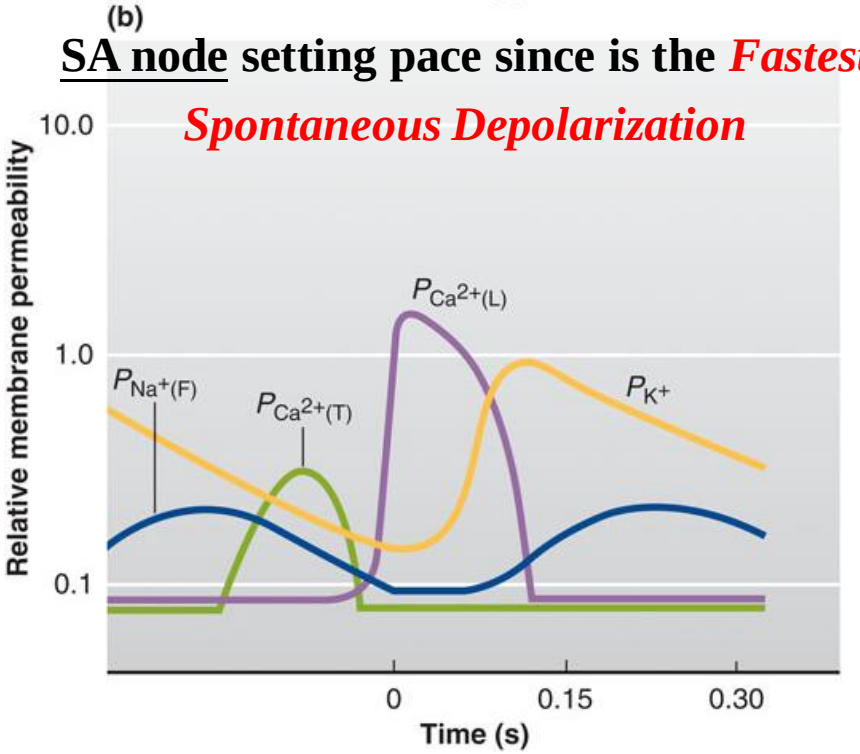
- Autorhythmic cells (**SA nodes**) have **pacemaker potentials**
- **Pacemaker potentials (slow depolarization)**: closing K^+ channels and opening Na^+ channels (***orange***)+ closing Na^+ channels and opening Ca^{++} channels (***yellow***)
- **Rapid depolarization phase** of AP: more opening Ca^{++} channels (***green***)
- **Repolarization phase:** closing Ca^{++} channels and opening K^+ channels (***pink***)



Sodium ions **"leaking" in through the F-type [funny] channels**

PLUS

Calcium ions moving in through the *T-type* Ca channels cause a threshold slow depolarization



SA node setting pace since is the *Fastest Spontaneous Depolarization*

The rapid opening of voltage-gated calcium channels (*L-type*) is responsible for the rapid depolarization phase

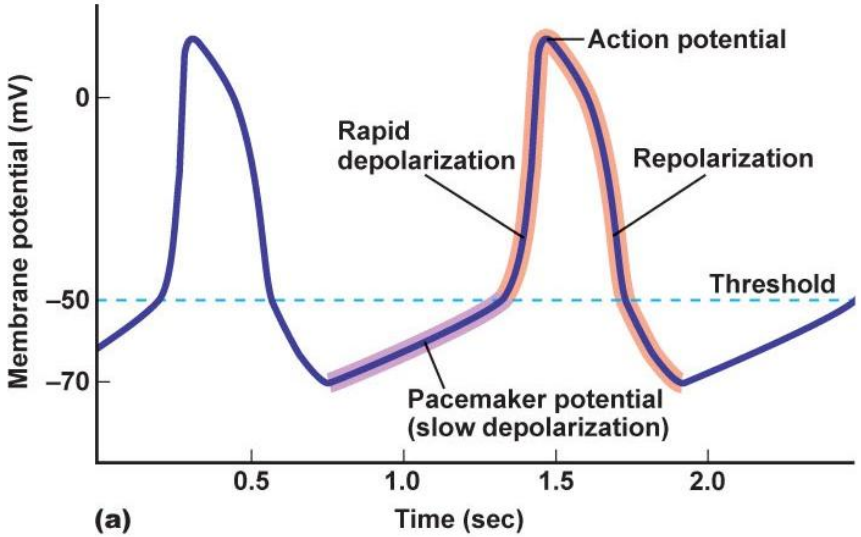
Reopening of potassium channels

PLUS

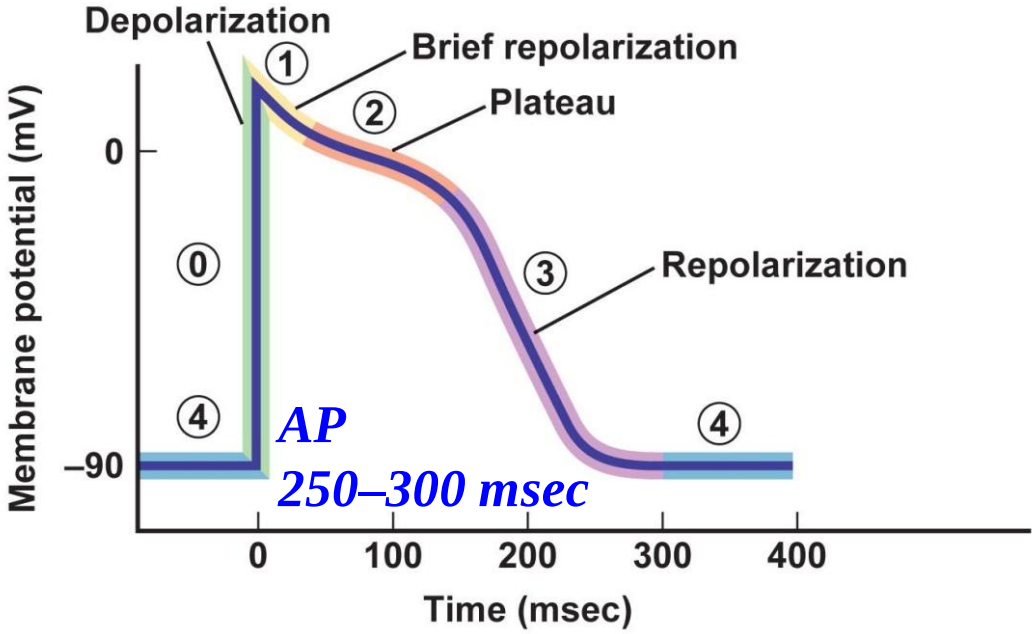
Closing of calcium channels are responsible for the repolarization phase

Ionic Basis of Action Potential in Pacemaker Cell

Autorhythmic cell potential change	Ion channel gating	Ion movement
Pacemaker potential		$P_{Na} > P_K$
Initial period of spontaneous depolarization to subthreshold	Funny channels open	Sodium moves in, potassium moves out
Latter period of spontaneous depolarization to threshold	T-type calcium channels open	Calcium moves in
	T= transient; L=long-lasting	
Rapid depolarization phase of action potential	L-type calcium channels open	Calcium moves in
Repolarization phase of action potential	Potassium channels open	Potassium moves out



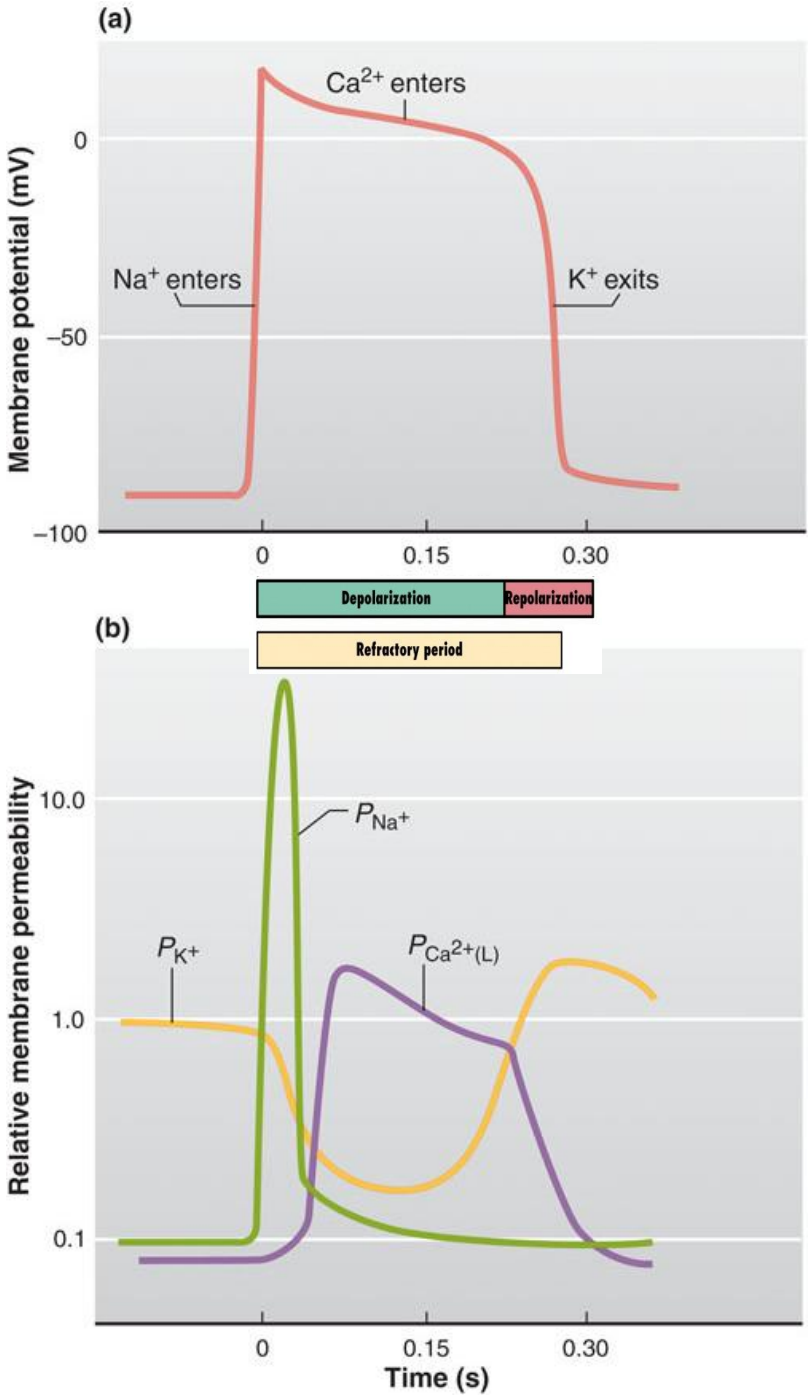
Ionic Basis of Electrical Activity in Cardiac Contractile Cell (Myocardial Cell)



1. **Some** voltage -gated **potassium channels close** in response to **depolarization**
2. **Depolarization opens** voltage-gated **calcium channels** which not only contributes to further **depolarization** but **triggers the muscle contraction**

Five phases:

- **Phase 0**—increased P_{Na}
- **Phase 1**—decreased P_{Na}
  1. ***Voltage-gated K channels close***
  2. ***L-type voltage-gated Ca channels open***
- **Phase 2**—increased P_{Ca}, decreased P_K
- **Phase 3**—increased P_K, decreased P_{Ca}
- **Phase 4**—resting membrane potential



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

Ionic Basis of Action Potential in Myocardial Cell

Phase of contractile cell action potential	Ion channel gating	Ion movement
0 Rapid depolarization	Sodium channels open	Sodium moves in
1 Small repolarization	Sodium channels inactivate	Sodium movement in decreases
2 Plateau	Potassium inward rectifier channels close Calcium L-type channels open	Potassium movement out decreases Calcium moves in
3 Repolarization	Potassium delayed rectifier channels open Calcium L-type channels close	Potassium moves out Calcium movement in decreases
4 Resting potential	Potassium channels (both types) open Sodium and calcium channels still closed	Potassium moves out Little sodium or calcium moves in

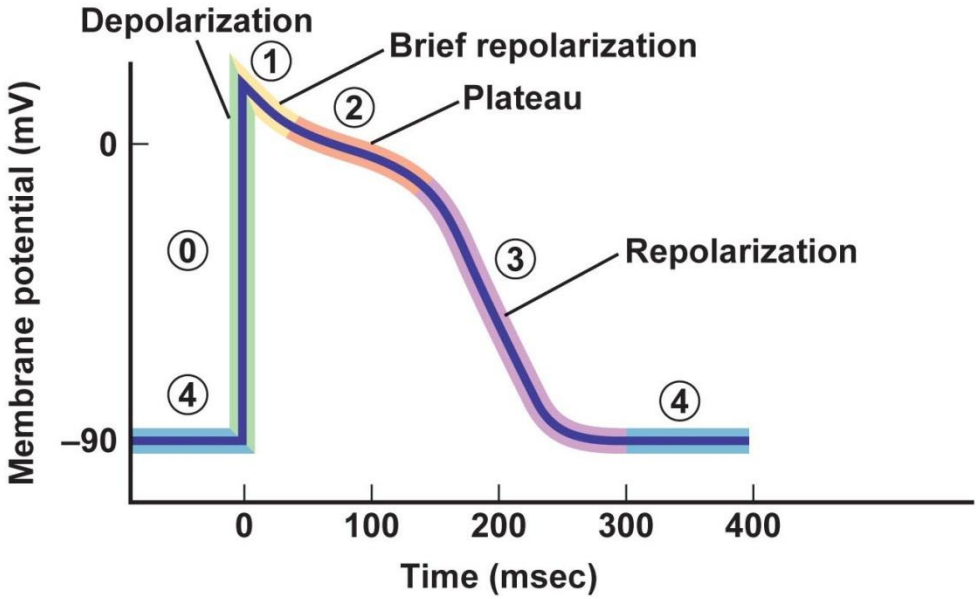
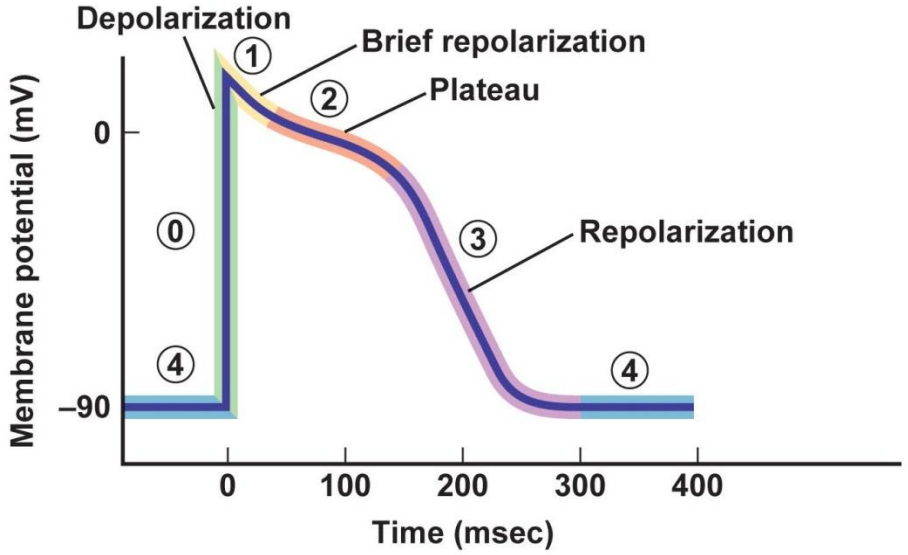


表 11-5　心室肌細胞的膜電位的形成機制

時 相			膜電位 (mV)	持續時間 (ms)	形成機制
靜止膜電位			-90	— —	K^+ 平衡電位
動作電位	去極化過程	0 期（去極化期）	-90 ~ +30	1~2	Na^+ 通道開放，大量 Na^+ 內流
	再極化過程	1 期（快速再極化初期）	+30 ~ 0	5~10	K^+ 通道開放，少量 K^+ 外流
		2 期（高原期）	0	100~150	Ca^{2+} 內流（及少量 Na^+ 內流）與 K^+ 外流相平衡
		3 期（快速再極化末期）	0 ~ -90	100~150	K^+ 通道開放，大量 K^+ 外流
		4 期（靜止期）	-90	— —	鈉鉀幫浦及鈉鈣交換體的共同活動



Action Potential in Different Positions of Heart

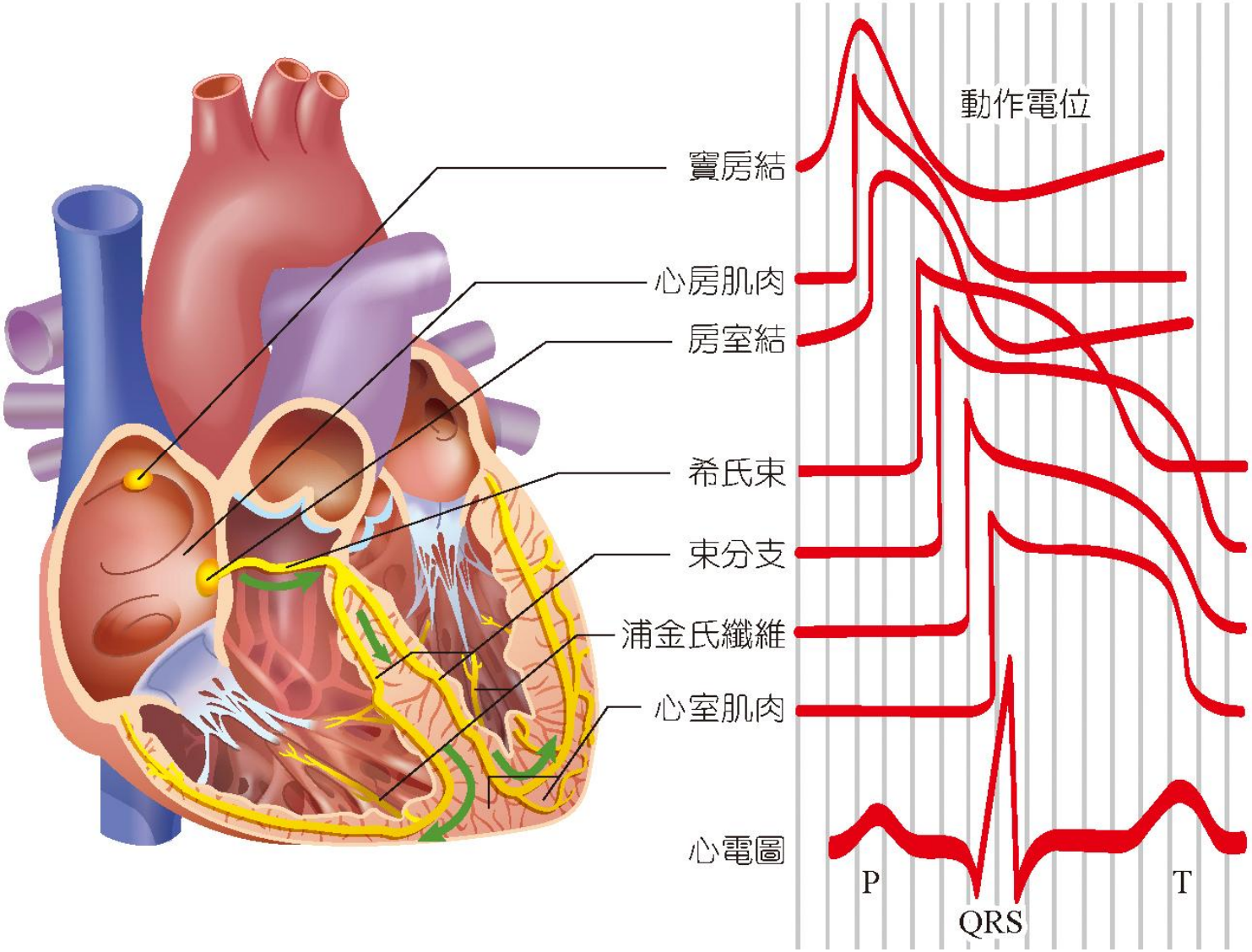
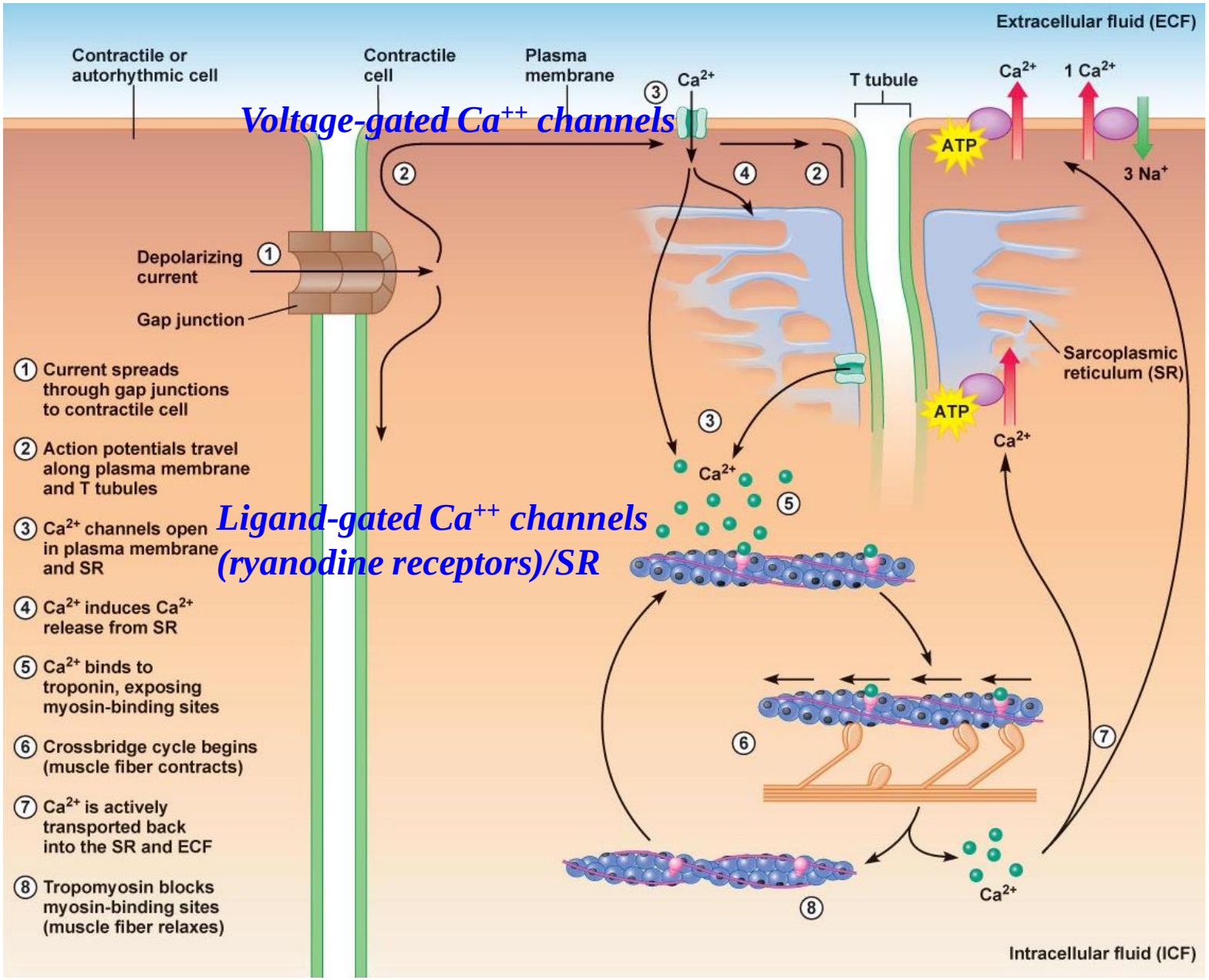


表 11-7　三類心肌細胞的電性活動比較

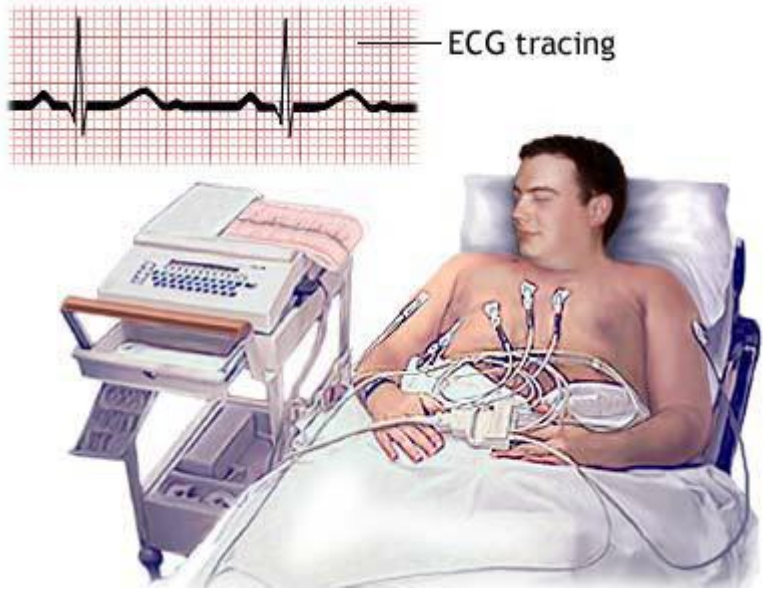
比較項目 ＼ 心肌細胞	心室肌細胞（快反應非自律性細胞）	竇房結細胞（慢反應自律性細胞）	浦金氏細胞（快反應自律性細胞）
膜電位分期	0、1、2、3、4 期	0、3、4 期	0、1、2、3、4 期
靜止膜電位／最大舒張電位值	靜止膜電位值 -90 mV	最大舒張電位 -70 mV	最大舒張電位 -90 mV
閾值電位	-70 mV	40 mV	-70 mV
0 期去極化幅度	大 (120 mV)	小 (70 mV)	大 (120 mV)
0 期時程	短 (1~2 ms)	長（7 ms 左右）	短 (1~2 ms)
0 期去極化速度	迅速	緩慢	迅速
0 期結束時膜電位值	+30 mV	0 mV	+30 mV
4 期自動去極化速度	——	快	慢
4 期膜電位	穩定	不穩定，自動去極化	不穩定，自動去極化

Excitation-Contraction Coupling in Myocardial Cells



Electrocardiogram

- **External measure** of electrical activity of the heart
- A simple, non-invasive test that records the heart's electrical changes accompany **each cardiac cycle (heartbeat)** is called an ***electrocardiogram* (*ECG* or *EKG*)**



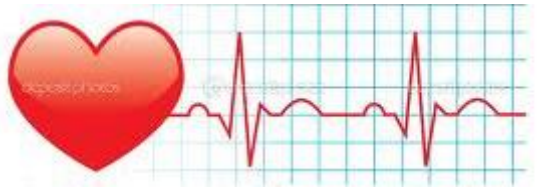
--***Body = conductor***

Currents in body can spread to surface (ECG, EMG, EEG)

--Distance and amplitude of ***size of potentials*** and ***synchronicity of potentials*** from other cells

--Heart electrical activity—**synchronized**

Leads of ECG



在身體兩個不同部位安置兩個金屬電極板，用導線連到心電圖描記器中的(+)、(-) 兩端，使電流進入電流計再回返到人體，構成一個完整電路，此記錄方法稱為**導程(leads)**

- 臨床上記錄心電圖通常採用**十二個導程**，分兩類

1. 雙極肢導(bipolar limb leads)：

--記錄放在手腕和腳踝上的電極之間的電壓

- ***第一肢導、第二肢導、第三肢導 (Lead I-III)***

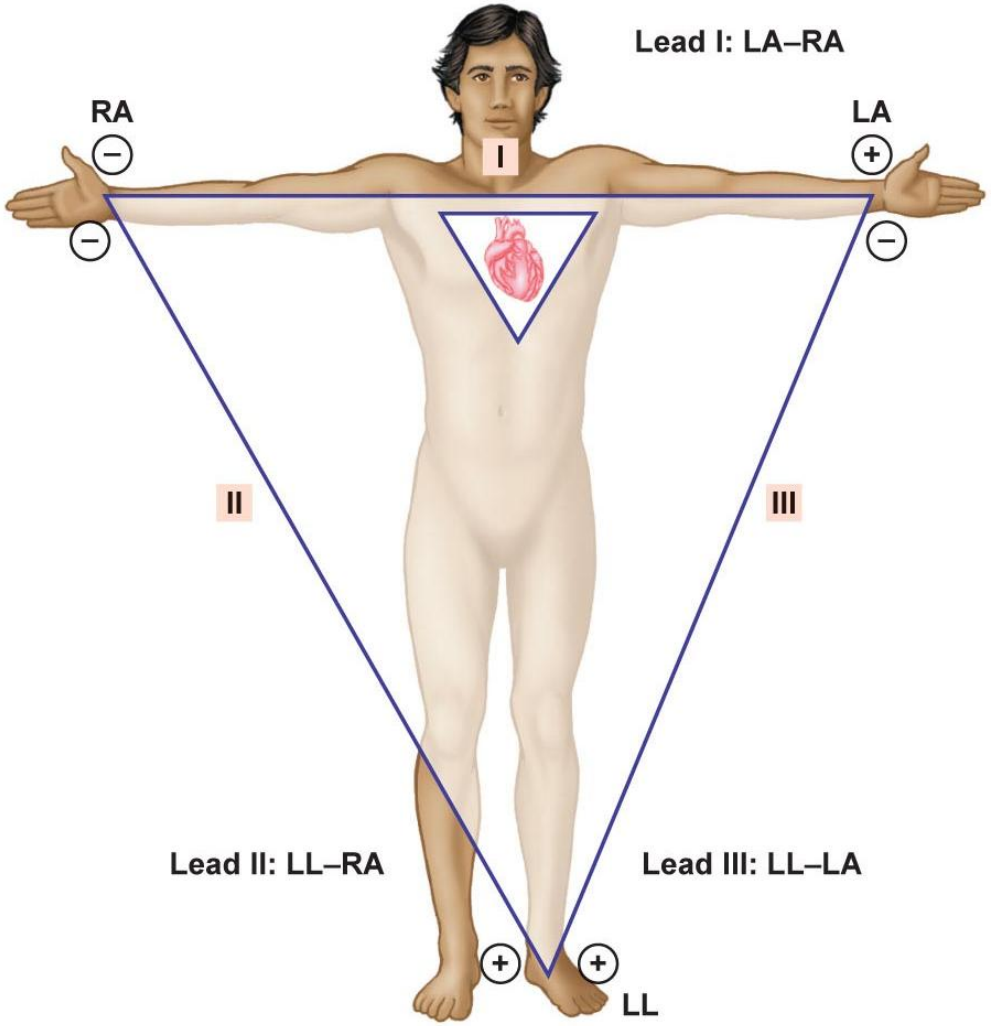
2. 單極導程(unipolar leads)：

--記錄放在身體的單一探查電極(-) 與無關電極(+) 之間的電位差

- ***單極肢導(unipolar limb leads): aVL, aVR, aVF***
- ***單極胸導(unipolar chest leads): V1-V6***

Leads of ECG

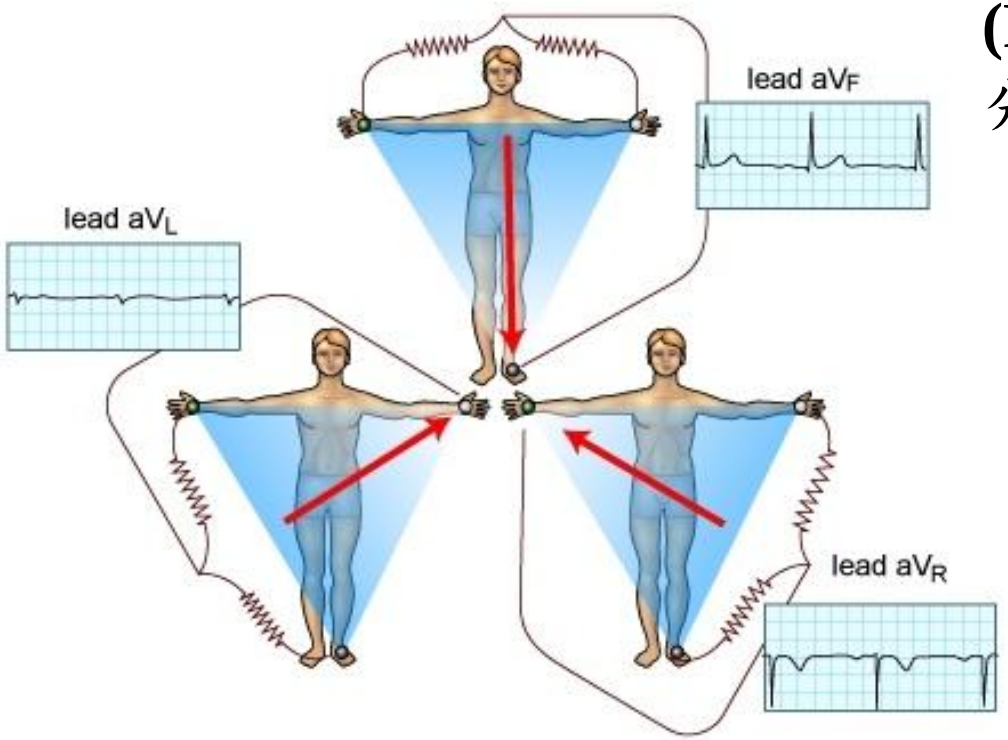
雙極肢導(bipolar limb leads)



1. **Lead I:** LA (+) and RA (-)
2. **Lead II:** LL (+) and RA (-)
3. **Lead III:** LL (+) and LA (-)

Leads of ECG

單極導程(unipolar leads): *單極肢導*



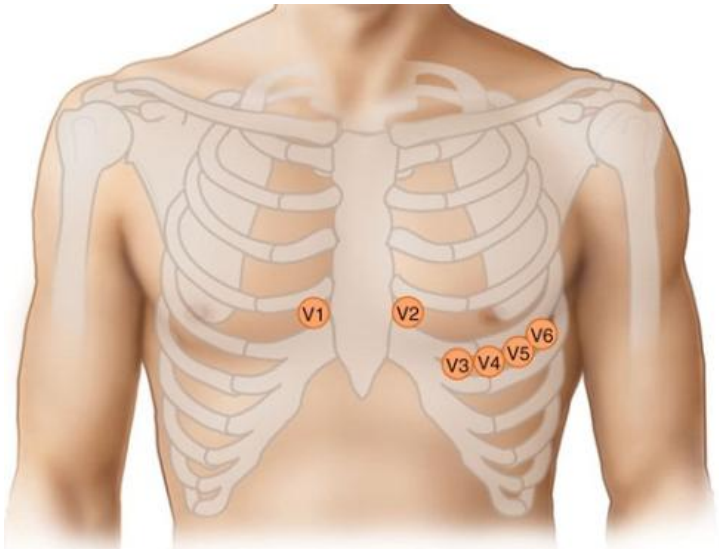
探查電極放在肢體的**右手臂(R)、左手臂(L)及左腳(F)**，分別簡寫:

1. **aVL:** 探查電極(-)與左手臂相連，無關電極(+)連接右手臂與左腳
2. **aVR:** 探查電極(-)與右手臂相連，無關電極(+)連接左手臂與左腳
3. **aVF:** 探查電極(-)與左腳相連，無關電極(+)連接左手臂與右手臂

Leads of ECG

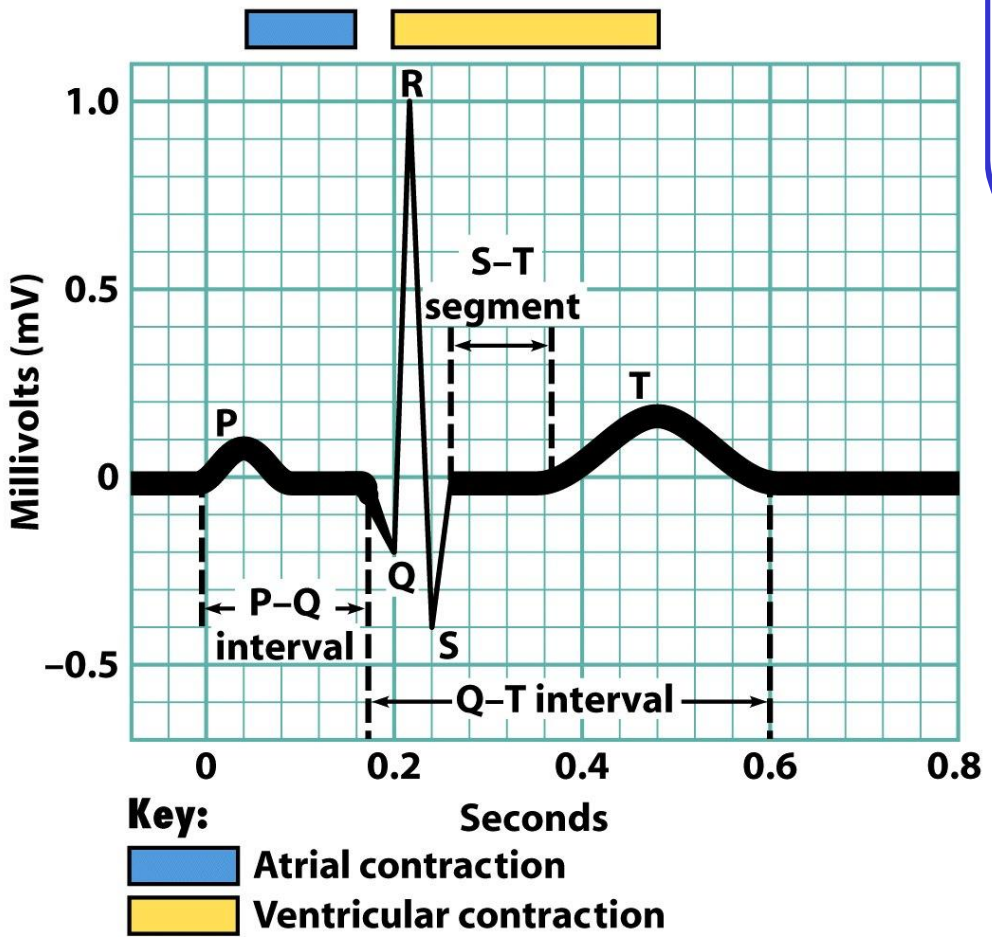
單極導程(unipolar leads): *單極胸導*

探查電極(-) 放在心前胸壁六個位置，即**V1~V6**

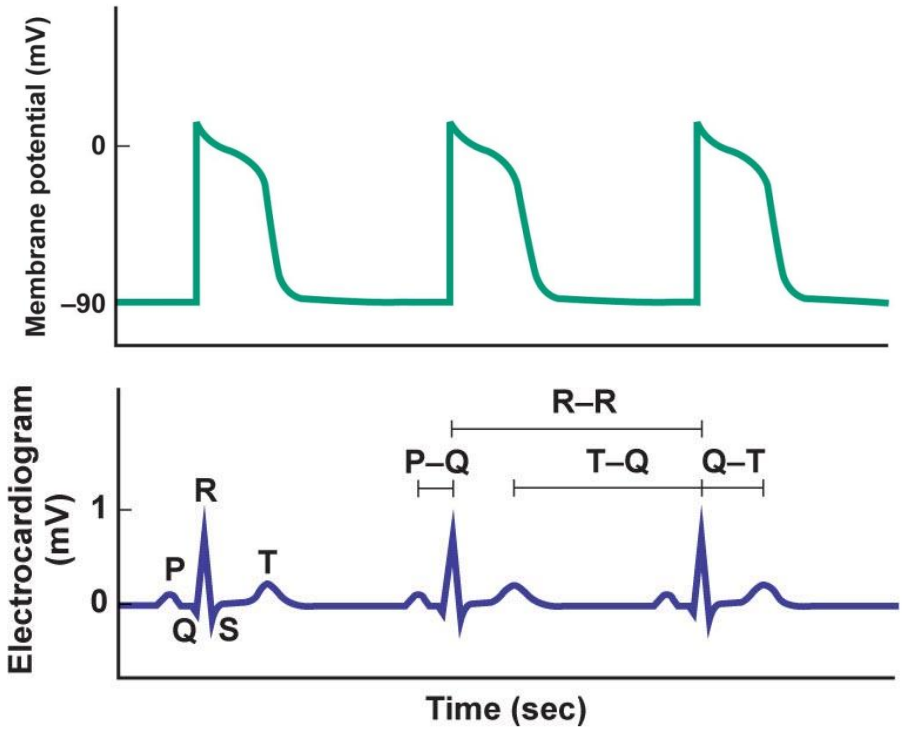


	電極配置
第一胸導 (V_1)	胸骨右側第四肋間
第二胸導 (V_2)	胸骨左側第四肋間
第三胸導 (V_3)	在 V_2 與 V_4 之間
第四胸導 (V_4)	鎖骨中線與第五肋間交界處
第五胸導 (V_5)	左腋前線與 V_4 同一水準
第六胸導 (V_6)	左腋中線與第五肋間交界處

Electrocardiogram



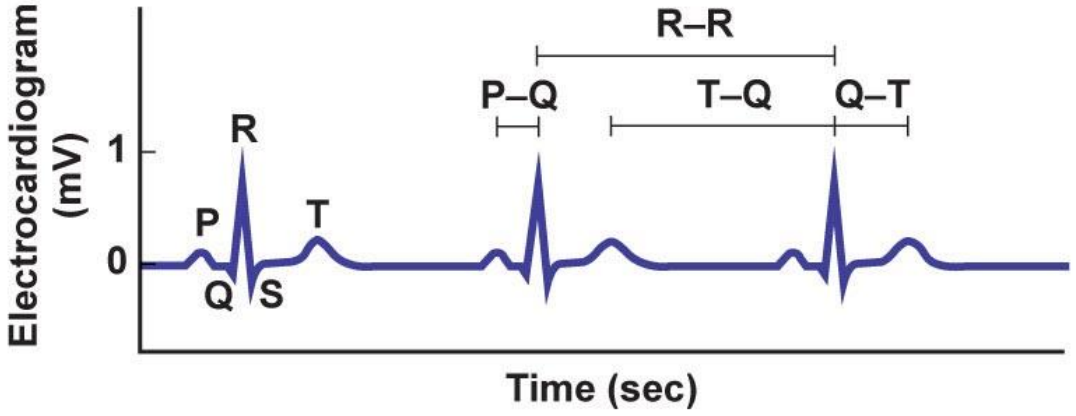
- **P wave:** ***atrial depolarization***
- **QRS complex:** ***ventricular depolarization*** and atrial repolarization
- **T wave:** ***ventricular repolarization***
- **PQ interval:** ***AV nodal delay*** (conduction time from ***atrial*** to ***ventricular excitation***)
- **QT interval:** ***ventricular systole***
- **TQ segment:** ***ventricular diastole***
- **ST segment:** ***time of complete ventricular depolarization***
- **RR interval:** ***time between heartbeats***



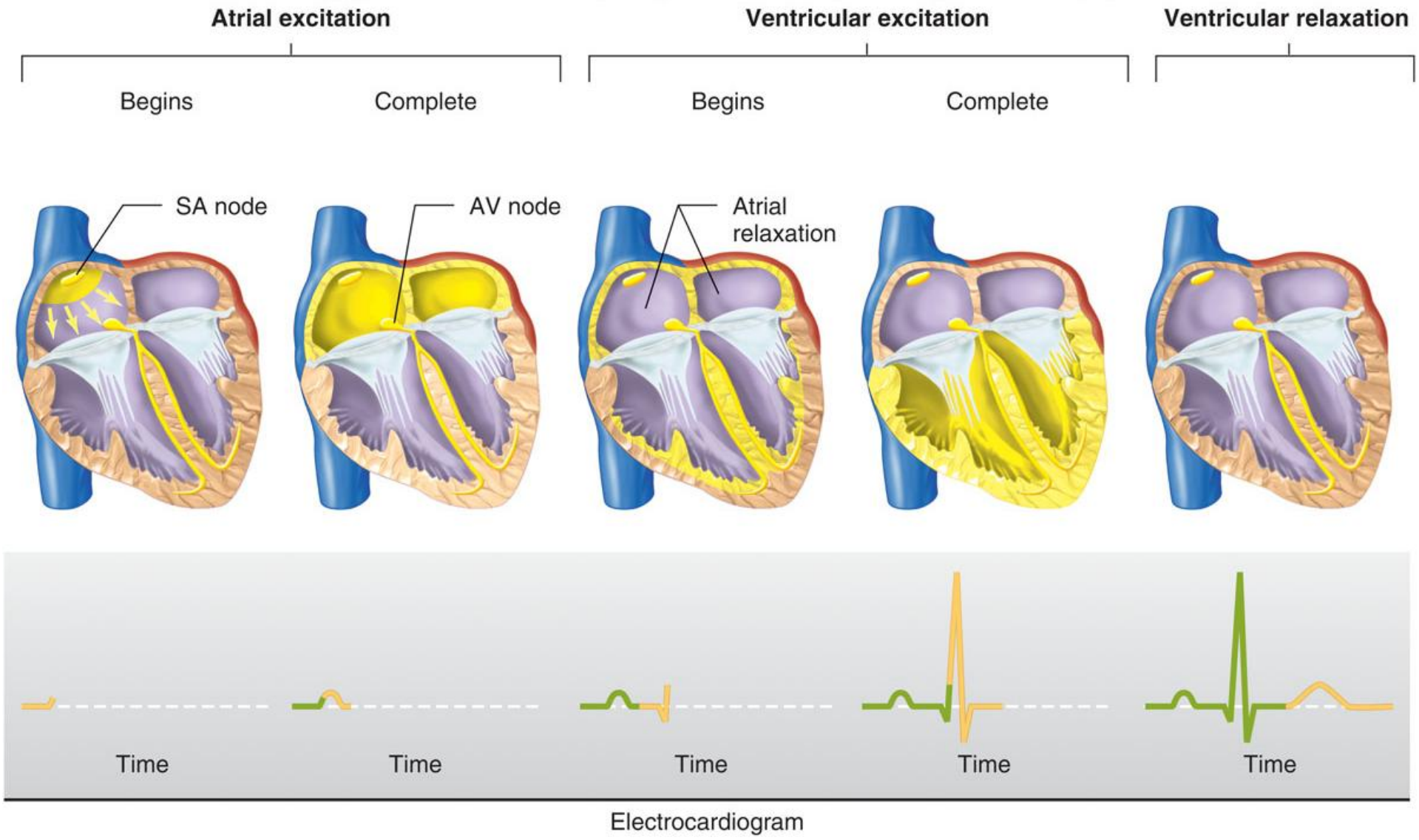
Component	Amplitude (mV)	Duration (sec)
P wave	0.2	0.10
QRS complex	1.0	0.08–0.12
T wave	0.2–0.3	0.16–0.27
P–Q interval	N/A	0.12–0.21
Q–T interval	N/A	0.30–0.43
T–Q segment	N/A	0.55–0.70
R–R interval	N/A	0.85–1.00

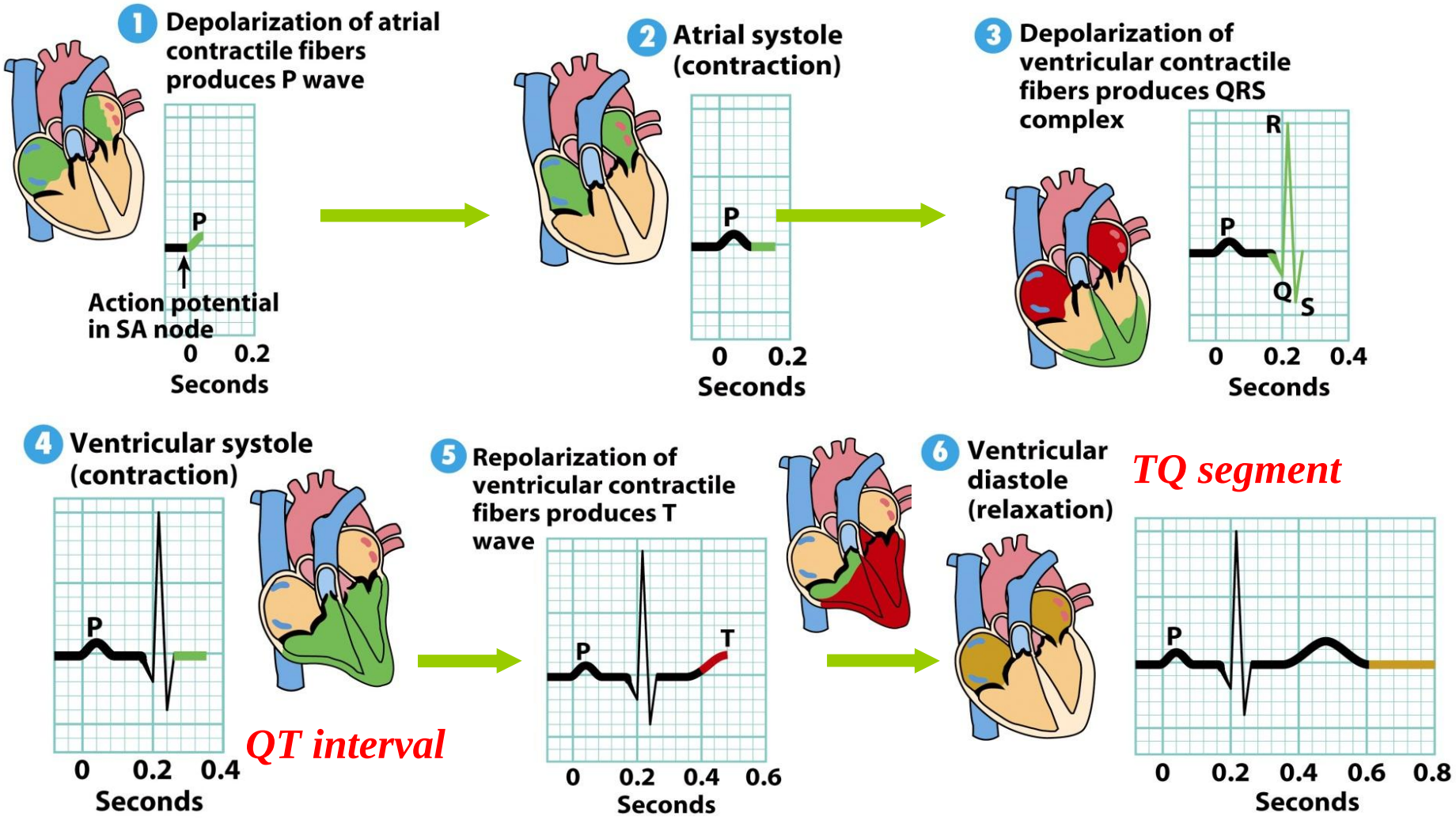
表 11-9　心電圖的定義與生理學意義

名稱	定義與生理學意義	波幅 (mV)	時間（秒）
P 波	心房去極化的電位波，代表心房收縮	0.05~0.25	0.08~0.11
QRS 複合波	心室去極化的電位波，代表心室收縮	不定（＜ 2）	0.06~0.10
T 波	心室再極化的電位波，代表心室舒張	0.1~0.8	0.05~0.25
PR 間隔	從 P 波起點到 QRS 複合波起點，代表心房去極化到心室去極化前的時間，即房－室傳導時間	—	0.12~0.20
QT 間隔	Q 波起點到 T 波終點，代表心室去極化到完全再極化的時間，即心室收縮時間	—	0.4~0.43
PQ 節段	從 P 波終點到 QRS 複合波起點，代表興奮在房室結的傳導時間	與基線相同	0.06~0.14
ST 節段	從 S 波終點到 T 波起點，心室完全去極化的時間	與基線相同	0.05~0.15



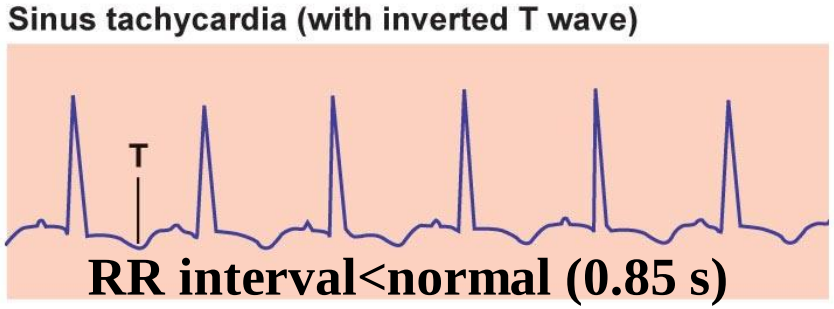
Sequence of Cardiac Excitation

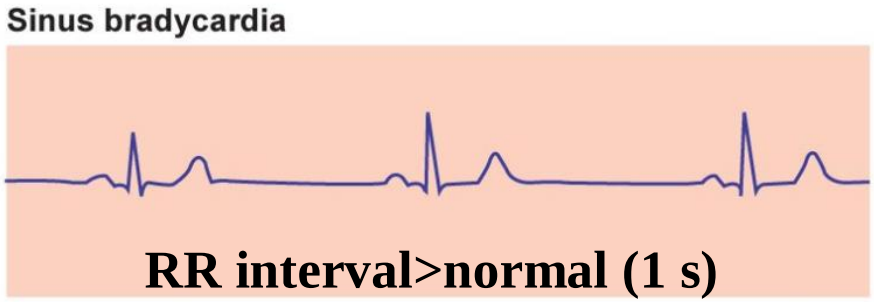



1 Depolarization of atrial contractile fibers produces P wave
P
Action potential in SA node
0 0.2
Seconds
2 Atrial systole (contraction)
P
0 0.2
Seconds
3 Depolarization of ventricular contractile fibers produces QRS complex
R
P
Q
S
0 0.2 0.4
Seconds
4 Ventricular systole (contraction)
P
0 0.2 0.4
Seconds
QT interval
5 Repolarization of ventricular contractile fibers produces T wave
P
T
0 0.2 0.4 0.6
Seconds
6 Ventricular diastole (relaxation)
TQ segment
P
0 0.2 0.4 0.6 0.8
Seconds

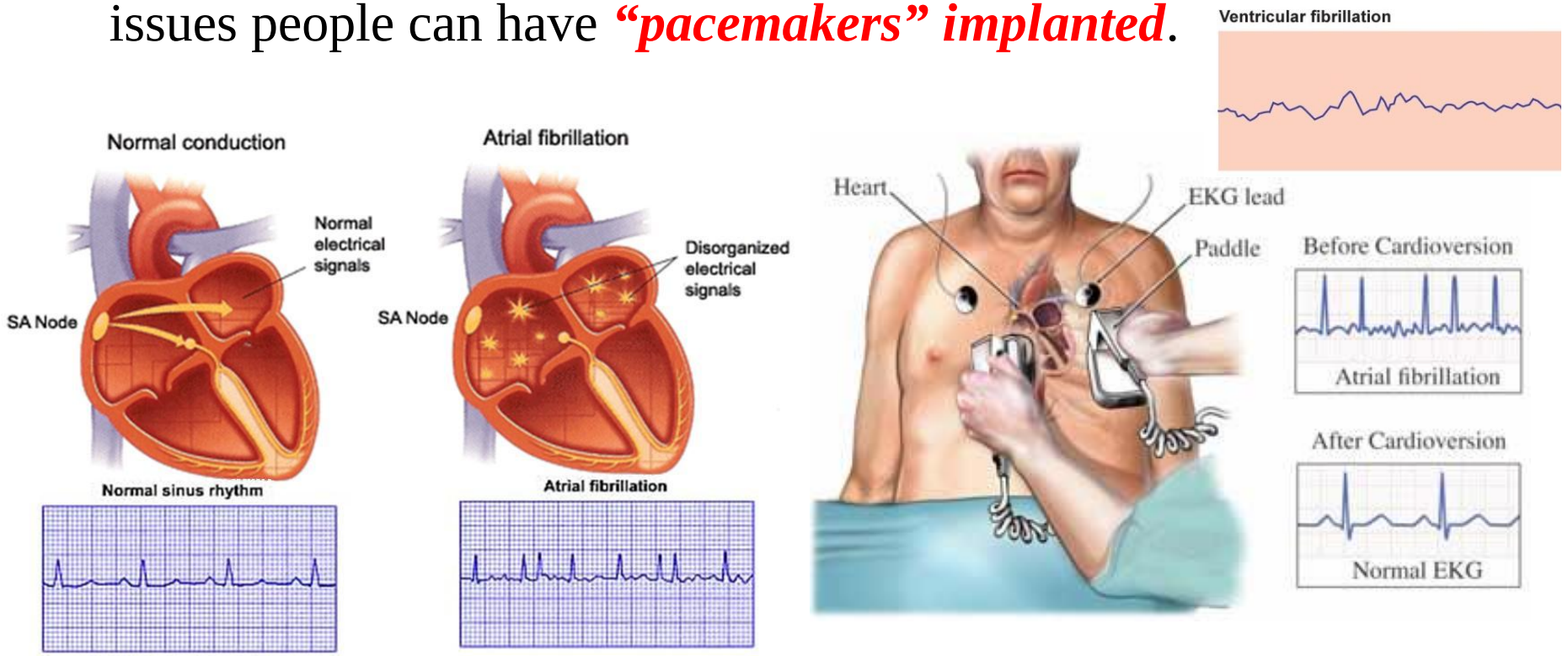
Clinical Application: Arrhythmias

- **Sinus rhythm** = **pace** generated by SA node
- Arrhythmias is an **irregular heartbeat** - the heart may beat too fast (***tachycardia*= fast rhythm**), too slowly (***bradycardia*= slow rhythm**), too early (***premature contraction***), or too rapid and irregular (***fibrillation***)
- Caused by a **defect in the conduction system**
- Classify by **rate** (tachycardia, bradycardia), or **mechanism** (automaticity, reentry, junctional, fibrillation), or **site of origin** (atria or ventricles)



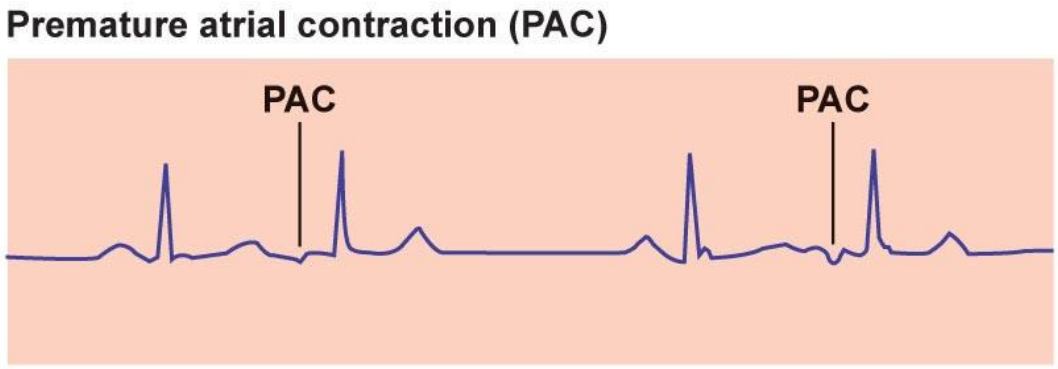


- **Atrial fibrillation** can result from **atrial flutter** (extremely fast:200-300 bpm and regular) and cause ***clotting and inefficient filling of the ventricles.***
- **Ventricular fibrillation** (ventricles can't pump blood and death occurs) can result from **ventricular tachycardia**.
- **Defibrillation** is the application of an electrical stimulus to shock the heart back into a normal SA rhythm. For chronic issues people can have ***"pacemakers" implanted***.



Arrhythmias

- **An ectopic focus** is an abnormal pacemaker that takes over the conduction system usually because it goes faster than the SA node.
- **Premature contraction** is called **Extrasystole**. The **preventricular contractions (PVCs)** are the most problematic.



PAC, followed by an ***extra ventricular contraction***

Arrhythmias: Heart Block

- A disease in the **electrical conduction system** of the heart ≠ angina (chest pain) or myocardial infarction (heart attack).
- **Slowed/diminished conduction** through **AV node** occurs in varying degrees.

1. First degree AV block (PR prolongation)

--**Increases duration PQ interval** **(>0.2 s)**

--**Increases delay** between atrial and ventricular contraction

--The most common causes are an **AV nodal disease**, **enhanced vagal tone** (for example in athletes), **electrolyte disturbances** and **medications** (ACh, Ca channel blockers, beta-blockers, digitalis)

Arrhythmias: Heart Block

2. Second degree AV block

--**Slowed, sometimes stopped** conduction through AV node

--**One or more (but not all) of the atrial impulses** fail to conduct to the ventricles due to impaired conduction

--**Lose 1-to-1 relationship** between P wave and QRS complex

--**Lose 1-to-1 relationship** between atrial and ventricular

Arrhythmias: Heart Block

3. Third degree AV block (Complete heart block)

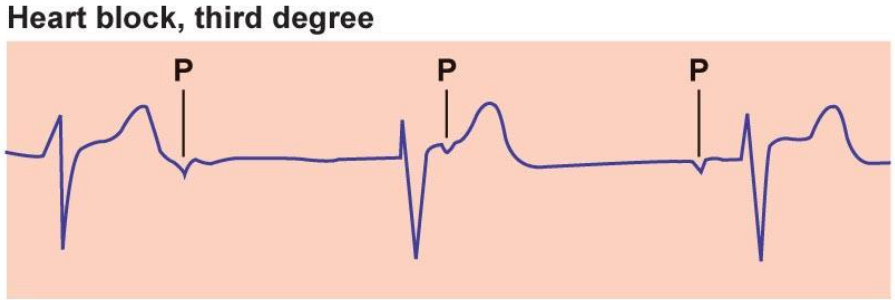
--**Loss of conduction** through the AV node

--Impulse generated in the SA node in the atrium does not propagate to the ventricles

--P wave becomes **independent of QRS**

--Atrial and ventricular contractions are **independent** (a pacemaker in the Purkinje fibers takes over, but this is slow (20–40 bpm)

--The most common cause is **coronary ischemia**

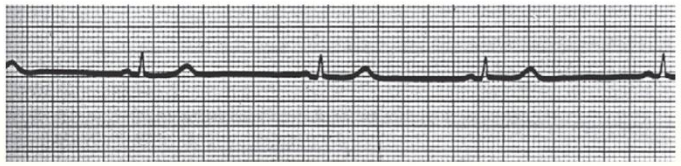


心律不整

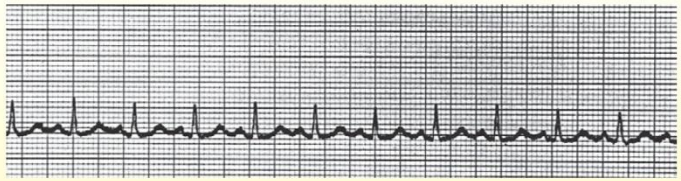
正常人心臟跳動節律規律，由竇房結控制，稱為竇性心律。如果心臟病變導致心臟搏動異常，例如過快、過慢或不規則，即稱為心律不整 (cardiac arrhythmia)。各種早期收縮 (premature beat)、竇性心搏過速、竇性心搏過緩、傳導阻滯、心房纖維顫動 (atrial fibrillation) 等都屬於心律不整（圖 11-18）。

心律不整可發生在健康人身上，如過度疲勞、吸菸、飲酒等引起，但最常見原因在於冠心病、心肌炎、心肌病、風濕性心臟病等引起。老年性的心律不整多見於器質性病變。心律不整可使心房和心室收縮模式改變，導致心排血量下降，引起病人心悸、胸悶或胸痛、頭暈、無力、呼吸短促等症狀。

透過心電圖檢查可以診斷各類心律不整。治療心律不整的方法包括：抗心律不整藥物、裝置心律調節器、電氣燒灼術 (radiofrequency ablation) 等。



竇性心搏過緩 (Sinus bradycardia)



竇性心搏過速 (Sinus tachycardia)

• **圖 11-18　心律不整的心電圖**。（圖片來源：Fox, 2006）

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)** ***SV = EDV - ESV***

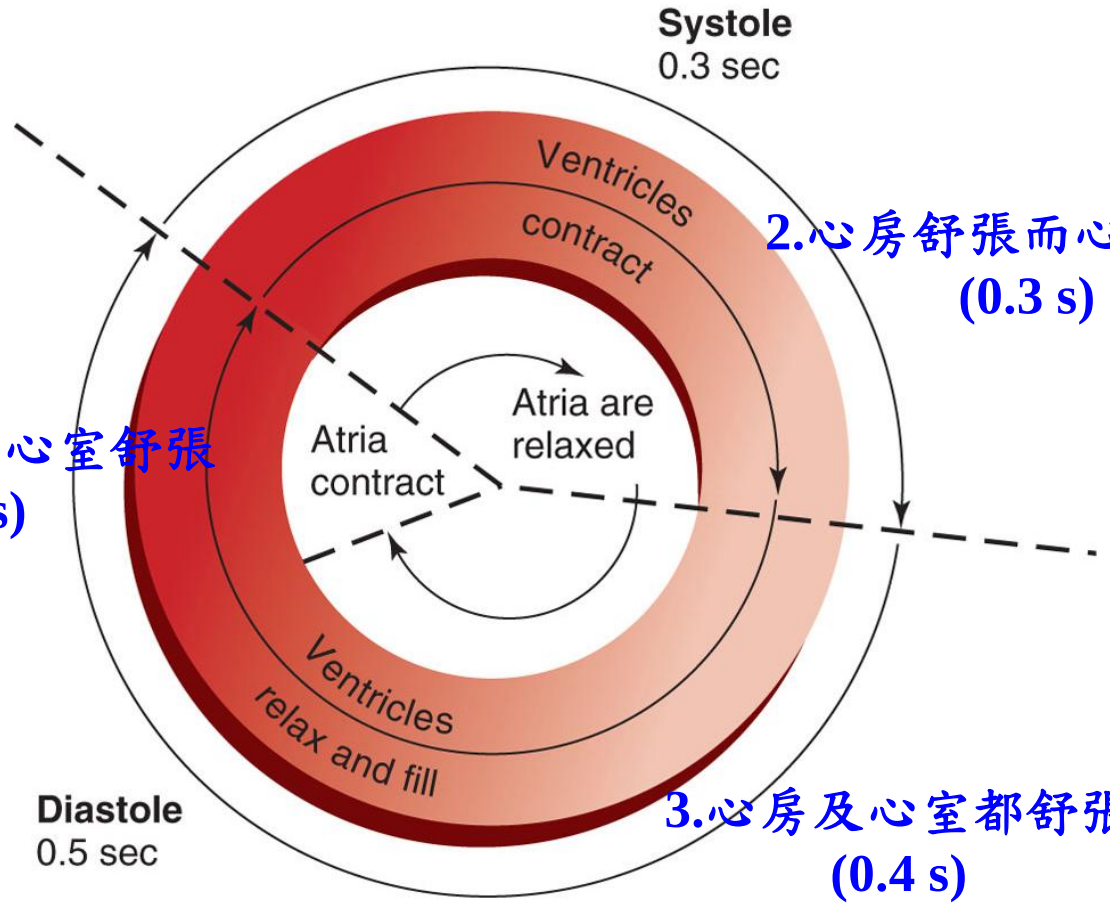
  --The volume ejected per beat from each ventricle, about 70 ml

Cardiac Cycle

Two main periods of cardiac cycle:

Systole (contraction) + Diastole (relaxation)

At 75 beats/min, one cycle requires 0.8 sec (60÷75)



1.心房收縮而心室舒張
(0.1 s)

2.心房舒張而心室收縮
(0.3 s)

3.心房及心室都舒張
(0.4 s)

Opening of Valves During the Cardiac Cycle

- **Valves open passively due to pressure gradients**

  --AV valves open when

  Pressure atria > pressure ventricles

  --Semilunar valves open when

  Pressure ventricles > pressure arteries

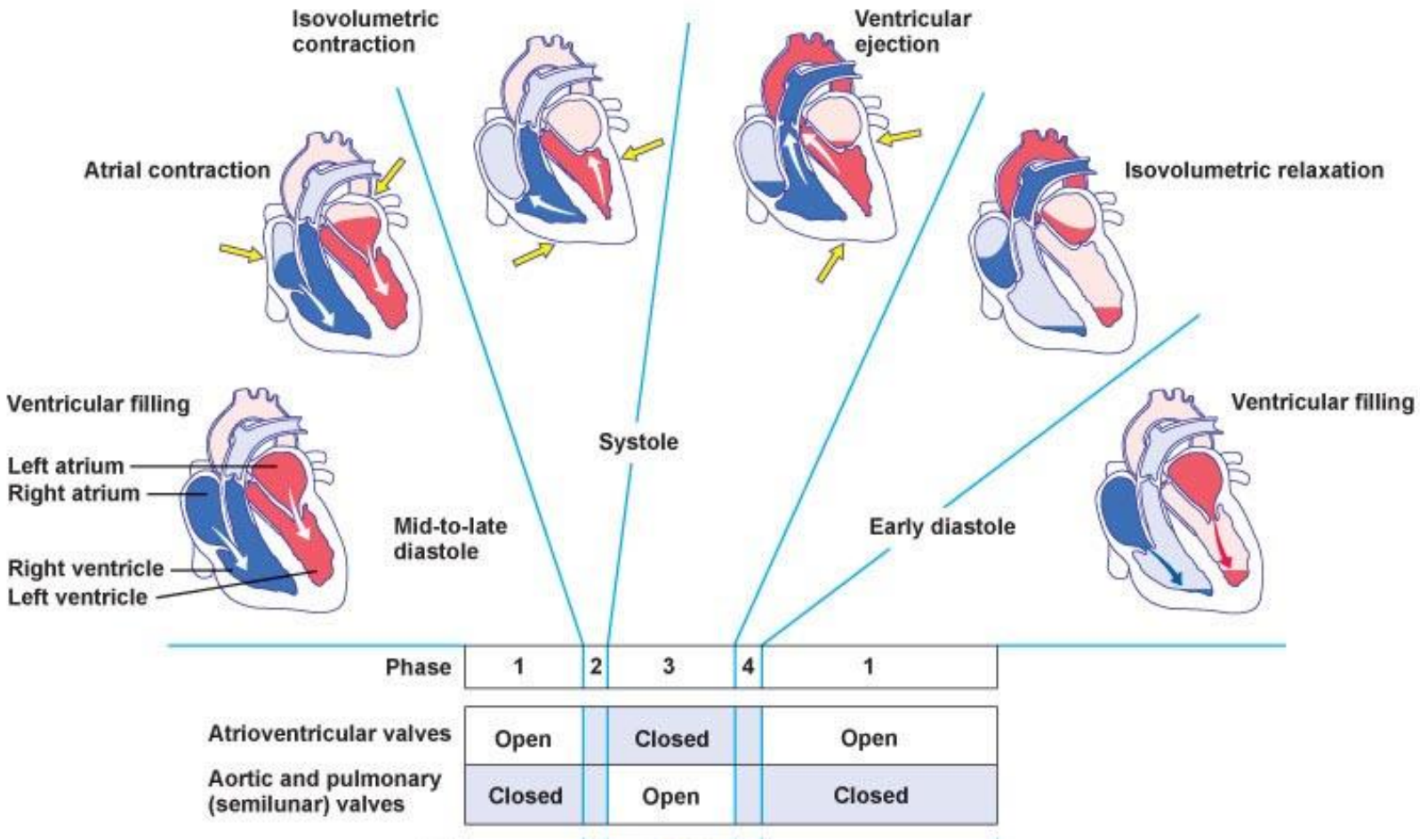
Four Phases of Cardiac Cycle

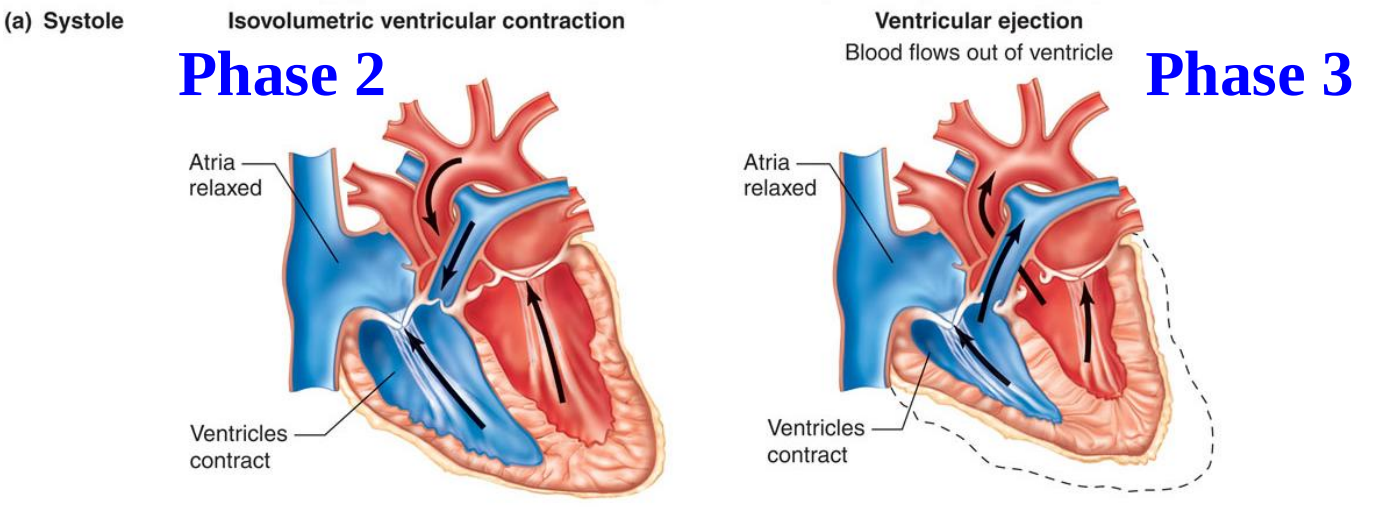
- **Ventricular filling (Phase 1)**
  - --**Pressure atria (venous return) > pressure ventricles**
  - --**AV valves open**
  - --**Passive phase**—no atria or ventricular contraction
  - --**Active phase—atria contract** (pushes final 20-25 ml blood into ventricle)
- **Isovolumetric ventricular contraction (Phase 2)**
  - --**Ventricle contracts**—increases pressure
  - --**AV and semilunar valves closed**
  - --**No blood entering or exiting ventricle**

Four Phases of Cardiac Cycle

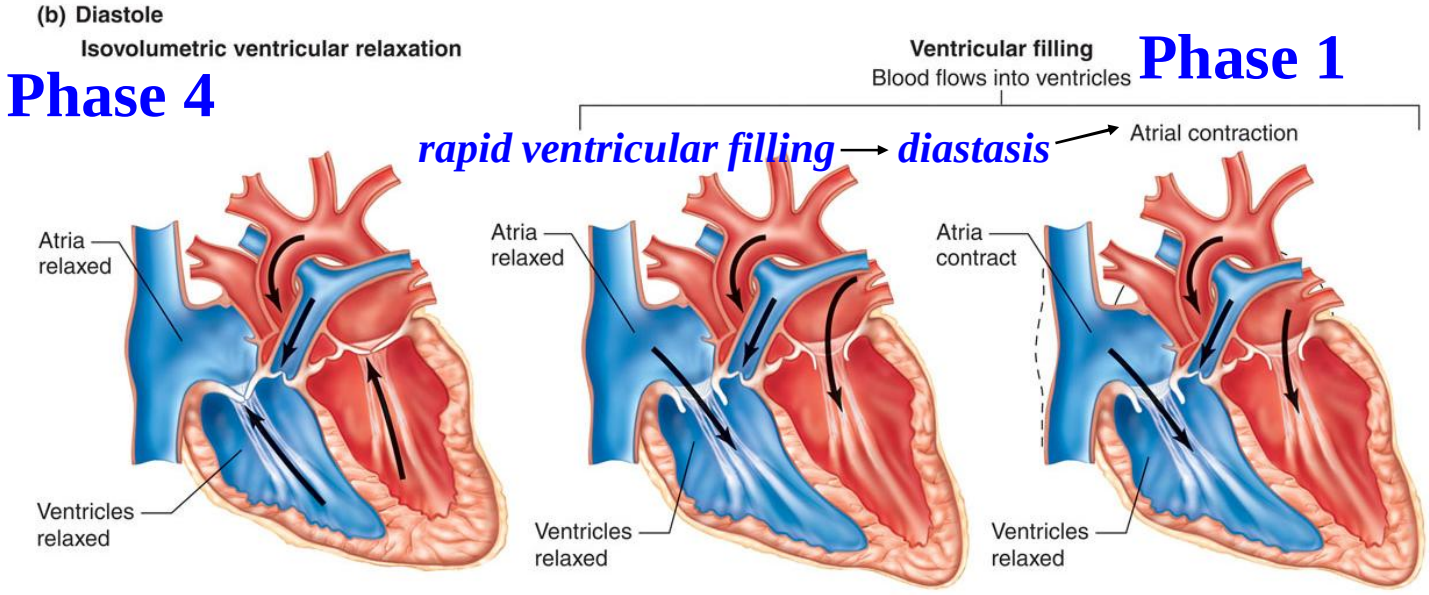
- **Ventricular ejection (Phase 3)**
  - **--Pressure ventricles > pressure arteries**
  - **--Semilunar valves open**
- **Isovolumetric ventricular relaxation (Phase 4)**
  - **--Ventricle relaxes**—decreases pressure
  - **--AV and semilunar valves closed**
  - **--No blood entering or exiting ventricle**

Four Phases of Cardiac Cycle





AV valves:	Closed	Closed
Aortic and pulmonary valves:	Closed	Open



AV valves:	Closed	Open	Open
Aortic and pulmonary valves:	Closed	Closed	Closed

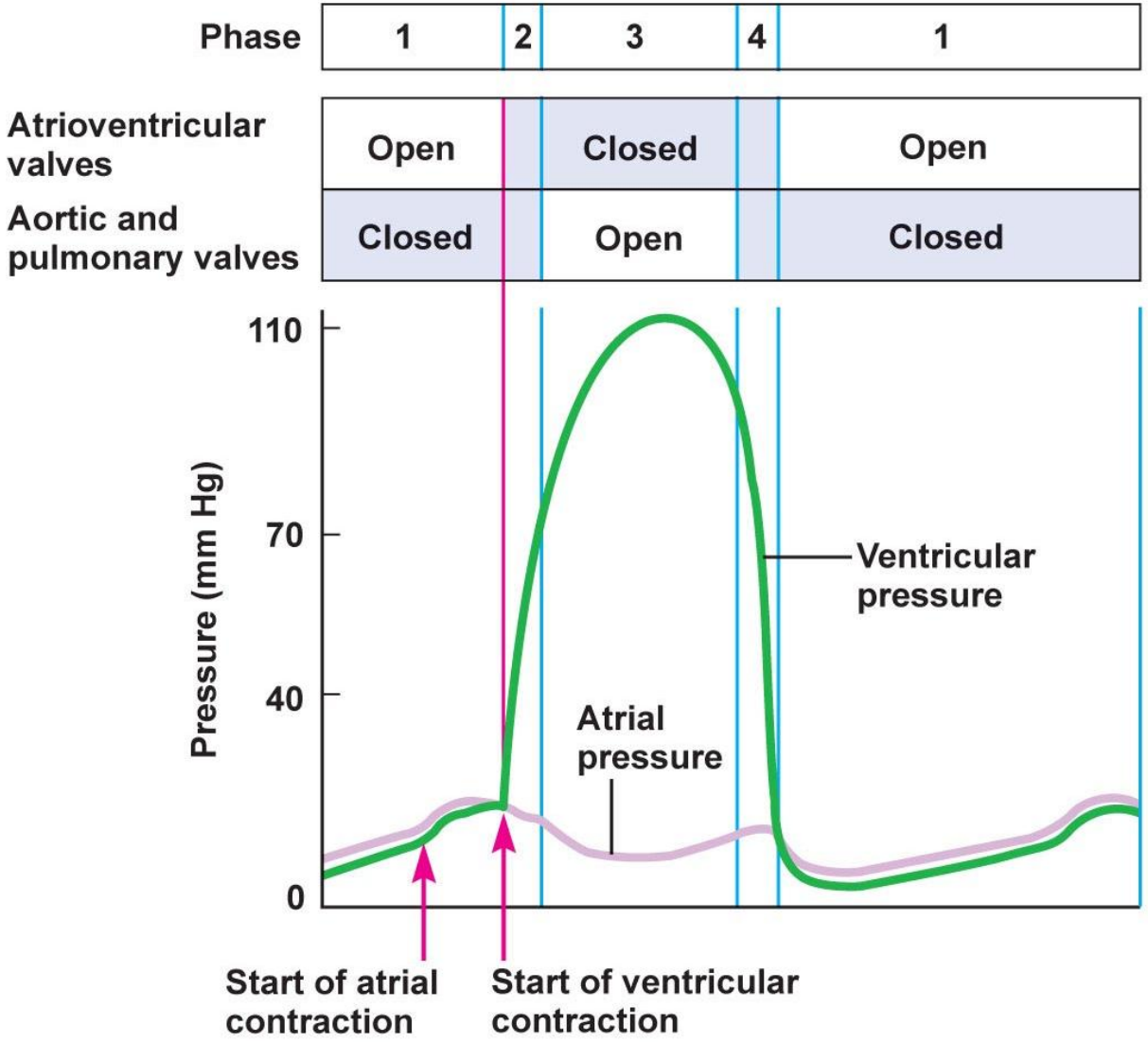
Ventricular Systole

- **Isovolumetric ventricular contraction**
  - --AV and aortic valves closed
  - --Ventricular pressure increases until it exceeds atrial pressure
- **Ventricular ejection**
  - --Aortic valve opens
  - --Blood moves from ventricle to aorta

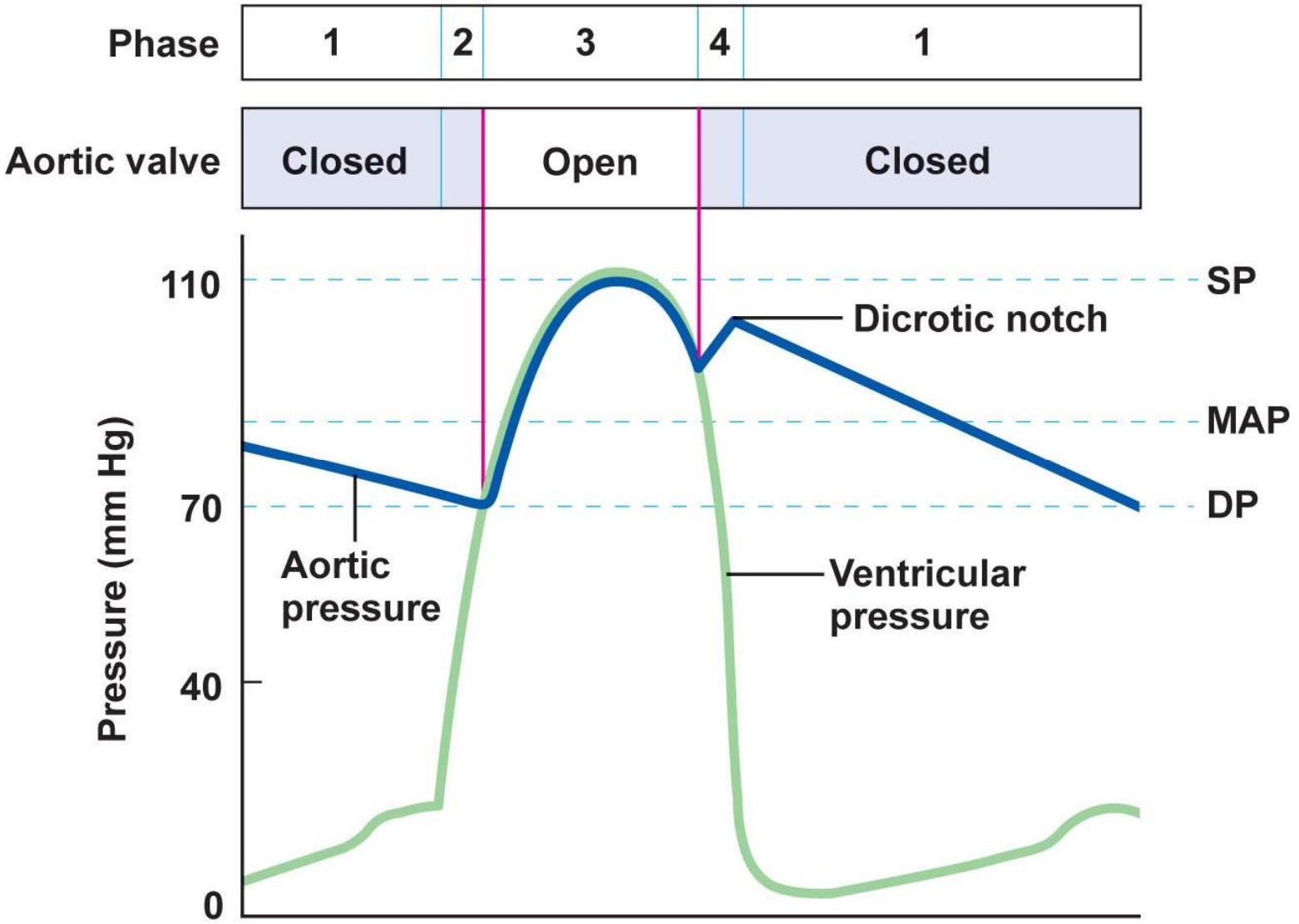
Ventricular Diastole

- **Isovolumetric ventricular relaxation**
  - --Ventricle muscle relaxes so that pressure is less than aorta
  - --Aortic valve closes
  - --Pressure in ventricle continues dropping until it is less than atrial pressure
- **Ventricular filling**
  - --AV valve opens
  - --Blood moves from atria to ventricle
  - --Passive until atrium contracts

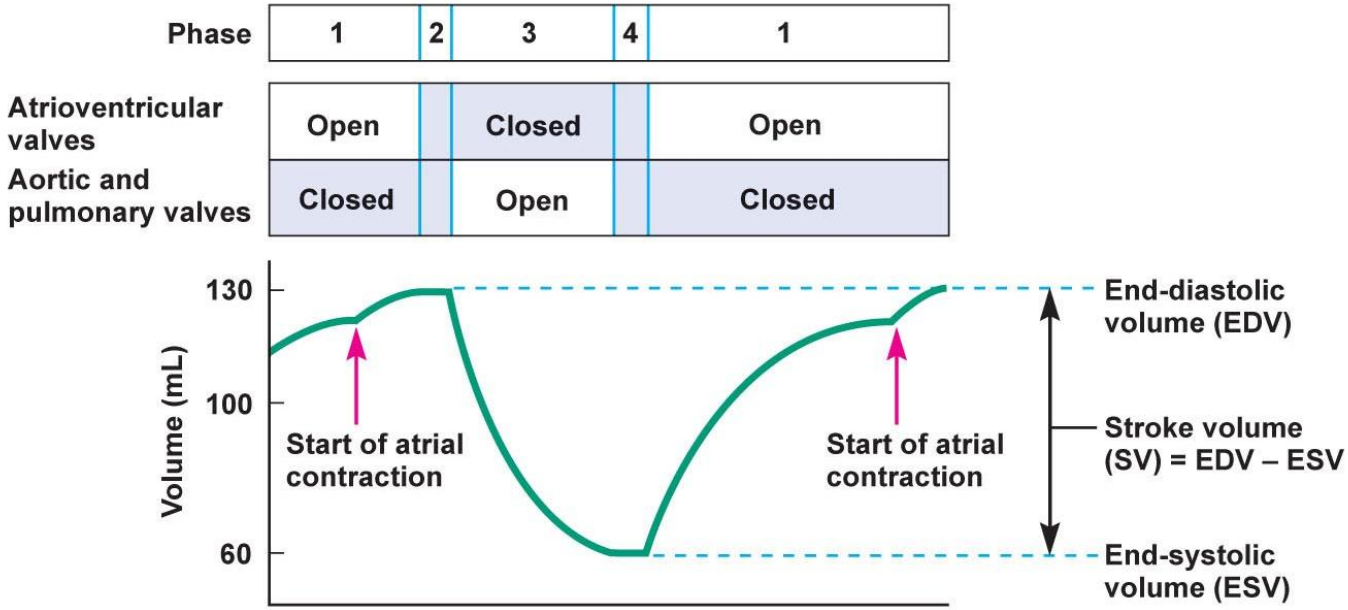
Ventricular Pressure



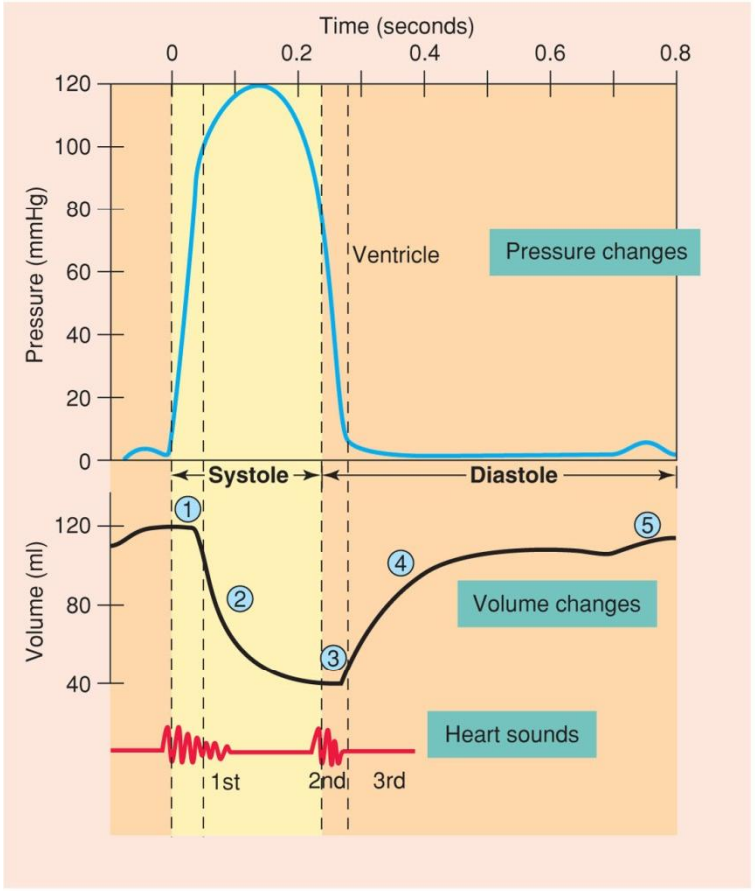
Aortic Pressure

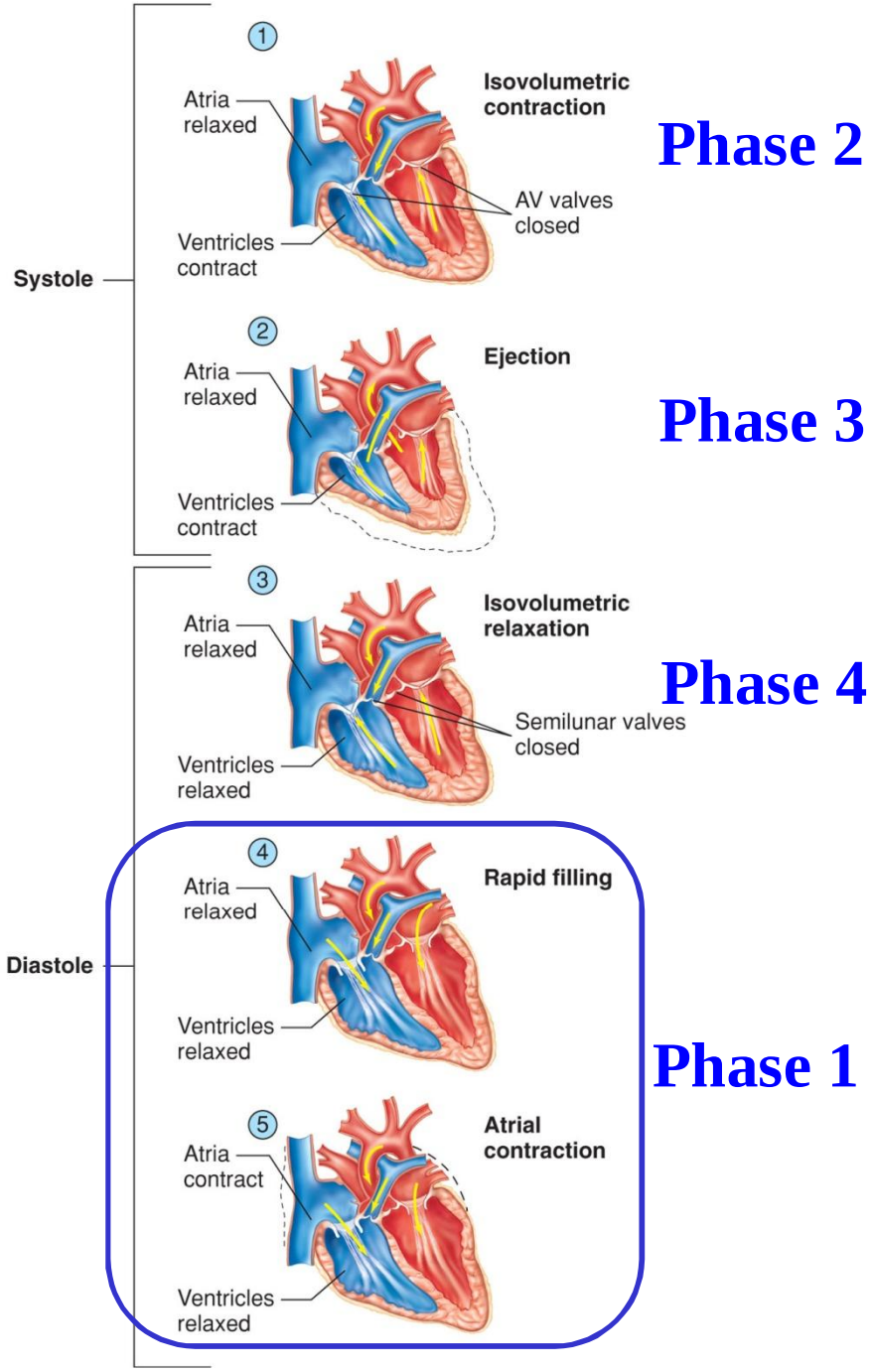


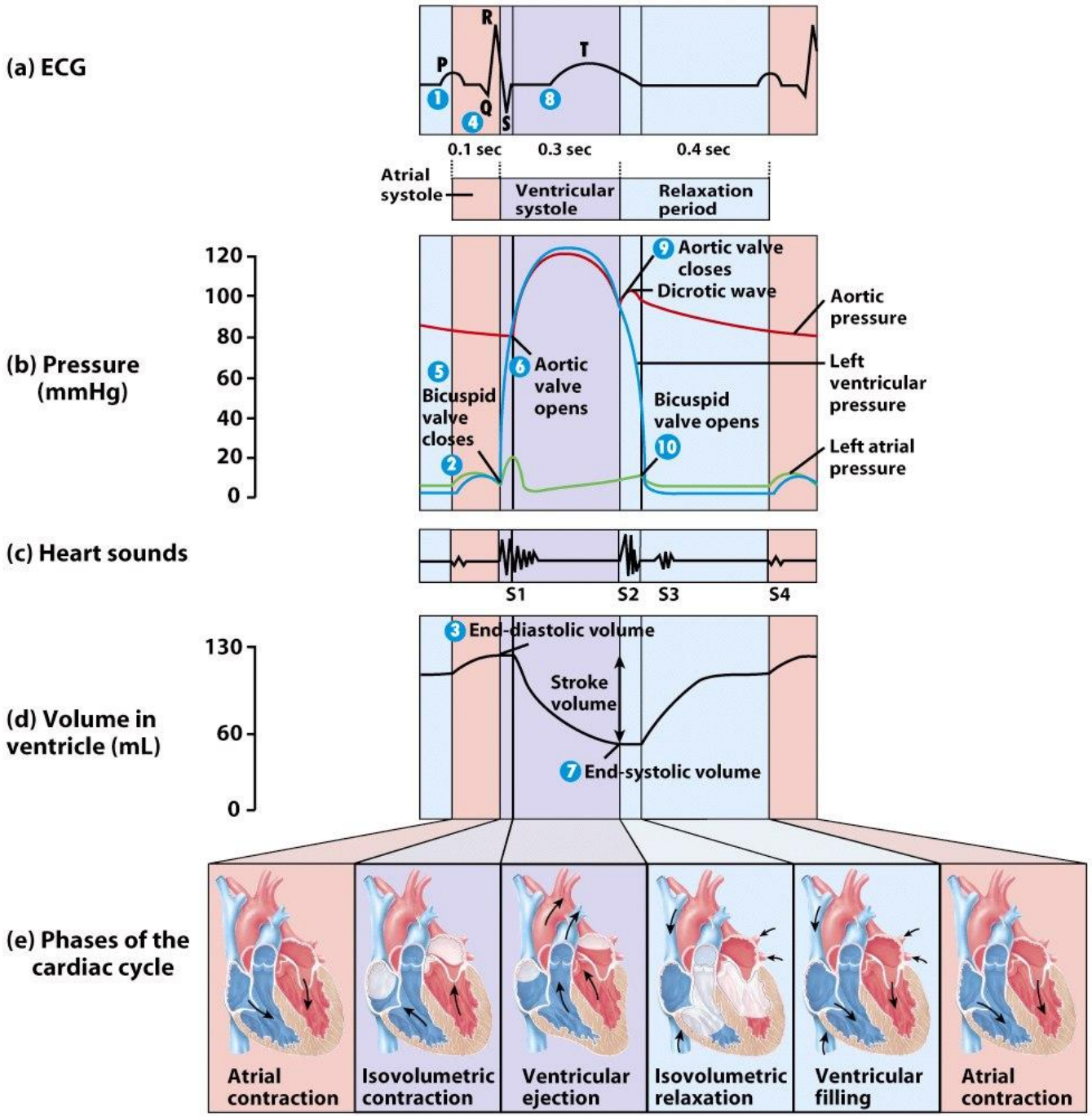
Ventricular Volume



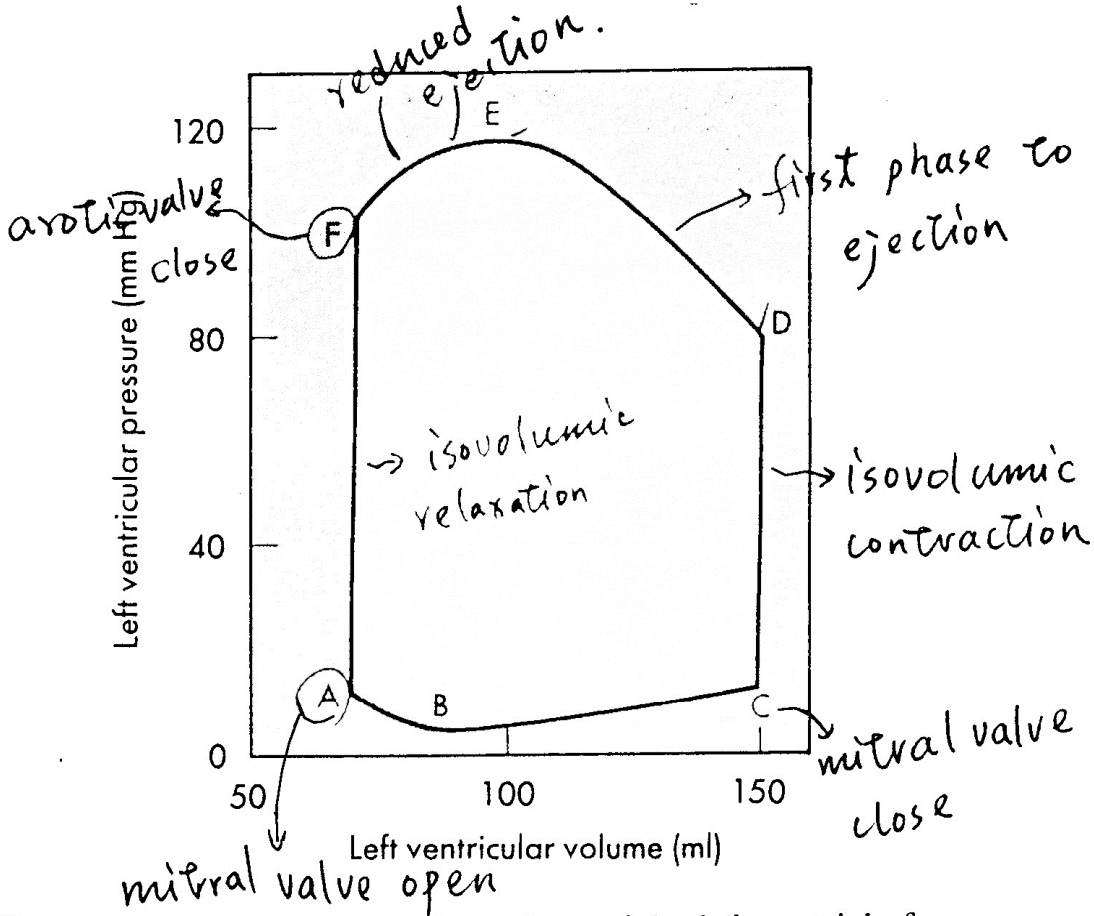
- **EDV = end-diastolic volume**, volume of blood in ventricle at the end of diastole (~130 ml)
- **ESV = end-systolic volume**, volume of blood in ventricle at the end of systole (~60 ml)
- **SV = stroke volume**, volume of blood ejected from ventricle each cycle (**SV = EDV –ESV**= 70 ml)
- **Ejection Fraction (EF)**, fraction of end-diastolic volume ejected during a heartbeat (**EF=SV/EDV**=0.54=54%~**50-75%** rest normal)


Time (seconds)
0
0.2
0.4
0.6
0.8
120
100
80
60
40
20
0
Pressure (mmHg)
Ventricle
Pressure changes
Systole
Diastole
120
80
40
Volume (ml)
1
2
3
4
5
Volume changes
Heart sounds
1st
2nd
3rd


Systole
Diastole
1
Atria relaxed
Isovolumetric contraction
AV valves closed
Ventricles contract
Phase 2
2
Atria relaxed
Ejection
Ventricles contract
Phase 3
3
Atria relaxed
Isovolumetric relaxation
Semilunar valves closed
Ventricles relaxed
Phase 4
4
Atria relaxed
Rapid filling
Ventricles relaxed
5
Atria contract
Atrial contraction
Ventricles relaxed
Phase 1


(a) ECG
R
P
T
Q
S
1
4
8
0.1 sec
0.3 sec
0.4 sec
Atrial systole
Ventricular systole
Relaxation period
(b) Pressure (mmHg)
120
100
80
60
40
20
0
9 Aortic valve closes
Dicrotic wave
Aortic pressure
5 Bicuspid valve closes
6 Aortic valve opens
Left ventricular pressure
Bicuspid valve opens
10
Left atrial pressure
2
(c) Heart sounds
S1
S2
S3
S4
(d) Volume in ventricle (mL)
130
60
0
3 End-diastolic volume
Stroke volume
7 End-systolic volume
(e) Phases of the cardiac cycle
Atrial contraction
Isovolumetric contraction
Ventricular ejection
Isovolumetric relaxation
Ventricular filling
Atrial contraction

Pressure-Volume Loop



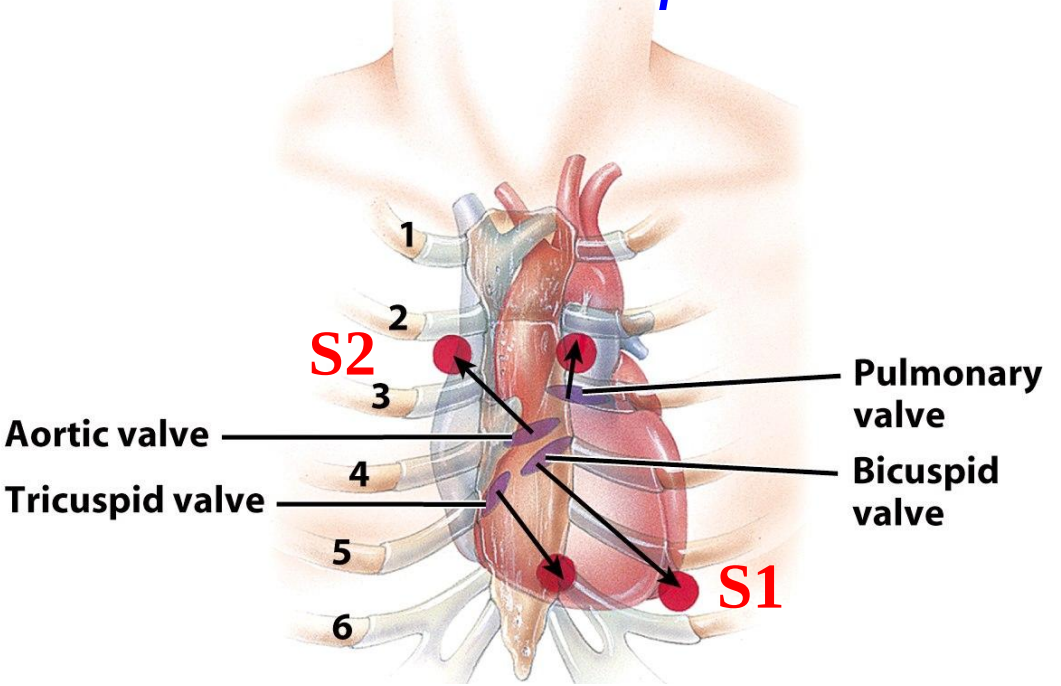
■ **Fig.** Pressure-volume loop of the left ventricle for a single cardiac cycle *(ABCDEF)*.

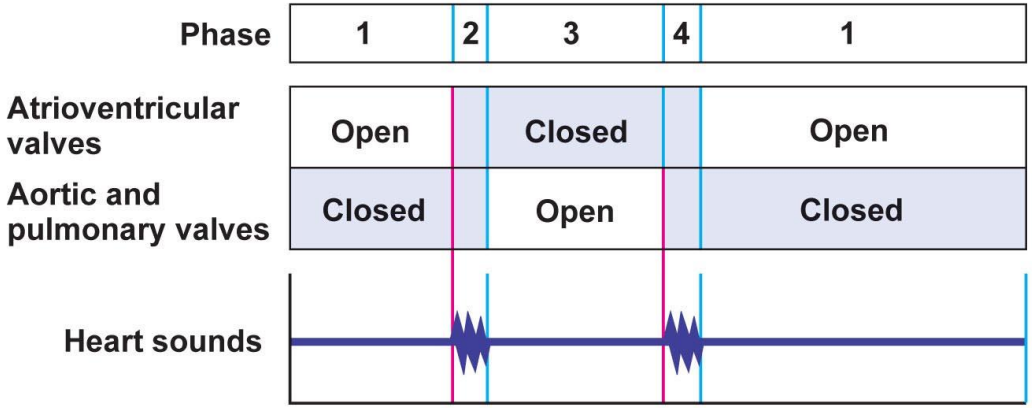
表 11-1　在心動週期中，壓力、瓣膜、血流方向、心室容積和心音的關係

心動週期的時相		壓力關係	房室瓣	半月瓣	血流方向	心室容積	心音
心室收縮期	等容收縮期 (0.05s)	房壓＜室壓≦主動脈壓	關閉	關閉	血液存心室	不變	S1
	快速射血期 (0.10s)	房壓＜室壓＞主動脈壓	關閉	開放	心室→動脈	↓	
	緩慢射血期 (0.15s)	房壓＜室壓＜主動脈壓	關閉	開放	心室→動脈	↓↓	
心室舒張期	等容舒張期 (0.07s)	房壓≦室壓＜主動脈壓	關閉	關閉	血液存心室	不變	S2
	快速充血期 (0.11s)	房壓＞室壓＜主動脈壓	開放	關閉	心房→心室	↑	S3
	緩慢充血期 (0.22s)	房壓＞室壓＜主動脈壓	開放	關閉	心房→心室	↑↑	
心房收縮期 (0.1s)		房壓＞室壓＜主動脈壓	開放	關閉	心房→心室	最大	S4

Heart Sounds

Where to listen on chest wall for heart sounds ?

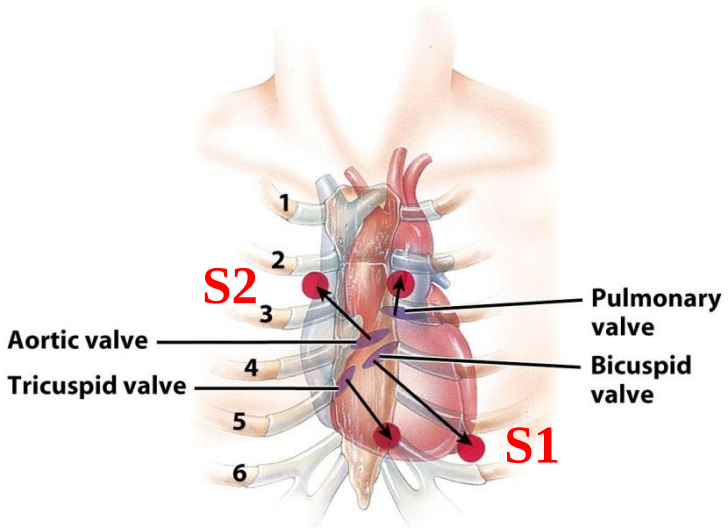




- The sound of a heartbeat comes primarily from the turbulent flow caused by the **closure of the valves**, not from the contraction of the heart muscle.
- The **first** heart sound (***soft Lubb***) = closing of **AV valves (*occurs at ventricular systole*)**.
- The **second** heart sound (***louder Dupp***) = closing of **semilunar valves (*occurs at ventricular diastole*)**.

表 11-2　心音的分類、產生時間、產生機制、特徵和生理意義

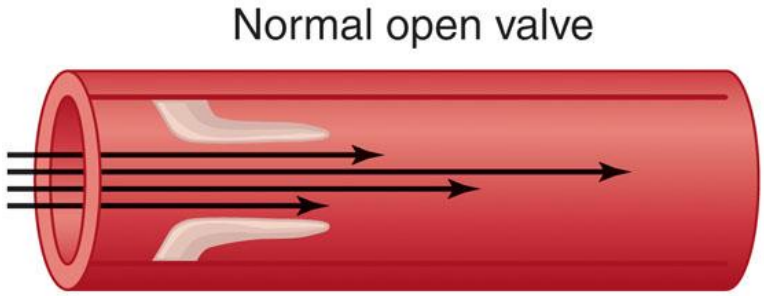
比較項目 ＼ 心音		第一心音 (S1)	第二心音 (S2)
心動週期時相		心室等容收縮期	心室等容舒張期
產生原因		房室瓣關閉	半月瓣關閉
聽診特徵	音調	低	高脆
	強度	響	較 S1 弱
	時程	長	較短（0.08 秒）
	最響部位	心尖（左第 5 肋間鎖骨中線）	心底（胸骨旁第 2 肋間）
生理意義		代表收縮期開始	代表舒張期開始
心電圖位置		QRS 複合波後 0.02~0.04 秒	T 波終末或稍後



Clinical Application: Murmurs

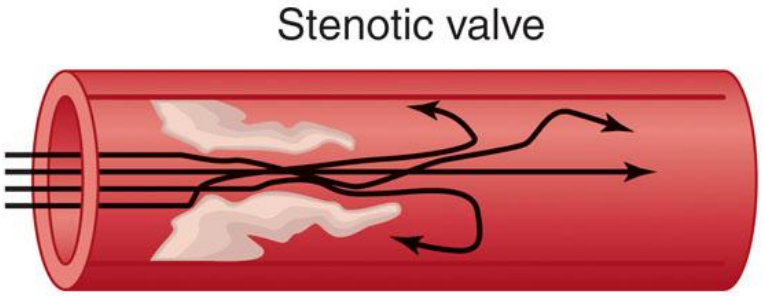
- A ***heart murmur*** is an abnormal sound that consists of a flow noise that is heard before, between, or after the lubb-dupp or that may mask the normal sounds entirely.
- Some murmurs are caused by turbulent blood flow around valves due to **abnormal anatomy** or **increased volume of flow**.
- Not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

Clinical Application: Murmurs



Normal open valve

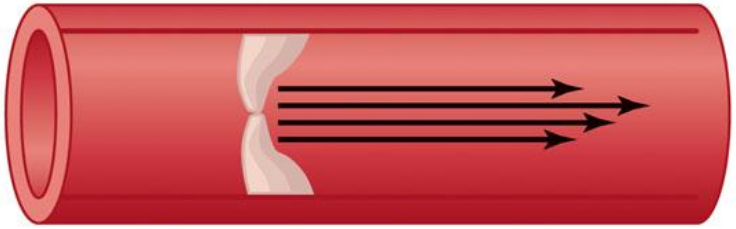
Laminar flow = quiet



Stenotic valve

Narrowed valve
Turbulent flow = murmur

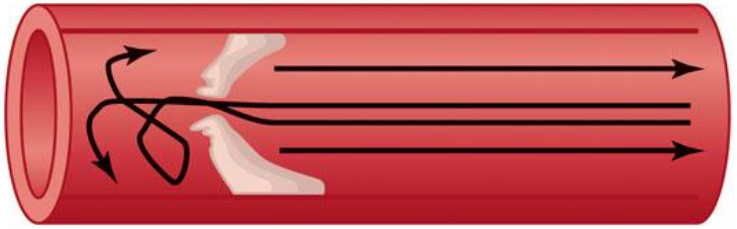
Mitral stenosis:
may result in pulmonary hypertension



Normal closed valve

No flow = quiet

(a)



Insufficient valve

Leaky valve
Turbulent backflow = murmur

(b)

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**

Measurement of Cardiac Function

- **Human cardiac output can be measured by a variety of methods**

  1. ***Echocardiography:*** a noninvasive technique that uses ultrasonic waves

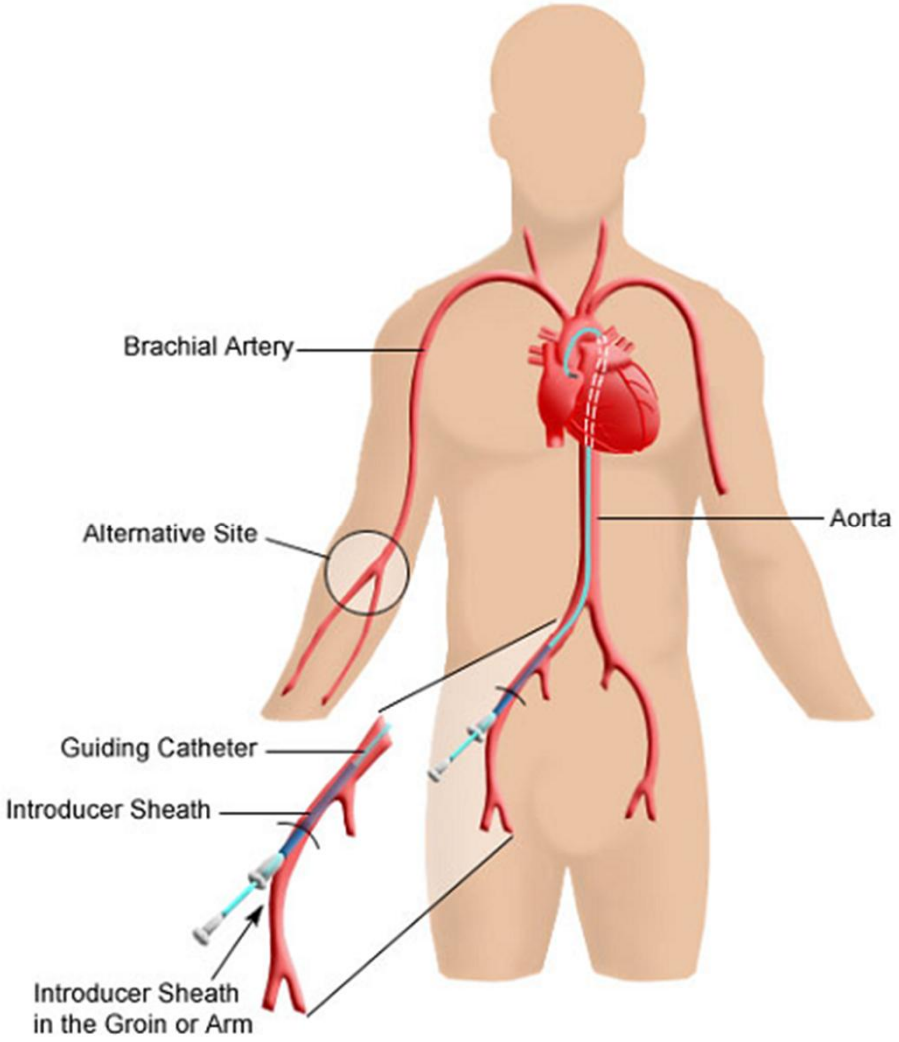
     --detect the abnormal functioning of **cardiac valves** or **contractions of the cardiac walls**, and can also be used to measure **ejection fraction**

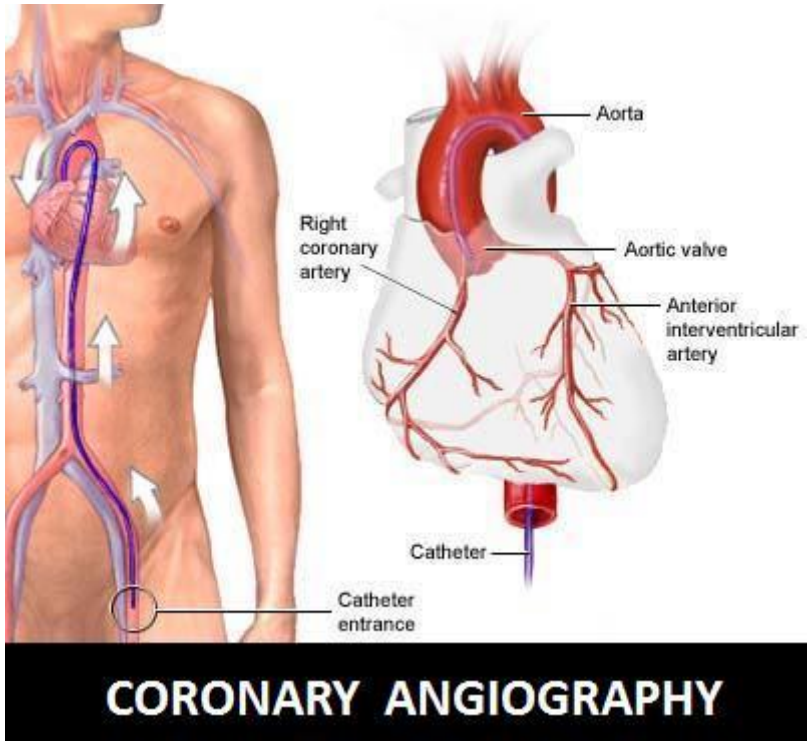
  2. ***Cardiac angiography:*** requires the temporary threading of a thin, flexible tube called a catheter through an artery or vein into the heart

     --a liquid containing radio-opaque contrast material is then injected through the **catheter** during **high-speed x-ray videography**

     --useful for evaluating **cardiac function** and for identifying **narrowed coronary arteries**

Cardiac Angiography





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

- **Average blood volume = 5.5 liters**
- **Volume of blood pumped by each ventricle per minute**
- **At 70 ml stroke volume (SV=EDV-ESV) & 72 beat/min (HR)-- 5 L/min at rest**
- **Regulate heart rate and stroke volume**

  --Extrinsic and intrinsic regulation

  1.Extrinsic—neural and hormonal

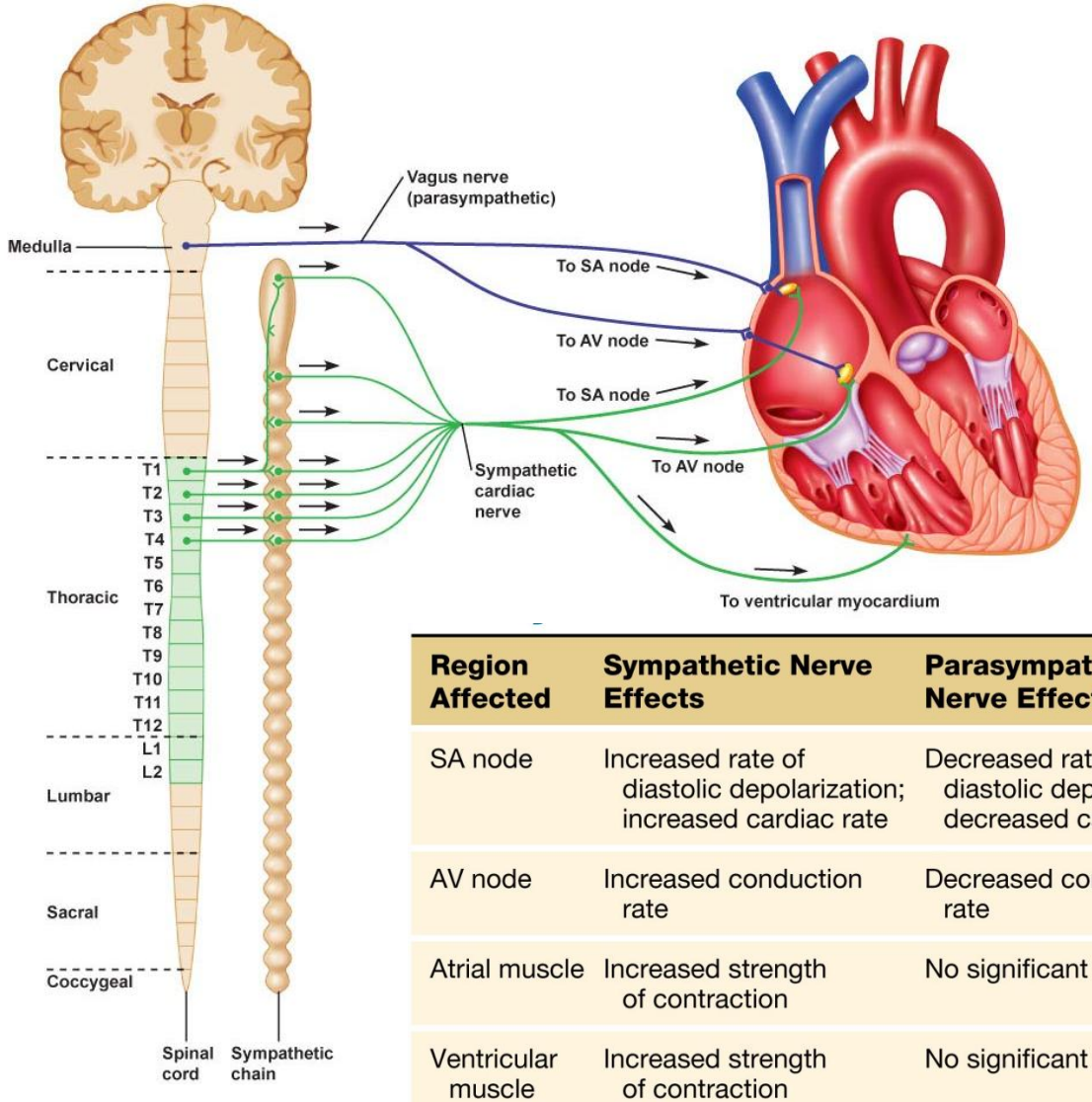
  2.Intrinsic—autoregulation

Regulation of Heart Rate

- In a healthy system **SV is fairly constant**. If blood volume drops or if the heart weakens, then SV declines and CO is maintained by **increasing HR** (CO= SV x HR)
- Things that **increase HR** are **positive chronotropic factors**
- Things that **decrease HR** are **negative chronotropic factors**
- Adjustments in heart rate important in short-term control of **cardiac output and blood pressure**
- **Autonomic nervous system (neural regulation)** and **epinephrine/norepinephrine (hormonal regulation)** most important
- Heart rate is also controlled by the input from the **ANS**: ***SNS increases heart rate***; ***PSNS decreases heart rate***

Regulation of Heart Rate

Autonomic Regulation

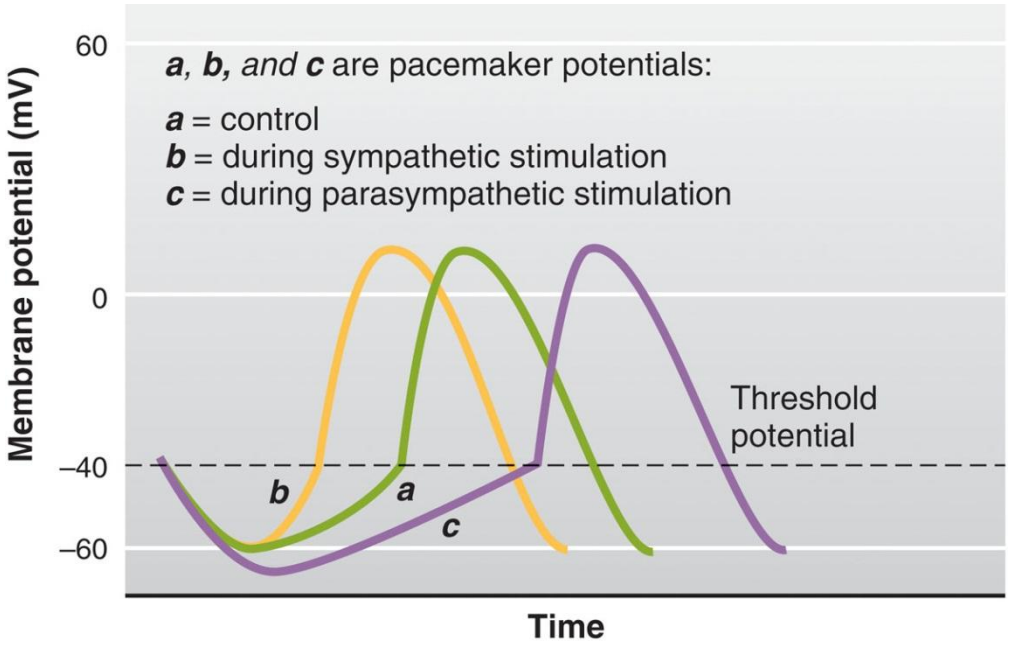


Region Affected	Sympathetic Nerve Effects	Parasympathetic Nerve Effects
SA node	Increased rate of diastolic depolarization; increased cardiac rate	Decreased rate of diastolic depolarization; decreased cardiac rate
AV node	Increased conduction rate	Decreased conduction rate
Atrial muscle	Increased strength of contraction	No significant effect
Ventricular muscle	Increased strength of contraction	No significant effect

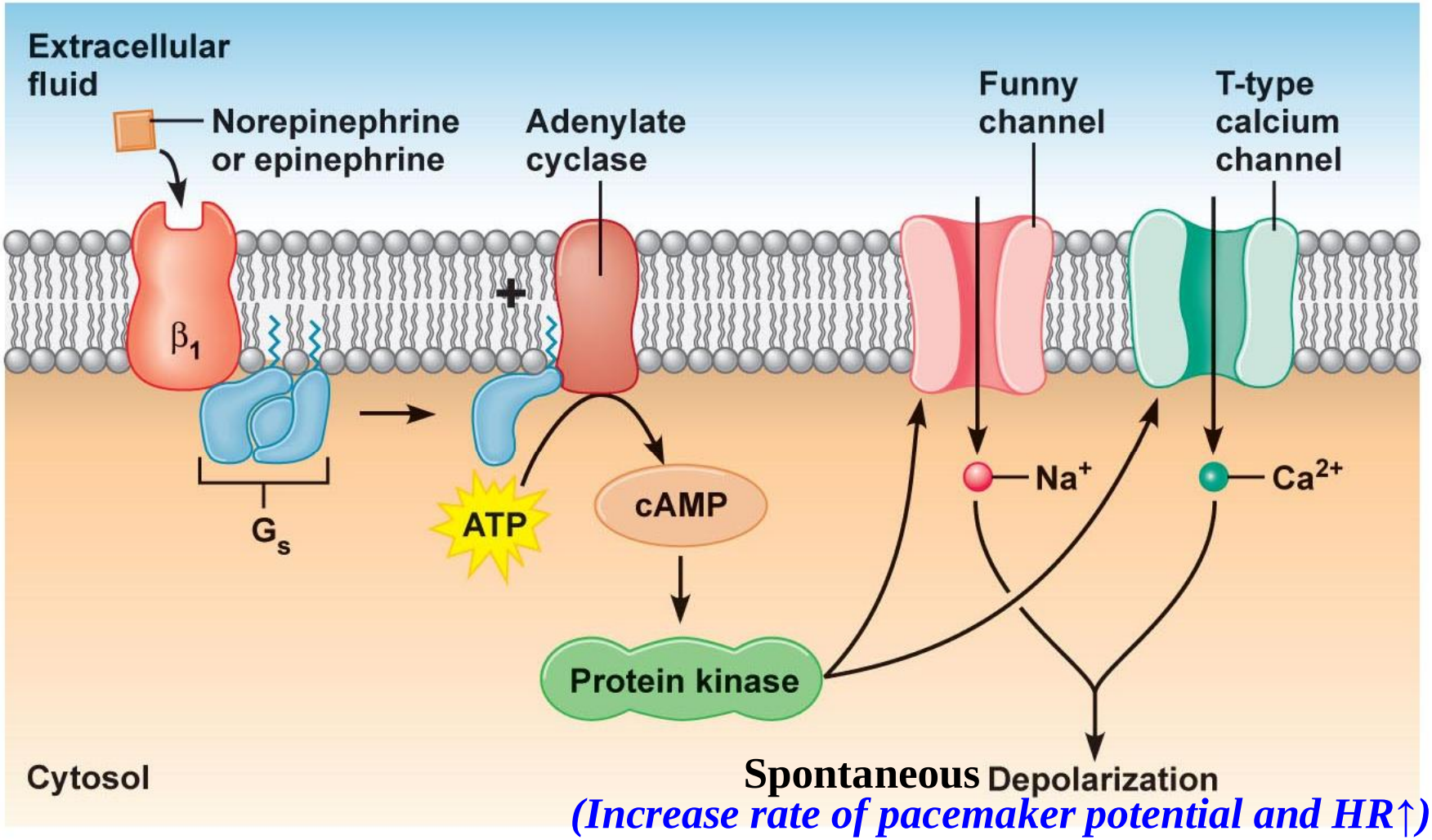
Regulation of Heart Rate

Autonomic Regulation

- SA node intrinsic firing rate = **100/min**
  - --No extrinsic control on heart, **HR = 100 bpm**
- SA node under **control of ANS and hormones**
  - **--Rest:** ***parasympathetic*** dominates, **HR = 75 bpm**
  - **--Excitement:** ***sympathetic*** takes over, **HR increases**

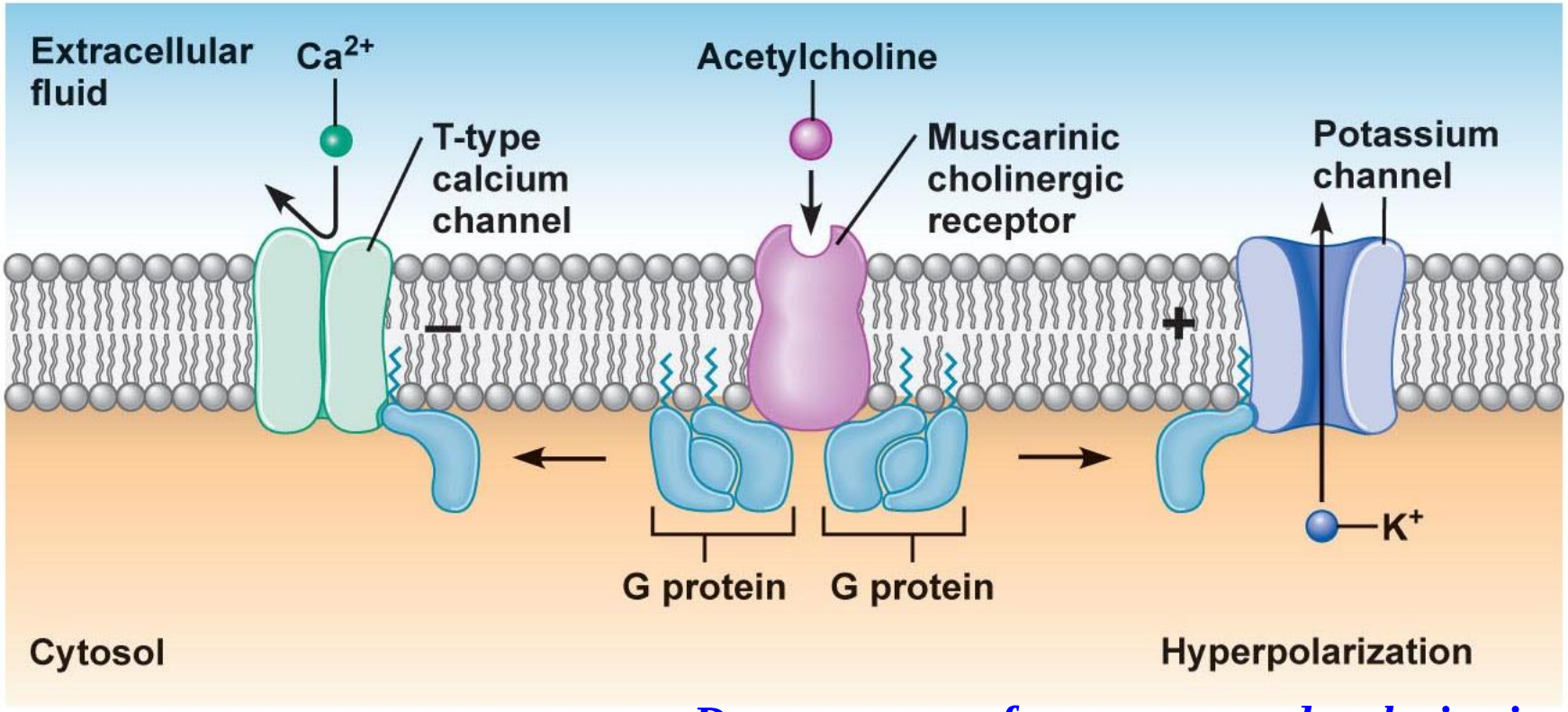


Sympathetic Regulation of SA cell (Heart Rate)



(a) Sympathetic

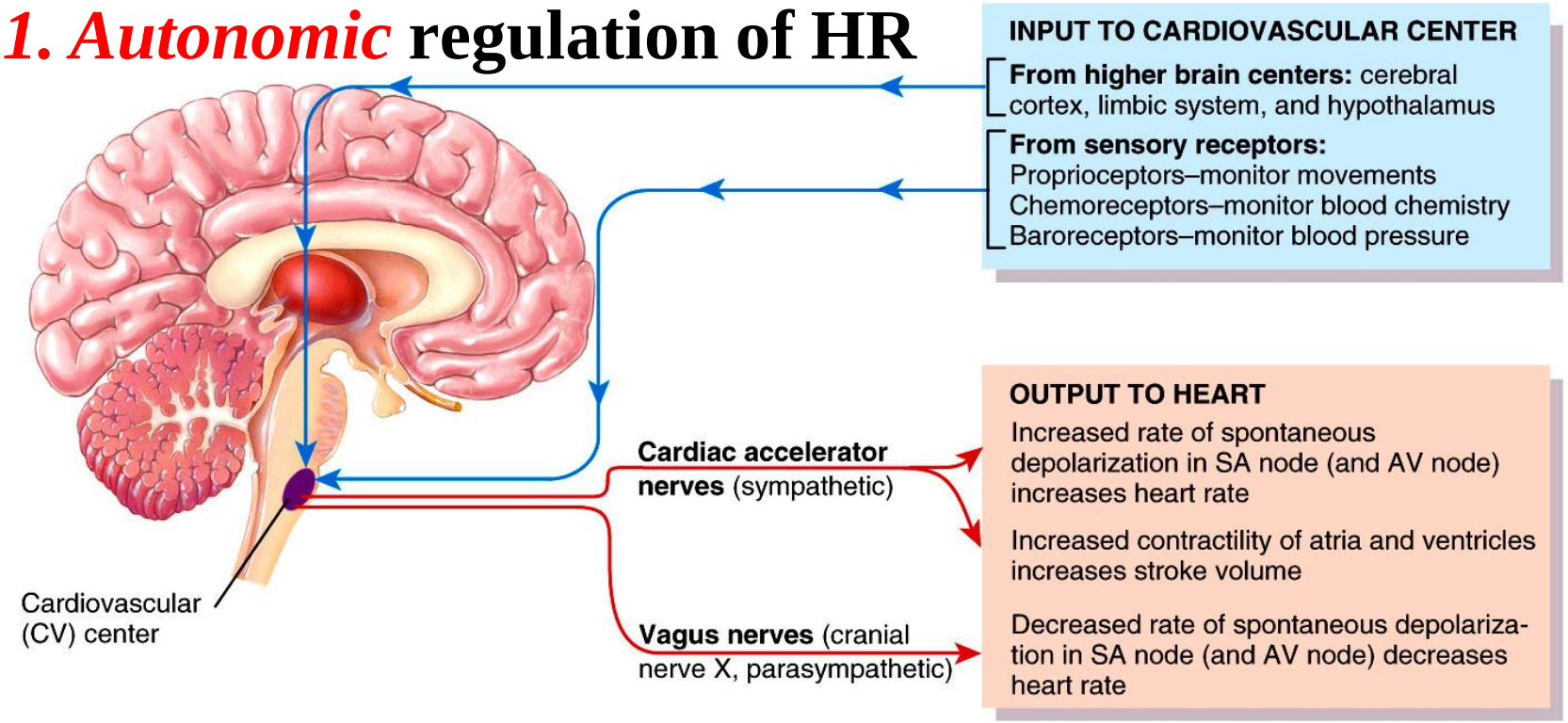
Parasympathetic Regulation of SA cell (Heart Rate)



(b) Parasympathetic

Decrease rate of spontaneous depolarization and hyperpolarize cell (HR↓)

1. Autonomic regulation of HR



2. Chemical regulation of HR

Hormones

--**Epinephrine** and **norepinephrine** increase heart rate and contractility (same effect as sympathetic effect)

--**Glucagon, insulin** and **thyroid hormones** also increase heart rate and contractility

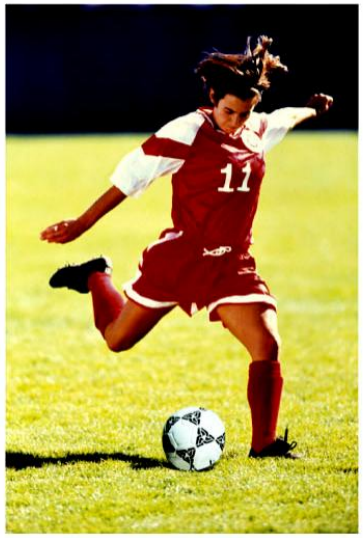
Cations

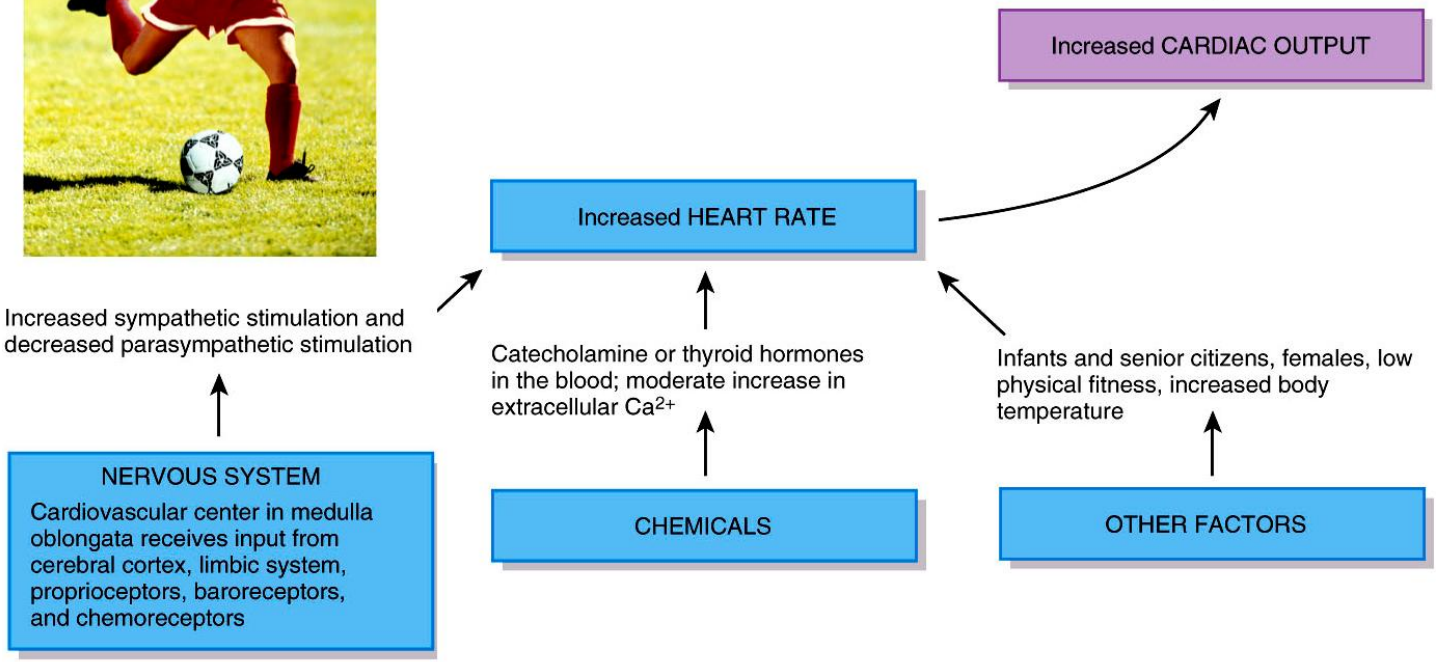
--**Ionic imbalance** can compromise pumping effectiveness

Relative concentration of **K^+, Ca^{2+}** and **Na^+** important

Cardiac Output(CO) =

Heart Rate(HR) × Stroke Volume(SV)





Regulation of Stroke Volume

- **SV= EDV-ESV**
- **3 primary factors affecting stroke volume**
  1. ***End-diastolic volume (preload)***
  2. ***Ventricular contractility (strength of ventricular contraction)***
  3. ***Afterload (total peripheral resistance)***
- **Ventricles never completely empty of blood**

  --Every beat the heart pumps about **60%** of the blood in its chambers or **70 mL**

  --More forceful contraction will expel more blood
- **Extrinsic controls** of SV: Change in **Contractility**

  --**Sympathetic** drive to ventricular muscle fibers

  --**Hormonal** control
- **Intrinsic controls** of SV: Changes in **EDV**

Regulation of Stroke Volume

1. Preload=EDV (Intrinsic controls)

--***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

2. Contractility

--Autonomic nerves, hormones, Ca^{+2} or K^{+} levels (**Extrinsic controls**)

--Is affected by ***positive*** and ***negative inotropic agents***

Positive inotropic agents increase contractility

Negative inotropic agents decrease contractility

3. Afterload

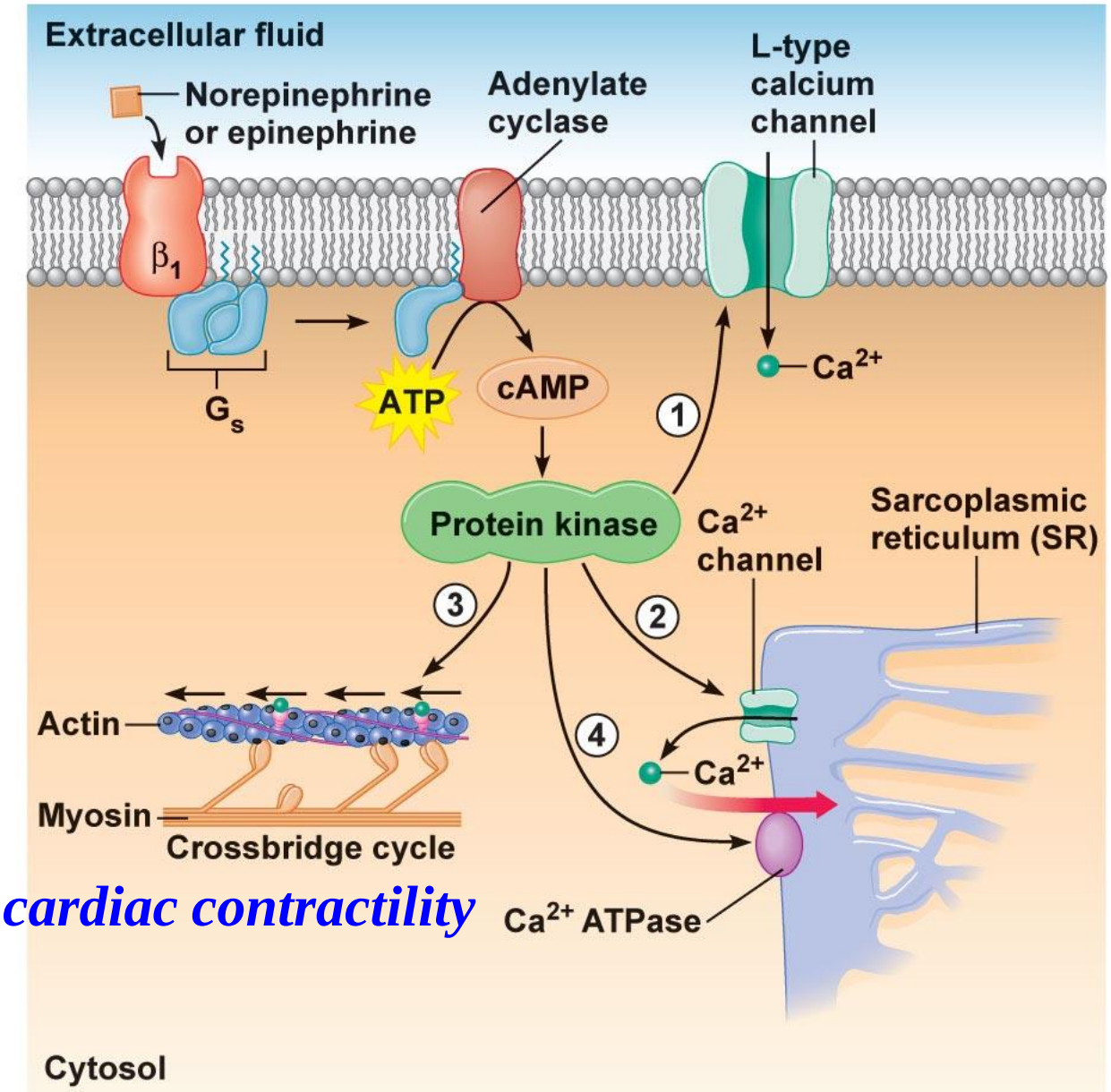
--Amount of **arterial pressure** created by the blood in the way

--High blood pressure creates high afterload

Extrinsic Controls of Stroke Volume

- **Sympathetic innervation of contractile cells**
  - *--Cardiac nerves*
  - *--NE binds to β_1 adrenergic receptors*
  - *--Increases cardiac contractility*
- **Parasympathetic innervation of contractile cells**
  - *--Not significant*
- **Hormones**
  - *--Thyroid hormones, insulin, and glucagon increase force of contraction*

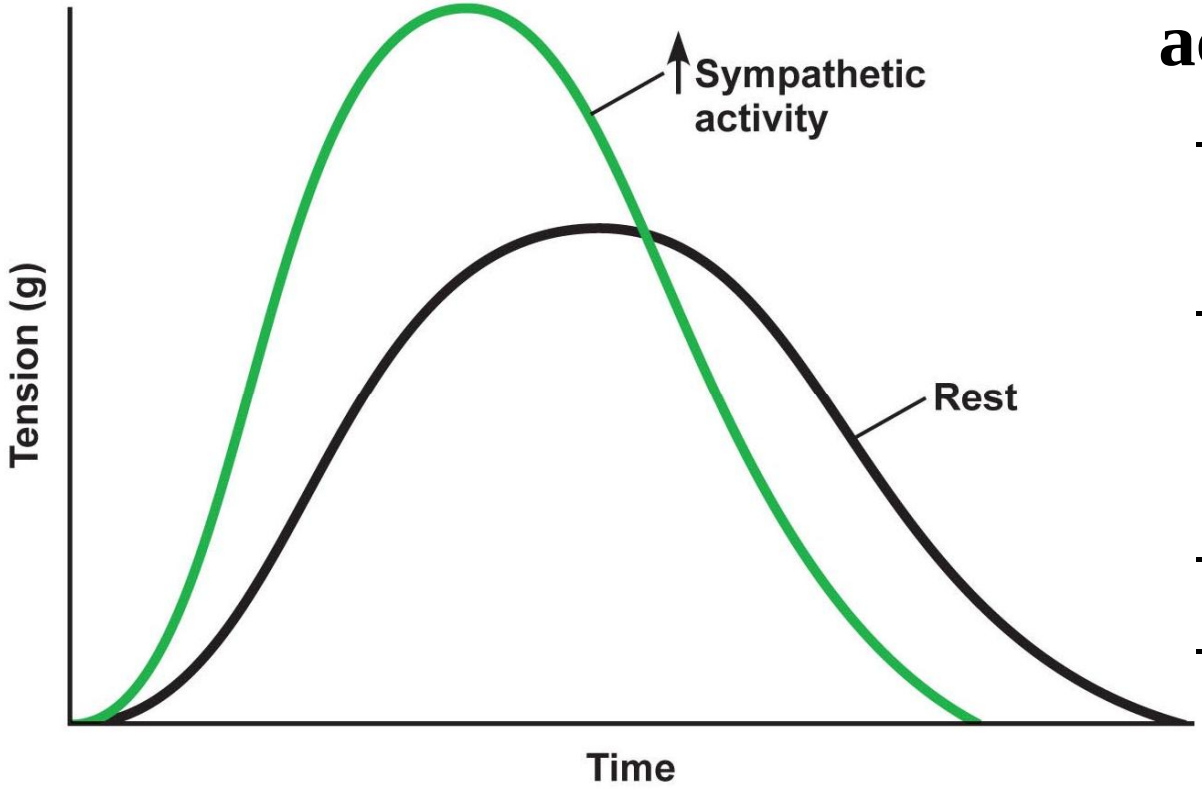
Sympathetic Effects on Contractility



Increases cardiac contractility

Extrinsic Controls of Stroke Volume

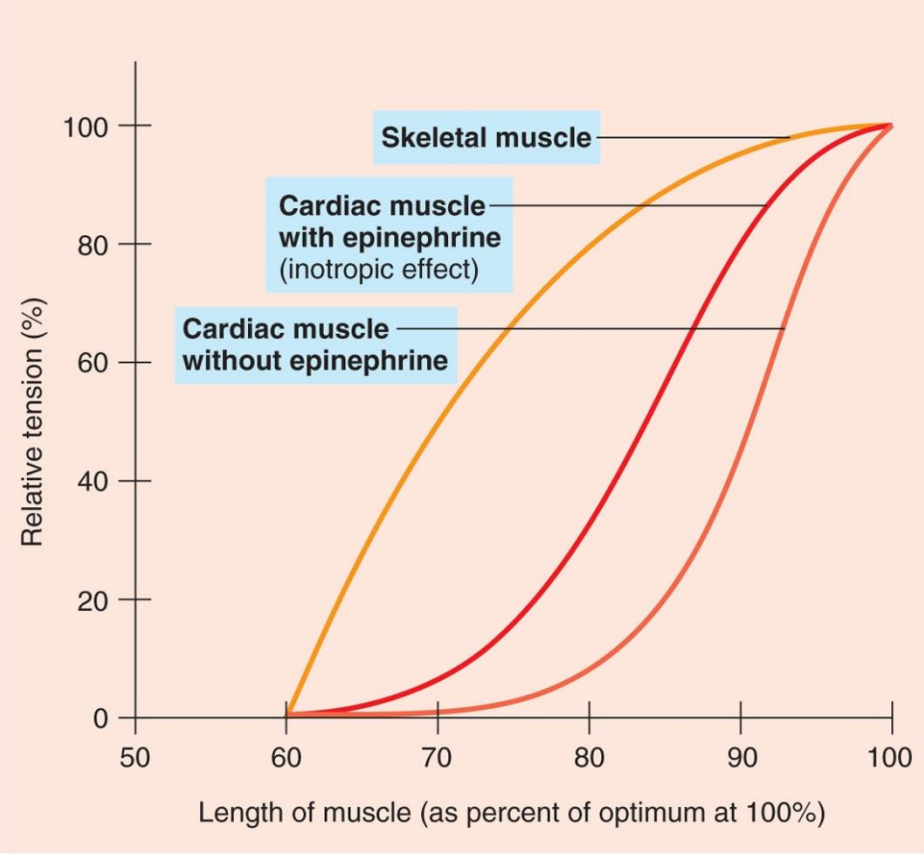
Sympathetic Regulation

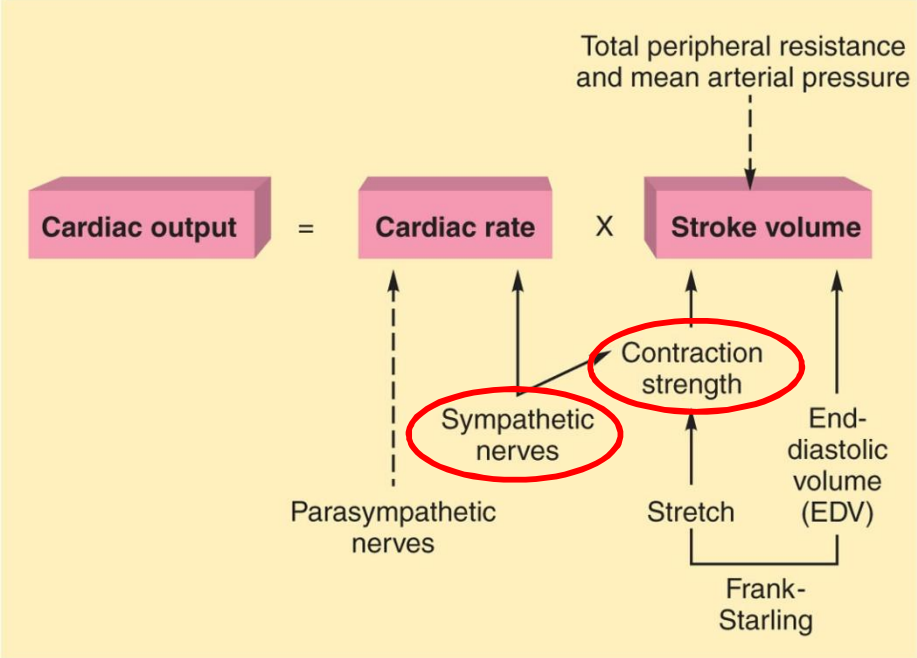


- **Increased sympathetic activity**
  - --Increased ***adrenal epinephrine*** release
  - --Increases strength of contraction (***contractility***)
  - --Increases ***SV***
  - --Increases ***rate of contraction***
  - --Increases ***rate of relaxation***

Extrinsic Controls of Stroke Volume

Sympathetic Regulation





Regulation of Stroke Volume

1. Preload=EDV (Intrinsic controls)

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--More muscle is stretched, greater force of contraction

--More blood more force of contraction results

2. Contractility

--Autonomic nerves, hormones, Ca^{+2} or K^{+} levels (**Extrinsic controls**)

--Is affected by ***positive*** and ***negative inotropic agents***

Positive inotropic agents increase contractility

Negative inotropic agents decrease contractility

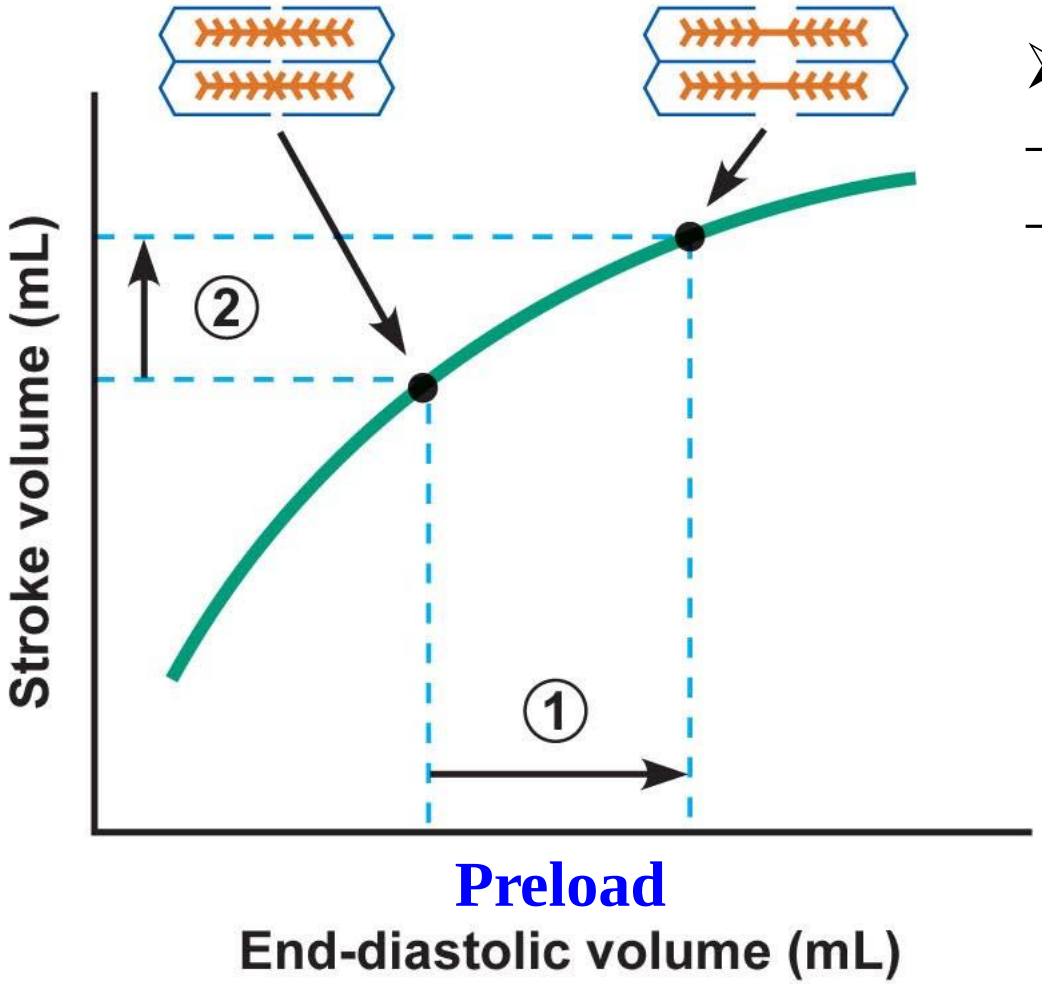
3. Afterload

--Amount of **arterial pressure** created by the blood in the way

--High blood pressure creates high afterload

Intrinsic Controls of Stroke Volume

Frank-Starling's Law



- **Increased EDV**

→ Increased contractility

→ Increased stroke volume

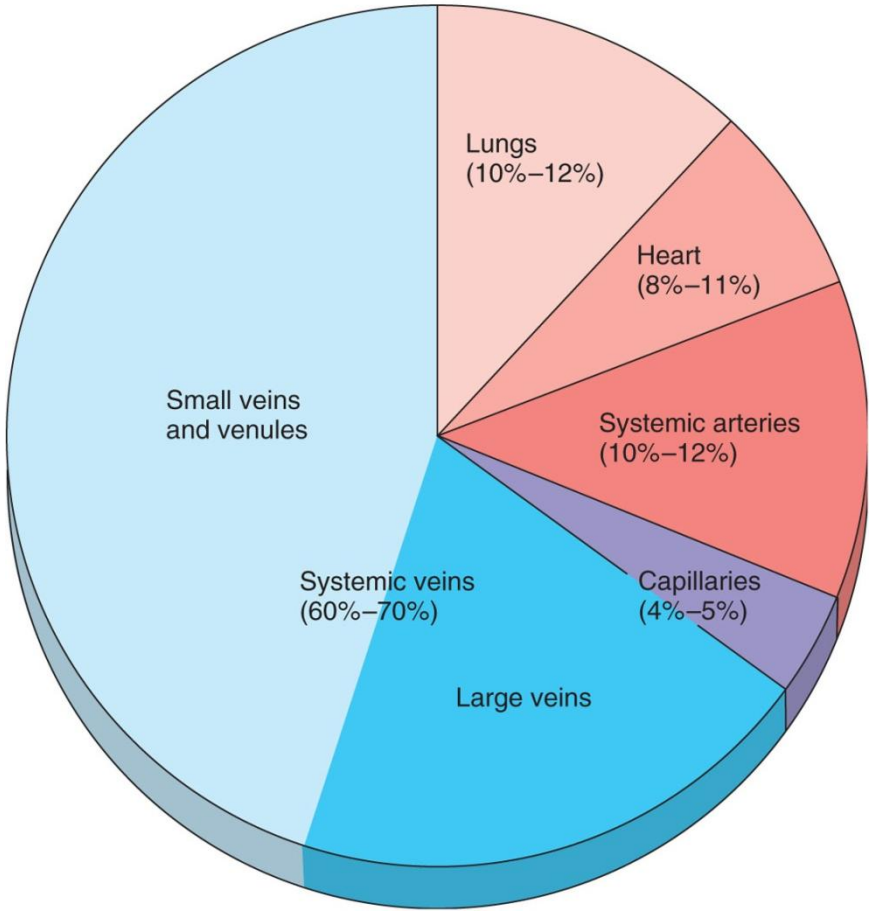
① An increase in EDV . . .
(Increase venous return)

② . . . causes stroke volume to increase

Intrinsic Controls of Stroke Volume

Frank-Starling's Law

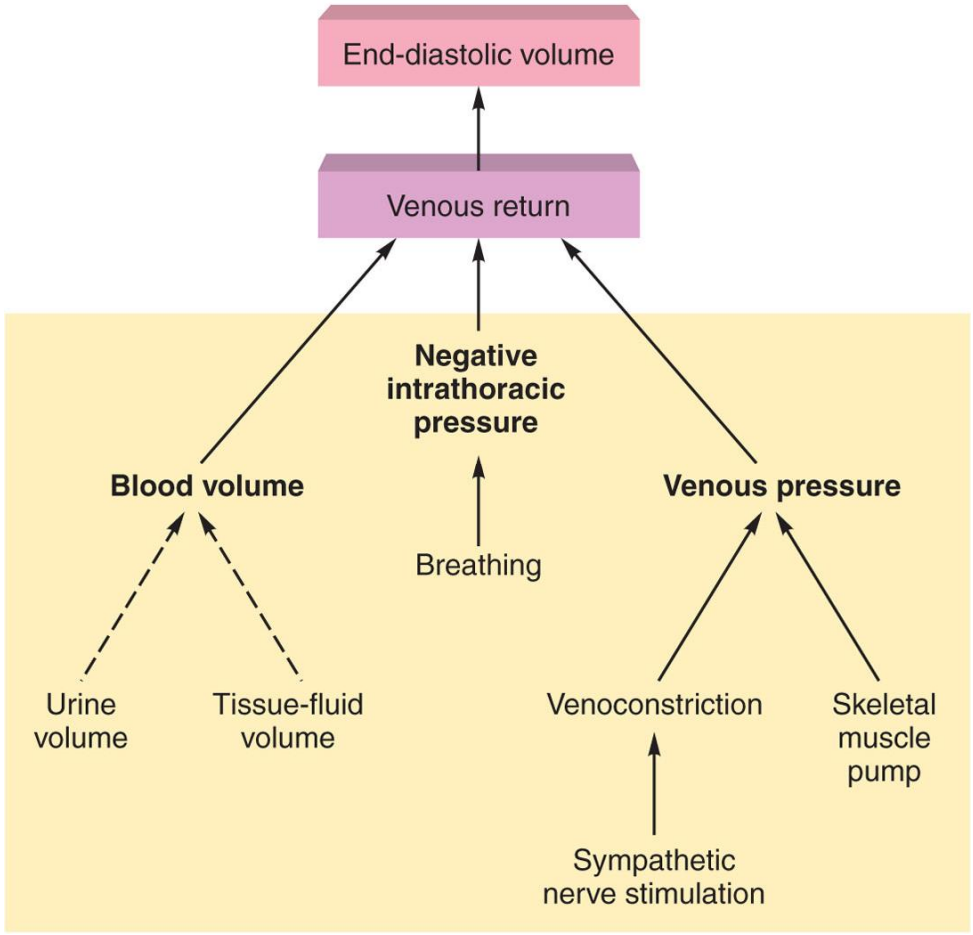
- **End diastolic volume = preload is controlled by factors that affect venous return:**
  - **--*Total blood volume***
  - **--*Venous pressure***

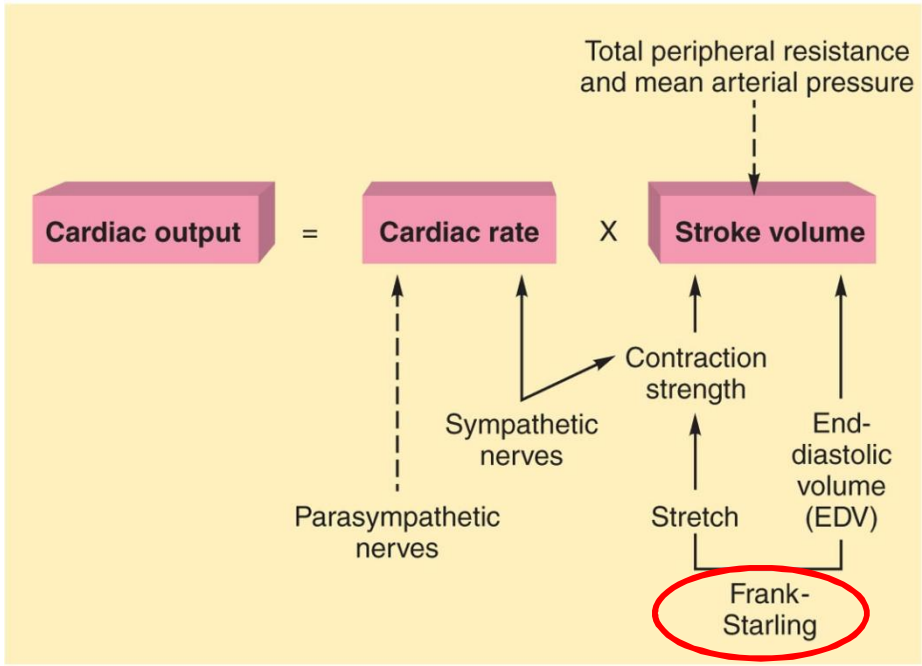


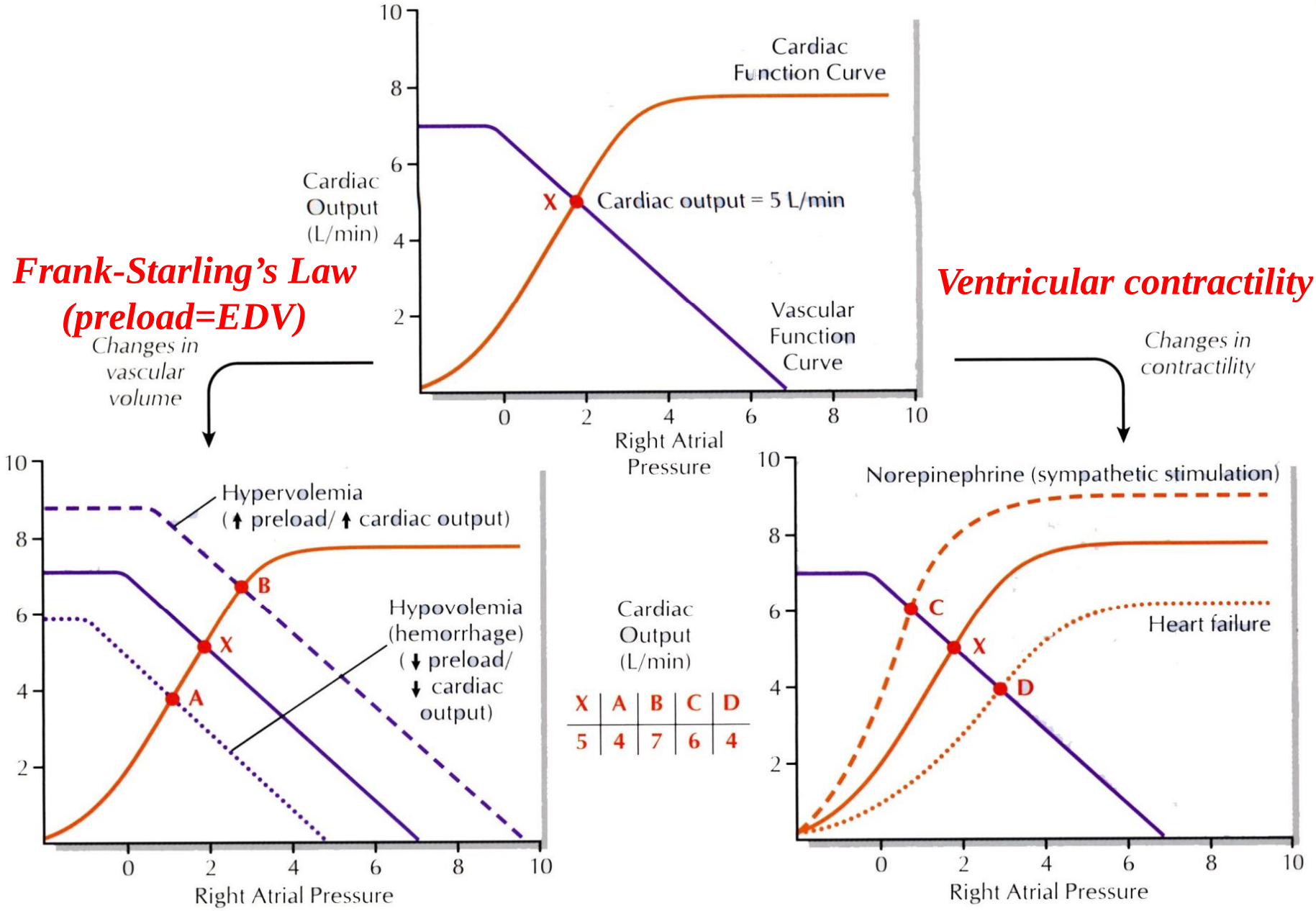
- ***Veins are compliant = stretch at a given pressure. They hold more blood than arteries but maintain lower pressure***

Intrinsic Controls of Stroke Volume

Frank-Starling's Law






Cardiac Function Curve
Cardiac Output (L/min)
X
Cardiac output = 5 L/min
Vascular Function Curve
Right Atrial Pressure
Frank-Starling's Law (preload=EDV)
Changes in vascular volume
Ventricular contractility
Changes in contractility
Hypervolemia (↑ preload/ ↑ cardiac output)
Hypovolemia (hemorrhage) (↓ preload/ ↓ cardiac output)
A
B
X
Right Atrial Pressure
Cardiac Output (L/min)
X A B C D
5 4 7 6 4
Norepinephrine (sympathetic stimulation)
Heart failure
C
X
D
Right Atrial Pressure

Regulation of Stroke Volume

1. Preload=EDV (Intrinsic controls)

--***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

2. Contractility

--Autonomic nerves, hormones, Ca^{+2} or K^{+} levels (**Extrinsic controls**)

--Is affected by ***positive*** and ***negative inotropic agents***

Positive inotropic agents increase contractility

Negative inotropic agents decrease contractility

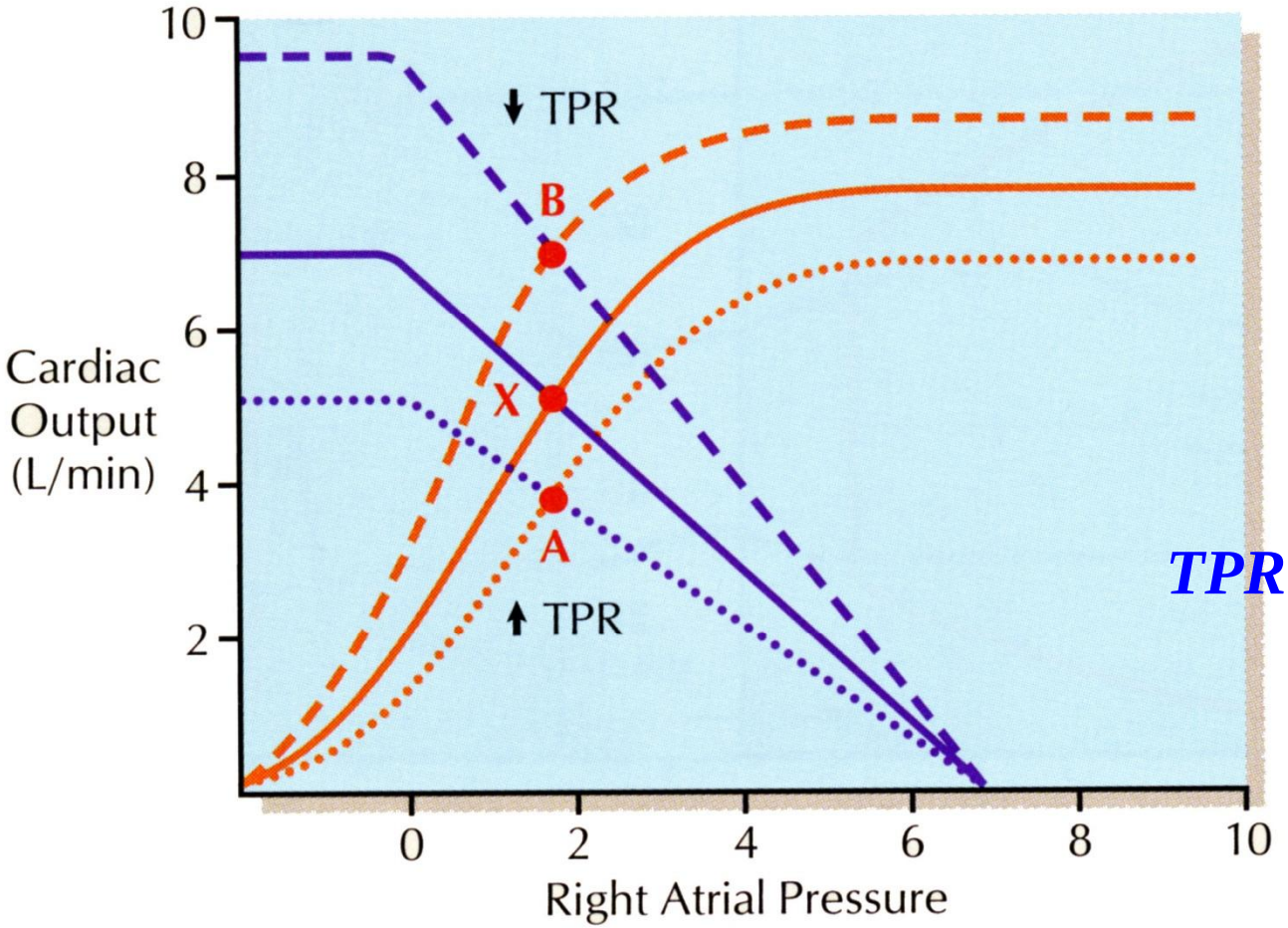
3. Afterload=Total peripheral resistance (TPR)

--Amount of **arterial pressure** created by the blood in the way

--High blood pressure creates high afterload

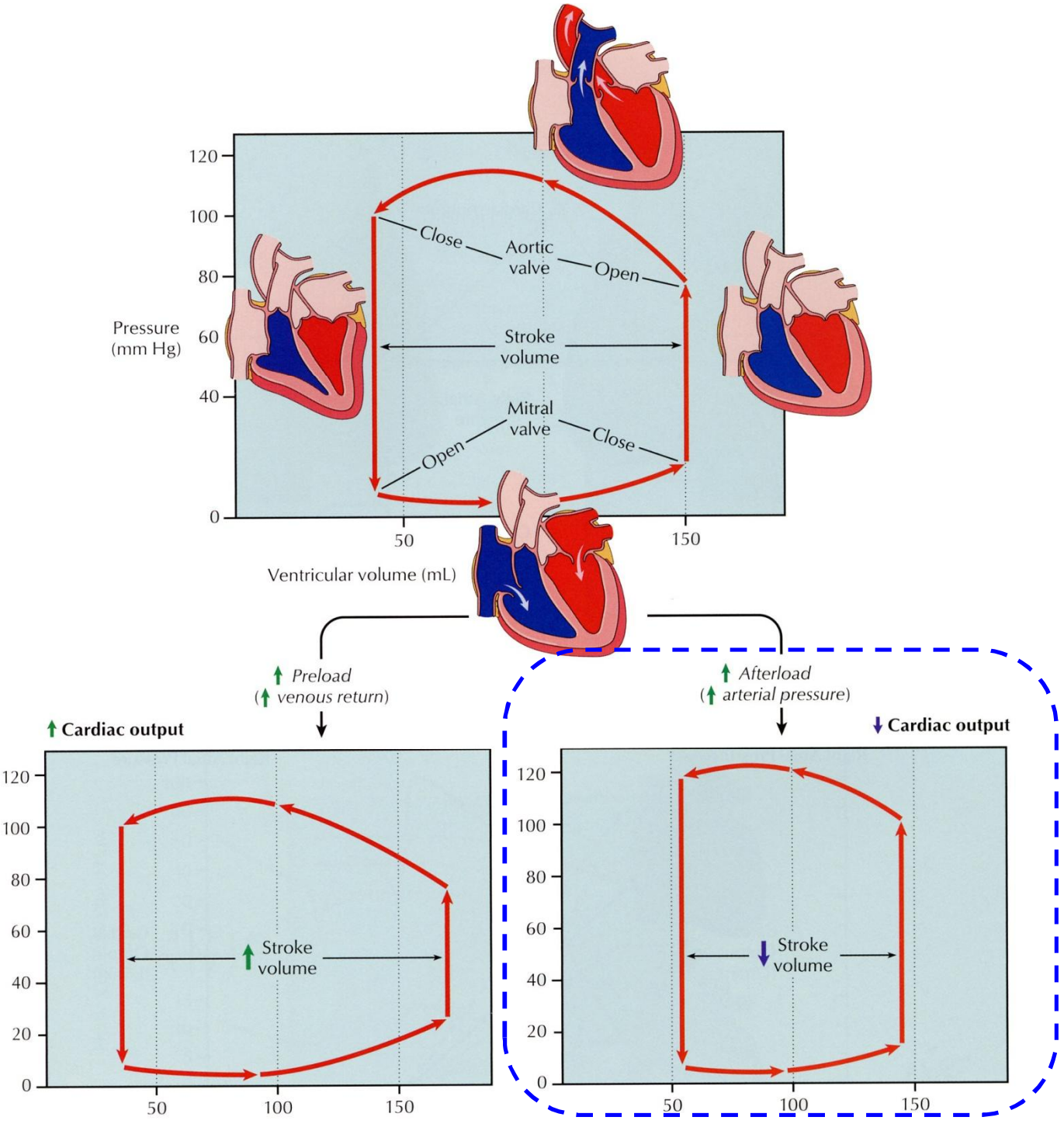
Regulation of Stroke Volume

Afterload (TPR)



A	X	B	Cardiac Output (L/min)
4	5	7	

TPR inversely related to SV or CO


120
100
80
60
40
0
Pressure
(mm Hg)
Close
Aortic
valve
Open
Stroke
volume
Mitral
valve
Open
Close
50
150
Ventricular volume (mL)
↑ Preload
(↑ venous return)
↑ Cardiac output
↑ Stroke
volume
↑ Afterload
(↑ arterial pressure)
↓ Cardiac output
↓ Stroke
volume

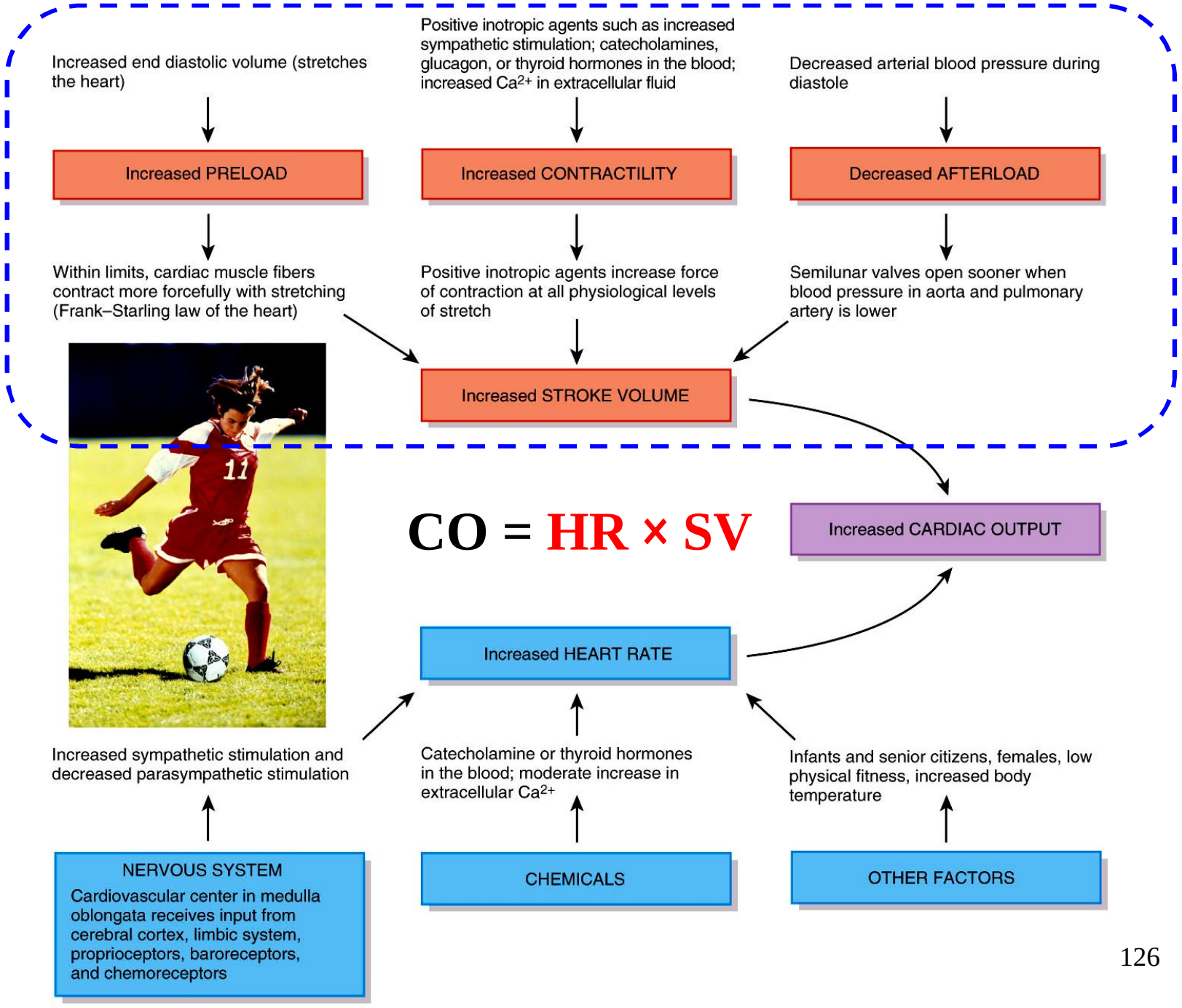
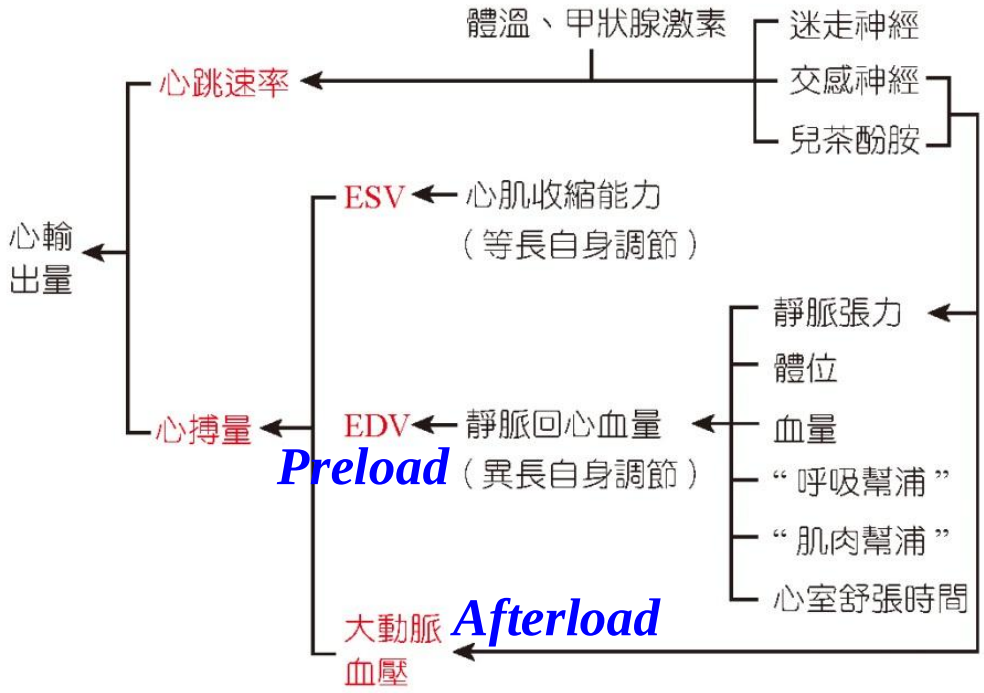

Increased end diastolic volume (stretches the heart)
Positive inotropic agents such as increased sympathetic stimulation; catecholamines, glucagon, or thyroid hormones in the blood; increased Ca^{2+} in extracellular fluid
Decreased arterial blood pressure during diastole
Increased PRELOAD
Increased CONTRACTILITY
Decreased AFTERLOAD
Within limits, cardiac muscle fibers contract more forcefully with stretching (Frank–Starling law of the heart)
Positive inotropic agents increase force of contraction at all physiological levels of stretch
Semilunar valves open sooner when blood pressure in aorta and pulmonary artery is lower
Increased STROKE VOLUME
CO = HR × SV
Increased CARDIAC OUTPUT
Increased HEART RATE
Increased sympathetic stimulation and decreased parasympathetic stimulation
Catecholamine or thyroid hormones in the blood; moderate increase in extracellular Ca^{2+}
Infants and senior citizens, females, low physical fitness, increased body temperature
NERVOUS SYSTEM
Cardiovascular center in medulla oblongata receives input from cerebral cortex, limbic system, proprioceptors, baroreceptors, and chemoreceptors
CHEMICALS
OTHER FACTORS

表 11-10　影響心輸出量的因素　$CO = HR \times SV$

影響因素 ＼ 影響效果		搏出量	心輸出量
心室舒張末期容積 (EDV) ↑		↑	↑
心室收縮末期容積 (ESV) ↑		↓	↓
心肌收縮能力 ↑		↑	↑
心跳速率 ↑	極限量小於 180 次 / 分		↑
	極限量大於 180 次 / 分	↓	↓



心衰竭 (Heart Failure)

心衰竭是指心臟結構或功能性疾病導致心肌收縮力下降，心臟不能排出足夠血液滿足組織代謝需要，以致於周圍組織灌注不足，出現肺循環或體循環淤血，臨床主要表現是呼吸困難和無力引起的體力活動受阻和水腫。

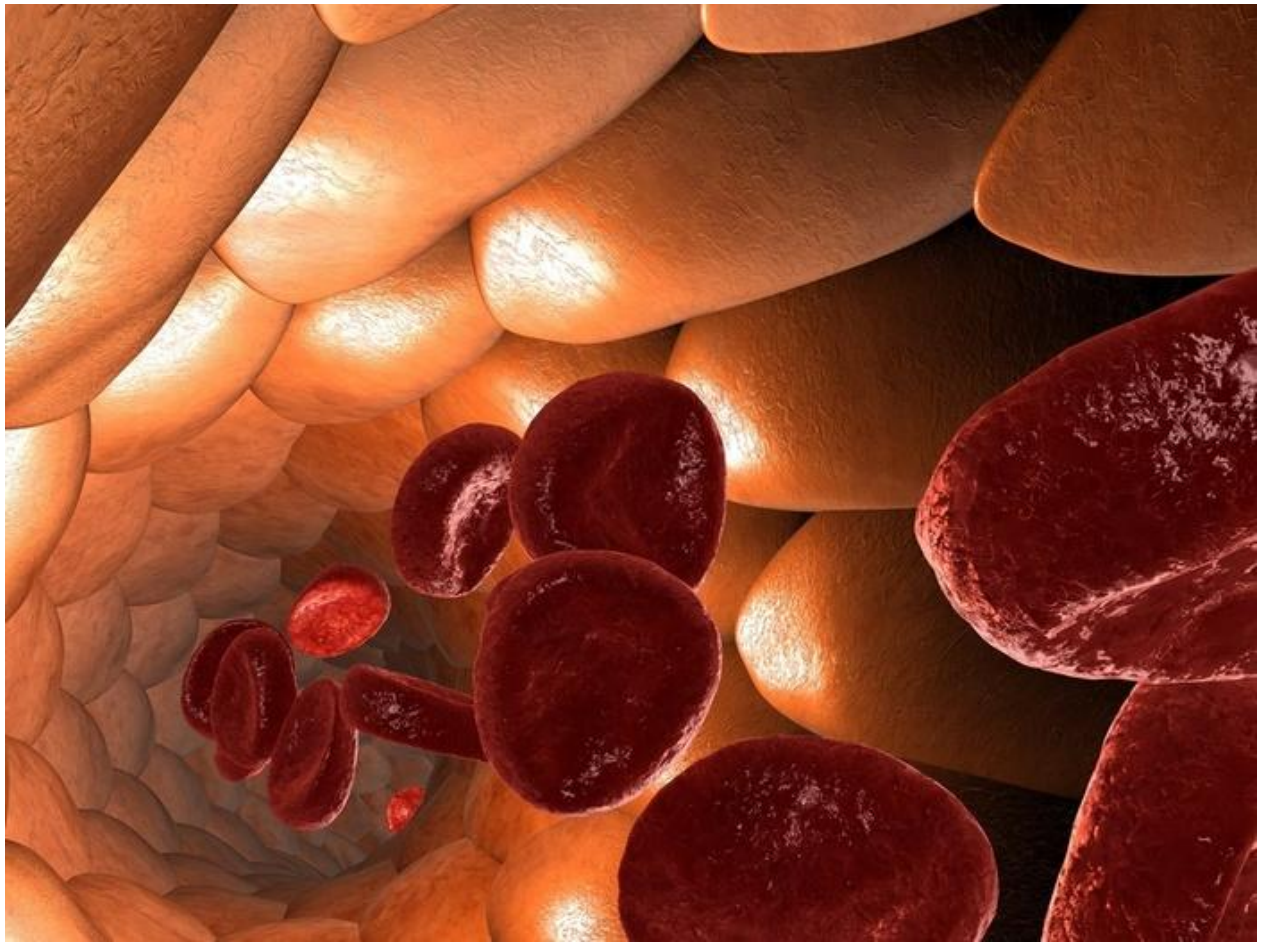
按發病部位和臨床表現常分為左心衰竭、右心衰竭和全心衰竭。左心衰竭是指左心室代償功能不全而發生的心衰竭，臨床上常見於高血壓、主動脈瓣狹窄、肥厚性梗阻性心肌病引起，以肺循環淤血為特徵。右心衰竭常見於肺心病、肺動脈高壓、肺動脈瓣狹窄等，以體循環淤血為特徵。左心衰竭後，肺動脈壓力增高，使右心負荷加重，長時間後，出現右心衰竭，即為全心衰竭。心肌炎、心肌病患者可出現全心衰竭。

按疾病的急緩分為急性和慢性心衰竭。急性心衰竭臨床上以急性左心衰竭最常見，表現為急性肺水腫或心源性休克；慢性心衰竭是一個緩慢的發展過程，一般有代償性心臟擴大或肥厚及其他代償機制參與。

按發病機制分為收縮性心衰竭和舒張性心衰竭。收縮性心衰竭的特點是心臟增大，收縮末期心室容積增加和射血率 (ejection fraction) 下降，是臨床上常見的心衰竭。舒張性心衰竭是由於心室鬆弛性降低，僵硬度增加，使心室舒張期充血受限，心室舒張末期壓力升高和心搏量減少，心肌常顯著肥厚，心臟大小正常、射血率無明顯減少，患者心衰竭症狀也不太明顯，可見於高血壓、冠心病的某一階段，嚴重者見於原發性限制型心肌病、原發性梗阻性肥厚型心肌病。通常舒張性心衰竭發生在先，進而發生收縮功能障礙。

Blood Vessels

The Cardiovascular System:
Blood Vessels, Blood Flow and Blood Pressure



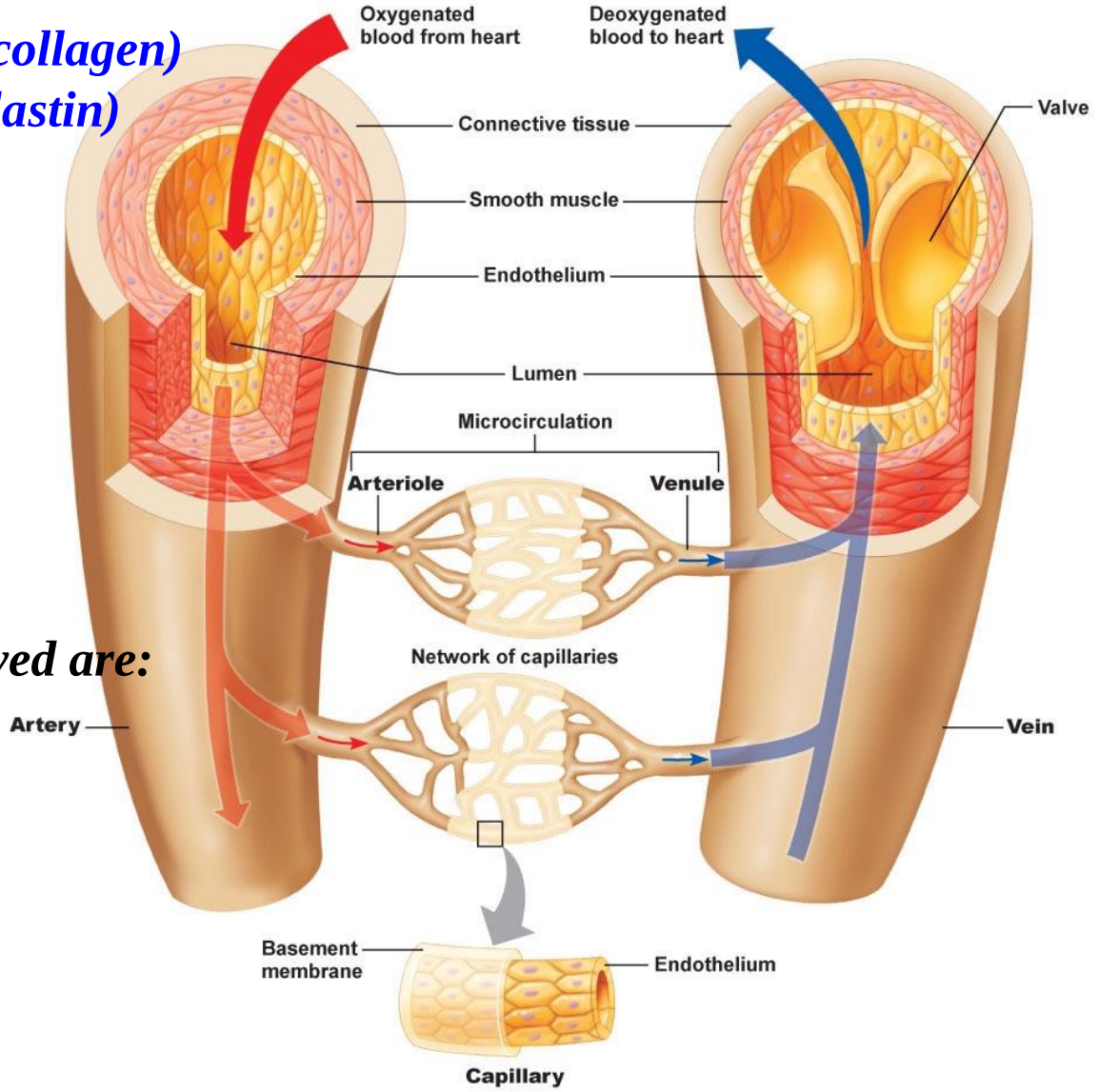
Structure and Function of Blood Vessels

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 **AWAY** from the heart
  - ***--Microcirculation***
    - ✓ ***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*** carry blood **TO** the heart

Types of Blood Vessels

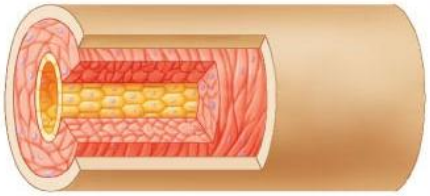
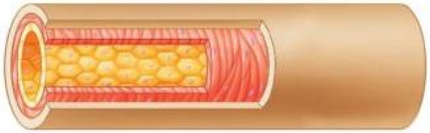
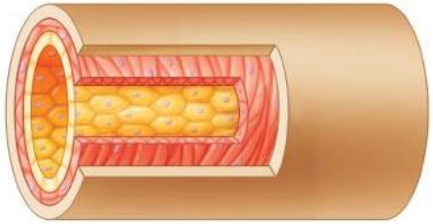
- *Fibrous connective tissue (collagen)*
- *Elastic connective tissue (elastin)*



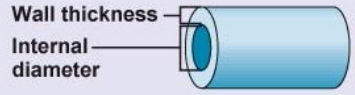
The types of structures involved are:

1. *Arteries*
   - *–Elastic arteries*
   - *–Muscular arteries*
   - *–Arterioles*
   - *–Capillaries*
2. *Veins*
   - *–Venules*

Blood Vessel Characteristics

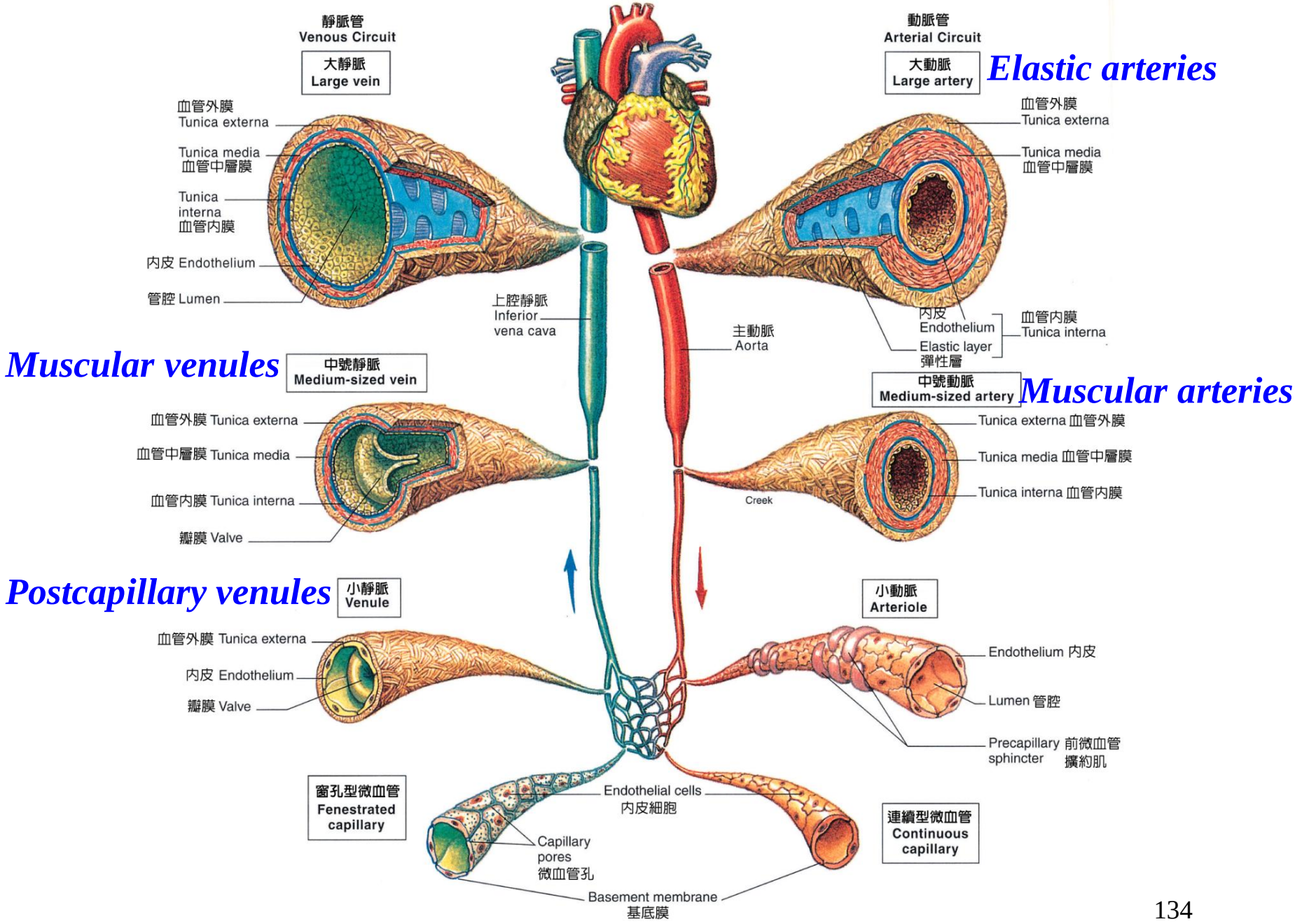
Average internal diameter (mm)	Average wall thickness (mm)		Special features
4.0	1.0	 Artery	Muscular, highly elastic
0.03	0.006	 Arteriole	Muscular, well innervated
0.008	0.0005	 Capillary	Thin-walled, highly permeable
0.02	0.001	 Venule	Thin-walled, some smooth muscle
5.0	0.5	 Vein	Thin-walled (compared to arteries), fairly muscular, highly distensible

= Endothelium
= Smooth muscle
= Connective tissue



Basic structure of Blood Vessel

- **The walls of arteries and veins have three layers or tunics:**
  - **--Tunica interna (intima):** inner layer; composed of simple squamous endothelium on a basement membrane and connective tissue
  - **--Tunica media:** middle layer; composed of smooth muscle tissue (regulates diameter of lumen)
  - **--Tunica externa:** outer layer; composed of connective tissue (helps anchor vessel to surrounding tissue)

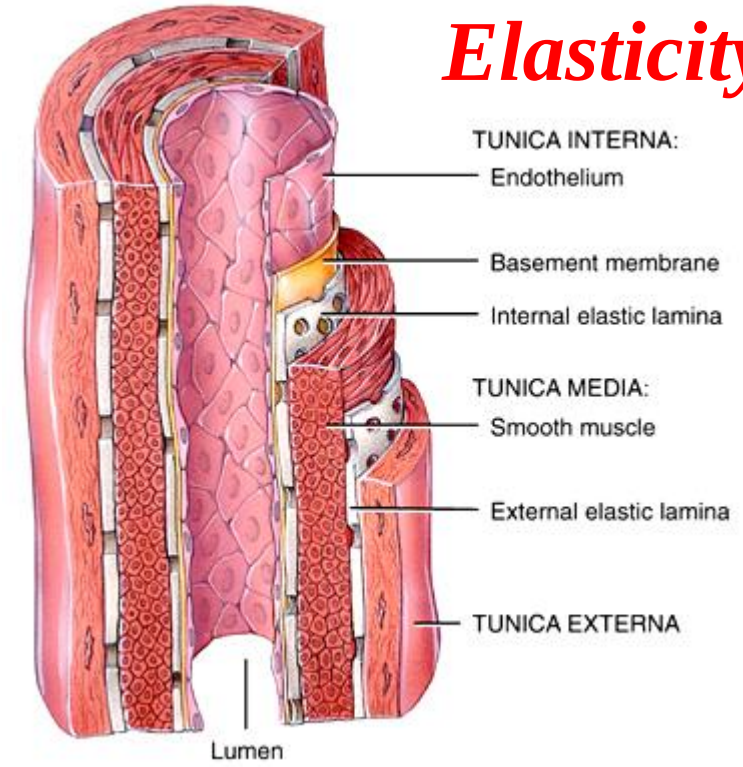

靜脈管
Venous Circuit
大靜脈
Large vein
血管外膜
Tunica externa
Tunica media
血管中層膜
Tunica
interna
血管內膜
內皮 Endothelium
管腔 Lumen
上腔靜脈
Inferior
vena cava
主動脈
Aorta
動脈管
Arterial Circuit
大動脈
Large artery
血管外膜
Tunica externa
Tunica media
血管中層膜
內皮
Endothelium
Elastic layer
彈性層
血管內膜
Tunica interna
Elastic arteries
Muscular venules
中號靜脈
Medium-sized vein
血管外膜 Tunica externa
血管中層膜 Tunica media
血管內膜 Tunica interna
瓣膜 Valve
中號動脈
Medium-sized artery
Muscular arteries
Tunica externa 血管外膜
Tunica media 血管中層膜
Tunica interna 血管內膜
Creek
Postcapillary venules
小靜脈
Venule
血管外膜 Tunica externa
內皮 Endothelium
瓣膜 Valve
小動脈
Arteriole
Endothelium 內皮
Lumen 管腔
Precapillary
sphincter
前微血管
擴約肌
窗孔型微血管
Fenestrated
capillary
Endothelial cells
內皮細胞
Capillary
pores
微血管孔
Basement membrane
基底膜
連續型微血管
Continuous
capillary

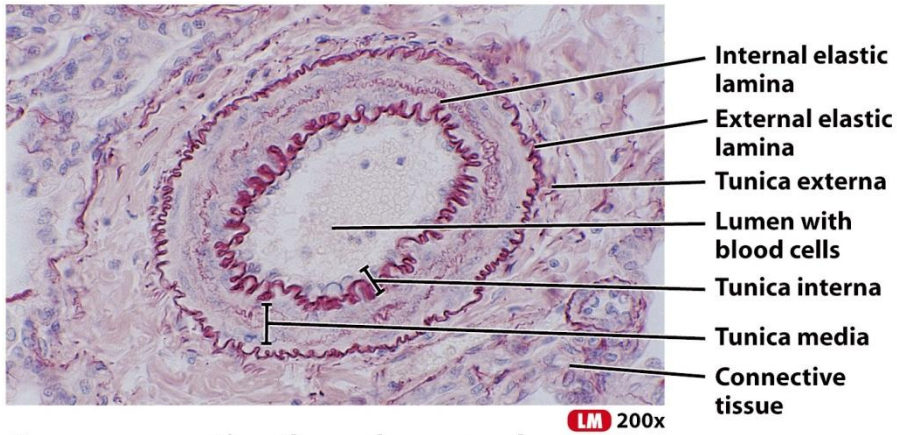
Distinguishing Features of Blood Vessels

BLOOD VESSEL	SIZE	TUNICA INTERNA	TUNICA MEDIA	TUNICA EXTERNA	FUNCTION
Elastic arteries	Largest arteries in the body.	Well-defined internal elastic lamina.	Thick and dominated by elastic fibers; well-defined external elastic lamina.	Thinner than tunica media.	Conduct blood from the heart to muscular arteries.
Muscular arteries	Medium-sized arteries.	Well-defined internal elastic lamina.	Thick and dominated by smooth muscle; thin external elastic lamina.	Thicker than tunica media.	Distribute blood to arterioles.
Arterioles	Microscopic (15–300 μm in diameter).	Thin with a fenestrated internal elastic lamina that disappears distally.	One or two layers of circularly oriented smooth muscle; distal-most smooth muscle cell forms a precapillary sphincter.	Loose collagenous connective tissue and sympathetic nerves.	Deliver blood to capillaries and help regulate blood flow from arteries to capillaries.
Capillaries	Microscopic; smallest blood vessels (5–10 μm in diameter).	Endothelium and basement membrane.	None.	None.	Permit exchange of nutrients and wastes between blood and interstitial fluid; distribute blood to postcapillary venules.
Postcapillary venules	Microscopic (10–50 μm in diameter).	Endothelium and basement membrane.	None.	Sparse.	Pass blood into muscular venules; permit exchange of nutri-ents and wastes between blood and interstitial fluid and function in white blood cell emigration.
Muscular venules	Microscopic (50–200 μm in diameter).	Endothelium and basement membrane.	One or two layers of circularly oriented smooth muscle.	Sparse.	Pass blood into vein; reservoirs for accumulating large volumes of blood (along with postcapillary venules.
Veins	Range from 0.5 mm–3 cm in diameter.	Endothelium and basement membrane; no internal elastic lamina; contain valves; lumen is much larger than in accompanying artery.	Much thinner than in arteries; no external elastic lamina.	Thickest of the three layers.	Return blood to the heart, facilitated by valves in veins in limbs.

Arteries

Elasticity & Contractility





Transverse section through a muscular artery

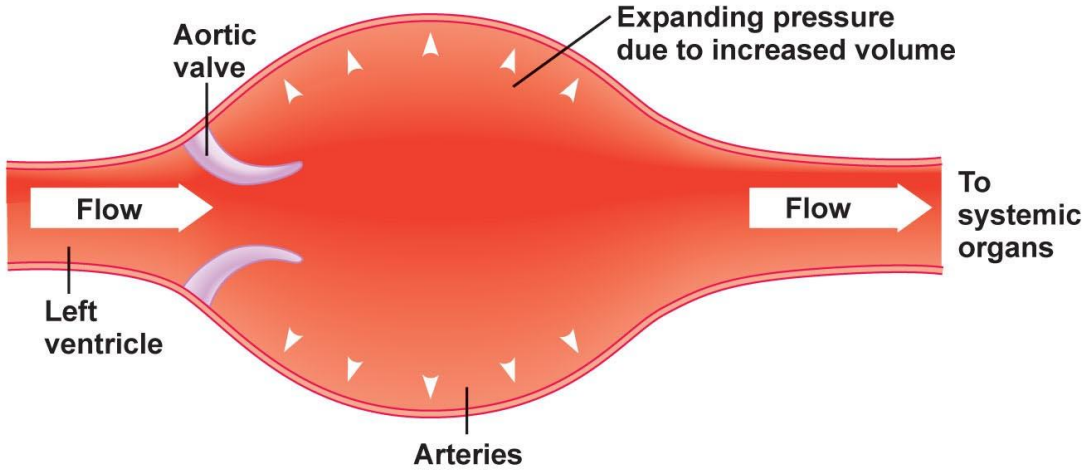
- The wall of an artery consists of three major layers
- **Tunica interna (intima)**
  - --simple squamous epithelium known as **endothelium**
  - --basement membrane
  - --internal elastic lamina
- **Tunica media**
  - --circular **smooth muscle** & elastic fibers
- **Tunica externa**
  - --elastic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

Arteries as Pressure Reservoirs

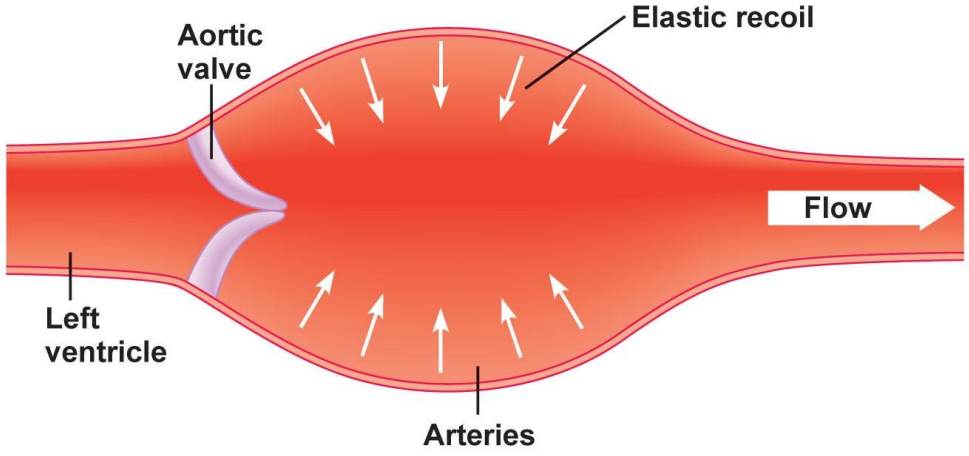
Elasticity & Contractility

- **Rapid transport pathway**
  - ***--Large diameter and Little resistance***
- **Walls contain elastic and fibrous (collagen) tissue**
  - ***--Under high pressure***
- **Arteries as a pressure reservoir =storage site for pressure**
  - ***--Thick elastic arterial walls***
  - ***--Low compliance***
  - ***--Expand as blood enters arteries during systole***
  - ***--Recoil during diastole***
- **Vasoconstriction** – decrease in lumen diameter
- **Vasodilation** – increase in lumen diameter

Arteries as Pressure Reservoirs



(a) Systole



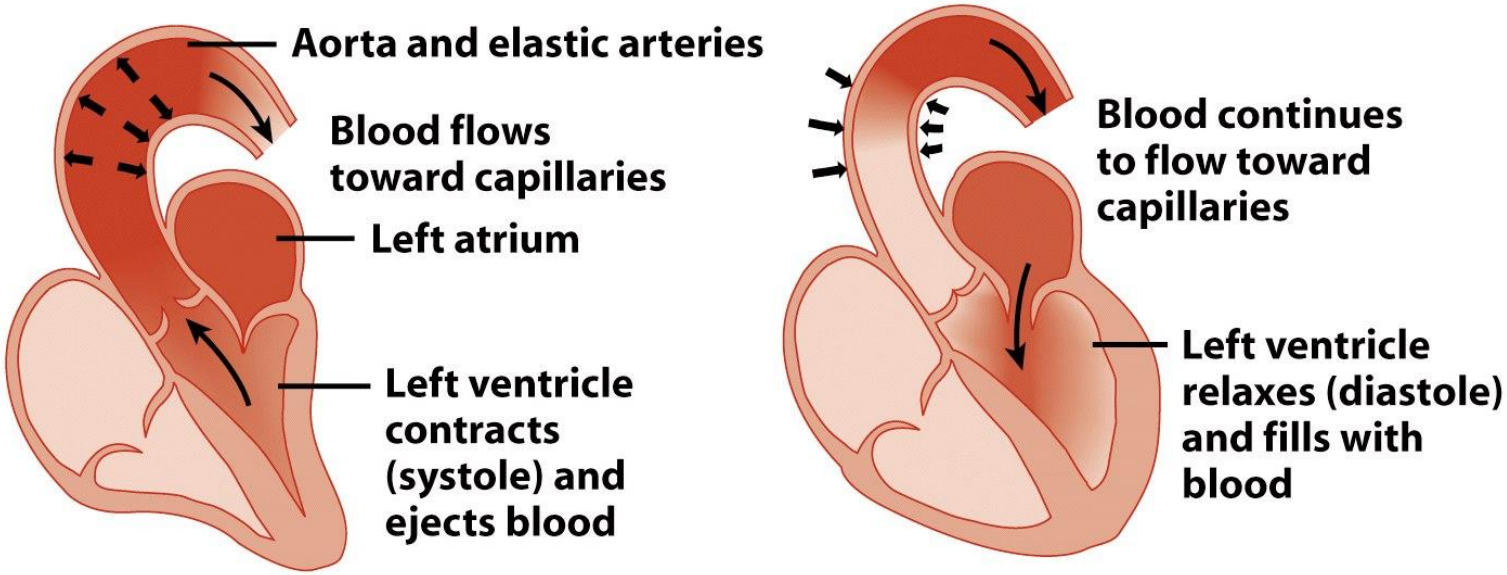
(b) Diastole

Sympathetic Innervation of Arteries

- **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

- **Largest arteries** with more elastic fibers and less smooth muscle are called ***elastic arteries*** (**aorta**) 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

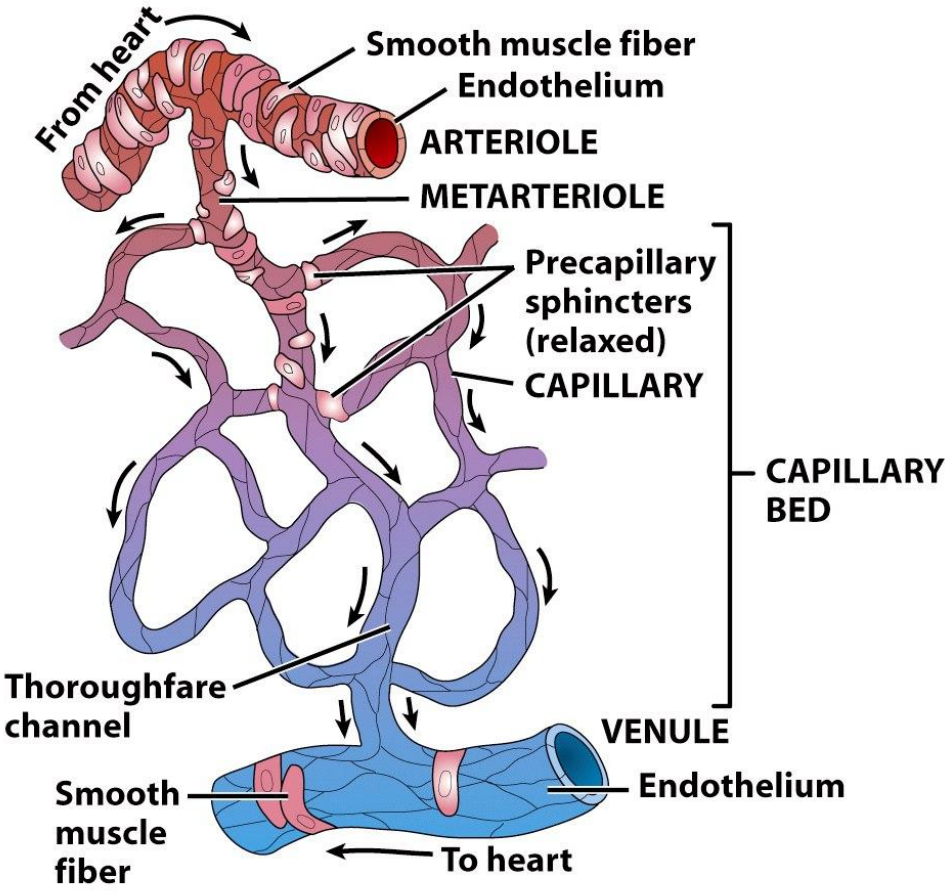
- These arteries deliver blood to **specific organs** (**mesenteric artery**, **renal artery** etc.)
- ***Medium-sized arteries*** with more muscle than elastic fibers in tunica media (little elastin)
- These arteries can play a large role in the regulation of **blood pressure (smooth muscle regulates radius)**
  --For example, the mesenteric artery carries ~25 % of the CO, so alterations in its diameter would have a large effect
- Capable of **greater vasoconstriction and vasodilation** to adjust **rate of flow**
  --walls are relatively thick
  --called ***distributing arteries*** because they direct blood flow

動脈粥狀硬化 (Atherosclerosis)

動脈粥狀硬化係指動脈發生非發炎性、退行性和增生性的病變。主要常見於體循環的大型動脈（如主動脈）和中型動脈（如冠狀動脈和腦動脈）。內膜有黃色粥狀外觀的脂質積聚、血栓形成、纖維組織增生，並合併有動脈中層的逐漸退化和鈣化等多種病變，而產生血管壁增厚變硬、失去彈性和管腔縮小堵塞的特徵，使得受阻動脈遠端缺血，導致局部組織壞死，是形成心臟和腦缺血疾病的主要原因。常見病因有高血壓、高血脂症、吸菸、糖尿病、肥胖等。

動脈粥狀硬化的症狀主要取決於血管病變及受波及器官的缺血程度，可能發生心絞痛、心肌梗塞、心律不整、腦缺血、腦萎縮、高血壓、下肢間歇性跛行等。臨床常用治療包括：均衡飲食、適量的活動、不吸菸、控制危險因素（如高血壓、高膽固醇、糖尿病等）及使用藥物（如降血脂藥、抗血小板藥物）等。

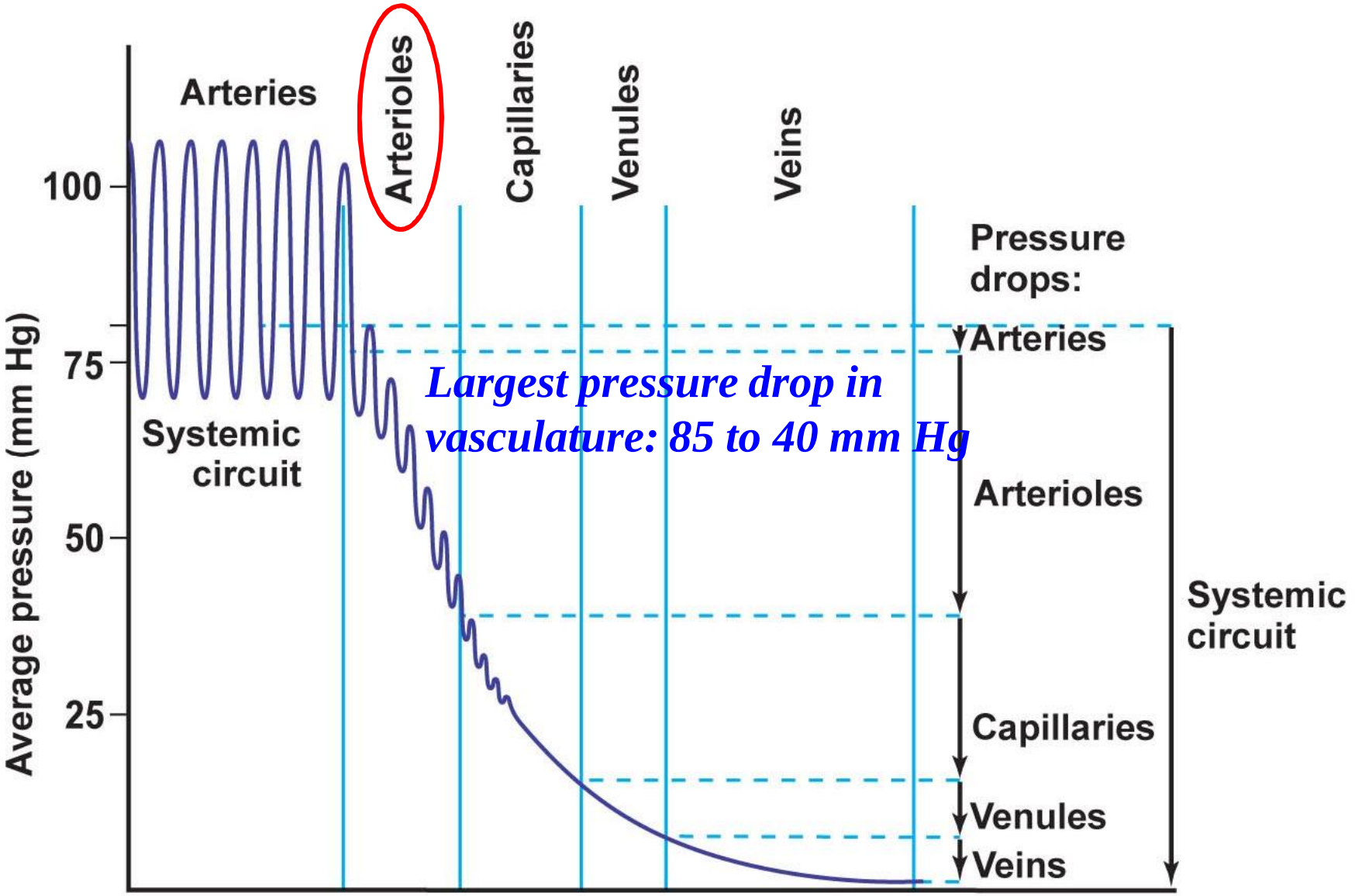
Arterioles



Sphincters relaxed: blood flowing through capillary bed

- ***Arterioles*** ***(resistance arteries)*** are the smallest arteries (tunica media containing few layers of muscle)
  - --Part of microcirculation
  - --Connect arteries to capillaries or metarterioles
  - --Contain rings of **smooth muscle** to regulate radius, and thus, resistance (**altering blood flow and arterial blood pressure**)
- Their diameter is controlled by **neural, hormonal, and local chemicals**
- Arterioles provide **greatest resistance to blood flow (*F* = Δ*P*/*R*)**

Blood Pressure in Vessels



Changes in Arteriole Radius

Radius dependent on ***contraction state of smooth muscle in arteriole wall***

- **Arteriolar tone**

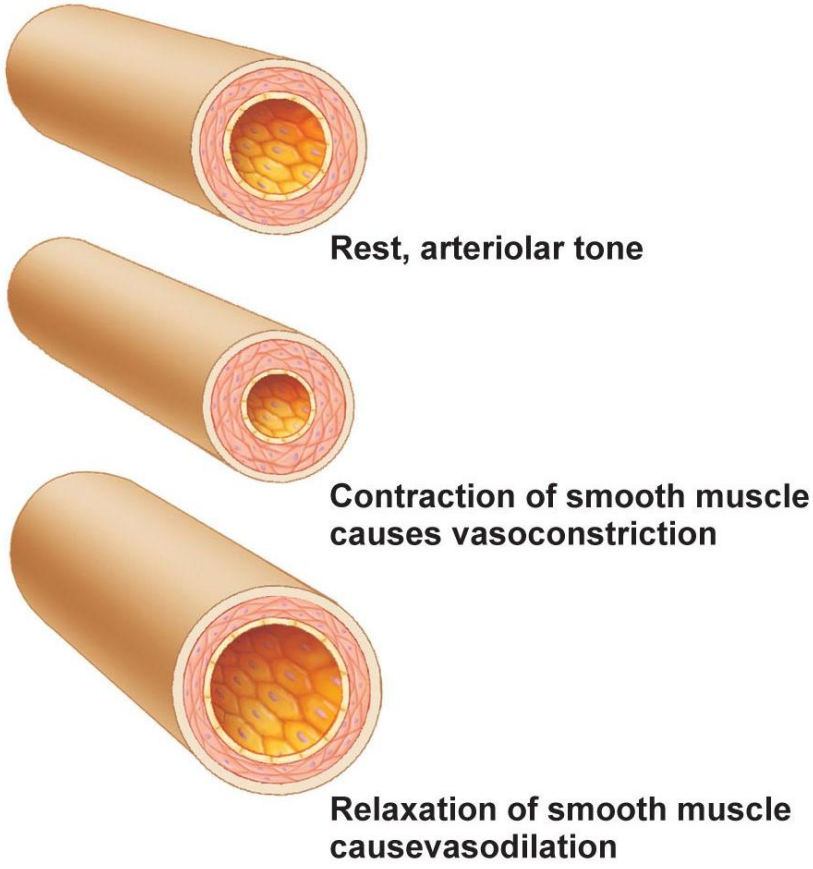
  --Contraction level (radius) independent of extrinsic influences

- **Vasoconstriction**

  --Increased contraction (decreased radius)

- **Vasodilation**

  --Decreased contraction (increased radius)



Functions: 1. Controlling blood flow to individual capillary beds

2. Regulating mean arterial pressure

Intrinsic Control of Arteriole Radius

- Regulation of **blood flow to organs** based on **need**
- Regulated by **varying resistance**

  $F = \Delta P/R$

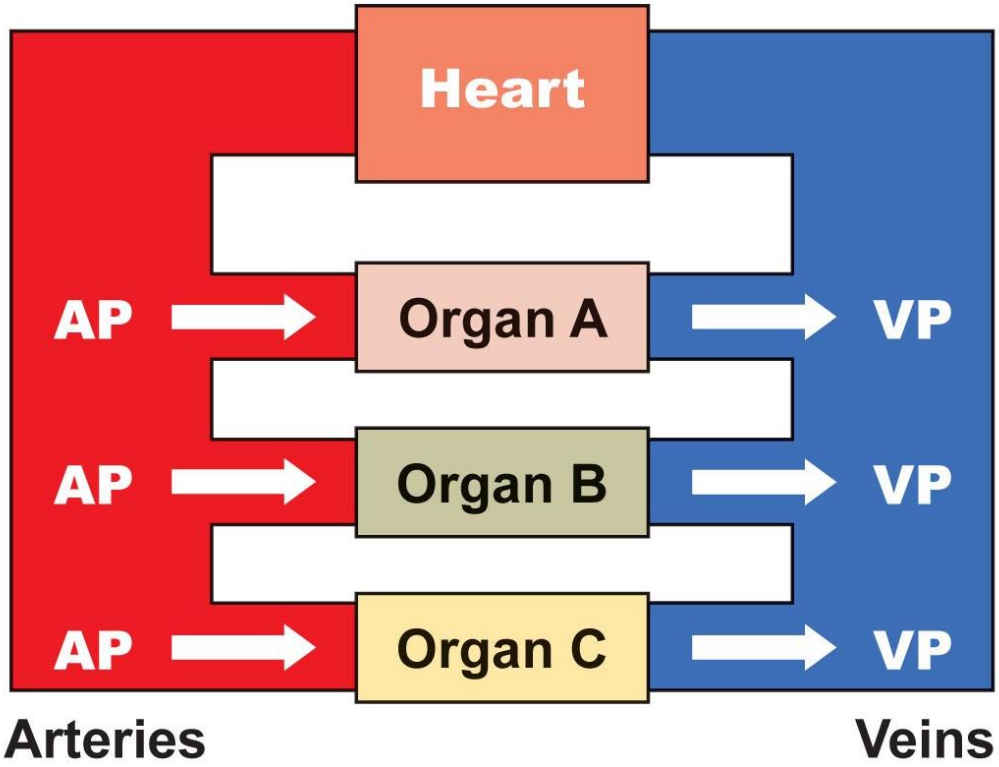
  --If you increase resistance by ***vasoconstriction*** and keep pressure the same, then flow to a tissue decreases

  --If you need to increase flow to a tissue, then you either ***increase the pressure*** or ***vasodilate*** to decrease resistance

  Ex. ***Organ blood flow = ΔP / organ resistance***

Arteriole Radius and Blood Flow

$$F = \Delta P/R$$



➢ **Pressure gradient (ΔP)**

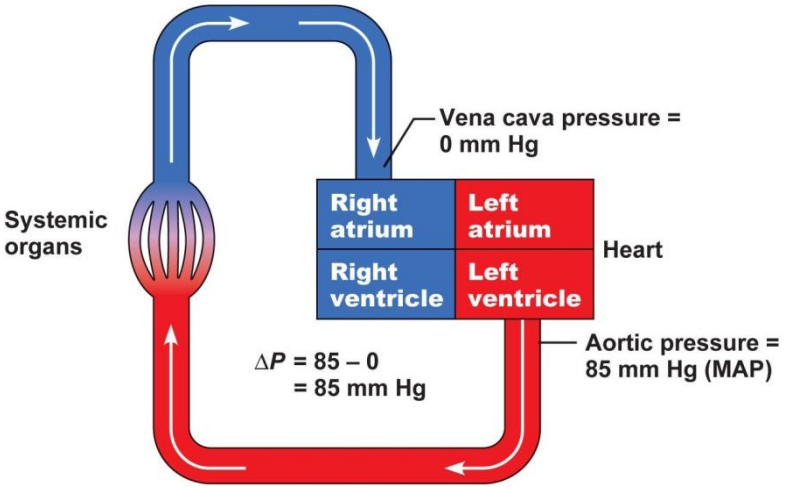
Organ blood flow driving force

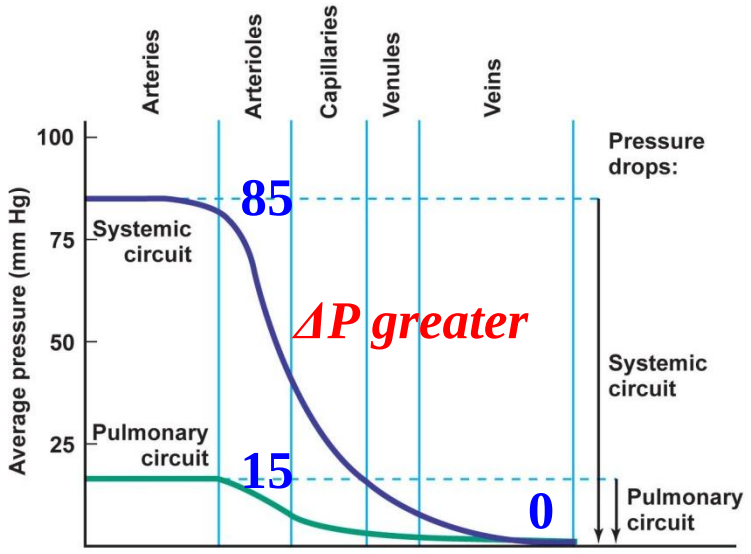
= Arterial pressure (AP) – Venous pressure (VP)

Arteriole Radius and Blood Flow

$$F = \Delta P/R$$

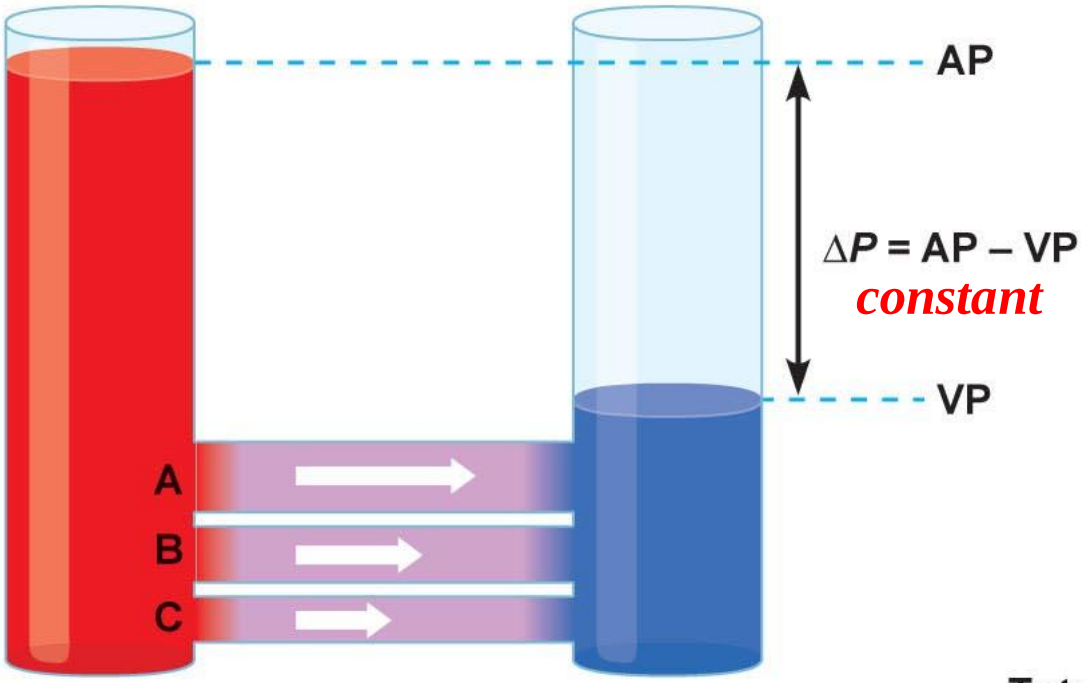
- ***Pressure gradients*** ***(ΔP)*** drive **blood flow** from high pressure to low pressure
- **Heart** creates pressure gradient for bulk flow of blood
- Pressure gradient = ***pressure in aorta minus pressure in vena cava*** just before it empties into right atrium
- Pressure in aorta = ***mean arterial pressure (MAP)*** = 85 mm Hg
- Pressure in vena cava = ***central venous pressure (CVP)*** = 0 mm Hg
- Pressure gradient = ***MAP – CVP*** = 85-0 = 85 mm Hg





Arteriole Radius and Blood Flow

$$F = \Delta P/R$$

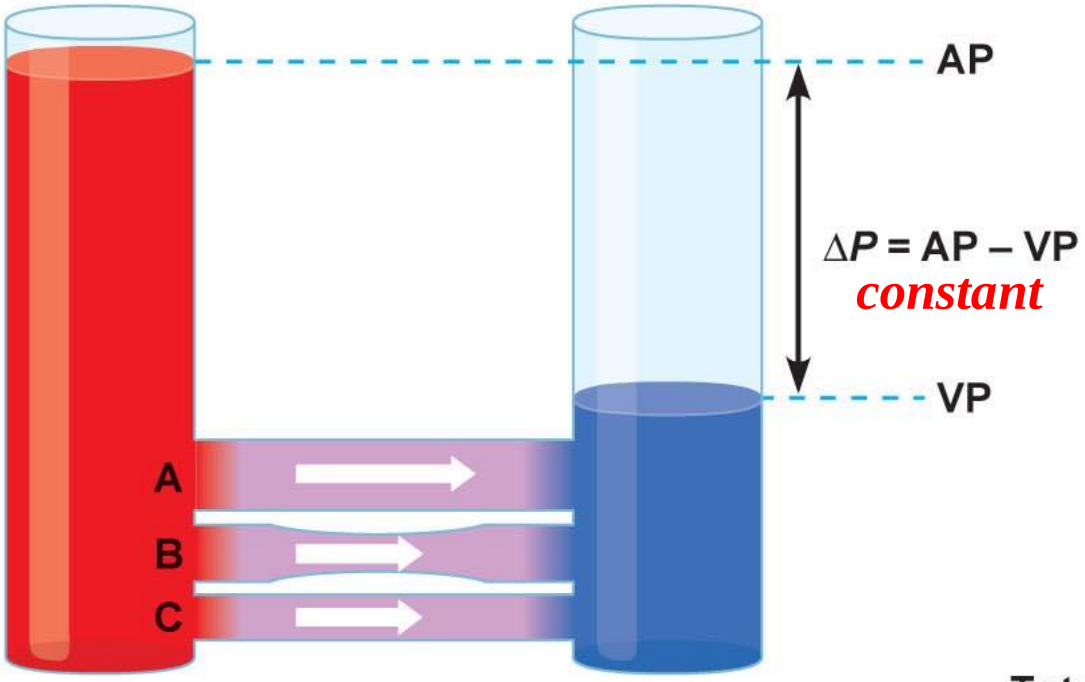


	Flow	Percent of cardiac output (total flow)
A	1.5 L/min	50%
B	1.0 L/min	33%
C	0.5 L/min	17%
Total flow:	3.0 L/min	

- Cardiac output is distributed unequally to different organs due to ***unequal resistance*** to blood flow through the organs
- **Flow varies** due to ***differences in resistance***

Arteriole Radius and Blood Flow

$$F = \Delta P/R$$



	Flow	Percent of cardiac output (total flow)
A	1.5 L/min	60%
B	0.5 L/min	20%
C	0.5 L/min	20%
Total flow:	2.5 L/min	

➢**Blood flow changes** when ***resistance changes***

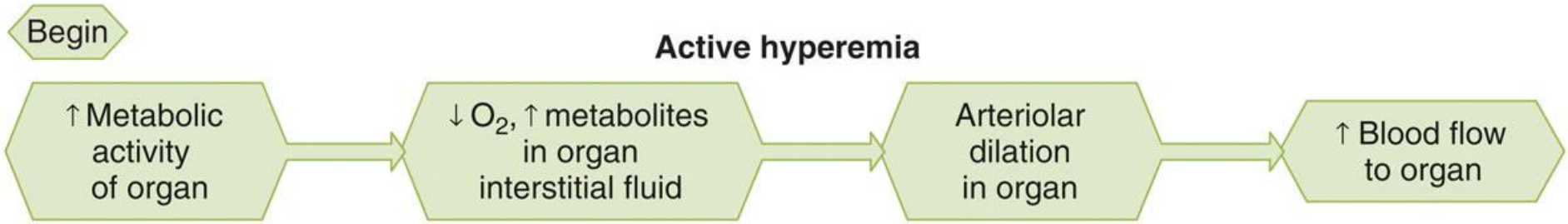
(Local and extrinsic regulation)

Local Control of Arteriole Radius

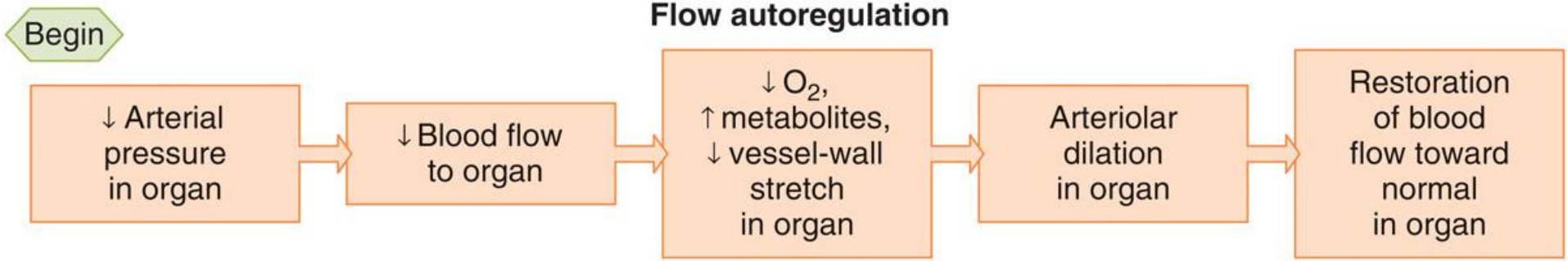
$$F = \Delta P/R$$

Contractile state of ***smooth muscle in Arteriole*** → ***Radius*** of arterioles → Vascular ***resistance*** → ***Blood flow and blood pressure***

(a) ***Metabolic Regulation***



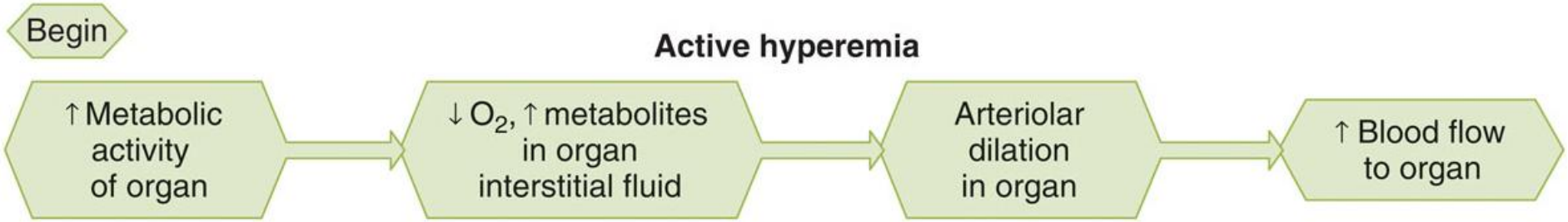
(b) ***Myogenic Autoregulation***



Local Control of Arteriole Radius

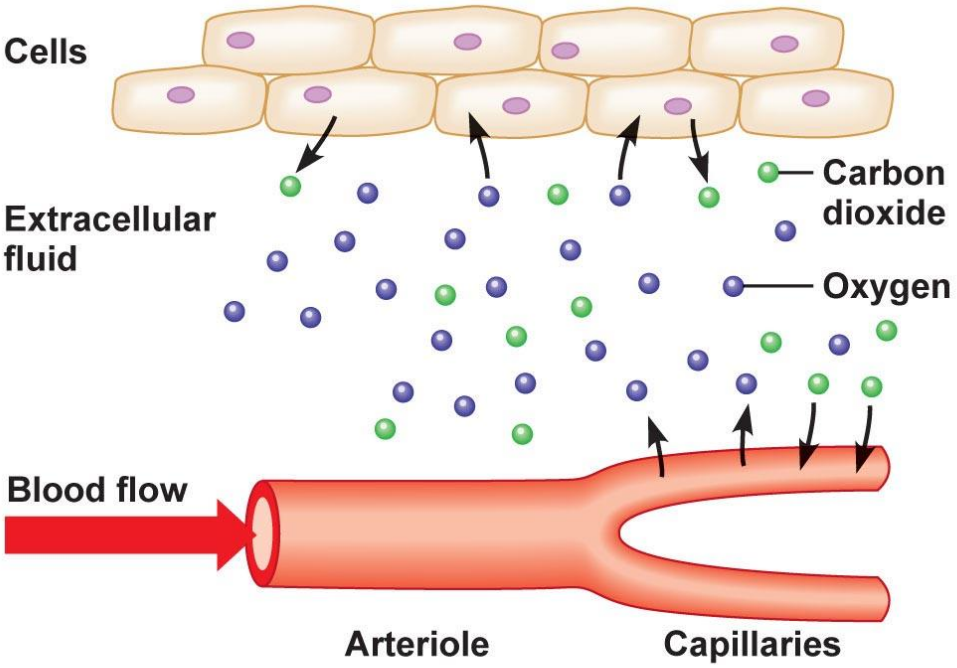
1. Metabolic Regulation=Active Hyperemia

- **Active Hyperemia:** increased blood flow in response to increased metabolic activity
- Changes associated with ***increased*** metabolic activity generally cause **vasodilation**
  --Carbon dioxide
  --Potassium
  --Hydrogen ions
- Changes associated with ***decreased*** metabolic activity generally cause **vasoconstriction**
  --Oxygen



Local Control of Arteriole Radius

1. Metabolic Regulation=Active Hyperemia

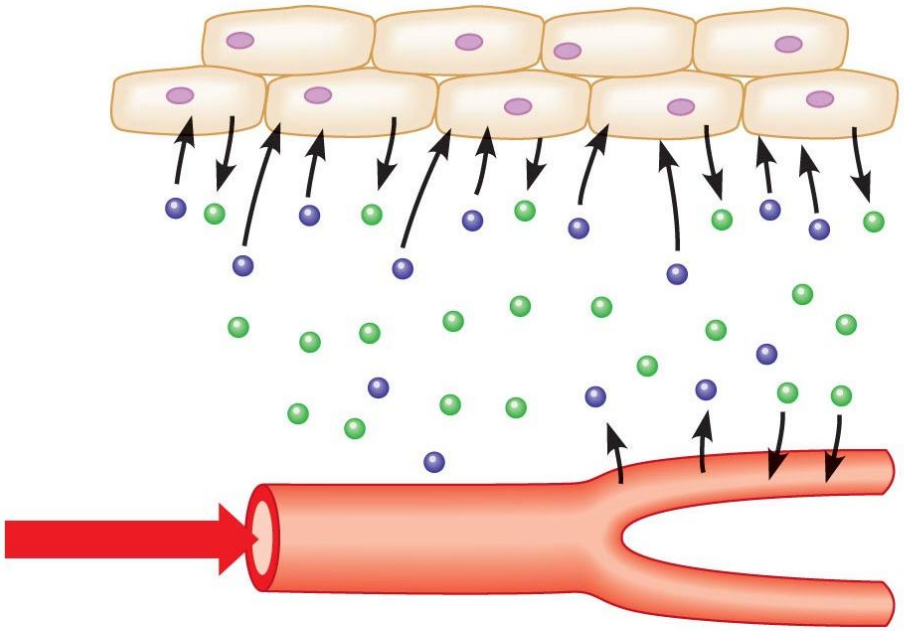


(a) Under normal steady-state conditions, oxygen (purple dots) is delivered to tissues by the blood as fast as it is consumed by cells, and carbon dioxide (green dots) is removed from tissues by the blood as fast as it is produced by cells.

- **Steady state**
  - *--O_2 delivered rate= consumed rate*
  - *--CO_2 removed rate= produced rate*

Local Control of Arteriole Radius

1. Metabolic Regulation=Active Hyperemia

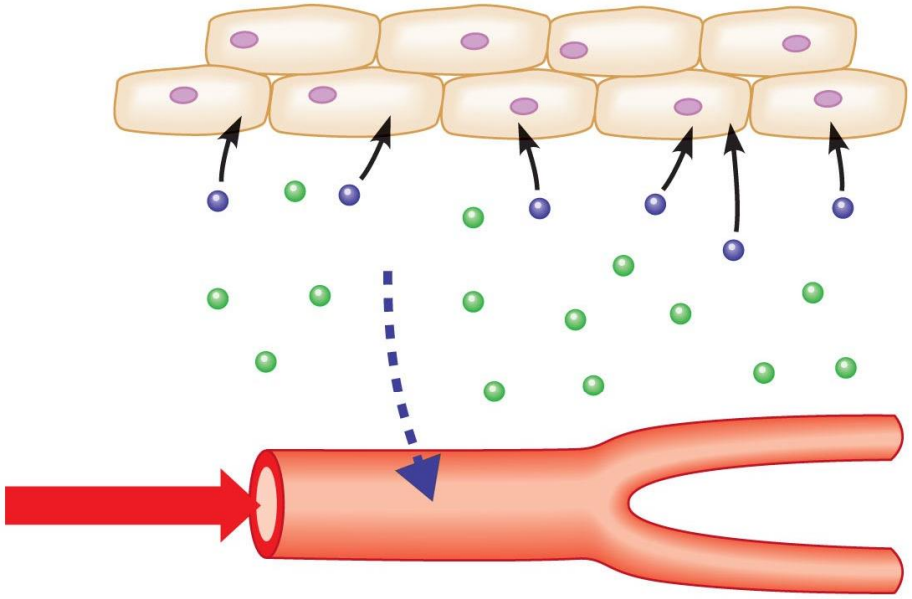


(b) An increase in the metabolic rate causes oxygen to be consumed faster than it is delivered and carbon dioxide to be produced faster than it is removed. The oxygen concentration in extracellular fluid decreases, while carbon dioxide concentration increases.

- **Increased metabolic rate**
  - *--O_2 delivered rate< consumed rate*
  - *--CO_2 removed rate< produced rate*

Local Control of Arteriole Radius

1. Metabolic Regulation=Active Hyperemia

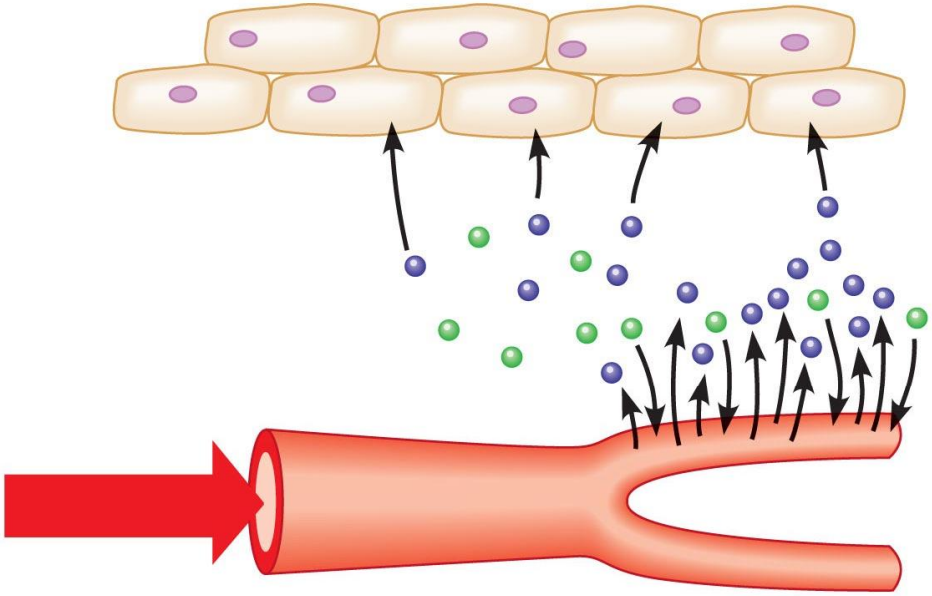


(c) The decreased oxygen concentration and increased carbon dioxide concentration act on arteriolar smooth muscle to promote vasodilation.

- **Response to low O_2 and high CO_2**
  - ***--Vasodilation***
  - ***--Vasodilation increases blood flow***

Local Control of Arteriole Radius

1. Metabolic Regulation=Active Hyperemia



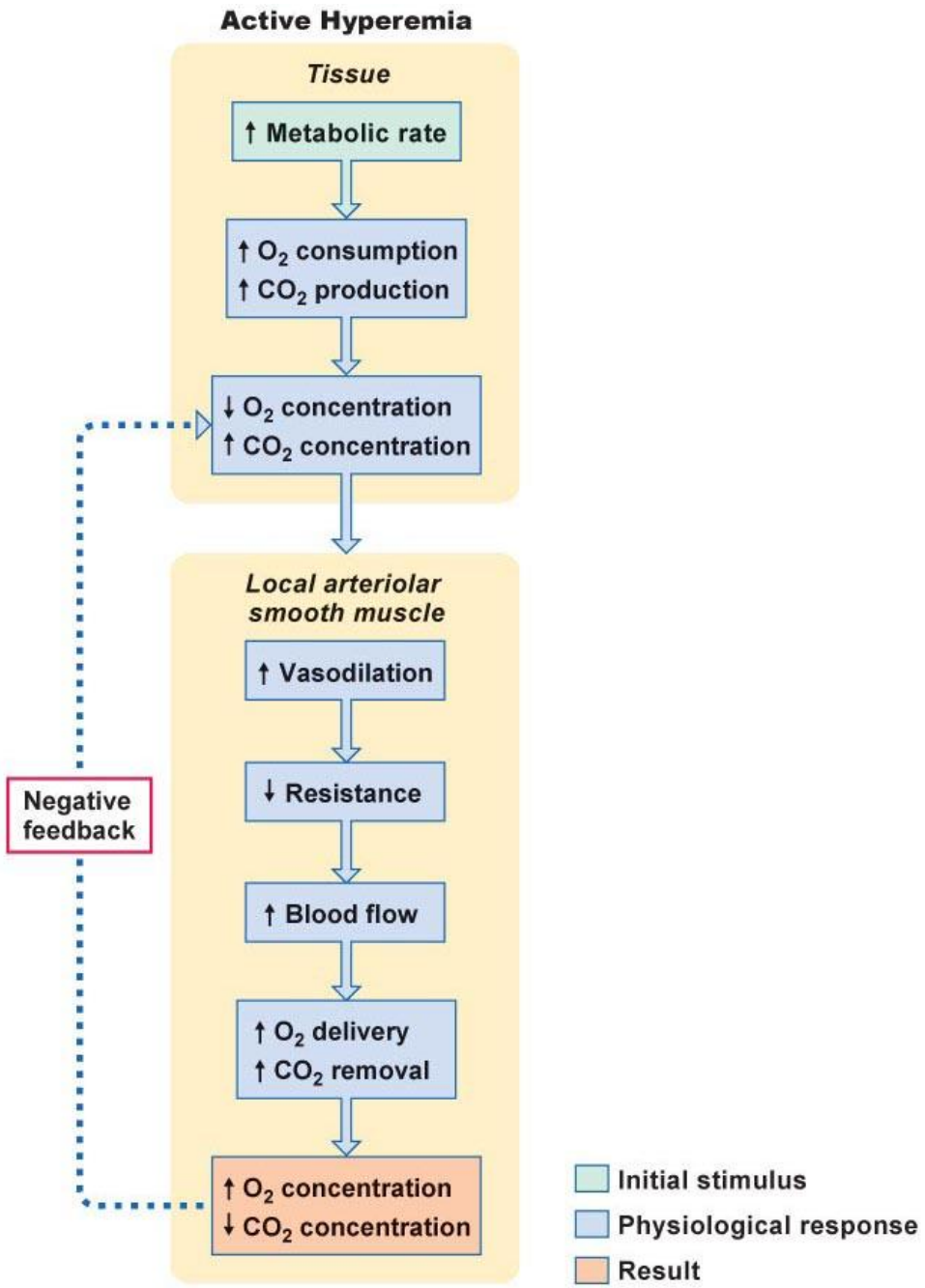
(d) Vasodilation promotes increased blood flow, which increases oxygen delivery to cells and carbon dioxide removal from cells.

- **Increased blood flow**
  - *--Delivers more O_2*
  - *--Removes more CO_2*

Local Control of Arteriole Radius

1. Metabolic Regulation

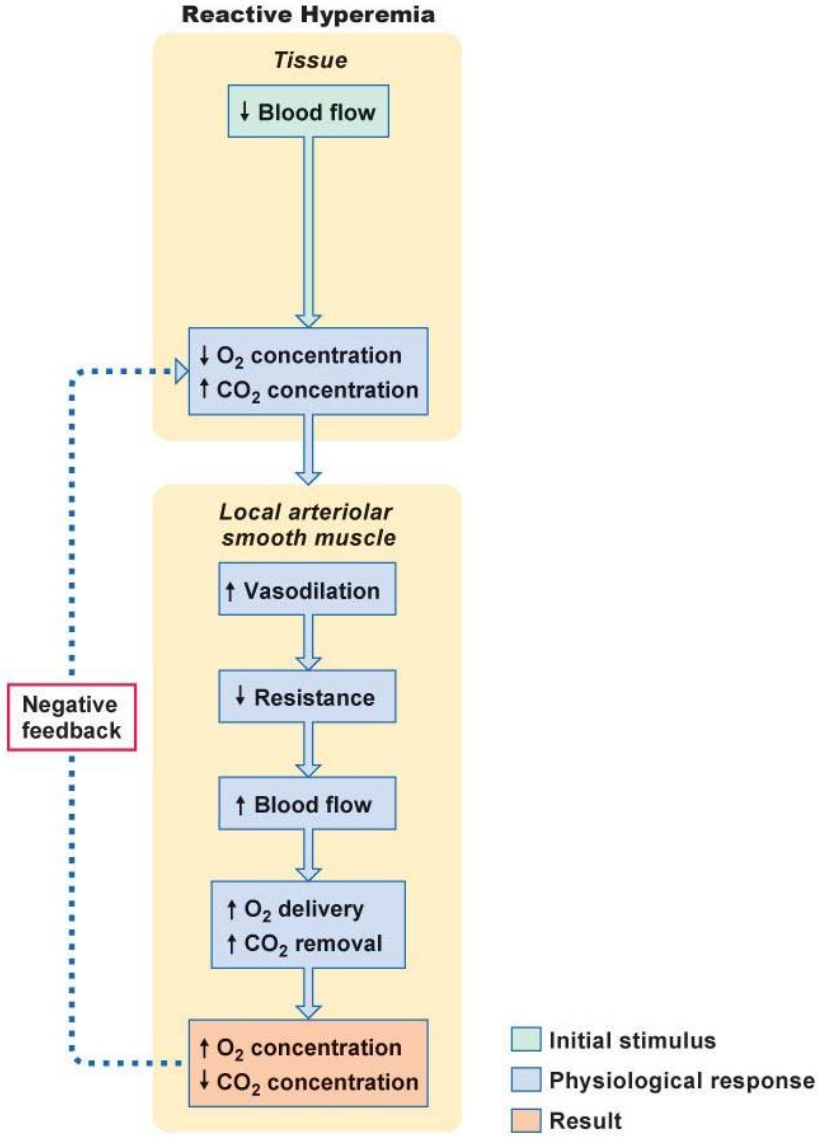
=Active Hyperemia



Local Control of Arteriole Radius

2. Blood flow Regulation=Reactive Hyperemia

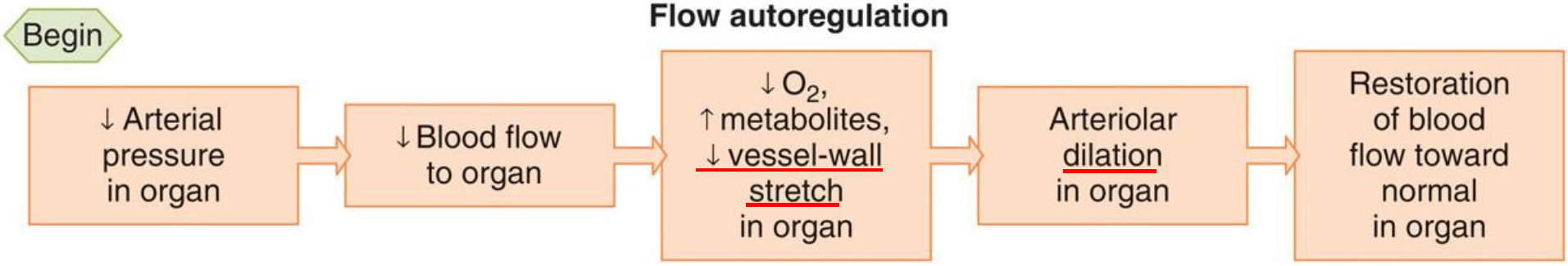
- **Blockage of blood flow to tissue**
  - *--Metabolites increase and oxygen decreases*
  - *--Vasodilation*
- **Release blockage**
  - *--Increased blood flow due to low resistance*
  - *--Metabolites removed, oxygen delivered*



Local Control of Arteriole Radius

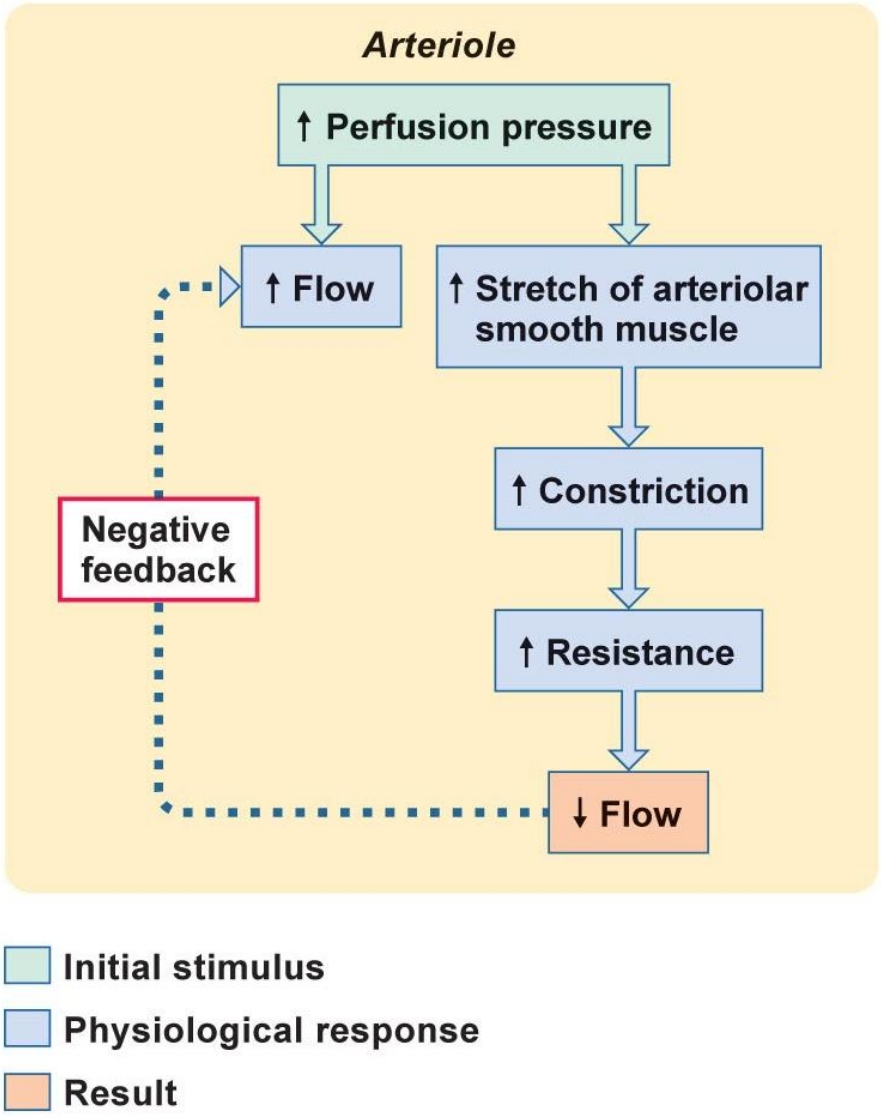
3. Myogenic Autoregulation=Myogenic Response

- **Myogenic Autoregulation:** change in vascular resistance in response to stretch of blood vessels in absence of any external factors
- **Increased perfusion pressure *increases*** blood flow and pressure in arterioles
- **Increased pressure in arteriole *stretches*** arteriole wall
- **Stretch of vascular smooth muscle *induces contraction*** of vascular smooth muscle (↓blood flow)—inherent property of smooth muscle
- Purpose—keep **blood flow constant (*autoregulate*)**



Local Control of Arteriole Radius

3. Myogenic Autoregulation=Myogenic Response



Local Control of Arteriole Radius

4. Chemical Messengers=Local Vasoactive Substances

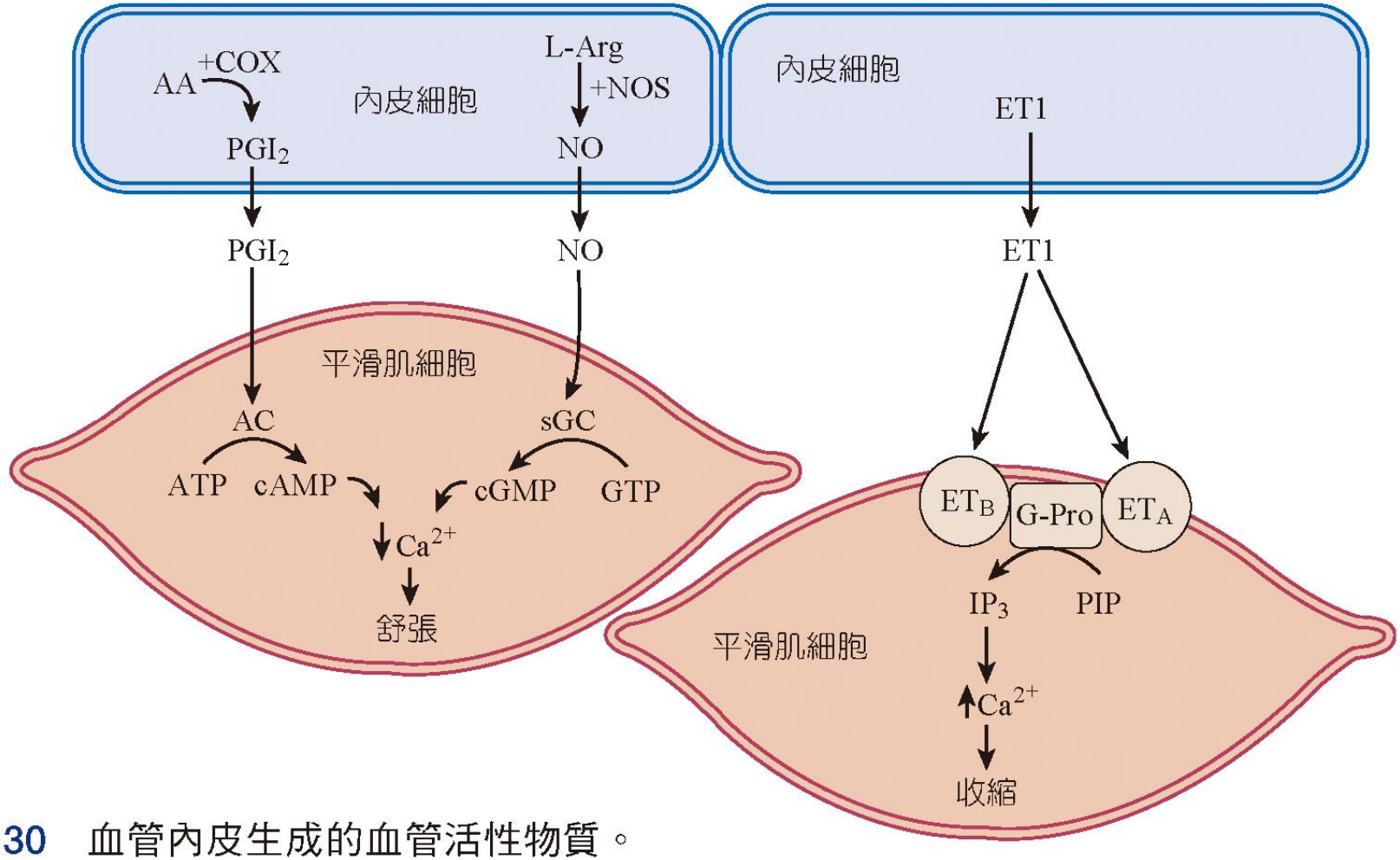
Actions on ***smooth muscle in Arteriole*** → ***Radius*** of arterioles
→ Vascular ***resistance*** → ***Blood flow and blood pressure***

Substance	Source	Effect on vascular smooth muscle
Oxygen	Delivered to tissues by blood; consumed in aerobic metabolism	Vasoconstriction
Carbon dioxide	Generated in aerobic metabolism	Vasodilation
Potassium ions	Released from cells (particularly in muscle) as a result of repeated depolarization occurring during activity	Vasodilation (vasoconstriction at high concentrations)
Acids (hydrogen ions)	Generated during anaerobic metabolism (lactic acid) and by reaction of carbon dioxide with water (carbonic acid)	Vasodilation
Adenosine	Released by cells in certain tissues in response to hypoxia	Vasodilation
Nitric oxide	Released by endothelial cells on a continuous basis and in response to various chemical signals	Vasodilation
Bradykinin	Generated from a precursor protein (kininogen) by action of an enzyme (kallikrein) secreted by cells in certain tissues in response to various chemical signals	Vasodilation
Endothelin-1	Released by endothelial cells in response to various chemical signals and mechanical stimuli	Vasoconstriction
Prostacyclin (PGI_2)	Released by endothelial cells in response to various chemical signals and mechanical stimuli	Vasodilation

ex. coronary arteries

ex. BK, histamine etc.

Vasoactive Substances of Vascular Endothelium

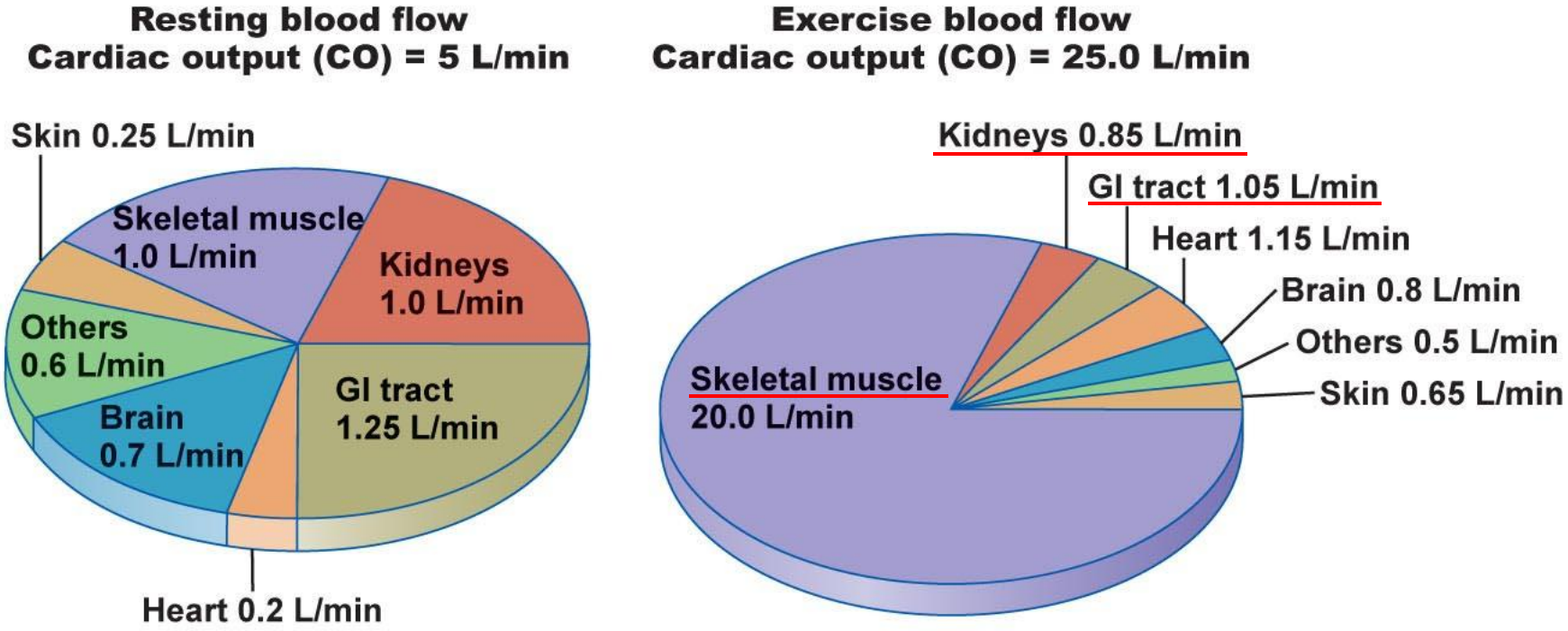


• 圖 11-30　血管內皮生成的血管活性物質。

Independent Regulation of Blood Flow

During Exercise

- Cardiac output ***increases*** during exercise
- Distribution of blood ***does not increase proportionally***
- Disproportionate flow diverts blood ***to muscles***



Independent Regulation of Blood Flow *During Exercise*

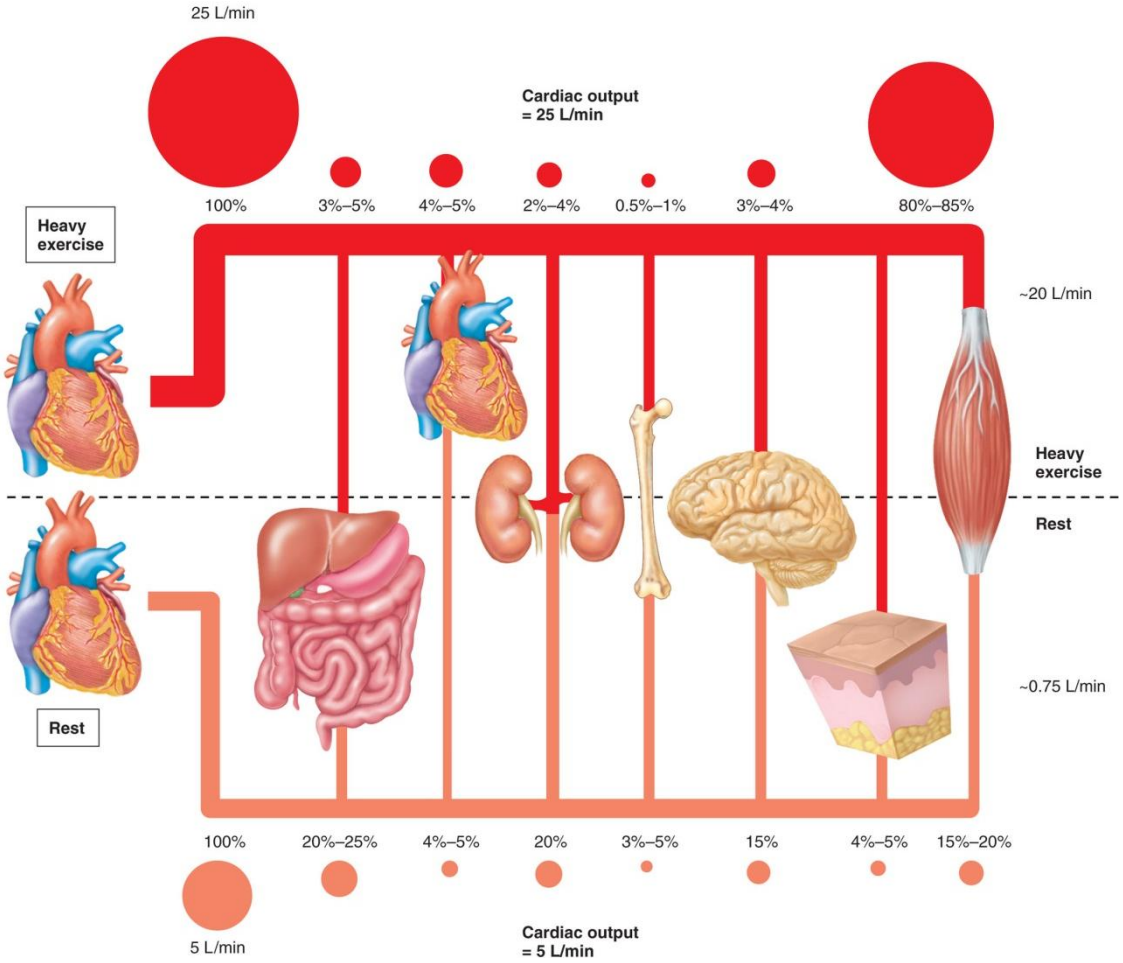


Table 14.5 | Changes in Skeletal Muscle Blood Flow Under Conditions of Rest and Exercise

Condition	Blood Flow (ml/min)	Mechanism
Rest	1,000	High adrenergic sympathetic stimulation of vascular alpha receptors, causing vasoconstriction
Beginning exercise	Increased	Dilation of arterioles in skeletal muscles due to cholinergic sympathetic nerve activity and stimulation of beta-adrenergic receptors by the hormone epinephrine
Heavy exercise	20,000	Fall in alpha-adrenergic activity Increased cholinergic sympathetic activity Increased metabolic rate of exercising muscles, producing intrinsic vasodilation

Extrinsic Control of Arteriole Radius

$$Flow\ (F) = \Delta P/R$$

$$CO = MAP / TPR$$

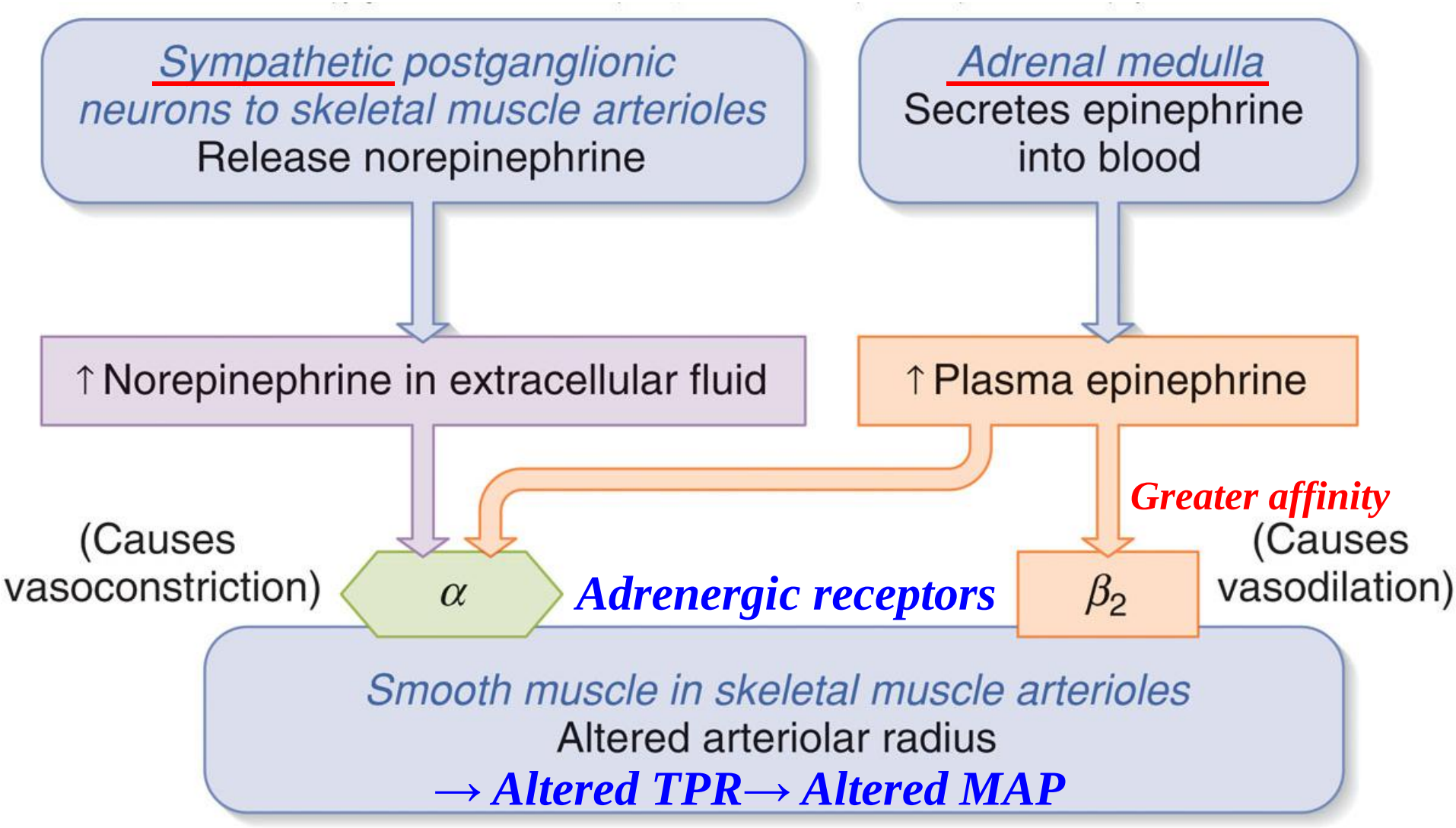
$$MAP = CO \times TPR$$

$$MAP = SV \times HR \times TPR$$

- Mean arterial pressure depends on ***TPR***
- TPR depends on ***radius of arterioles***
- Radius of arterioles regulated by ***extrinsic mechanisms*** to control ***mean arterial pressure***
  - ***--Sympathetic activity***
  - ***--Hormones***

Extrinsic Control of Arteriole Radius

$$F = \Delta P/R$$



Extrinsic Control of Arteriole Radius

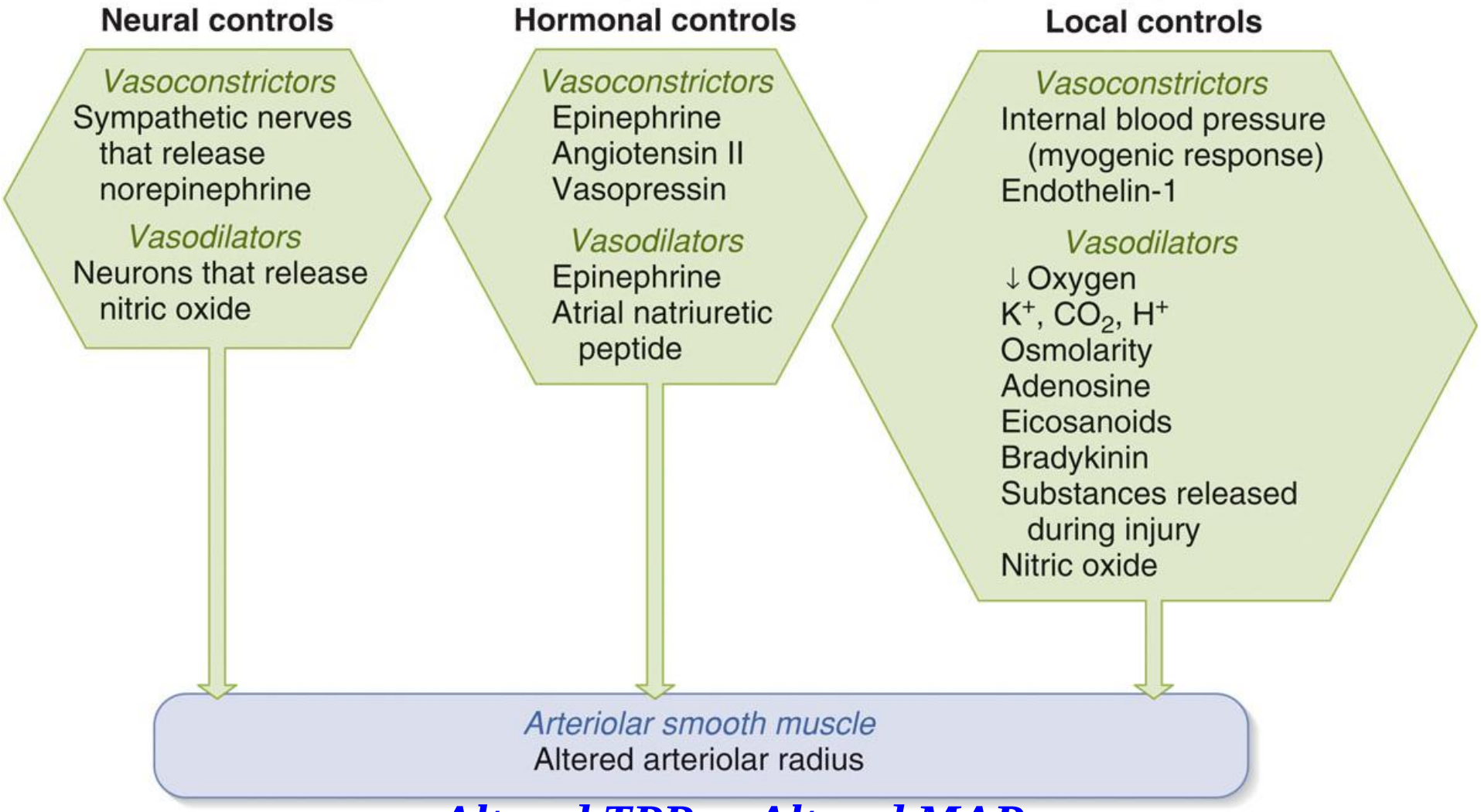
Extrinsic factor	Change in radius	Effect on MAP
Sympathetic nerves	Vasoconstriction	Increase
Epinephrine	Depends on receptor type α Adrenergic: vasoconstriction β_2 Adrenergic: vasodilation	Increase (dominant effect is at α receptors)
Vasopressin ***(ADH)***	Vasoconstriction	Increase
Angiotensin II	Vasoconstriction	Increase

- **AII** is synthesized from **angiotensinogen** **(precursor)**
- Angiotensinogen ***renin*** angiotensin I ***ACE*** angiotensin II
- Action

  --Vasoconstriction

  --Increases TPR (total peripheral resistance)

Control of Arteriole Radius



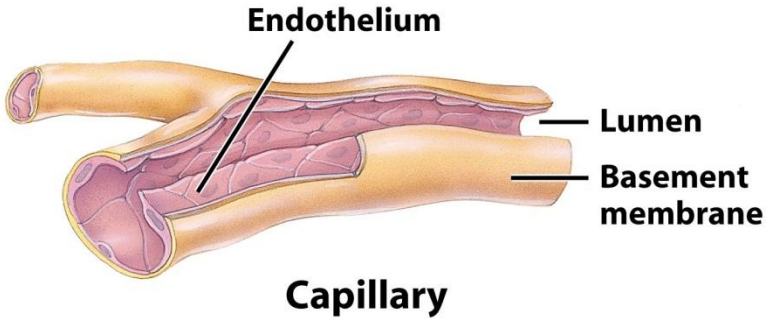
→ Altered TPR→ Altered MAP

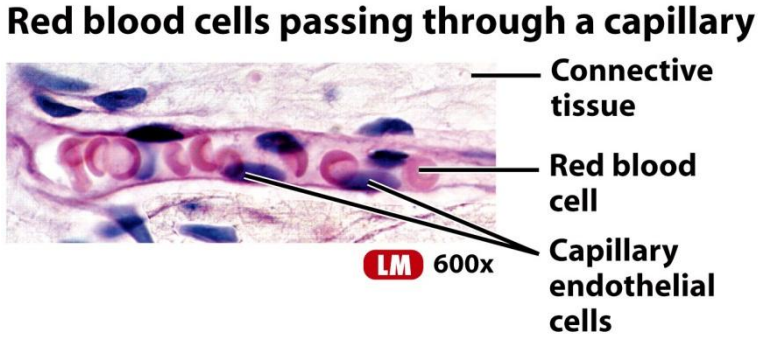
Capillaries

- **Microscopic vessels** (5−10 µm in diameter) that connect arterioles to venules (***smallest blood vessels***)
- 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

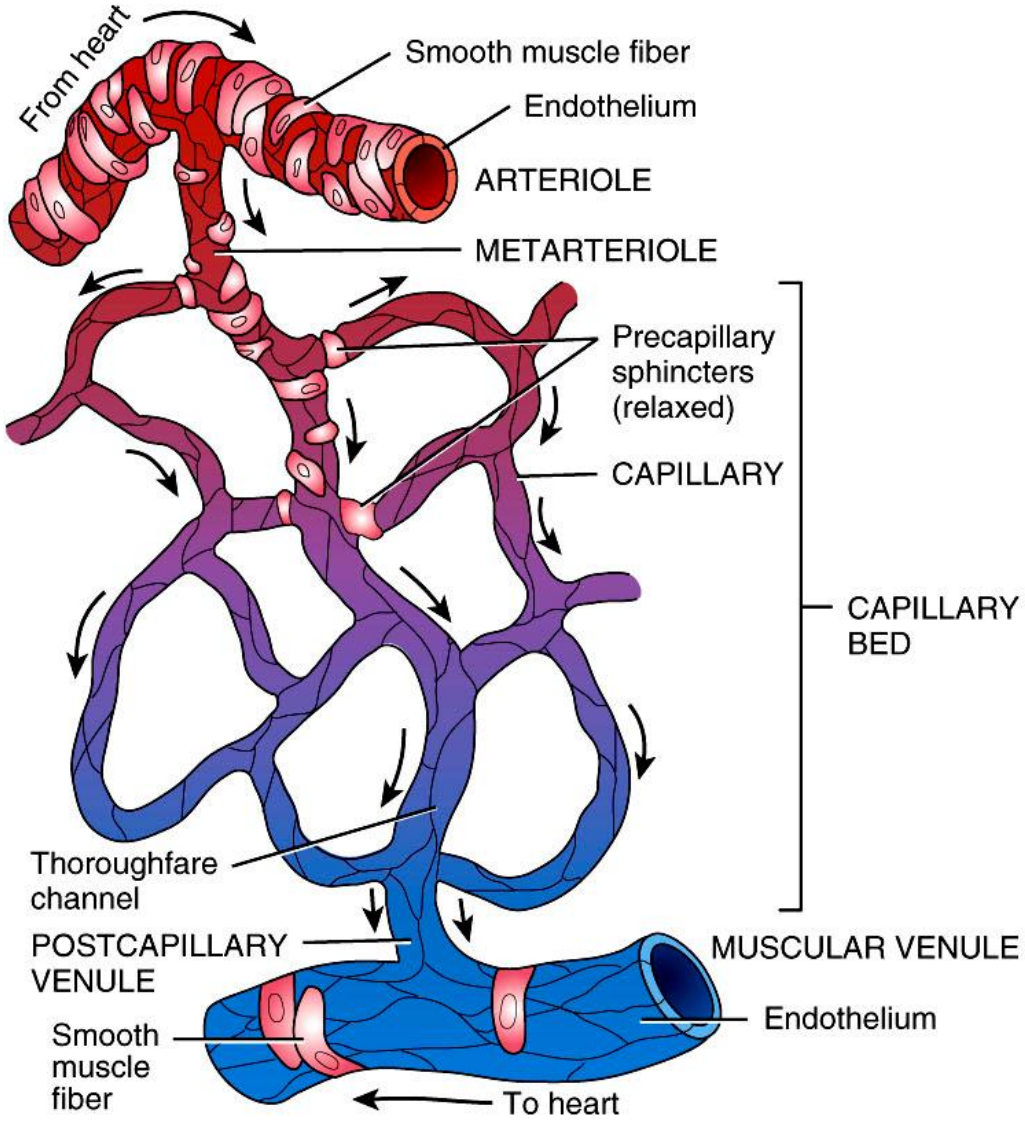
  --Lacking in **epithelia, cornea and lens of eye & cartilage**
- **Exchange vessels**− exchange of nutrients & wastes between blood and tissue fluid (total SA = 600 m^2)
- Capillary walls (lack tunica media and tunica externa)= a single layer of cells (**endothelium=**simple squamous epithelium tissue) and a **basement membrane**





Capillaries

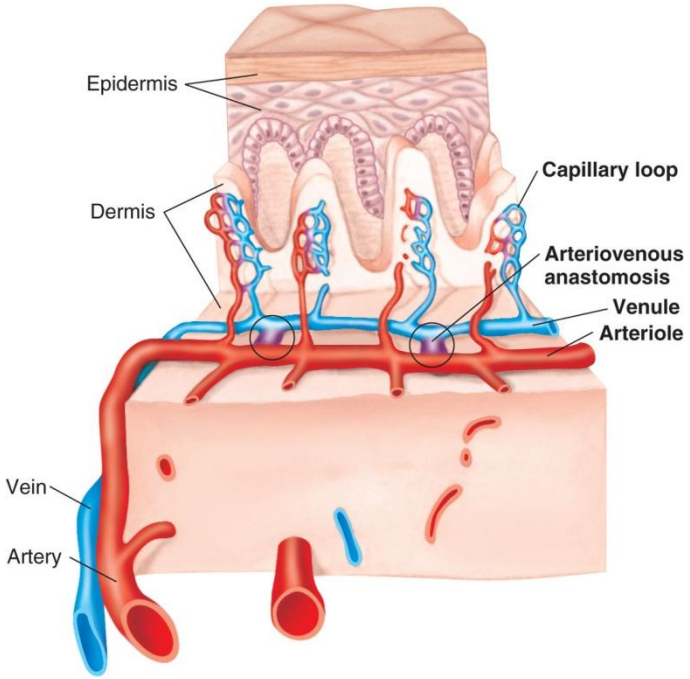
- **Capillaries form microcirculation –**flow from metarteriole through capillaries and into postcapillary venule
- **Capillary beds –arise from single metarteriole**
  - --***Vasomotion*:** intermittent contraction and relaxation
  - --***Thoroughfare channel*:** bypasses capillary bed
- **Blood flow to capillaries is regulated by:**
  - --***Vasoconstriction and vasodilation of arterioles***
  - --***Precapillary sphincters***



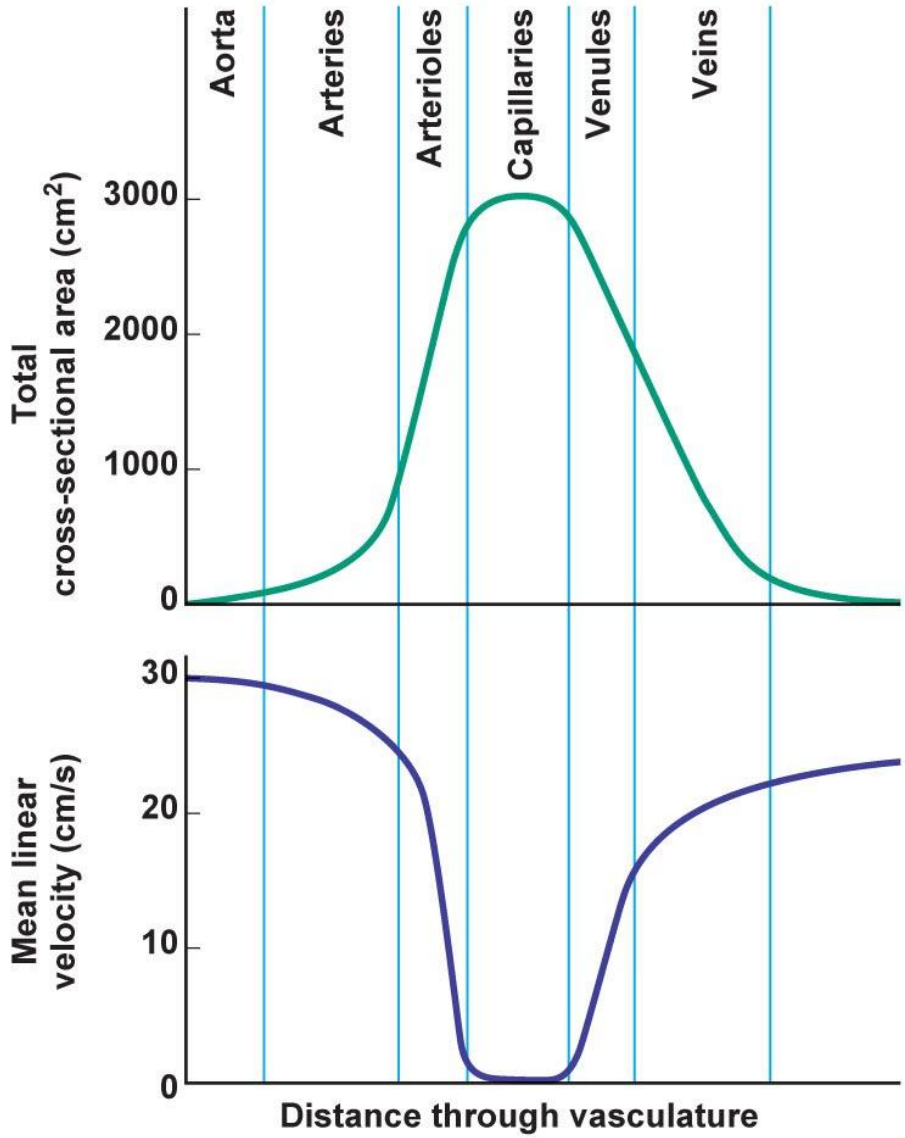
(a) Sphincters relaxed: blood flowing through capillaries

表 11-11　直捷通路與動靜脈吻合支的比較

途徑	直捷通路 *Thoroughfare channel*	動靜脈吻合支 *Arteriovenous anastomosis*
血管組成	小動脈→後小動脈→直捷通路→小靜脈	小動脈→動靜脈吻合支→小靜脈
血流速度	快	迅速（更快）
物質交換	少	無
主要分布	骨骼肌	皮膚
血管狀況	通常開放	平時關閉，體溫升高時開放
生理意義	血液迅速回流心臟	體溫調節

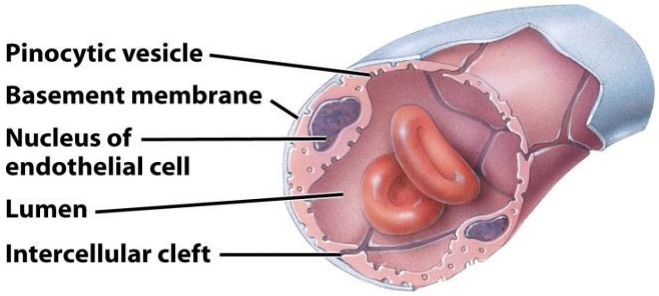


Vessel Area and Velocity of Blood

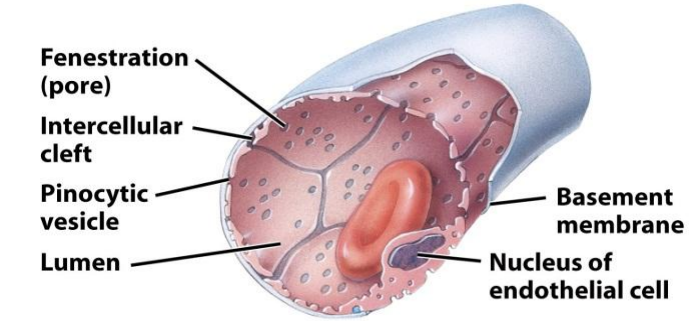


- **Capillaries**
  - --Have ***greatest*** ***total cross-sectional area***
  - --Have ***slowest*** ***velocity of blood flow, enhances exchange***

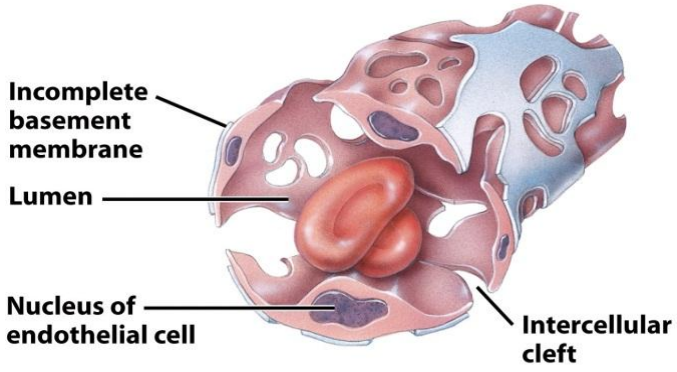
Types of Capillaries



Continuous capillary formed by endothelial cells



Fenestrated capillary



Sinusoid

❖ Continuous capillaries

--Intercellular clefts are ***gaps*** between neighboring cells

--***Skin, muscle, adipose tissue, skeletal & smooth, connective tissue, CNS and lungs***

--***Most common kind*** have tight junctions

❖ Fenestrated capillaries

--Plasma membranes have many holes (more permeable)

--***Kidneys, small intestine, choroid plexuses, ciliary process & endocrine glands***

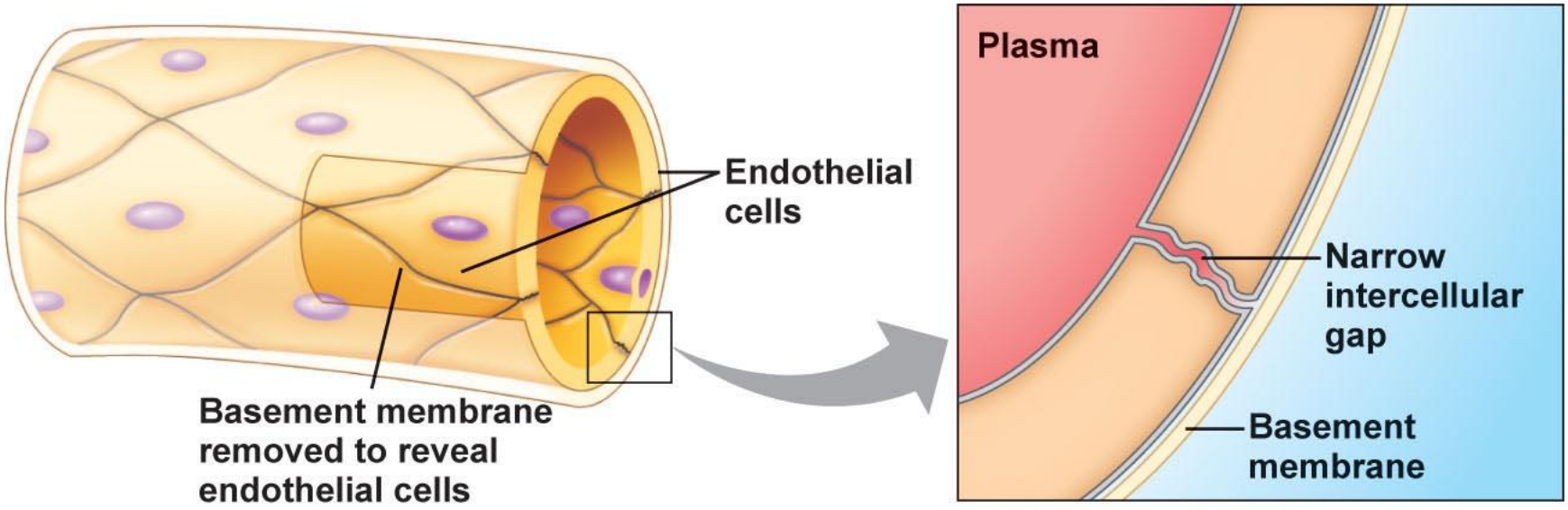
❖ Sinusoid (Discontinuous)

--Very large fenestrations

--Incomplete basement membrane

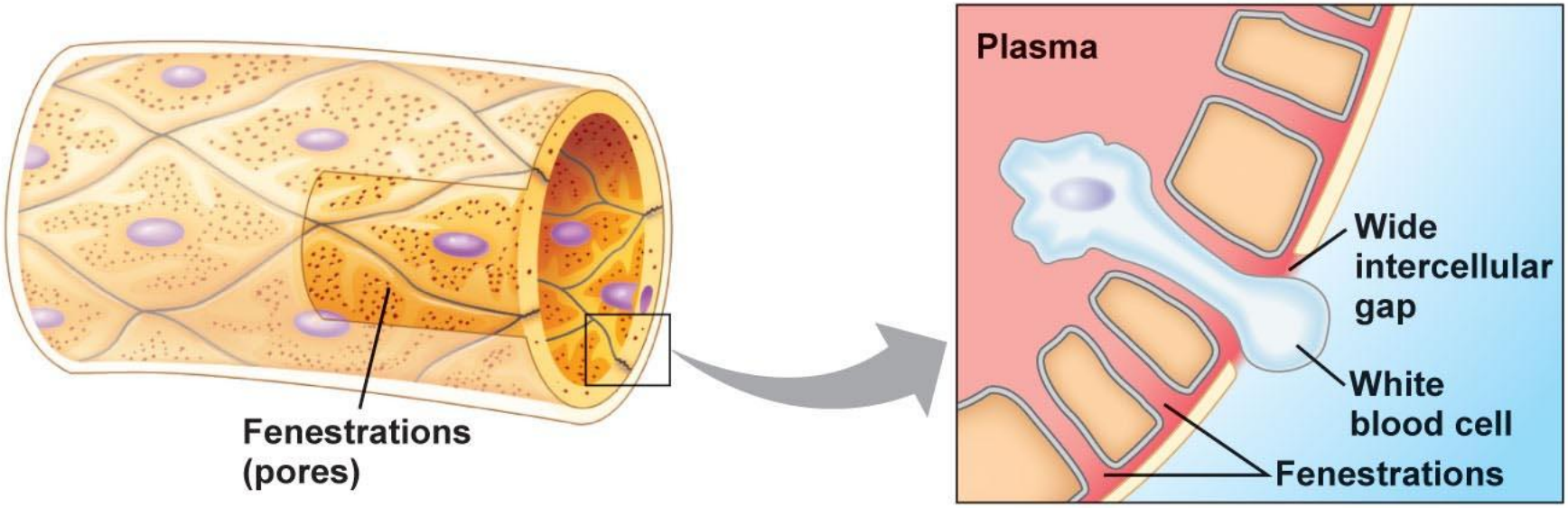
--***Liver, bone marrow, spleen, anterior pituitary, & parathyroid gland***

Continuous Capillaries



- ***Most common***
- ***Small gaps* between endothelial cells**
  --Allows **small water-soluble molecules** to move through

Fenestrated Capillaries



- ***Large gaps* between endothelial cells forming pores or fenestrations**
  - --Allow **proteins and in some cases blood cells** to move through

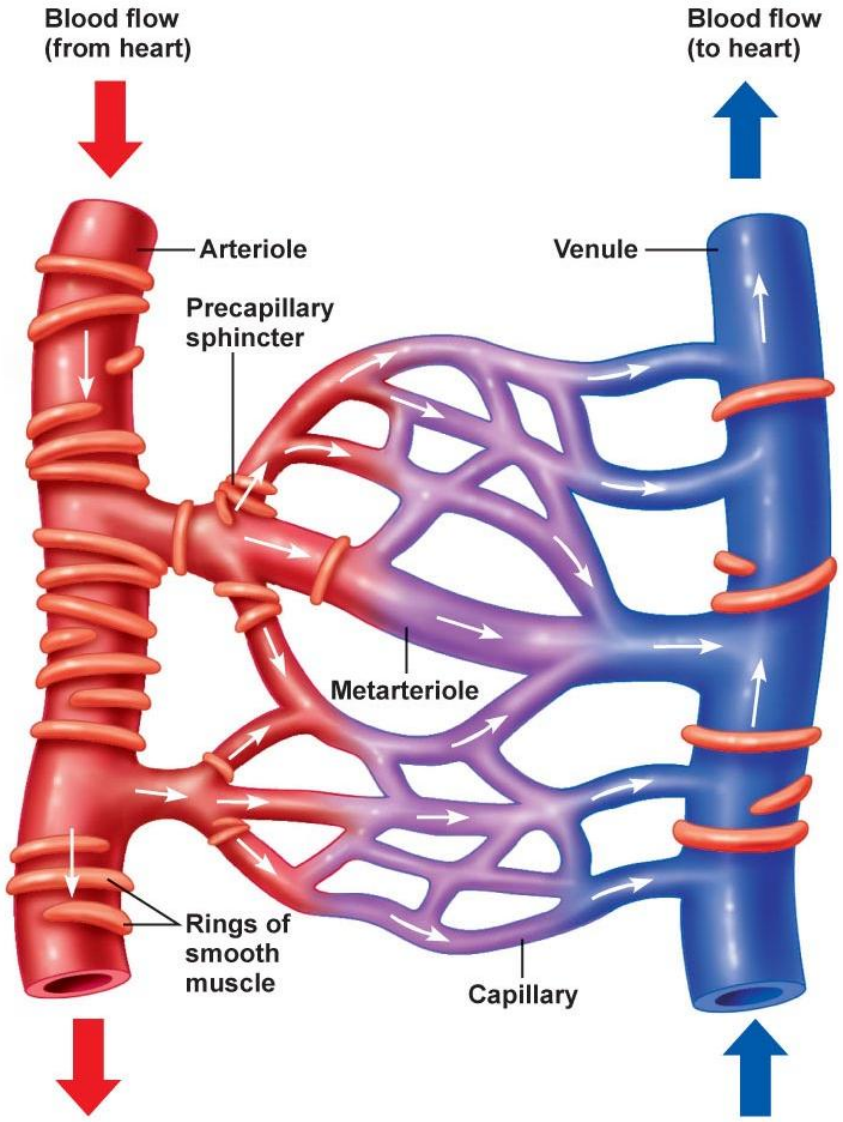
Types of Capillaries

種類 / 特性	連續型微血管	窗孔型微血管	不連續型微血管
內皮細胞型態	緊密相連	細胞間有 80~100 nm 的孔隙，並附著黏液蛋白	細胞間隙較大，約 1 μm
部位	主要在肌肉、肺、皮膚及血腦障壁上	腎臟、小腸絨毛、內分泌腺等部位	骨髓、肝脾的血竇中
通透性	對水和蛋白質的通透性都很低	水及蛋白質能通過	對水和蛋白都有高通透

Local Control of Blood Flow Through Capillary Beds

- Local control of **smooth muscle** in microcirculation
  - ***1. Arterioles***
  - ***2. Metarterioles***
    - ➢ Intermediate between arterioles and capillaries
    - ➢ Directly connect arterioles to venules
    - ➢ Function as shunts to bypass capillaries
    - ➢ Rings of smooth muscle at strategic locations
      - --Contract and relax in response to local factors
      - --***Contract*** → **increase** blood flow through capillaries
      - --***Relax*** → **decrease** blood flow through capillaries
  - ***3. Precapillary sphincters***

Local Control of Blood Flow Through Capillary Beds



***3. Precapillary Sphincters*:**
Rings of smooth muscle that surround capillaries on the arteriole end

--Contract and relax in response to local factors only

--***Contraction*** → constrict capillary → **decrease** blood flow

--***Relaxation*** → **increase** blood flow

--***Metabolites*** cause **relaxation**

Capillary Exchange

- Movement of substances between blood and interstitial fluid
- **3 exchange mechanisms** across capillary walls

1. Diffusion (most important method)

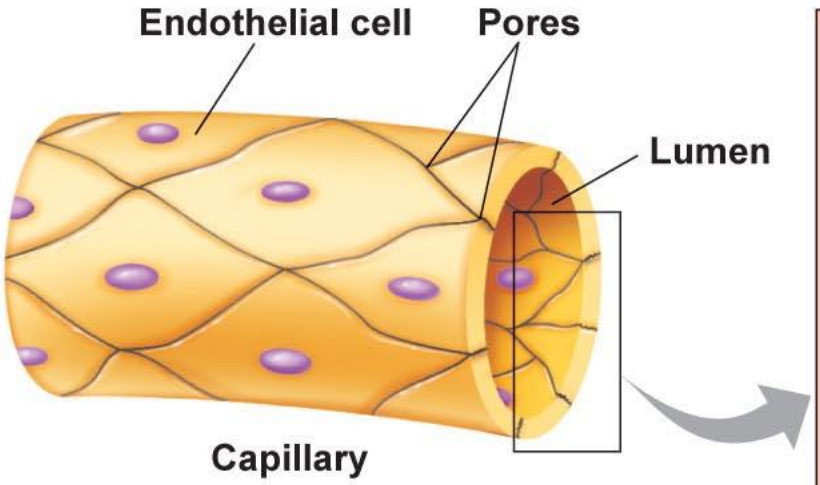
- Substances move ***down their concentration gradient***
  - --O_2 and nutrients from blood to interstitial fluid to body cells
  - --CO_2 and wastes move from body cells to interstitial fluid to blood
- Can cross capillary wall through ***intracellular clefts, fenestrations or through endothelial cells (lipid bilayer)***
  - --Most plasma proteins cannot cross
  - --Except in sinusoids – proteins and even blood cells leave
  - --Blood-brain barrier (Mediated transport)– tight junctions limit diffusion

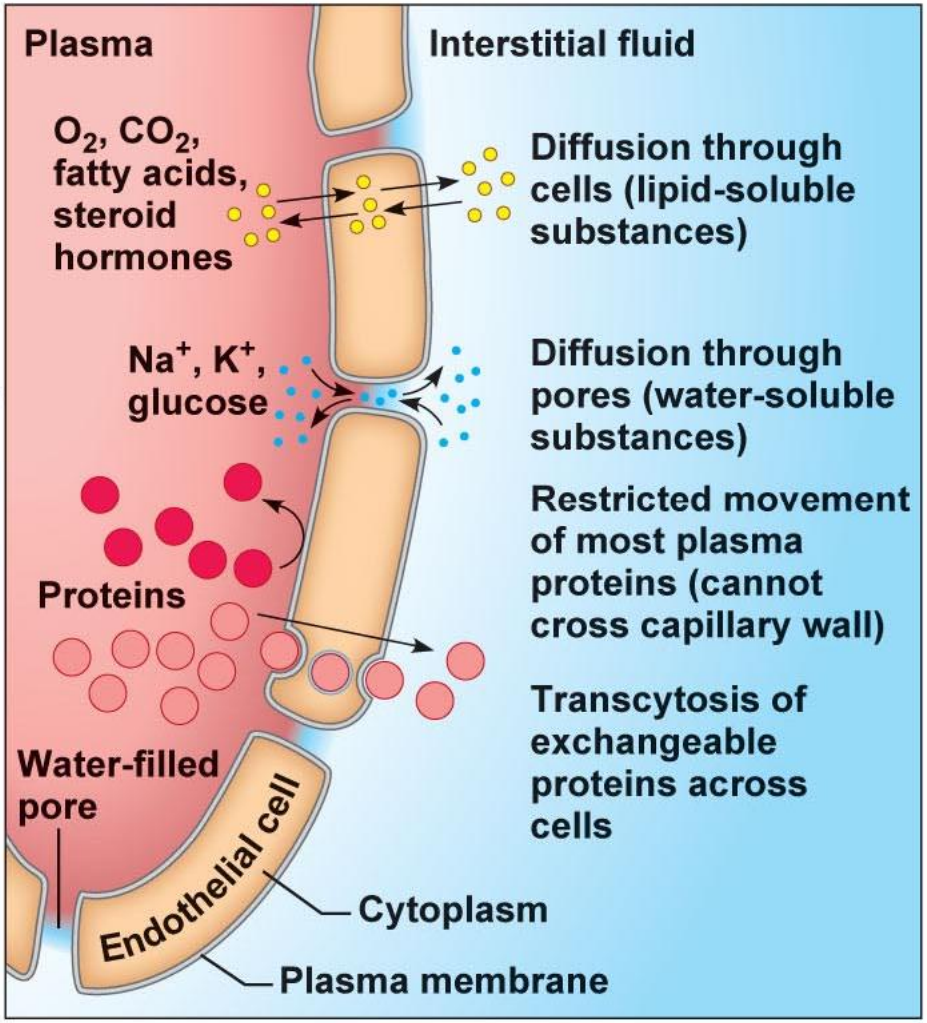
2. Transcytosis

- 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

3. Bulk flow

Capillary Exchange





- ***Diffusion*--most common mechanism**
  - *--Lipophilic—across membrane*
  - *--Lipophobic—through pores*
- ***Transcytosis*--exchangeable proteins**
- ***Mediated transport*--in brain**

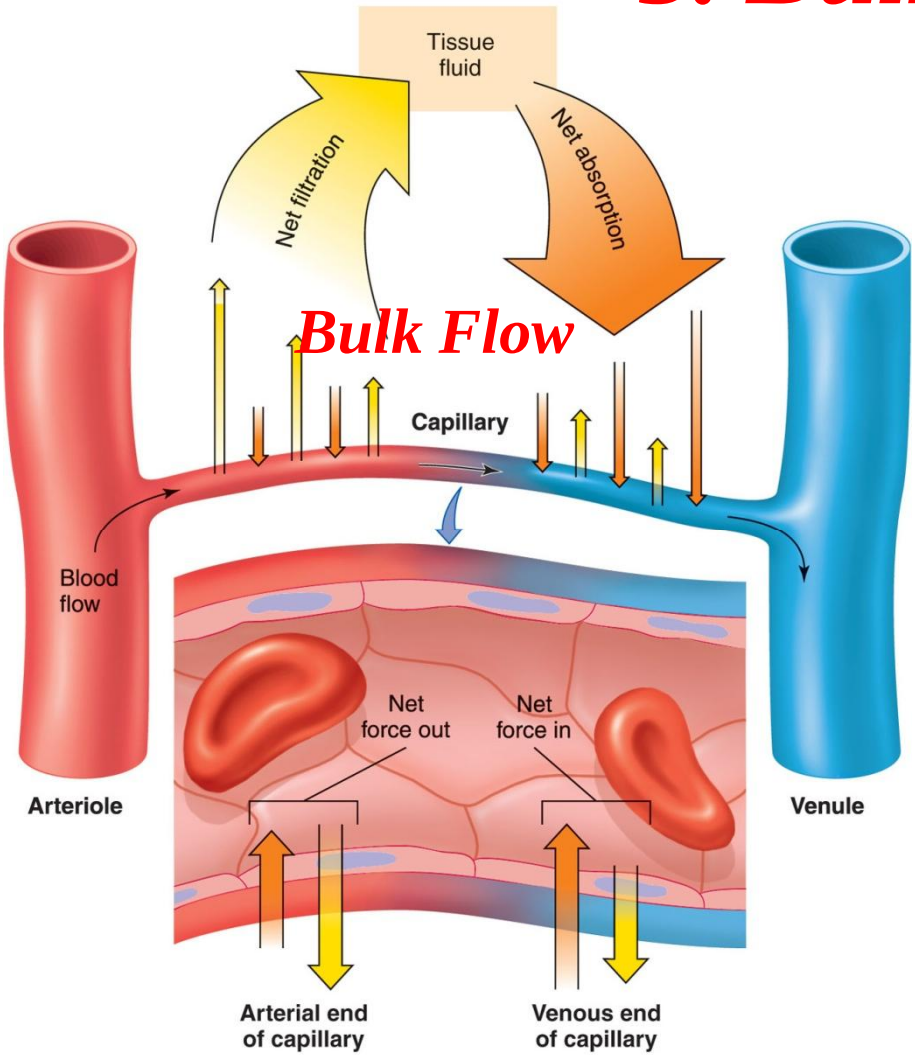
Capillary Exchange

3. Bulk Flow

- **Bulk flow** = Passive process in which large numbers of ions, molecules, or particles in a fluid move together in the same direction
- Based on ***pressure gradient***
- Diffusion is more important for solute exchange
- Bulk flow more important for regulation of ***relative volumes*** of blood and interstitial fluid
- **Filtration**= from capillaries into interstitial fluid
- **Reabsorption**= from interstitial fluid into capillaries

Capillary Exchange

3. Bulk Flow



- **Net filtration pressure =** hydrostatic pressure of the blood in the capillaries - hydrostatic pressure of the fluid outside the capillaries
- **Net reabsorption =** movement of fluid into the capillaries

  --Blood plasma has higher colloid osmotic pressure than interstitial fluid

Starling Forces
Across Capillary Walls

- **Starling forces for bulk flow: *hydrostatic and osmotic pressures***
- **Hydrostatic pressure gradient = force due to fluid**
- **Osmotic pressure = osmotic force exerted on water by nonpermeating solutes**
  - --Only nonpermeating solute = **proteins**
  - --***Oncotic pressure (colloid osmotic pressure)*** = osmotic force of proteins

Hydrostatic Pressure Gradient

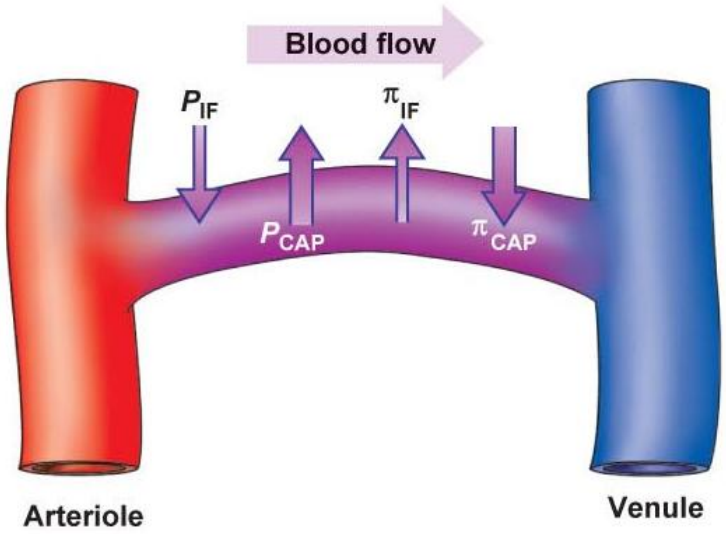
- **Capillary hydrostatic pressure = capillary BP**
  - --Arteriole end = 38 mm Hg
  - --Venous end = 16 mm Hg
  - --Favors **filtration**
- **Interstitial hydrostatic pressure = 0–1 mm Hg**
  - --Favors **reabsorption**
- **Hydrostatic pressure gradient**
  - --Arteriole end: 38 – 1 = 37 mm Hg, **filtration**
  - --Venous end: 16 – 1 = 15 mm Hg
  - --Favors **reabsorption**

Osmotic Pressure Gradient

- **Capillary oncotic osmotic pressure**
  - --25 mm Hg (plasma protein 6-8 g/100 ml)
  - --Favors **reabsorption**
- **Interstitial fluid oncotic osmotic pressure**
  - --0–1 mm Hg (relatively few protein)
  - --Favors **filtration**
- **Osmotic pressure gradient**
  - --25 – 0 = 25 mm Hg
  - --Favors **reabsorption**

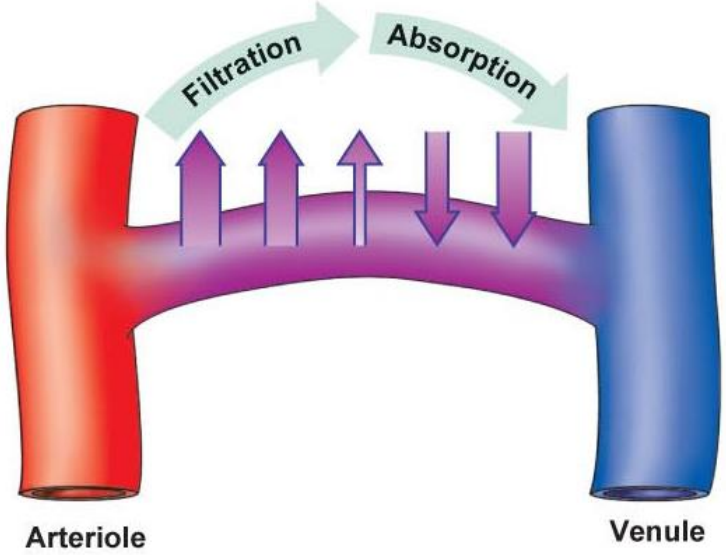
Starling Forces
Across Capillary Walls

- **2 pressures promote filtration**
  1. ***Capillary (blood) hydrostatic pressure***
     generated by pumping action of heart
  2. ***Interstitial fluid colloid osmotic pressure***
- **2 pressures promote reabsorption**
  1. ***Capillary (blood) colloid osmotic pressure***
     promotes reabsorption (due to blood plasma proteins > ISF)
  2. ***Interstitial fluid hydrostatic pressure***

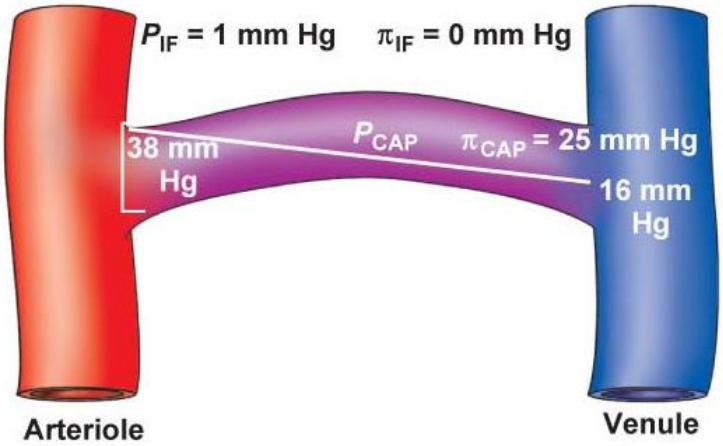


(a)

Starling's Law



(c) ***Filtration ≈ Reabsorption***



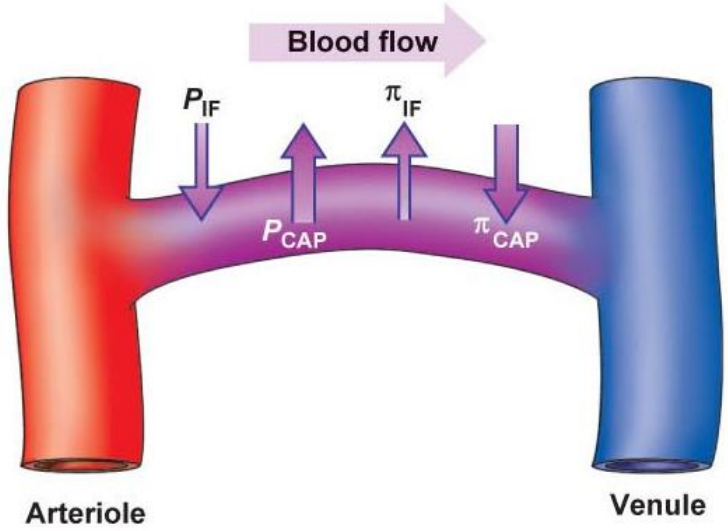
Arteriole end		Venule end	
Filtration pressure:	Absorption pressure:	Filtration pressure:	Absorption pressure:
P_{CAP} = 38 mm Hg	π_{CAP} = 25 mm Hg	P_{CAP} = 16 mm Hg	π_{CAP} = 25 mm Hg
π_{IF} = 0 mm Hg	P_{IF} = 1 mm Hg	π_{IF} = 0 mm Hg	P_{IF} = 1 mm Hg
38 mm Hg	26 mm Hg	16 mm Hg	26 mm Hg
NFP = Filtration pressure – Absorption pressure		NFP = Filtration pressure – Absorption pressure	
= 38 mm Hg – 26 mm Hg = 12 mm Hg		= 16 mm Hg – 26 mm Hg = –10 mm Hg	

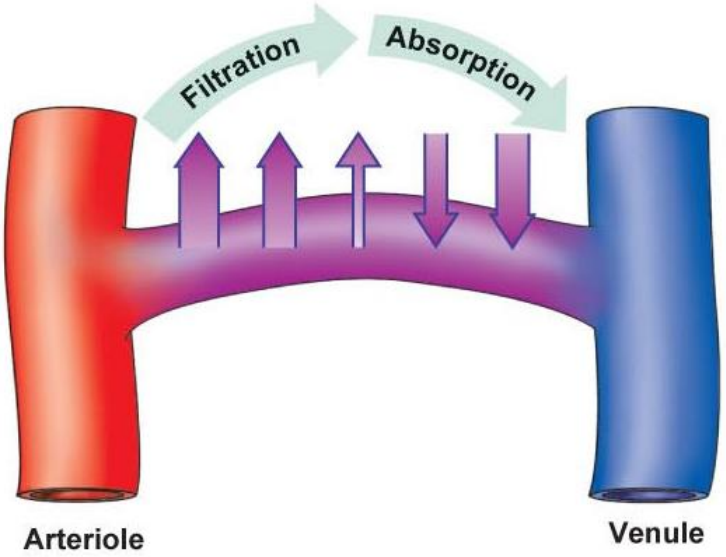
(b)

- ***Net filtration pressure (NFP)= $(P_{CAP} + \pi_{IF}) - (\pi_{CAP} + P_{IF})$***
- ***Net across capillary: filtration > absorption***
- ***Net filtration = 3 L/day***
- ***Lymphatic system picks up excess filtrate and returns it to circulation***

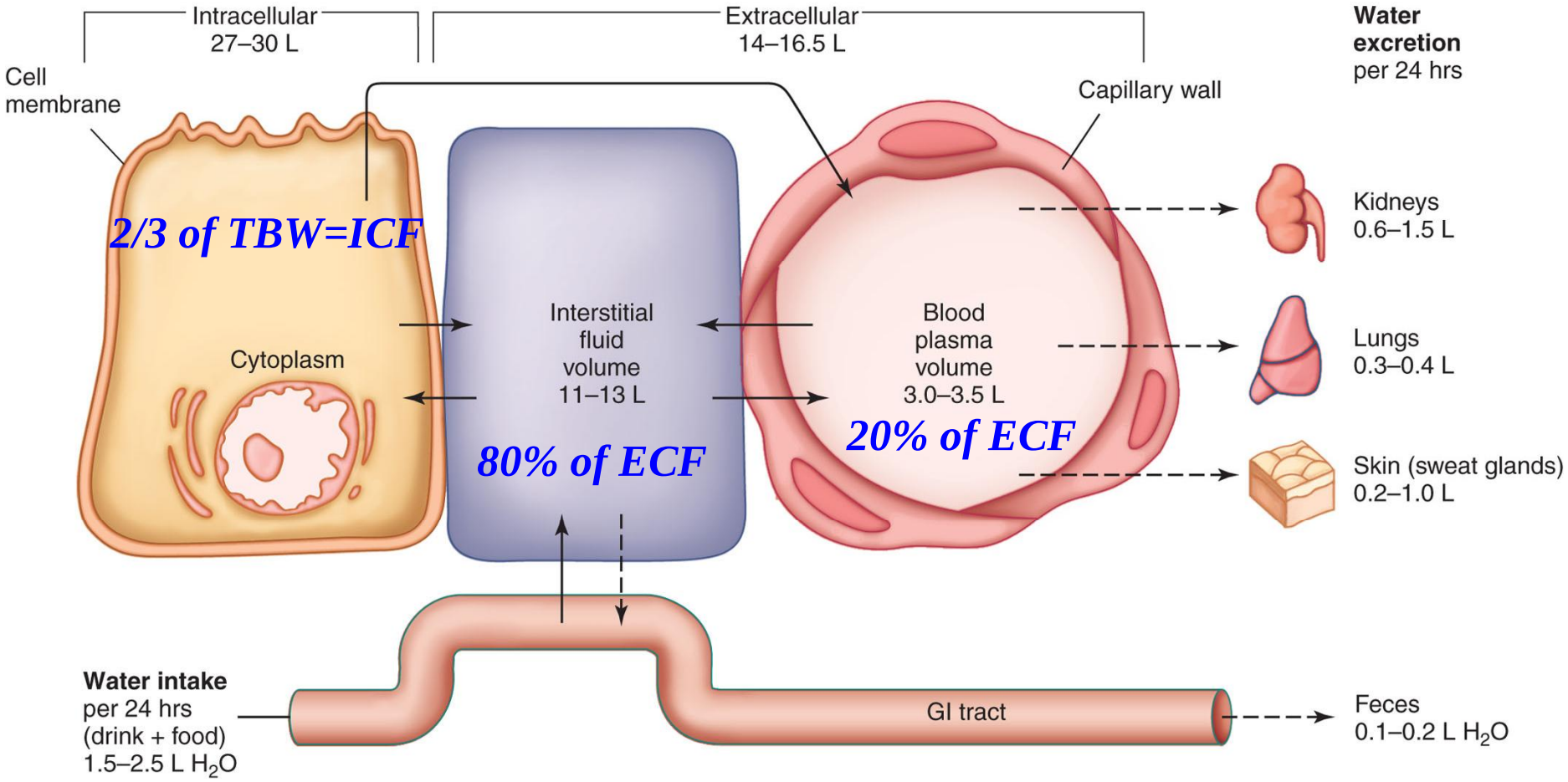
Starling Forces
Across Capillary Walls

Force	Definition	Direction of force	Approximate value
Capillary hydrostatic pressure, P_{CAP}	Hydrostatic pressure exerted by the presence of fluid inside the capillary	Filtration	16–38 mm Hg
Interstitial fluid hydrostatic pressure, P_{IF}	Hydrostatic pressure exerted by the presence of fluid outside the capillary	Absorption	1 mm Hg
Capillary osmotic pressure, π_{CAP}	Osmotic force due to presence of proteins in plasma	Absorption	25 mm Hg
Interstitial fluid osmotic pressure, π_{IF}	Osmotic force due to presence of proteins in interstitial fluid	Filtration	0 mm Hg
Net filtration pressure, NFP	**Difference between forces for filtration and absorption**	**If positive: filtration if negative: absorption**	**2 mm Hg**





Body Water Distribution



- **Osmotic forces** (control the movement of water: ISF-capillaries; ISF-ICF), **water excretion** (urine formation) and **water intake** (drinking) play a important role in <u>blood volume homeostasis</u>

Clinical Application: 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 P_{CAP}	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 π_{IF}	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 π_{CAP}	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

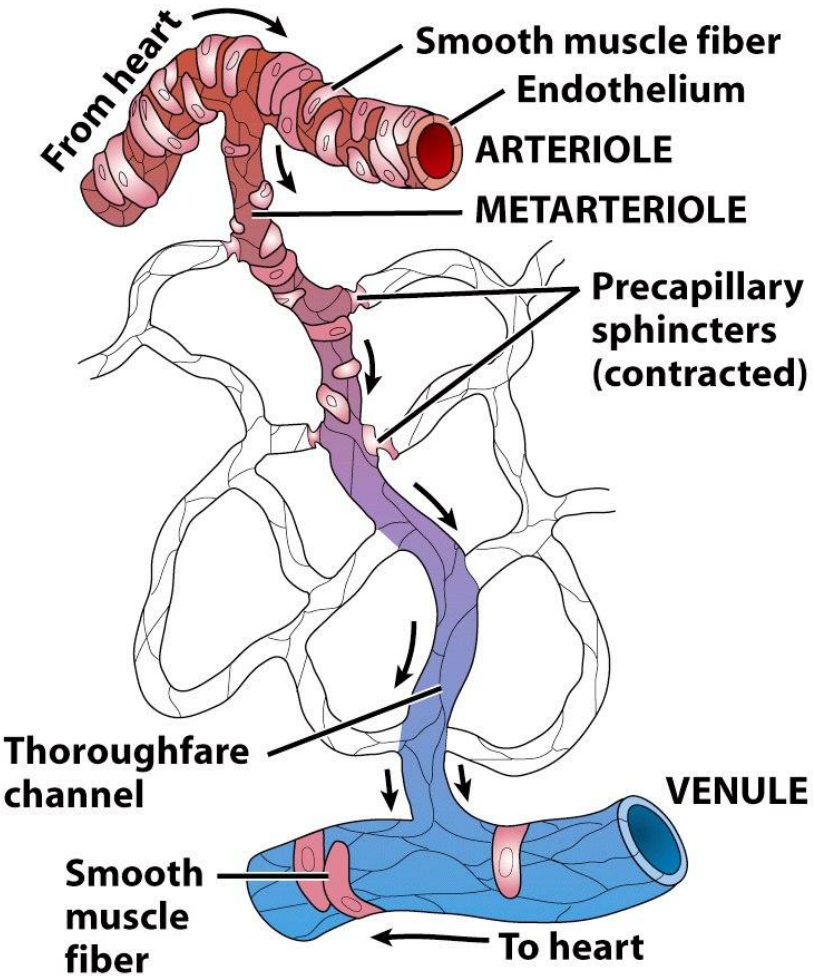
Clinical Application: Edema

An abnormal increase in interstitial fluid

表 11-19　組織液增多的影響因素

原因	實例
1. 微血管血壓↑ P_{CAP}	靜脈回流受阻 ***ex. CHF***
2. 組織液膠體滲透壓↑ π_{IF}	病理性微血管通透性上升，部分血漿蛋白過濾進入組織液
3. 血漿膠體滲透壓↓ π_{CAP}	低蛋白血症
4. 淋巴回流受阻	絲蟲病導致淋巴管阻塞引起的象皮腿；乳腺癌阻塞淋巴管
5. 微血管通透性↑ π_{IF}	炎症、過敏反應 ***ex. histamine etc.***

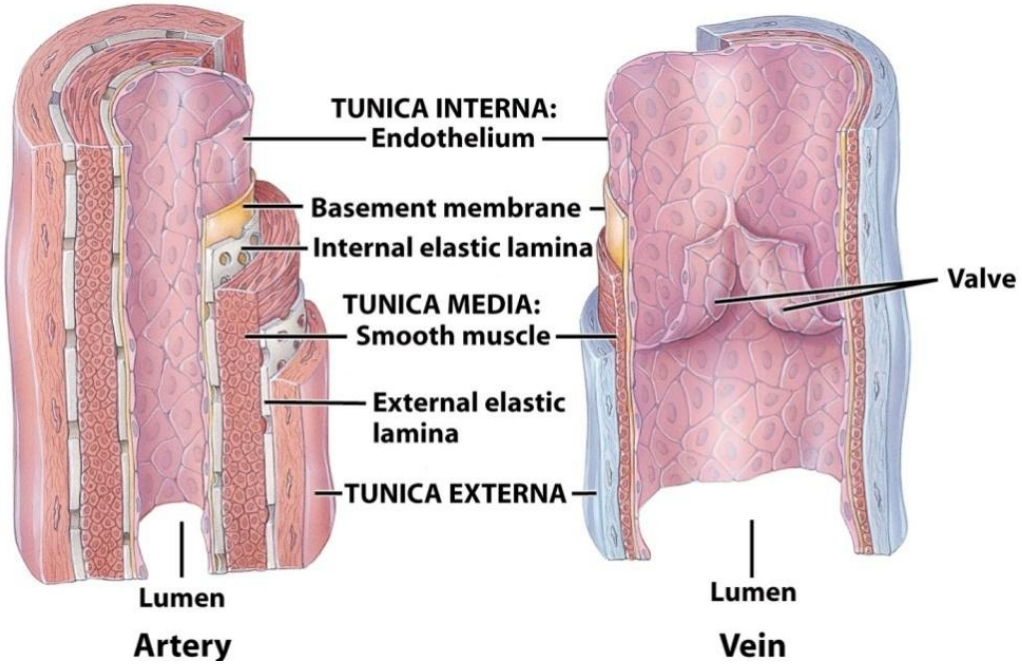
Venules

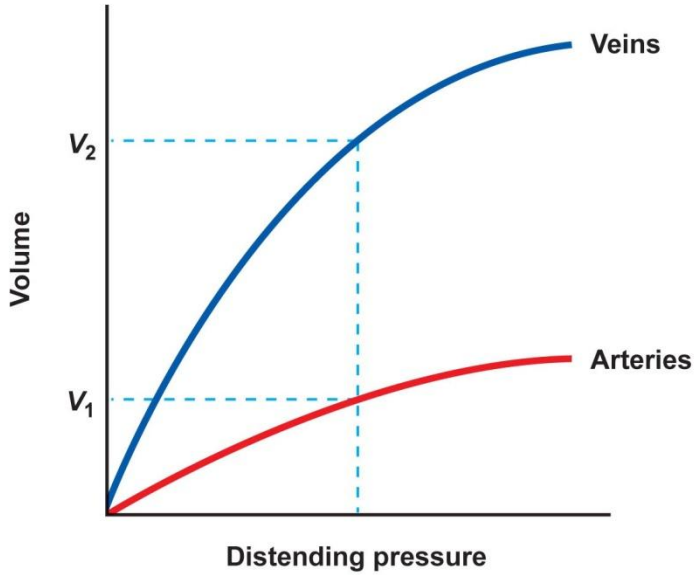


Sphincters contracted: blood flowing through thoroughfare channel

- **Small veins** collecting blood from capillaries
- **Smaller** than arterioles
- Form part of microcirculatory exchange unit with capillaries
- Tunica media contains only a few smooth muscle cells & scattered fibroblasts
  - --Very porous endothelium allows for escape of many phagocytic white blood cells

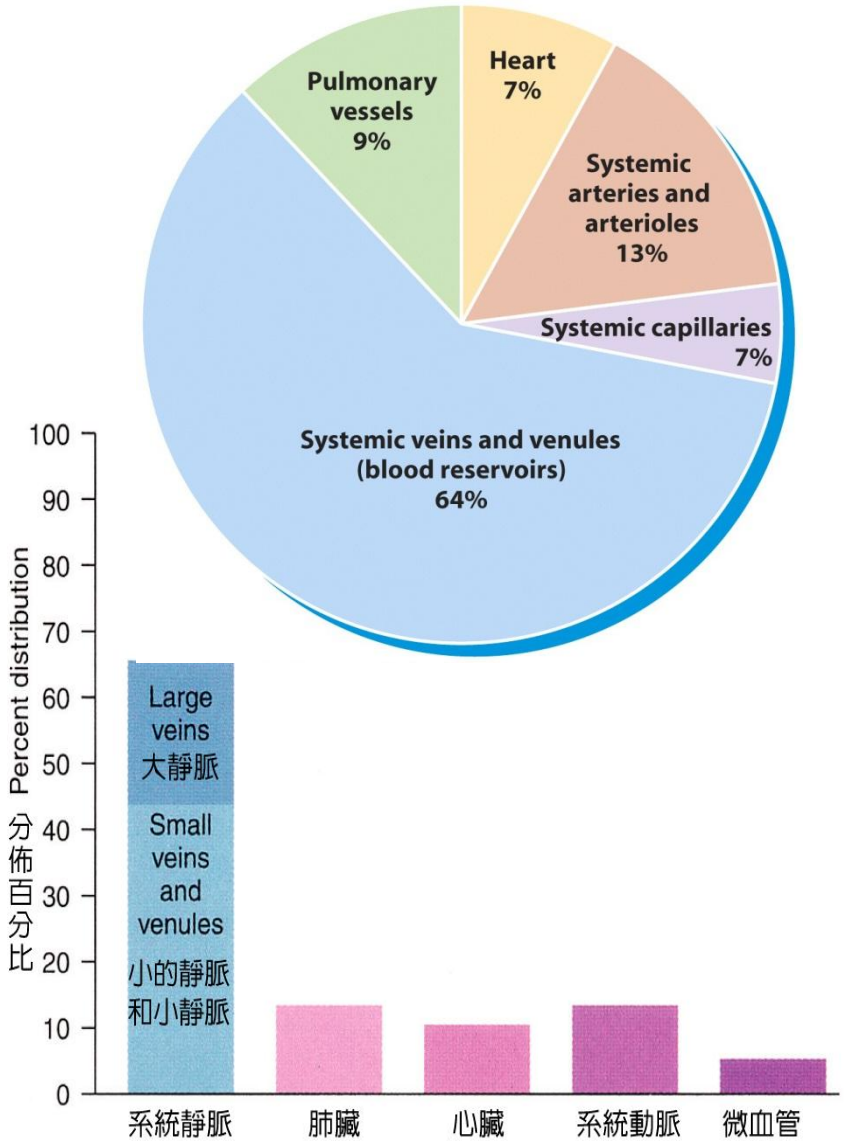
Veins





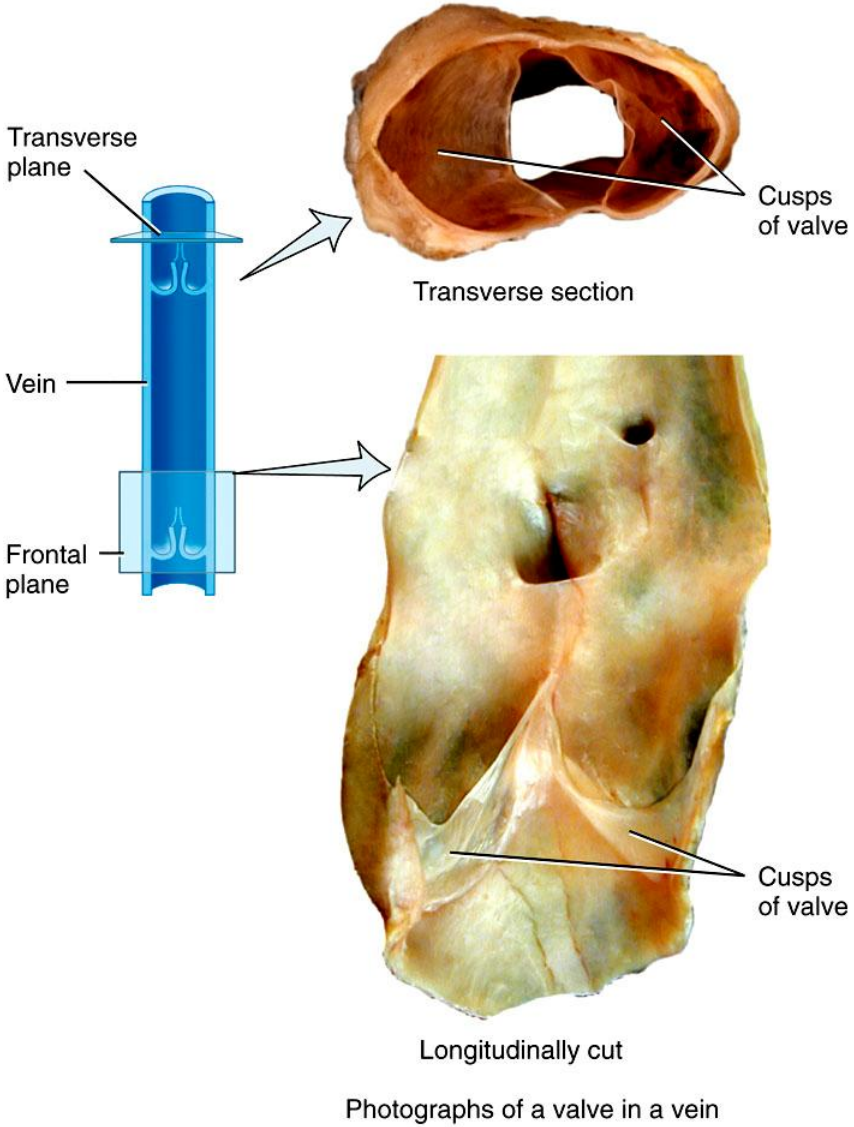
- ***Veins*** consist of the same three tunics as arteries but have a thinner tunica interna and media and a thicker tunica externa
  - --**Less** elastic tissue and smooth muscle
  - --**Thinner**-walled than arteries
  - --Contain ***valves*** to prevent the backflow of blood
- Veins are highly distensible= ***capacitance (compliant) vessels*** that act as **blood reservoirs**
  - --64% total blood volume in systemic veins at rest

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

Venous Valves



Photographs of a valve in a vein

- Valves allow ***unidirectional blood flow***
  - --Present in peripheral veins
  - --Absent from central veins
- Valves – folds on tunica interna forming cusps
  - --Aid in ***venous return*** by preventing backflow
- ***Portal vein*** – blood passes through second capillary bed
  - --Hepatic or hypophyseal
- ***Vascular (venous) sinuses*** are veins with very thin walls with no smooth muscle to alter their diameters
  - --***Brain's superior sagittal sinus*** and the ***coronary sinus*** of the heart

Venous Pressure

- Blood pressure in veins is ~15 mm Hg. This is not sufficient to move blood back to the heart. So there are the "**pumps**":

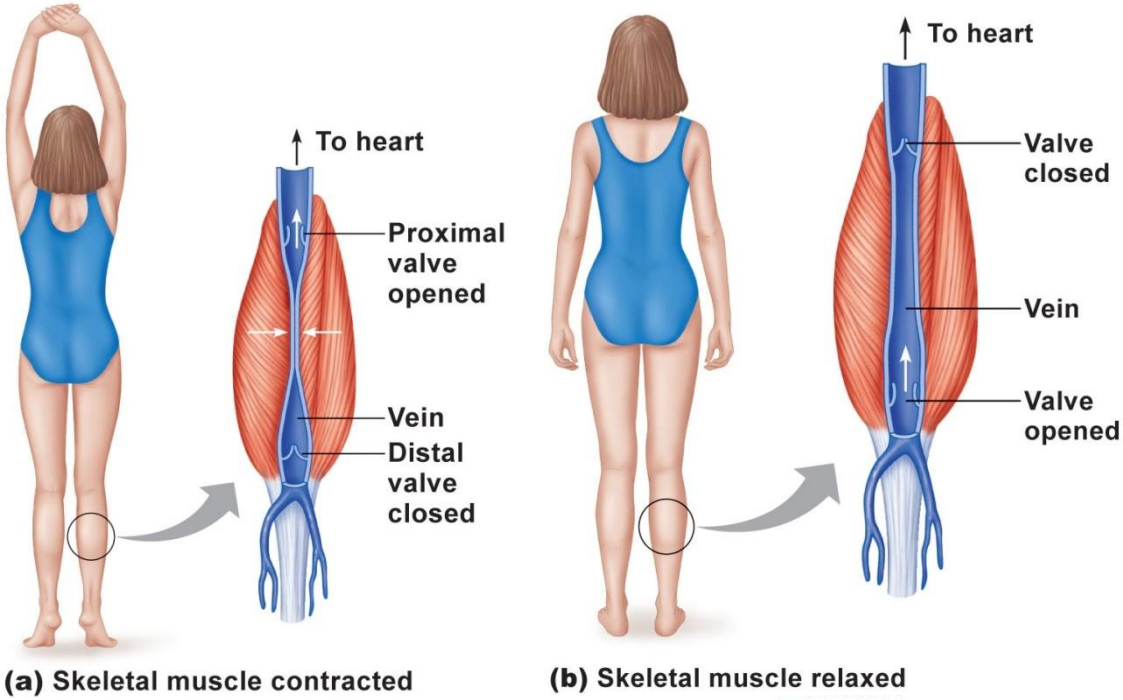
  1. **Respiratory pump: *Inhalation*** increases abdominal cavity pressure in relation to thoracic pressure and helps to propel blood back to the heart

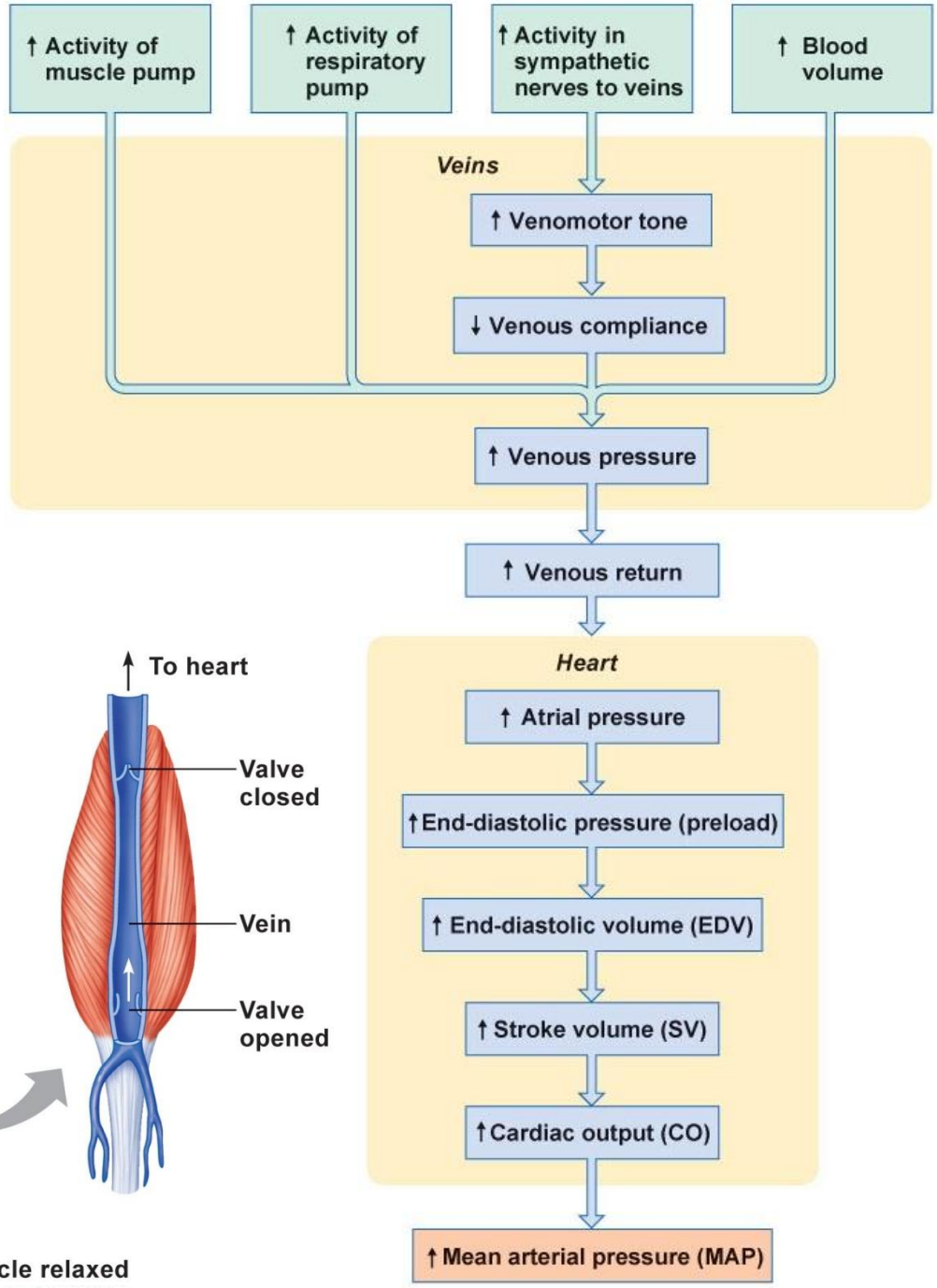
  2. **Muscular pump: *Muscles contract*** blood moving forward and being prevented from backflow by the ***venous valves***. This moves blood toward the heart

- The smooth muscle in the veins is under ***SNS control*** and contract (***venoconstriction***) when stimulated, similar to the arterial smooth muscle. This causes contraction and a narrowing of the lumen

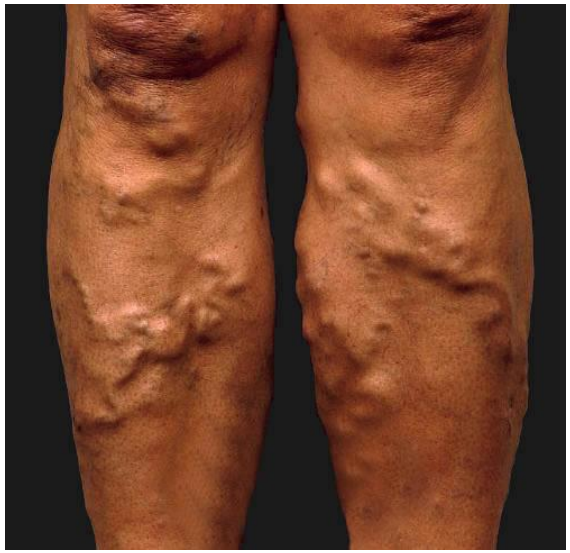
Factors Affecting Venous Pressure

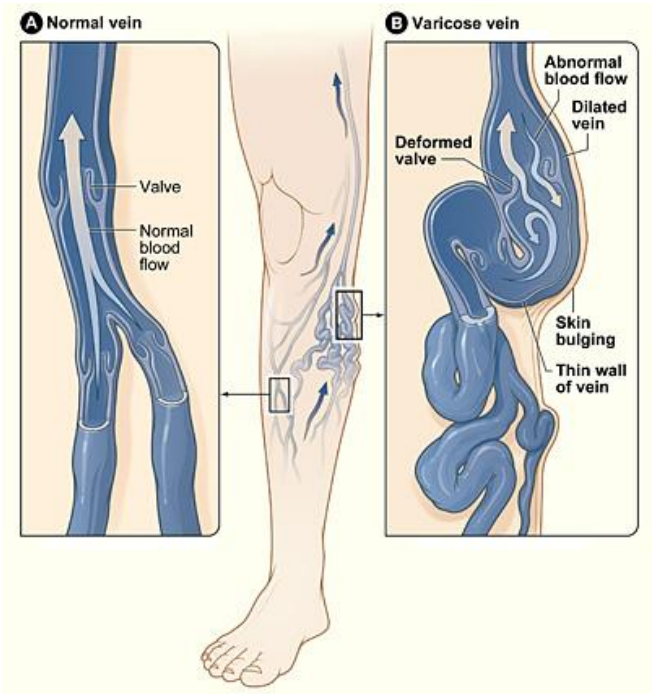
- ***Skeletal muscle pump***
- ***Respiratory pump***
- ***Blood volume***
- ***Venomotor tone***





Clinical Application: Varicose Veins

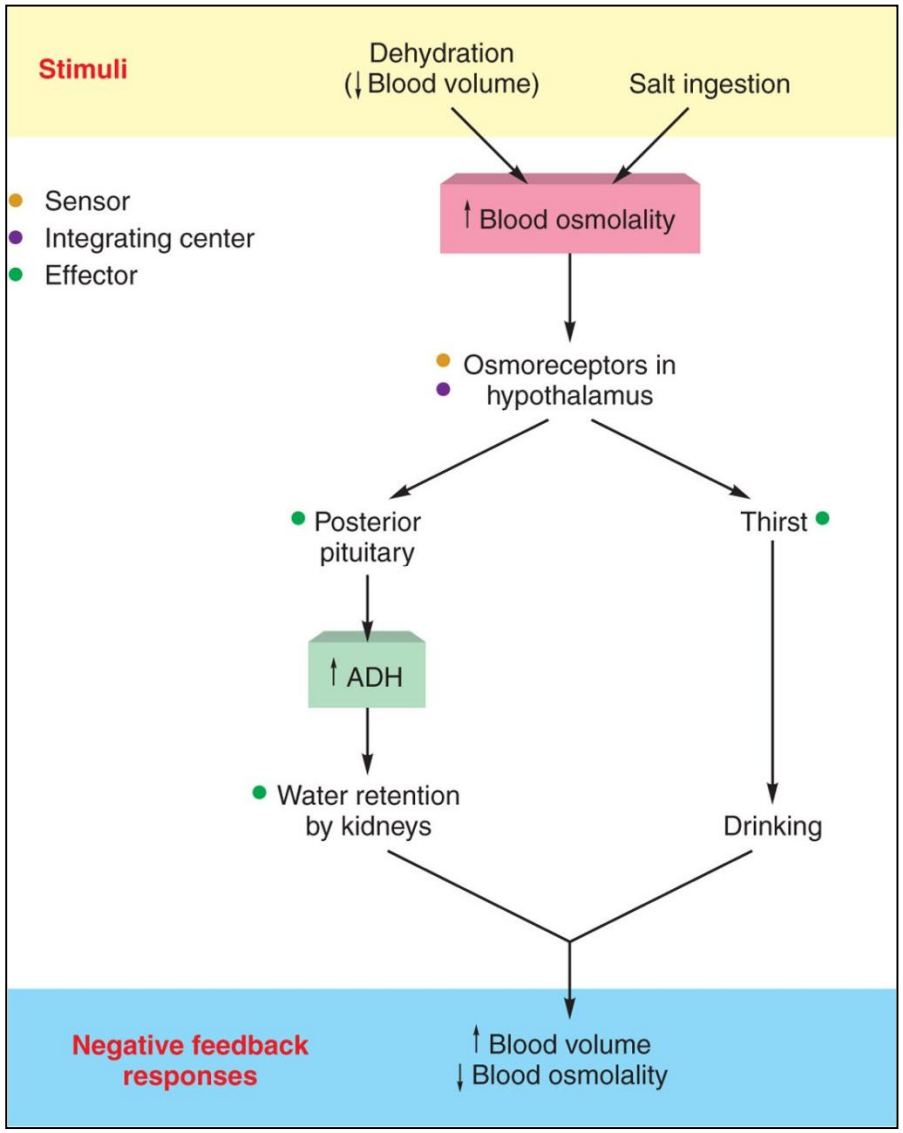




- **Twisted, dilated superficial veins**
  - --Caused by **leaky venous valves**
    - Congenital or mechanically stressed from prolonged standing or pregnancy
  - --Allow **backflow and pooling of blood**
    - Extra pressure forces fluids into surrounding tissues
    - Nearby tissue is inflamed and tender
- The most common sites are in the **esophagus**, 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***

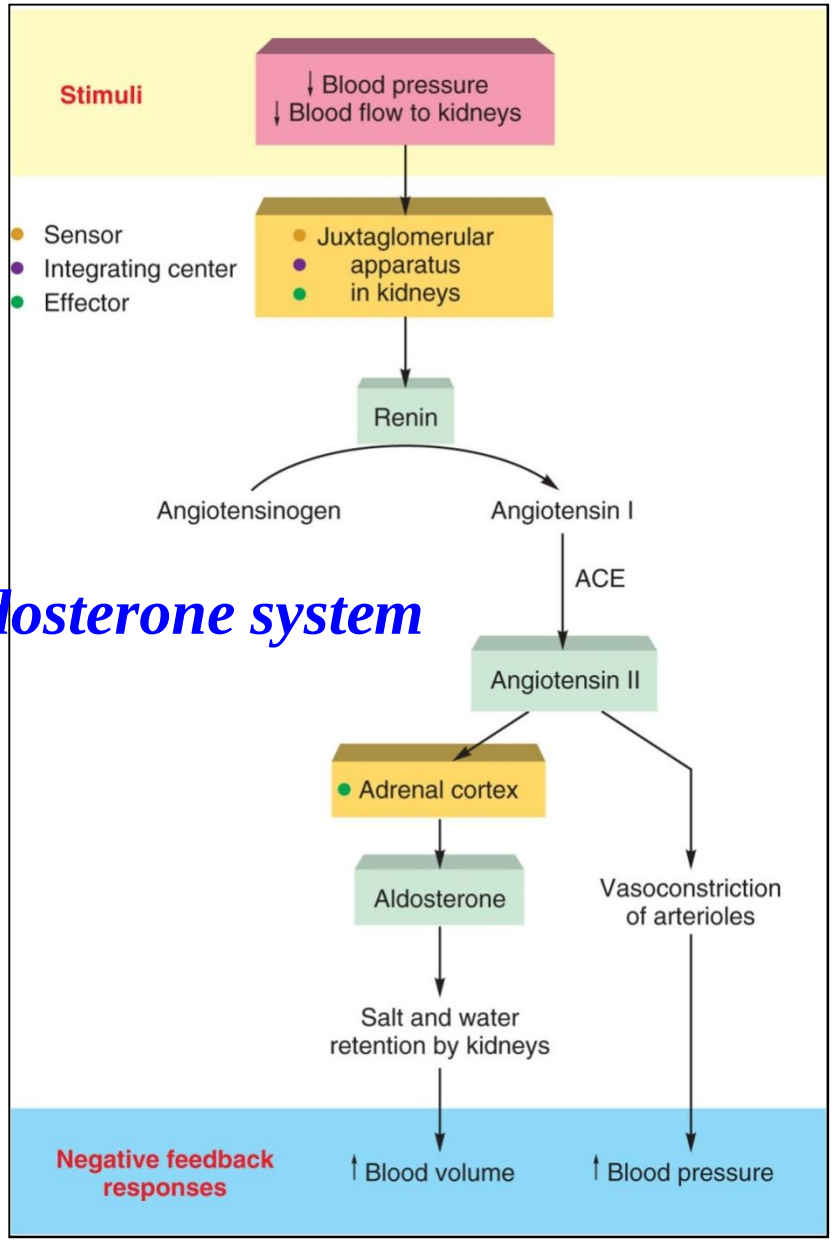
Regulation of Blood Volume by Kidneys

- **180 L** of filtrate is moved across the glomeruli per day, yet only about **1.5 L** is actually removed as urine. The rest is reabsorbed into the blood
- The amount of fluid reabsorbed is controlled by ***several hormones*** in response to the body's needs
- ***Antidiuretic hormone (ADH)=vasopressin (AVP)***
- Stretch receptors in left atrium, carotid sinus, and aortic arch also ***inhibit*** ADH release



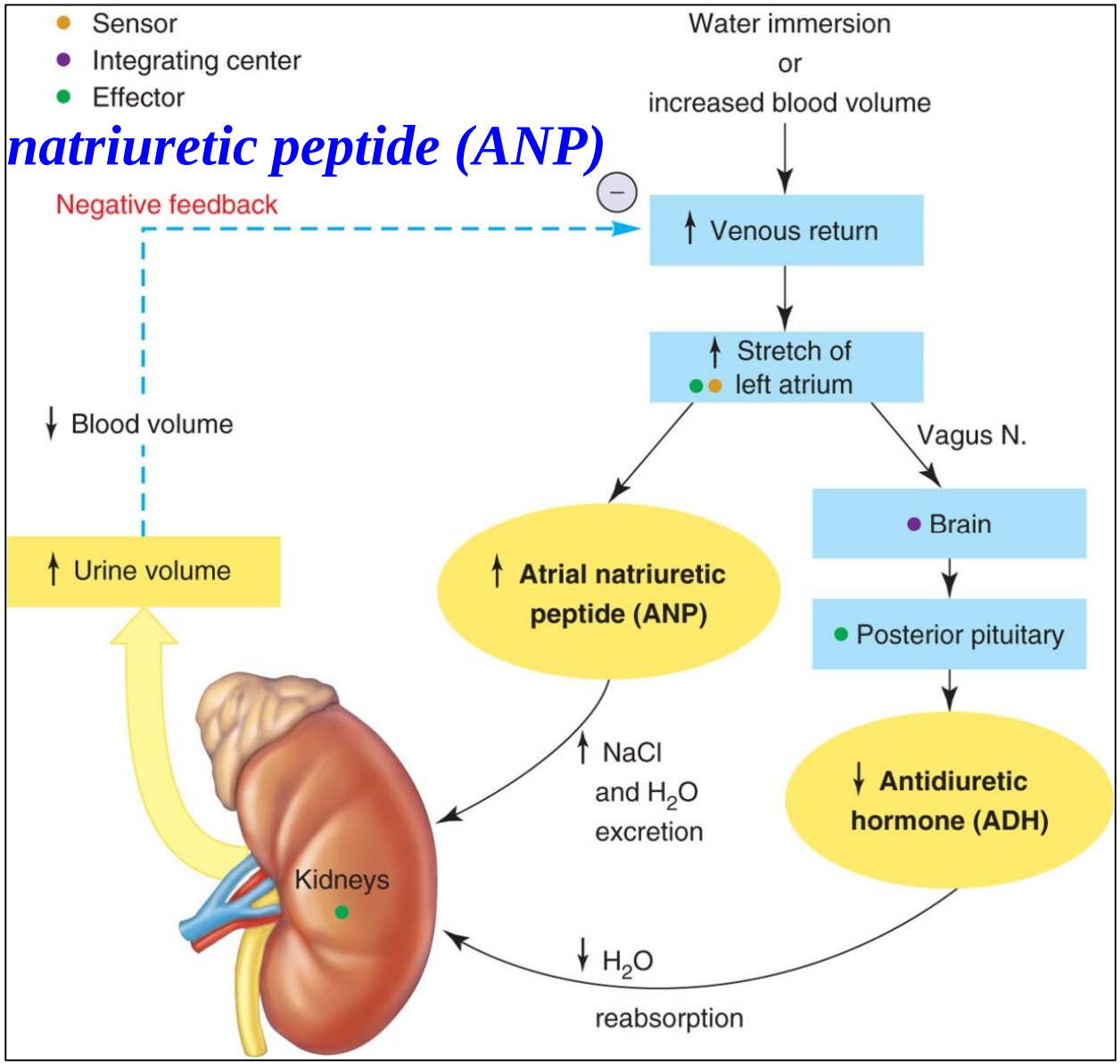
Regulation of Blood Volume by Kidneys

➢ ***Renin-angiotensin-aldosterone system (RAAS)***



Regulation of Blood Volume by Kidneys

➢ ***Atrial natriuretic peptide (ANP)***



Hemodynamics

$$Flow = \Delta P/R$$

$$CO = MAP / TPR$$

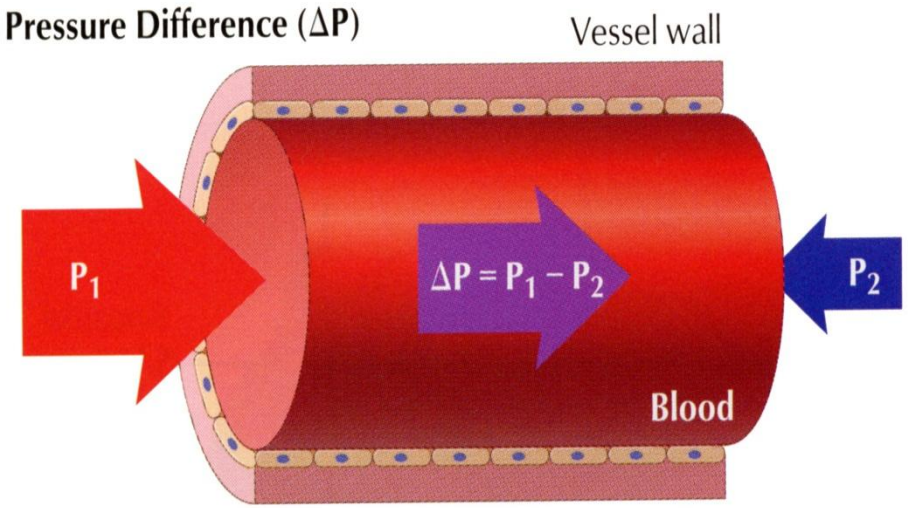
$$MAP = CO \times TPR$$

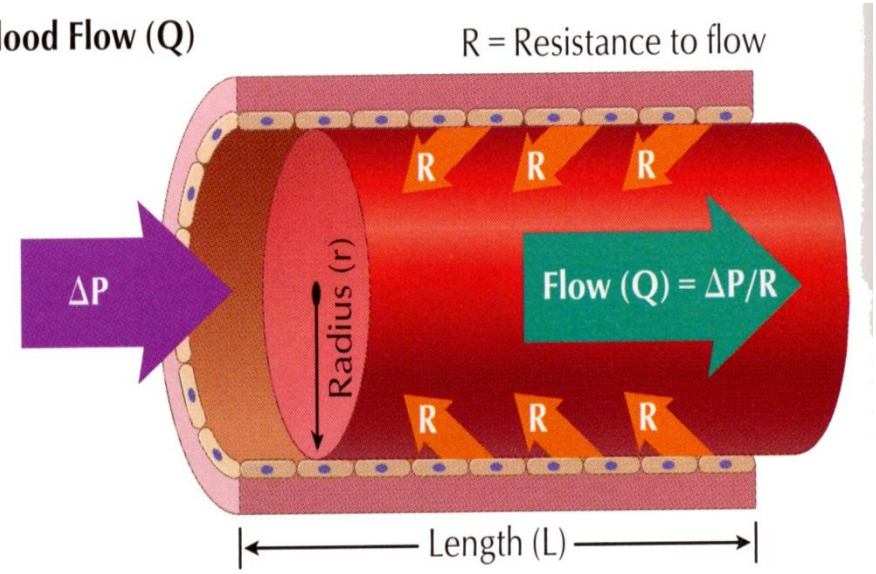
$$MAP = SV \times HR \times TPR$$

- **Factors affecting circulation**
  - **--Pressure differences (△P)** that drive the blood flow
    - ***Velocity of blood flow* (inversely related to the cross-sectional area)**
    - ***Volume of blood flow* (CO=MAP / TPR)**
      - ***--venous return (4 factors)***
    - ***Blood pressure* (MAP=CO × TPR)**
  - **--Resistance to flow (R)**
- **An interplay of forces result in blood flow**

Hemodynamic: Pressure Difference

血流量指每分鐘流經血管某一截面的血量，
取決於血管兩端的壓力差(△P)和血流阻力(R)





Hemodynamics: Resistance

Resistance to Flow (R)

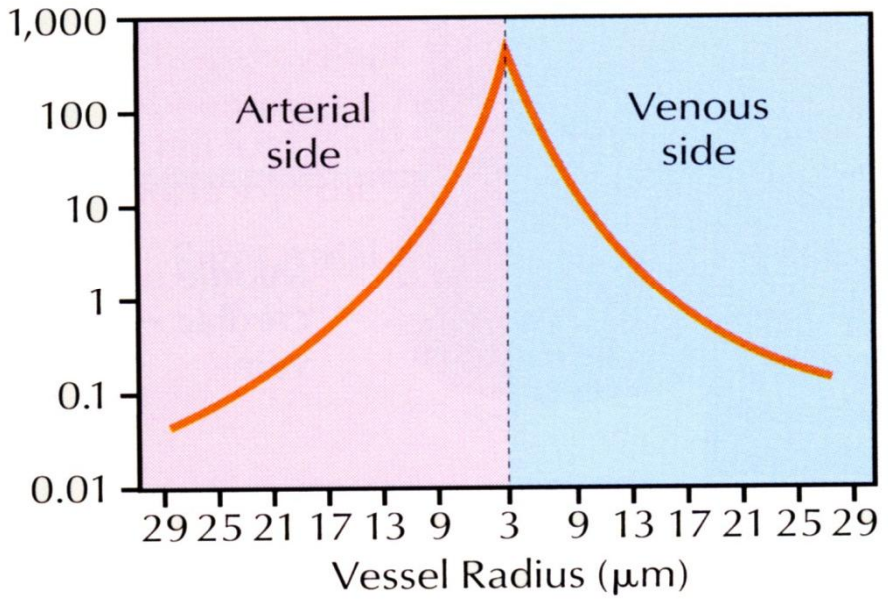
Poiseuille's Law

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

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 (***Flow = ΔP/R***)
- Vascular resistance depends on the ***vessel radius***, ***blood viscosity***, and ***total blood vessel length***
- ***Systemic vascular resistance*** (***total peripheral resistance=TPR***) refers to all of the vascular resistances offered by systemic blood vessels

Factors Affecting Resistance to Flow

- **Radius of vessel**

  --In ***arterioles*** (and small arteries) — can regulate radius

- **Length of vessel**

  --In ***obesity (↑body size)*** — can ↑total vessel length (↑R)

- **Viscosity of fluid = η**

  --Blood viscosity dependent on ***amount of RBCs (Hct) and shear rate***

Resistance to Flow (R)

Poiseuille's Law

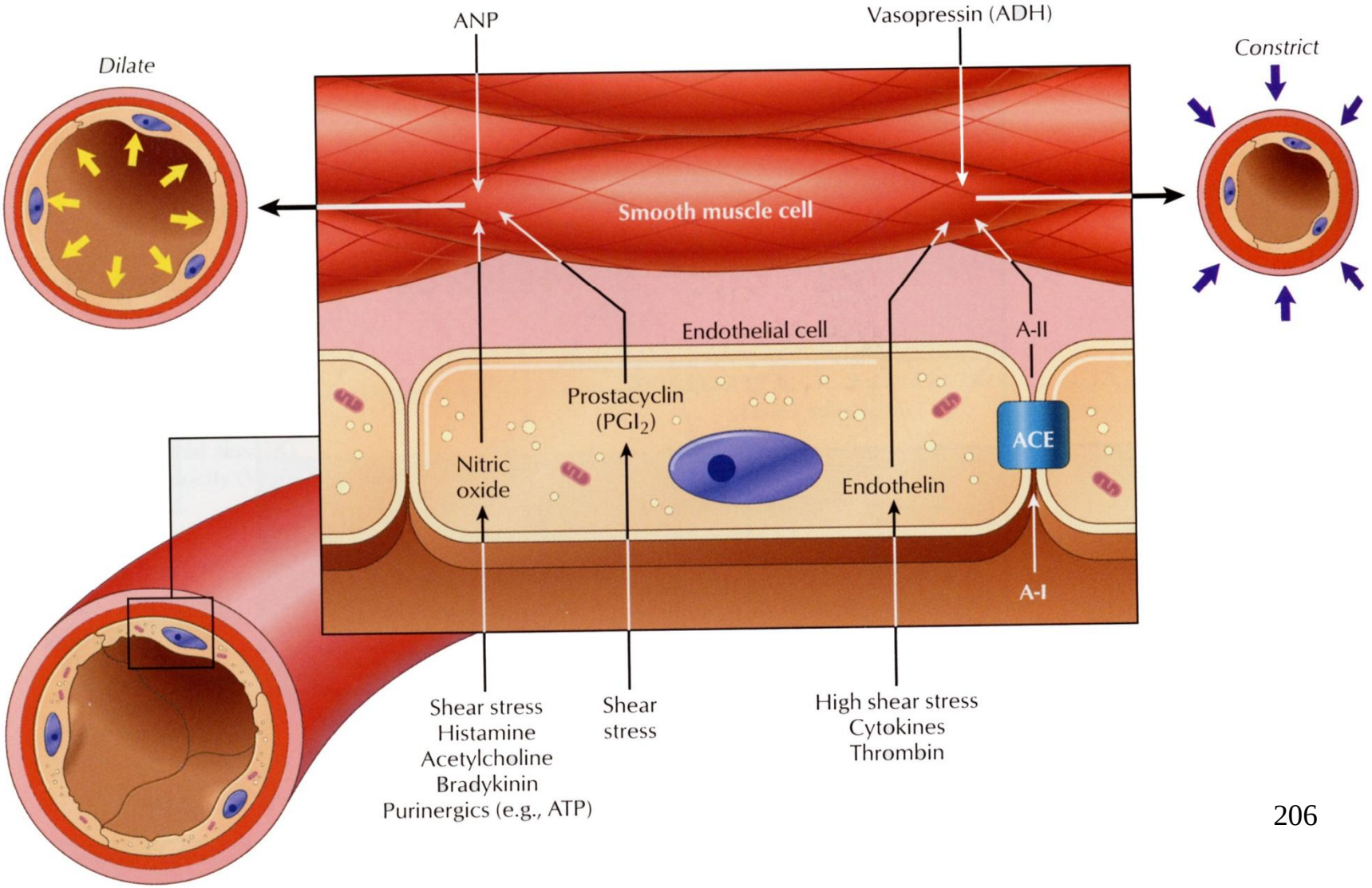
$$R = \frac{\eta \times L \times 8}{\pi r^4}$$

η = viscosity
L = vessel length
r = vessel radius

- 血流阻力(R) 與**血管長度(L) 及血液黏稠度(η) 成正比**，與**血管半徑的四次方(r^4)成反比**
- 當其他條件都相同時，若管徑變為原先的**一半**，則血流阻力便會增加 2^4 = **16 倍**
- 對血流阻力影響最大的因素為**血管管徑**

Total peripheral resistance (TPR)

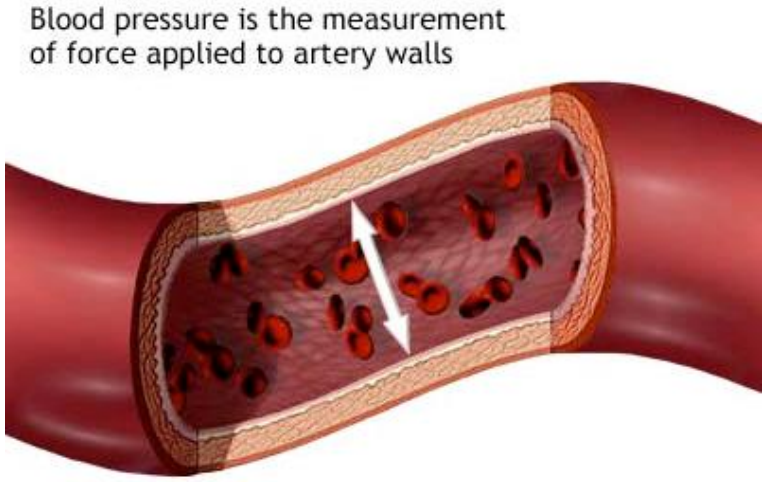
- ✓ ***Neural Controls***
- ✓ ***Hormone Controls***
- ✓ ***Local Controls***

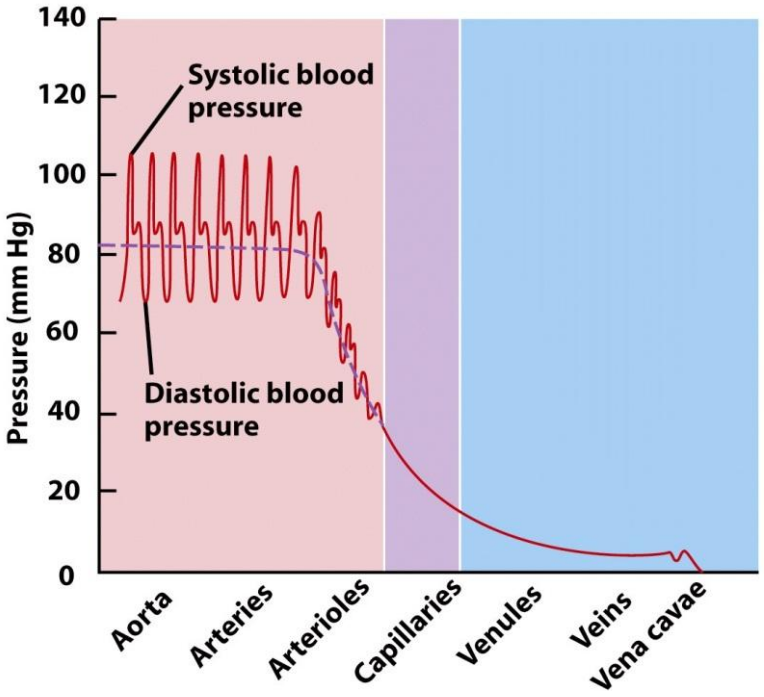


Extrinsic Control of Vascular Resistance

Extrinsic Agent	Effect	Comments
Sympathetic nerves		
Alpha-adrenergic	Vasoconstriction	Vasoconstriction is the dominant effect of sympathetic nerve stimulation on the vascular system, and it occurs throughout the body.
Beta-adrenergic	Vasodilation	There is some activity in arterioles in skeletal muscles and in coronary vessels, but effects are masked by dominant alpha-receptor-mediated constriction.
Cholinergic	Vasodilation	Effects are localized to arterioles in skeletal muscles and are produced only during defense (fight-or-flight) reactions.
Parasympathetic nerves	Vasodilation	Effects are restricted primarily to the gastrointestinal tract, external genitalia, and salivary glands and have little effect on total peripheral resistance.
Angiotensin II	Vasoconstriction	A powerful vasoconstrictor produced as a result of secretion of renin from the kidneys; it may function to help maintain adequate filtration pressure in the kidneys when systemic blood flow and pressure are reduced.
ADH (vasopressin)	Vasoconstriction	Although the effects of this hormone on vascular resistance and blood pressure in anesthetized animals are well documented, the importance of these effects in conscious humans is controversial.
Histamine	Vasodilation	Histamine promotes localized vasodilation during inflammation and allergic reactions.
Bradykinins	Vasodilation	Bradykinins are polypeptides secreted by sweat glands and by the endothelium of blood vessels; they promote local vasodilation.
Prostaglandins	Vasodilation or vasoconstriction	Prostaglandins are cyclic fatty acids that can be produced by most tissues, including blood vessel walls. Prostaglandin I_2 is a vasodilator, whereas thromboxane A_2 is a vasoconstrictor. The physiological significance of these effects is presently controversial.

Blood Pressure





- Pressure exerted by blood on walls of a vessel
  - --Caused by **contraction of 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

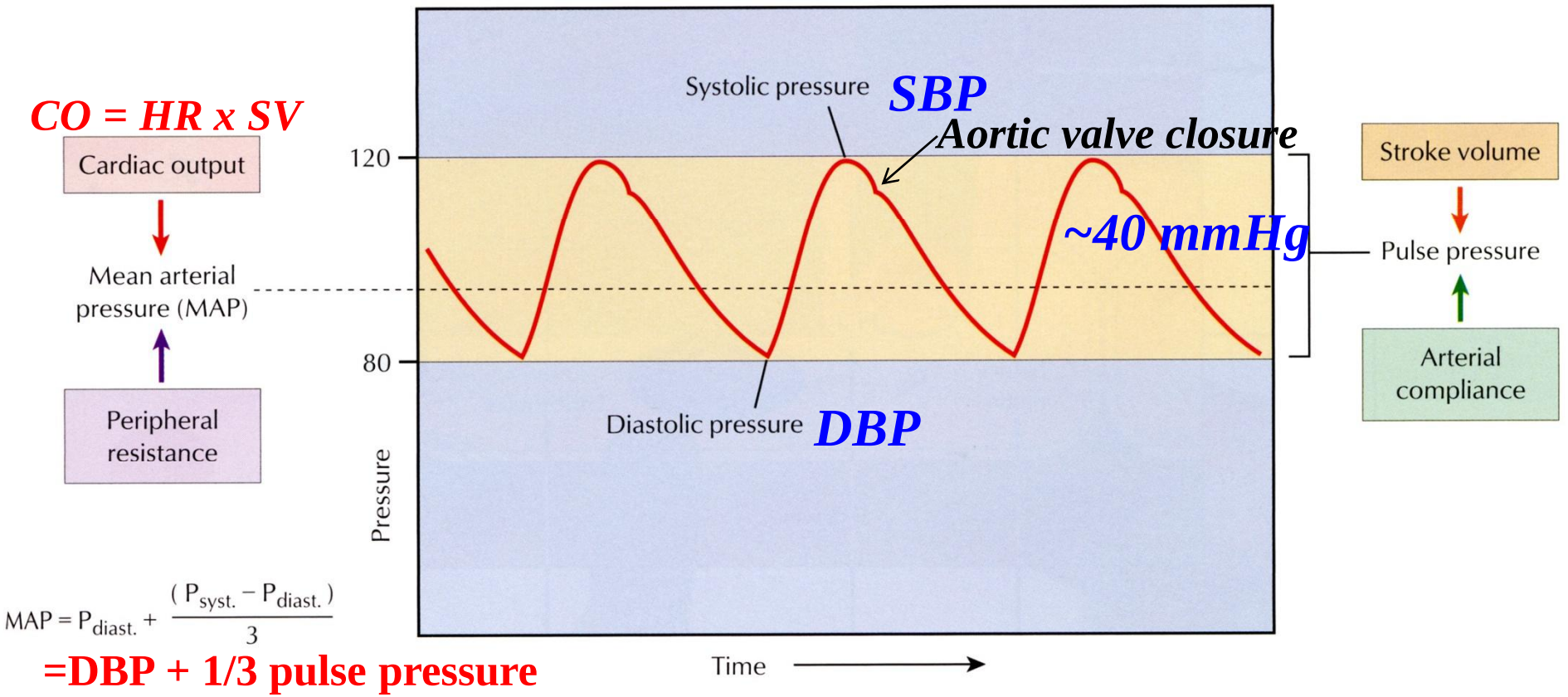
Arterial Pressure

MAP = CO x TPR

MAP determined by

- ***Heart rate***
- ***Stroke volume***
- ***Total peripheral resistance***

CO = HR x SV

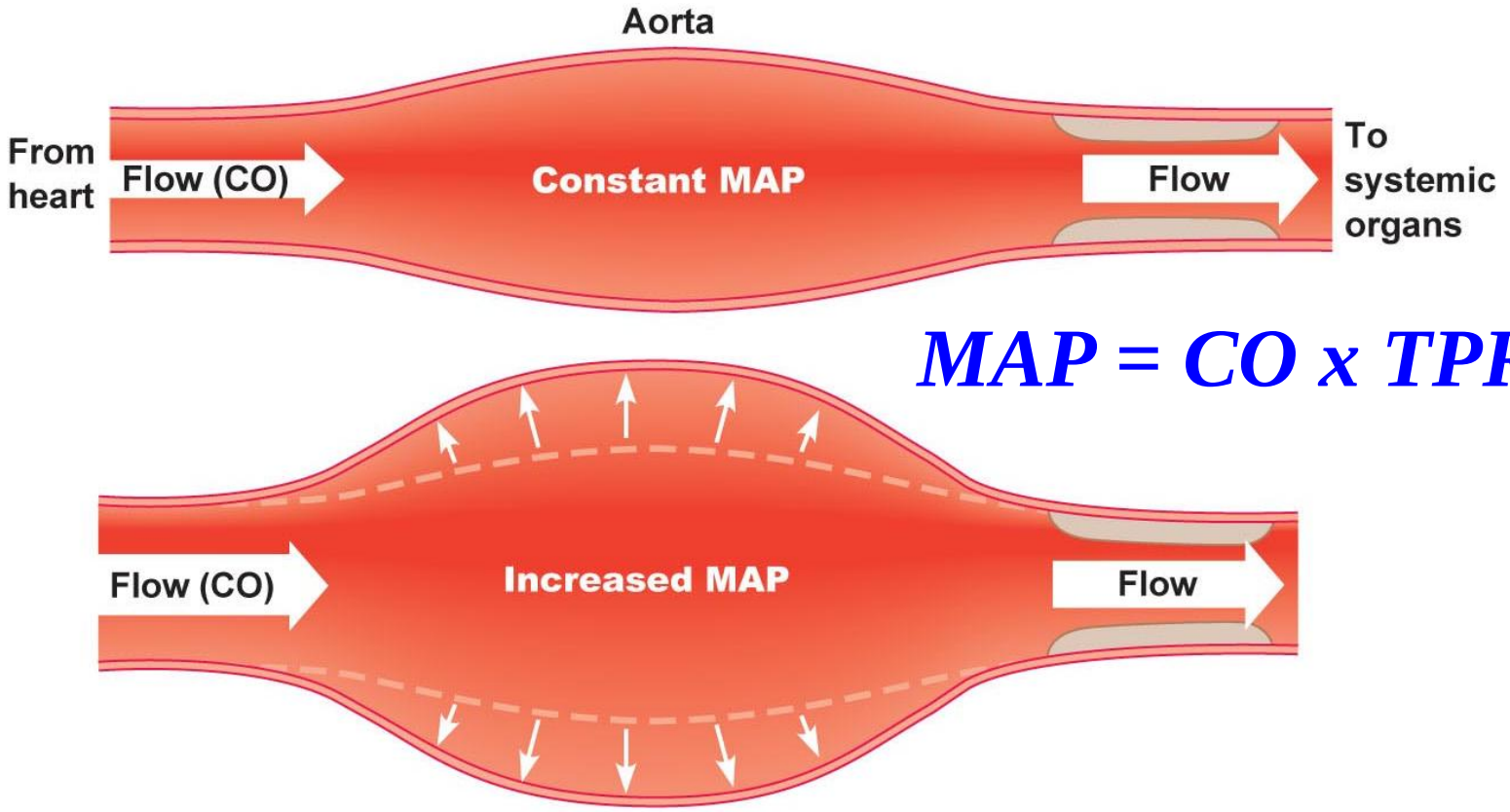


$$MAP = P_{diast.} + \frac{(P_{syst.} - P_{diast.})}{3}$$

=DBP + 1/3 pulse pressure

SBP:DBP:PP= 3:2:1

Effects of Cardiac Output on Mean Arterial Pressure

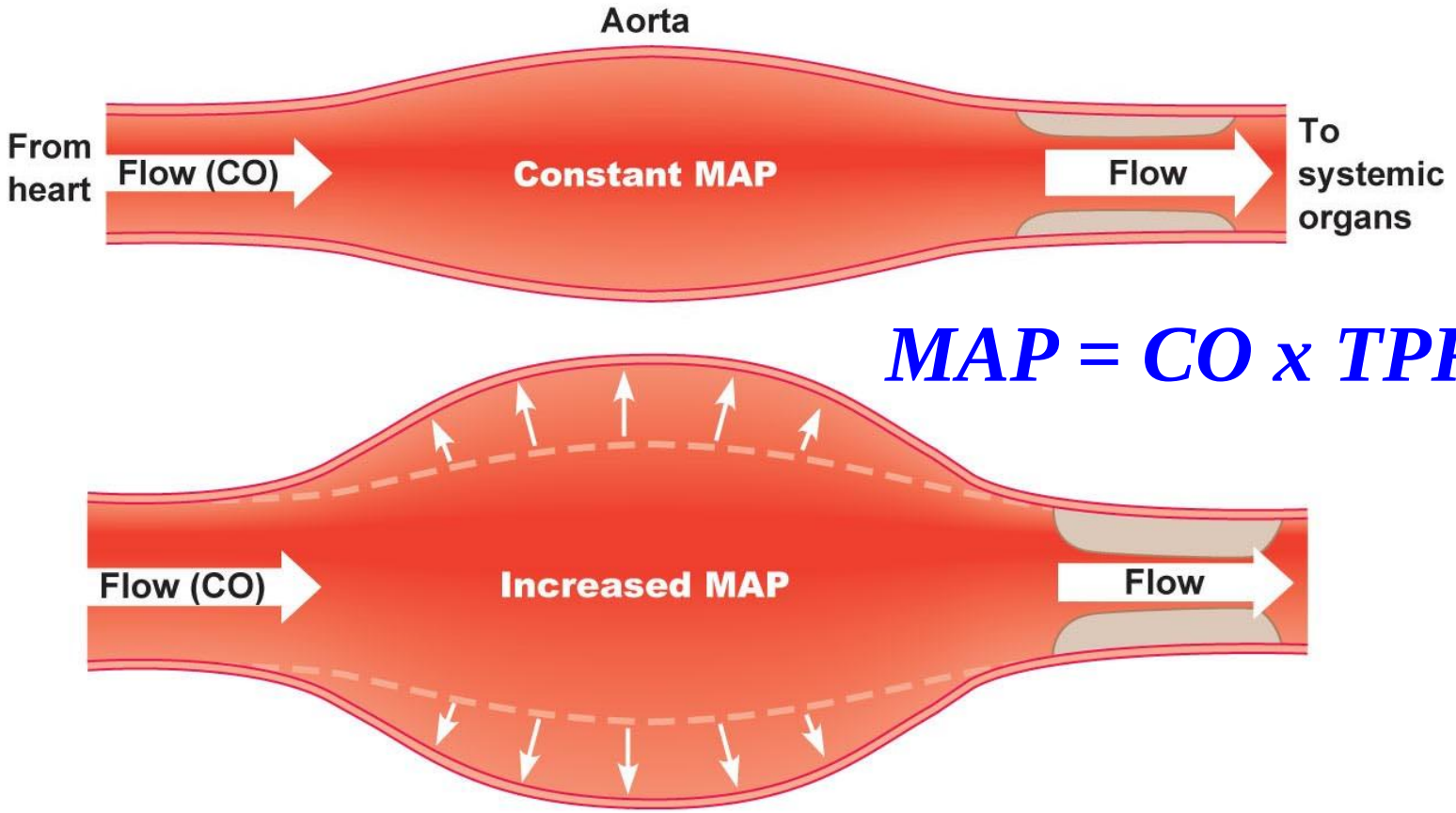


An increase in cardiac output . . .

. . . leads to an increase in the volume of blood contained in the aorta and an increase in mean arterial pressure . . .

. . . when total peripheral resistance remains the same.

Effects of TPR on Mean Arterial Pressure



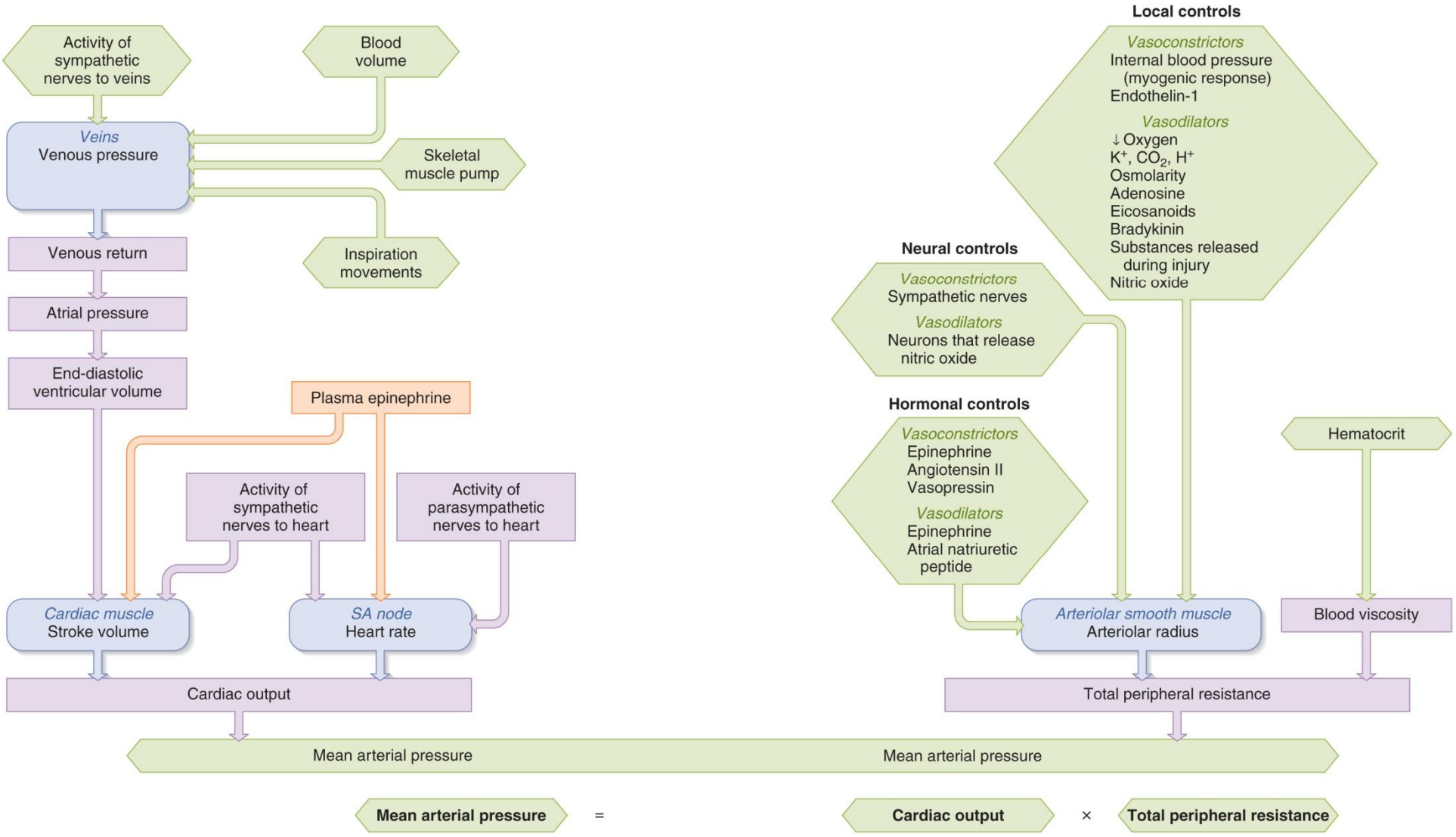
$$MAP = CO \times TPR$$

A constant cardiac output . . .

. . . leads to an increase in the volume of blood contained in the aorta and an increase in mean arterial pressure . . .

. . . when total peripheral resistance increases.

Control of Blood Pressure



MAP=CO × TPR

Determinants of Arterial Pressure

MAP = HR x SV x TPR

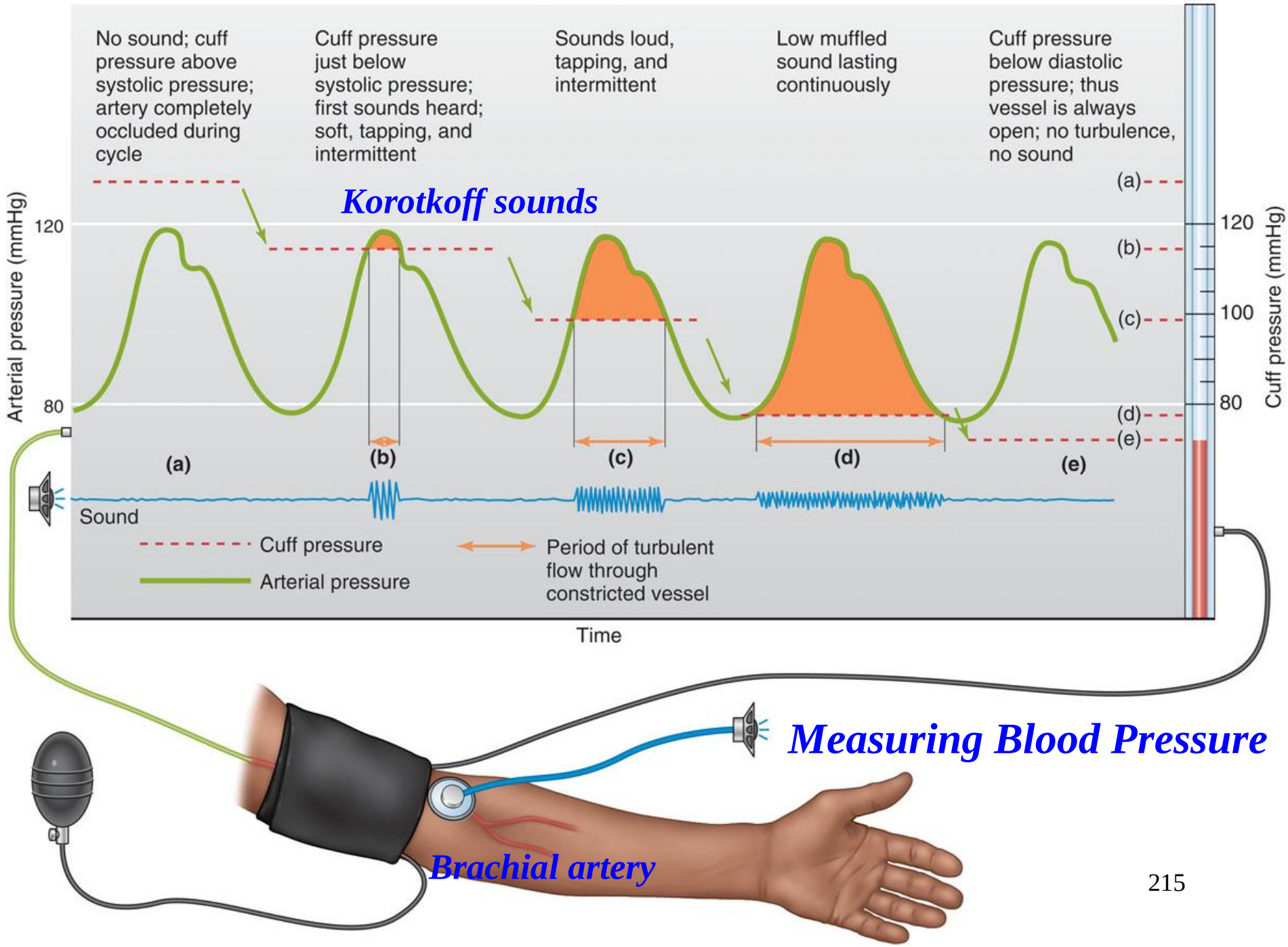
影響因素 \ 血壓變化	收縮壓	舒張壓	脈搏壓	主要作用
心搏量↑	↑↑	↑	↑	收縮壓
心跳速率↑	↑	↑↑	↓	舒張壓
周邊總阻力↑	↑	↑↑	↓	舒張壓
單純大動脈彈性↓	↑	↓	↑↑	脈搏壓
循環血量↓或失血	↓	↓	↓	

註：增加↑；明顯增加↑↑。

Determinants of Mean Arterial Pressure

MAP = HR x SV x TPR

Target organ or tissue	Neural or hormonal factor	Factor's effect on target	Influence on mean arterial pressure
Heart			
Sinoatrial node	Sympathetic nerves	↑HR	↑MAP
	Parasympathetic nerves	↓HR	↓MAP
	Epinephrine	↑HR	↑MAP
Ventricular myocardium	Sympathetic nerves	↑Contractility (↑SV)	↑MAP
	Epinephrine	↑Contractility (↑SV)	↑MAP
Arteriolar smooth muscle (most tissues)	Sympathetic nerves	Vasoconstriction (↑TPR)	↑MAP
	Epinephrine	Vasoconstriction or vasodilation, depending on concentration and location	Variable
	Vasopressin	Vasoconstriction (↑TPR)	↑MAP
	Angiotensin II	Vasoconstriction (↑TPR)	↑MAP
Venous smooth muscle	Sympathetic nerves	↑Venomotor tone	↑MAP
	Epinephrine	↑Venomotor tone	↑MAP


No sound; cuff pressure above systolic pressure; artery completely occluded during cycle
Cuff pressure just below systolic pressure; first sounds heard; soft, tapping, and intermittent
Sounds loud, tapping, and intermittent
Low muffled sound lasting continuously
Cuff pressure below diastolic pressure; thus vessel is always open; no turbulence, no sound
Korotkoff sounds
Arterial pressure (mmHg)
120
80
(a)
(b)
(c)
(d)
(e)
Sound
Cuff pressure
Arterial pressure
Period of turbulent flow through constricted vessel
Time
Cuff pressure (mmHg)
120
100
80
Measuring Blood Pressure
Brachial artery

血壓的測量

血壓的測量通常採用肱動脈的血壓計測量方法（圖 11-32）。水銀柱血壓計的組成包括壓脈帶、充氣橡皮球、水銀柱壓力計以及橡皮導管連接。測量血壓時，將壓脈帶繞住上臂，聽診器置於肘窩肱動脈處監聽動脈搏動聲音。

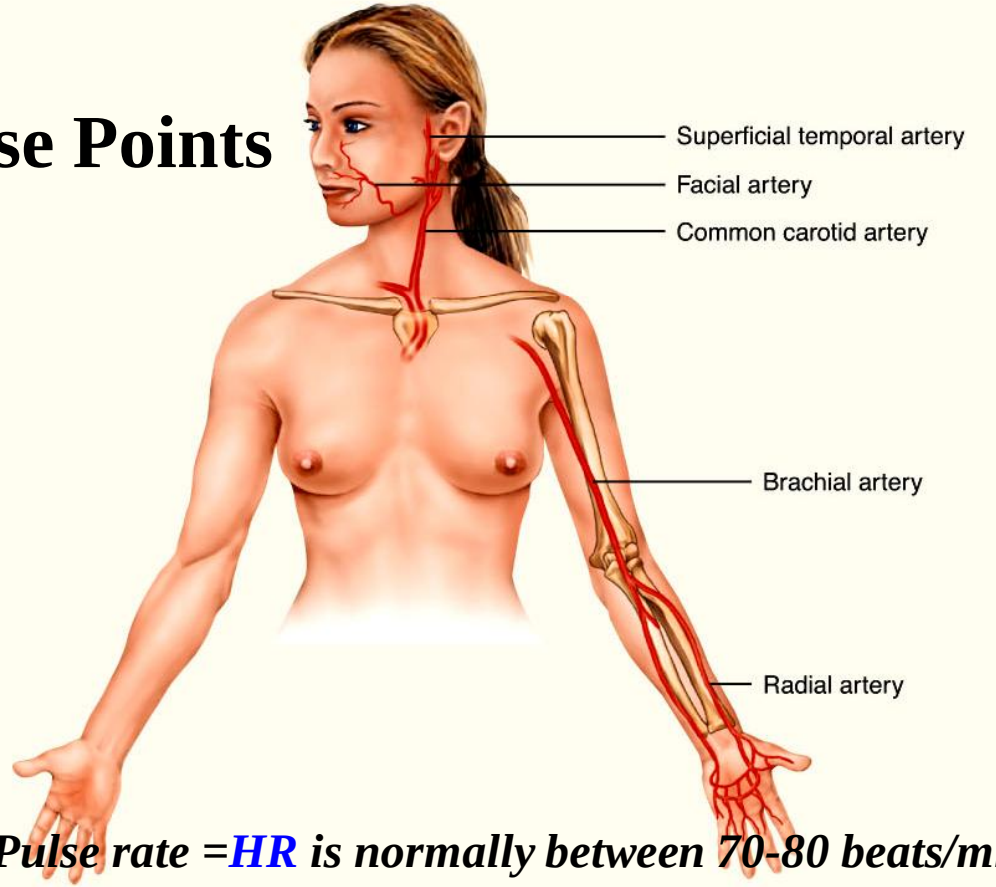
測壓初始向壓脈帶內充氣加壓，當壓脈帶的氣囊壓力超過動脈收縮壓後，使動脈完全閉陷，並阻止心動週期各期血流。然後逐漸放氣，氣囊壓力逐漸下降。當氣囊壓力降至與動脈收縮壓相等時，心臟射出的血液僅在動脈血壓處於最大時流出肱動脈，每次流過都將產生一次亂流，亂流引起血管壁振動。此時放在壓脈帶下方的聽診器可聽到亂流引起的拍擊聲。第一個拍擊聲出現時的水銀數值即為動脈收縮壓。

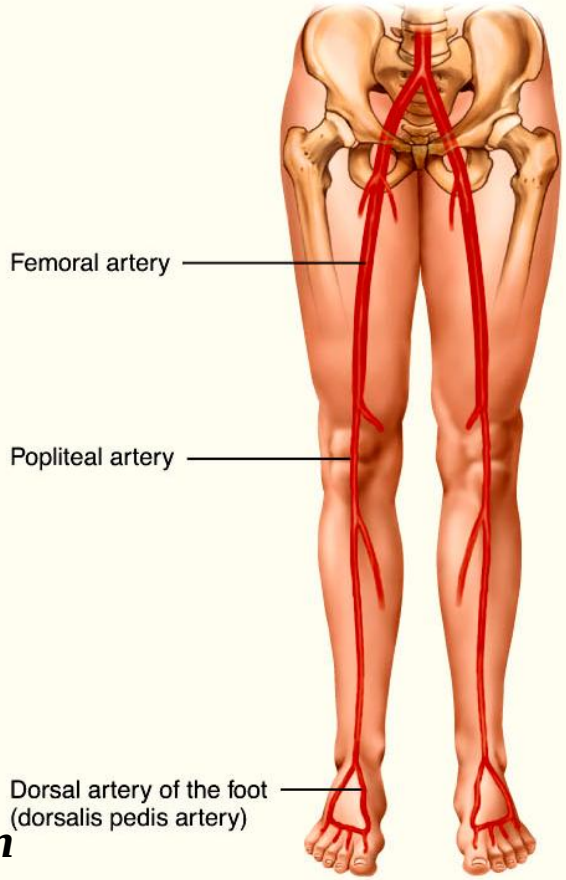
隨著氣囊壓力逐漸下降，每一次心臟收縮將會有更多的血液流過肱動脈，產生的拍擊聲轉變為較響的重擊聲。此後，氣囊壓力繼續下降。當氣囊壓力下降至動脈舒張時，肱動脈在心動週期的任何階段都不能被閉陷，通過肱動脈的血流為層流，層流血液不引起血管壁振動。因此，聽診器聽不到聲音，表現為聲音變弱或消失。此時對應的水銀數值為動脈舒張壓。收縮壓反映左心室收縮力，舒張壓反映血管的阻力。兩者之差為脈搏壓。

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

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.
		Radial artery	Distal aspect of wrist.
Common carotid artery	Lateral to larynx (voice box).	Dorsal artery of the foot (dorsalis pedis artery)	Superior to instep of foot.
Brachial artery	Medial side of biceps brachii muscle.		

Pulse Points

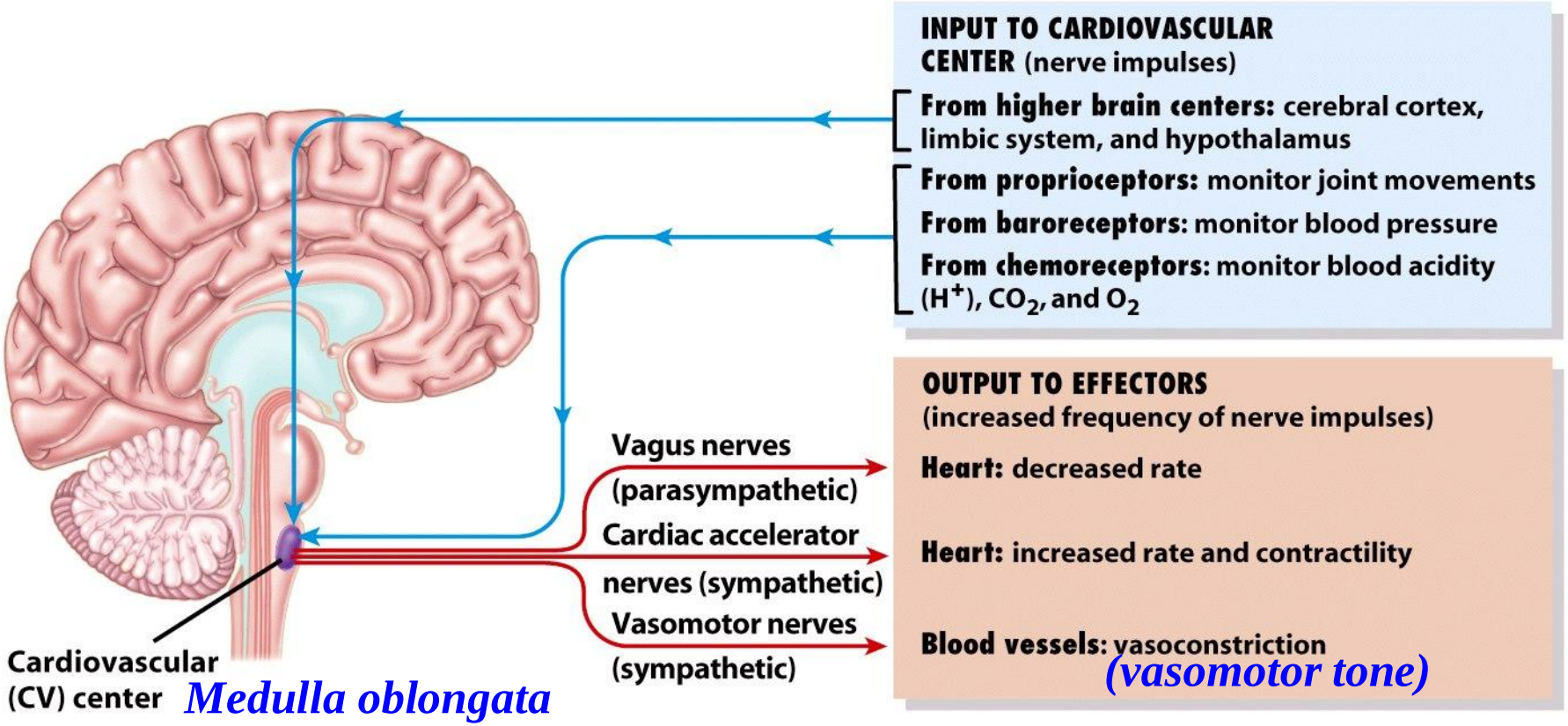




- ***Pulse rate =HR is normally between 70-80 beats/min***
- ***Tachycardia is rate over 100 beats/min & Bradycardia under 50***

Control of Blood Pressure

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



Input to CV Center

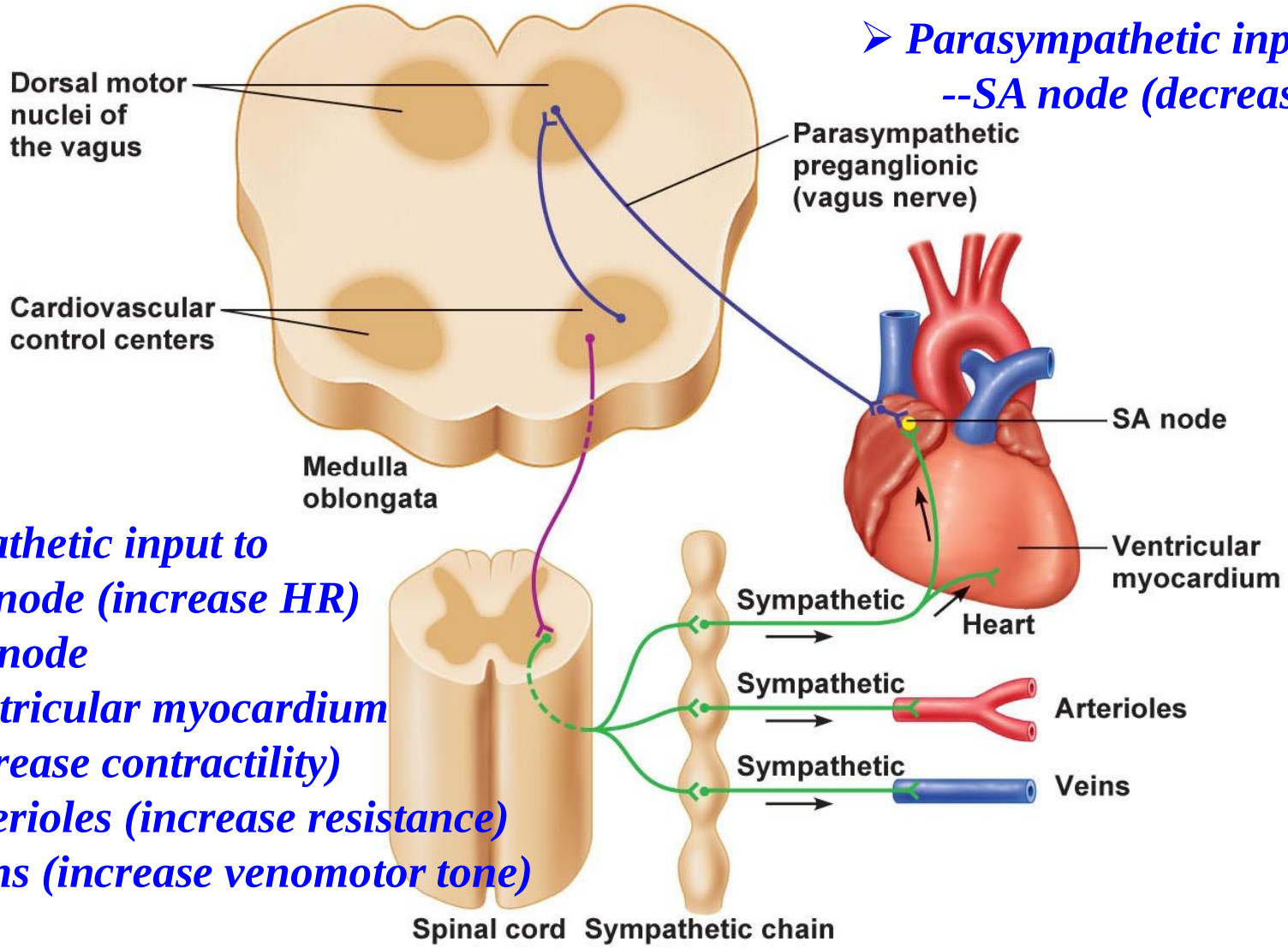
- **Higher brain centers** such as cerebral cortex, limbic system & hypothalamus
  - --Anticipation of competition
  - --Increase in body temperature
- **Proprioceptors**
  - --Input during physical activity
- **Baroreceptors**
  - --Changes in pressure within blood vessels
- **Chemoreceptors**
  - --Monitor 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 producing vasoconstriction (vasomotor tone)
    - Increased stimulation produces constriction & increased BP

Cardiovascular Neural Pathways

- *Parasympathetic input to*
  - *--SA node (decrease HR)*



- *Sympathetic input to*
  - *--SA node (increase HR)*
  - *--AV node*
  - *--Ventricular myocardium (increase contractility)*
  - *--Arterioles (increase resistance)*
  - *--Veins (increase venomotor tone)*

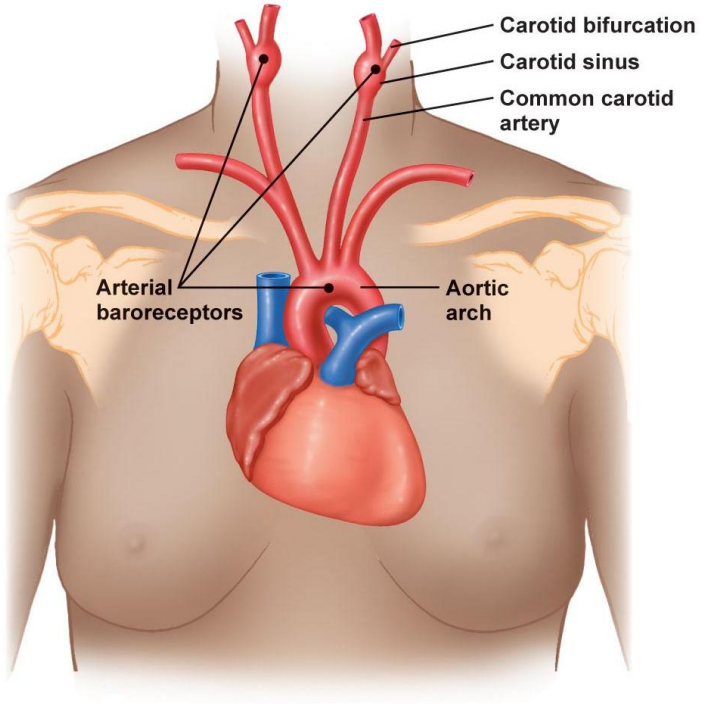
Short- and Long-Term Regulation of MAP

- **Short-term regulation—seconds to minutes**
  - --Regulate ***cardiac output*** and ***total peripheral resistance (MAP=CO × TPR)***
  - --Involves ***heart*** and ***blood vessels***
  - --Primarily ***neural control***
- **Long-term regulation—minutes to days**
  - --Regulate ***blood volume***
  - --Involves ***kidneys***
  - --Primarily ***hormonal control***

Neural Regulation of Blood Pressure

Negative feedback loops

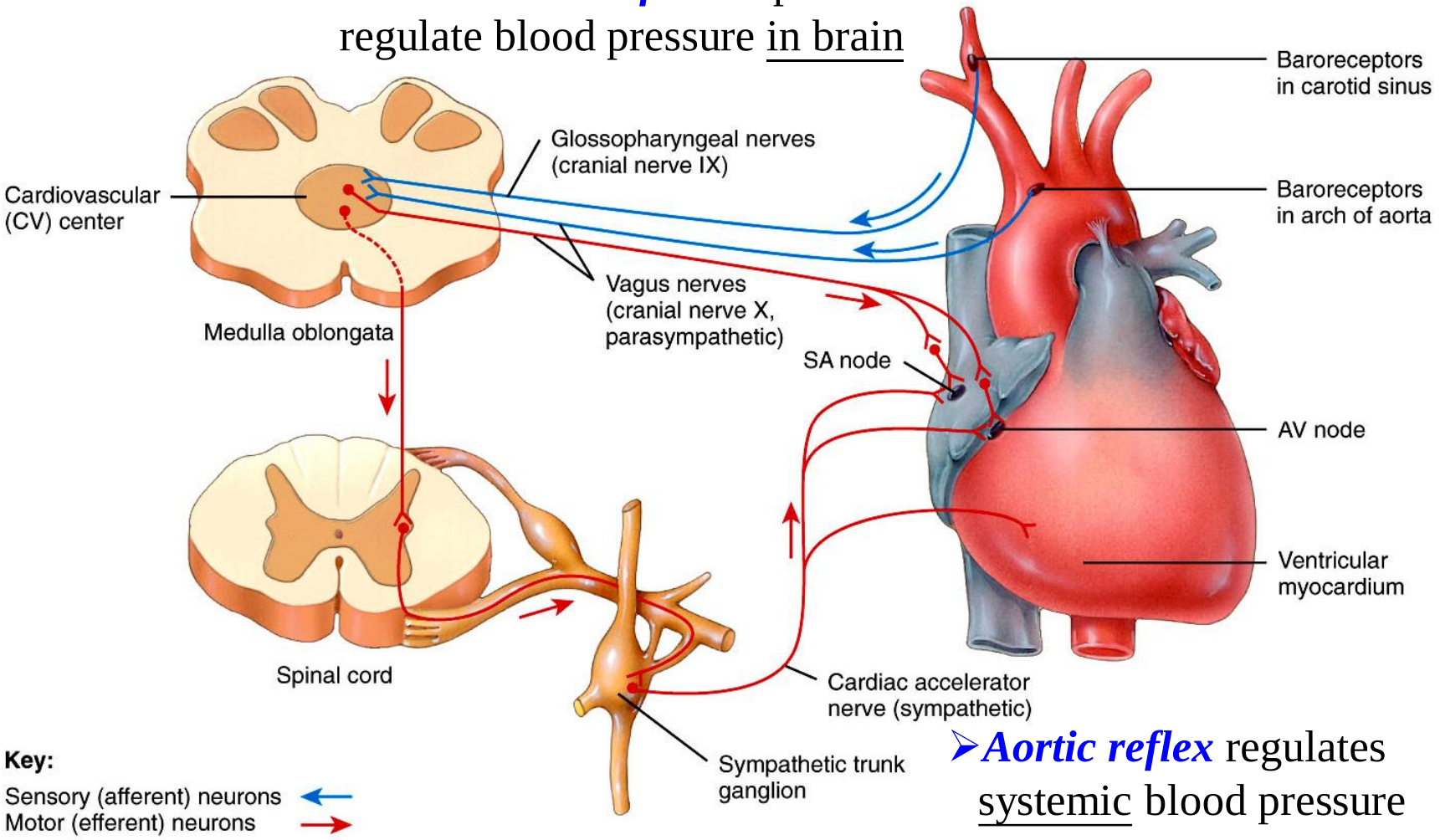
- **Detector = baroreceptors (pressure-sensitive sensory neurons)**
- **Afferent = CN. IX+X**
- **Integration Center = CV centers in the brainstem**
- **Controllers (efferent) = ANS**
- **Effectors = heart and blood vessels**
- **Locations = aortic arch+carotid sinuses**
- **Baroreceptors = pressure receptor**
  - --Sometimes called stretch receptors
  - --Arterial baroreceptors = sinoaortic receptors
- Respond to **stretching** due to pressure changes in arteries



Neural Regulation of Blood Pressure

1. Baroreceptor Reflexes (BRR)

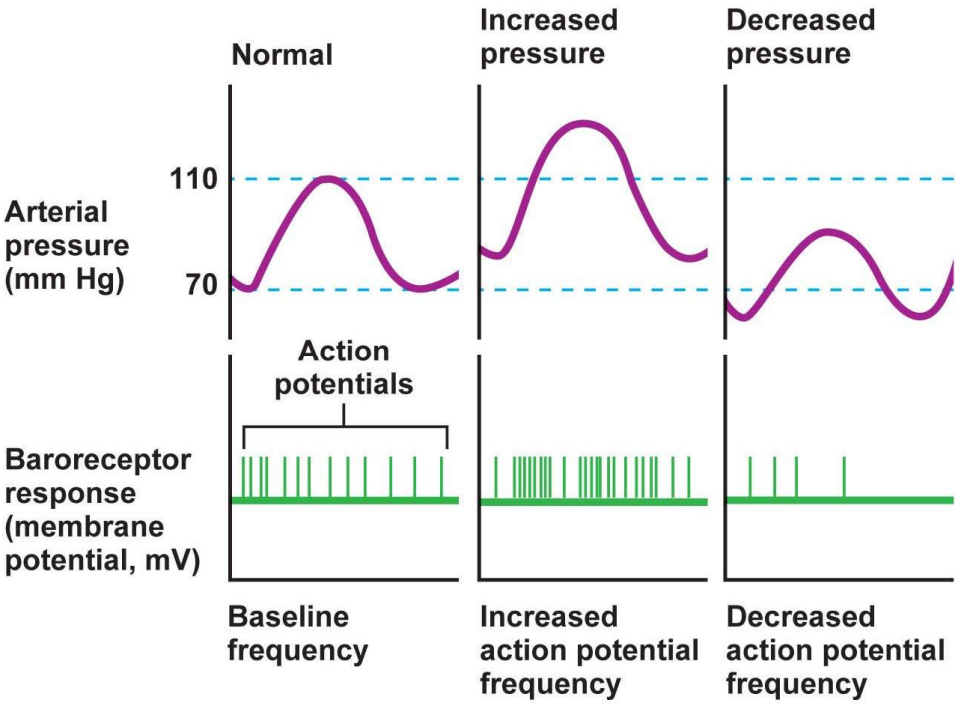
➢ ***Carotid sinus reflex*** helps regulate blood pressure in brain

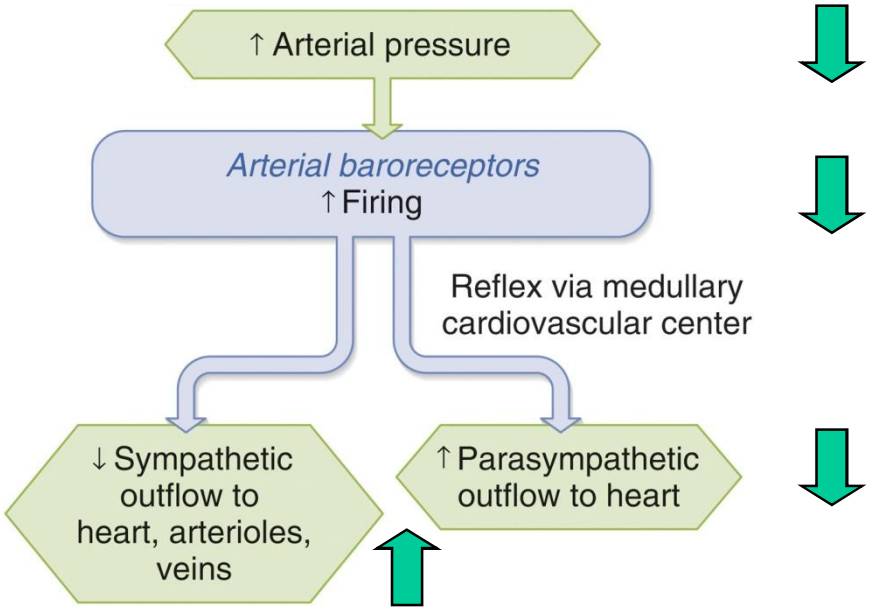


➢ ***Aortic reflex*** regulates systemic blood pressure

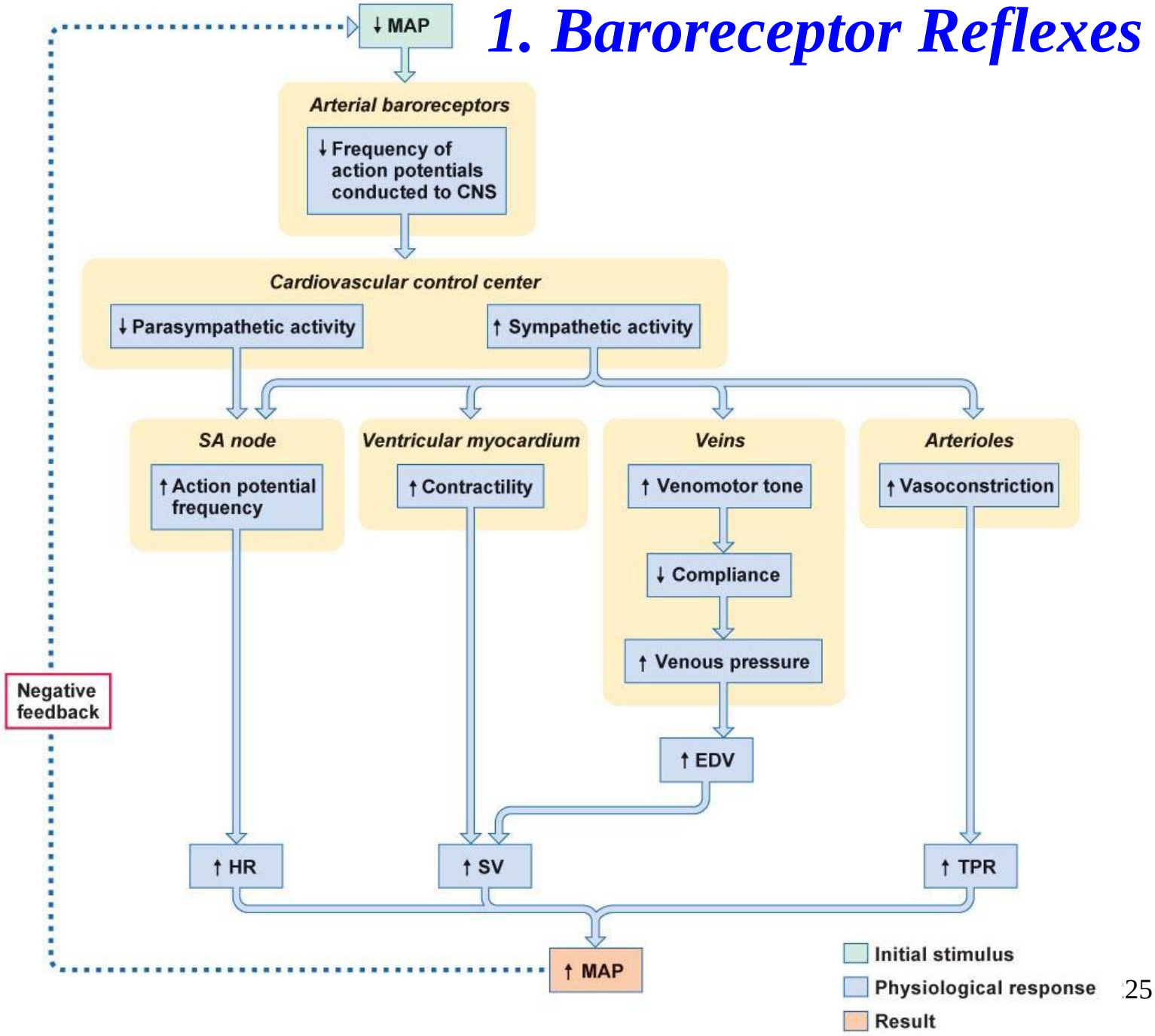
Neural Regulation of Blood Pressure

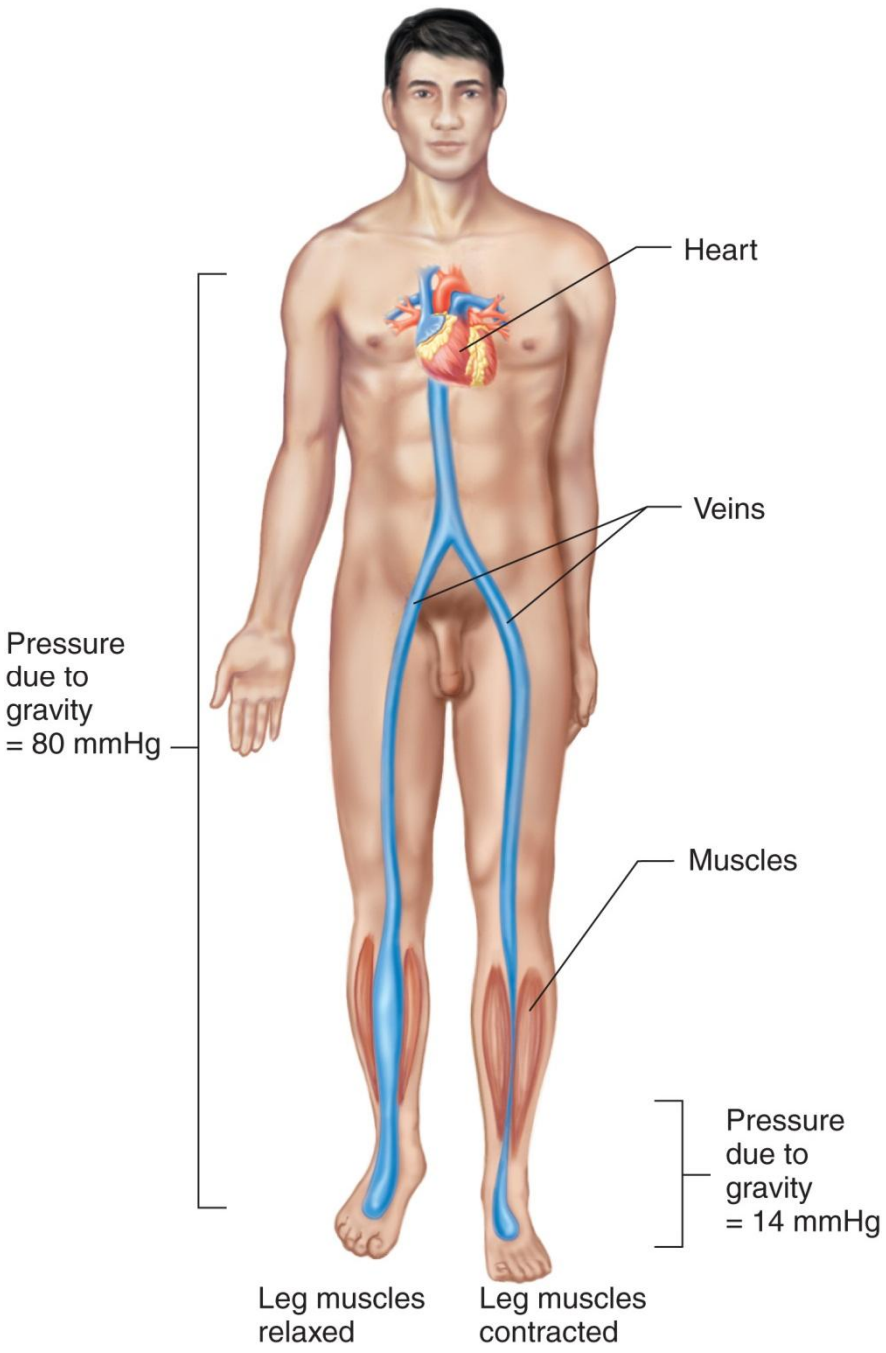
1. Baroreceptor Reflexes (BRR)

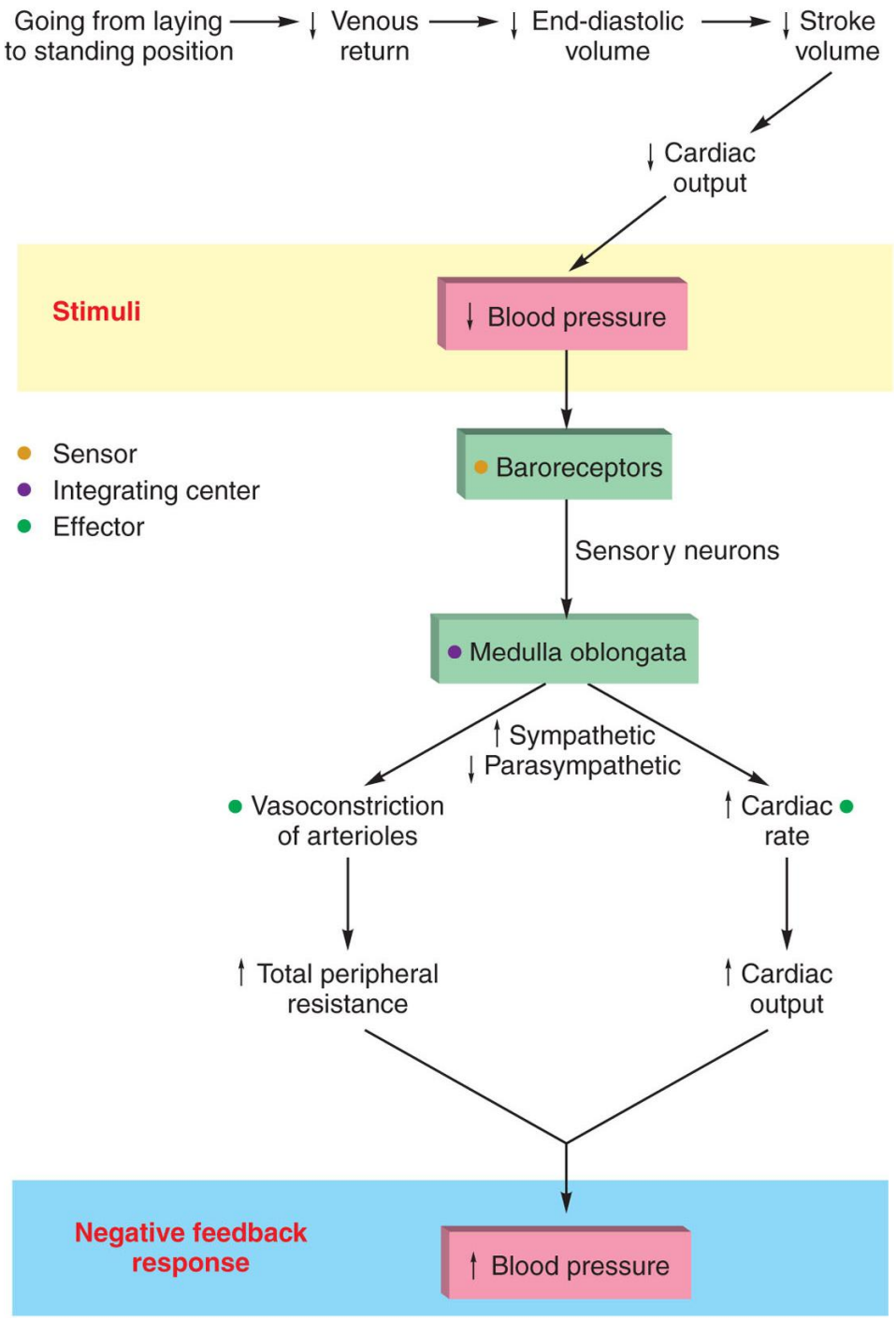




1. Baroreceptor Reflexes




Heart
Veins
Muscles
Pressure due to gravity = 80 mmHg
Pressure due to gravity = 14 mmHg
Leg muscles relaxed
Leg muscles contracted


Going from laying to standing position
↓ Venous return
↓ End-diastolic volume
↓ Stroke volume
↓ Cardiac output
Stimuli
↓ Blood pressure
Sensor
Integrating center
Effector
Baroreceptors
Sensory neurons
Medulla oblongata
↑ Sympathetic
↓ Parasympathetic
Vasoconstriction of arterioles
↑ Cardiac rate
↑ Total peripheral resistance
↑ Cardiac output
Negative feedback response
↑ Blood pressure

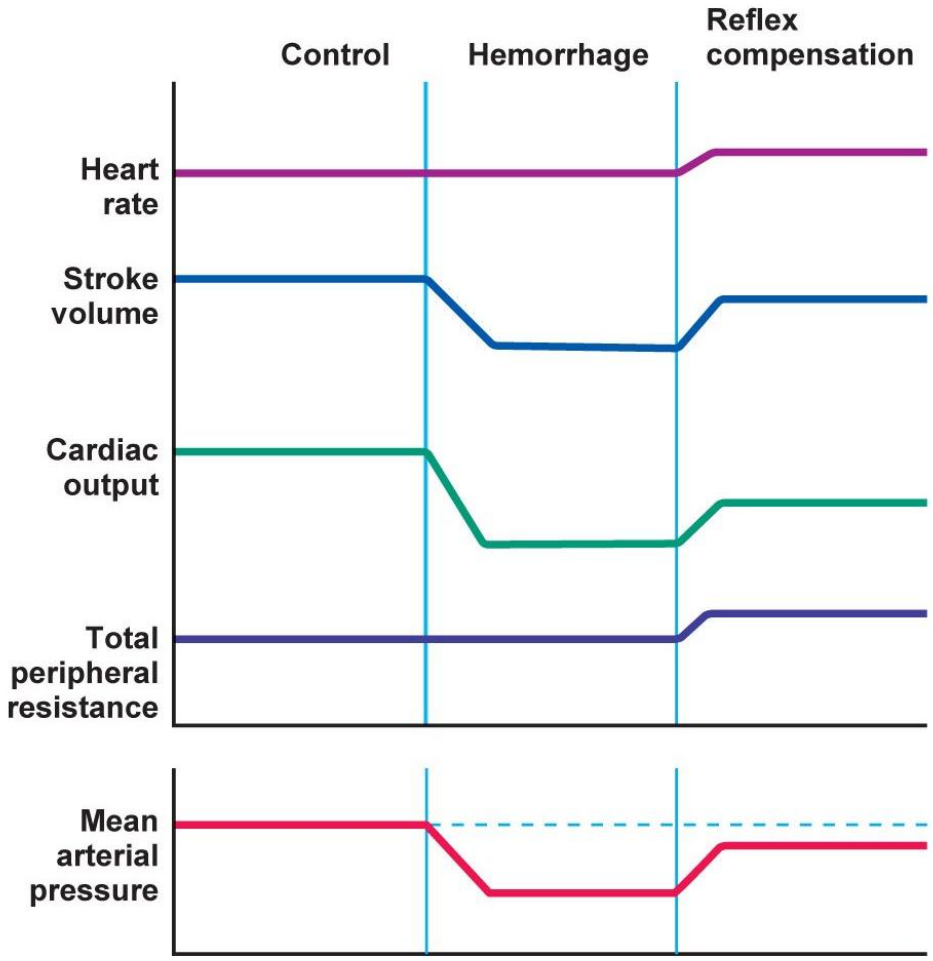
Neural Regulation of Blood Pressure

1. Baroreceptor Reflexes (BRR)

血壓	壓力感受器	傳入神經	心血管中樞		傳出神經	動作器	對血壓的作用
突然增高	頸動脈竇 (+) 主動脈弓 (+)	舌咽 N (+) 迷走 N (+)	延腦	心迷走中樞 (+) 心交感中樞 (-) 血管收縮中樞 (-)	心迷走神經 (+) 心交感神經 (-) 交感性血管收縮神經 (-)	心臟 (-) 心臟 (-) 血管舒張	→心輸出量↓→血壓↓ →心輸出量↓→血壓↓ →周邊總阻力↓→血壓↓

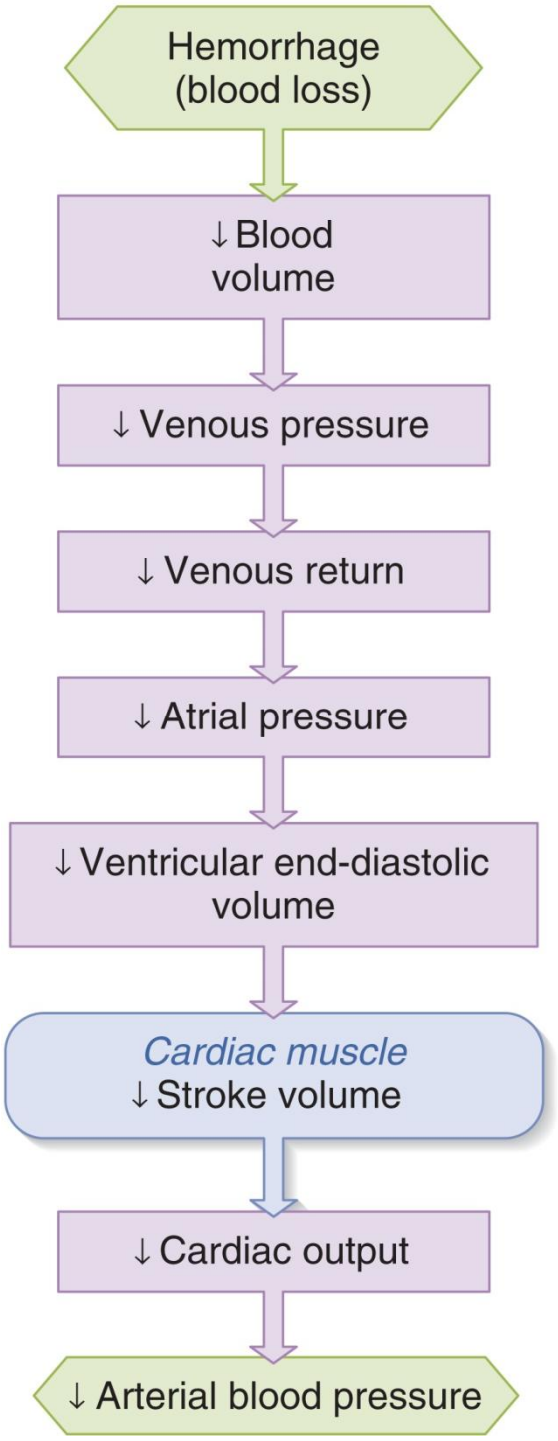
註：(＋)興奮；(－)抑制。

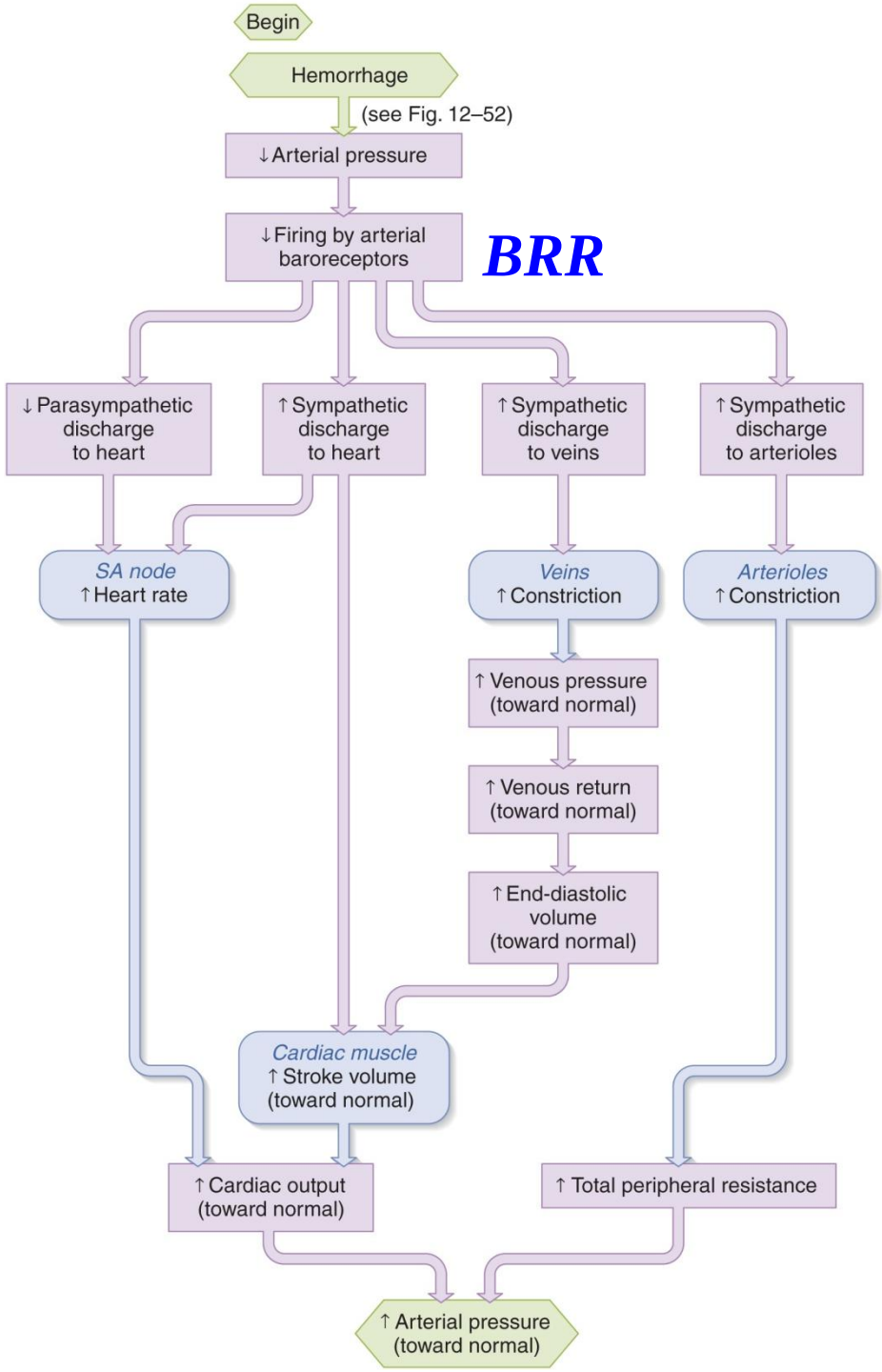
Clinical Application: Hemorrhage



MAP = HR x SV x TPR

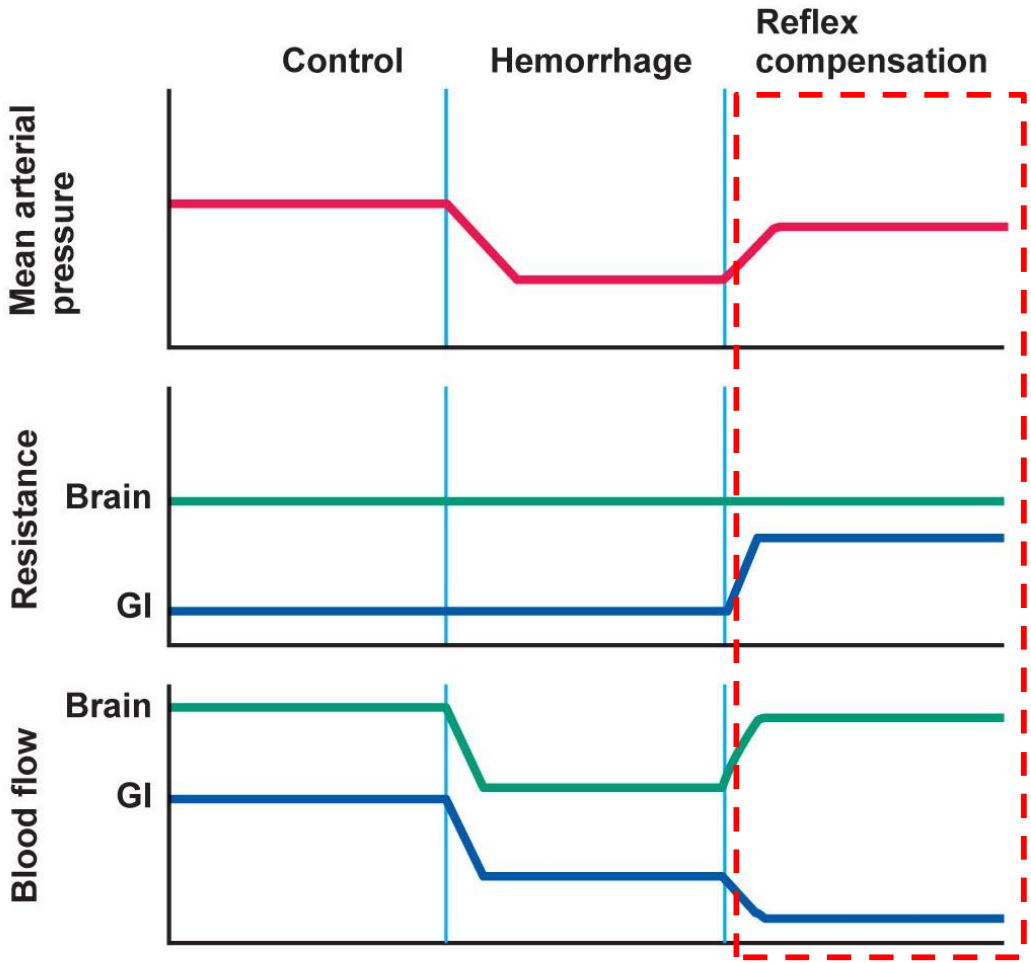
- Hemorrhage results in a **decrease in blood volume**
- Blood volume decrease → **decrease in MAP**
- Hemorrhage causes
  - ***--Baroreceptor reflex***
  - ***--Increase in sympathetic activity***
  - ***--Decrease in parasympathetic activity***
- **Reflex compensation**


Hemorrhage (blood loss)
↓ Blood volume
↓ Venous pressure
↓ Venous return
↓ Atrial pressure
↓ Ventricular end-diastolic volume
Cardiac muscle
↓ Stroke volume
↓ Cardiac output
↓ Arterial blood pressure

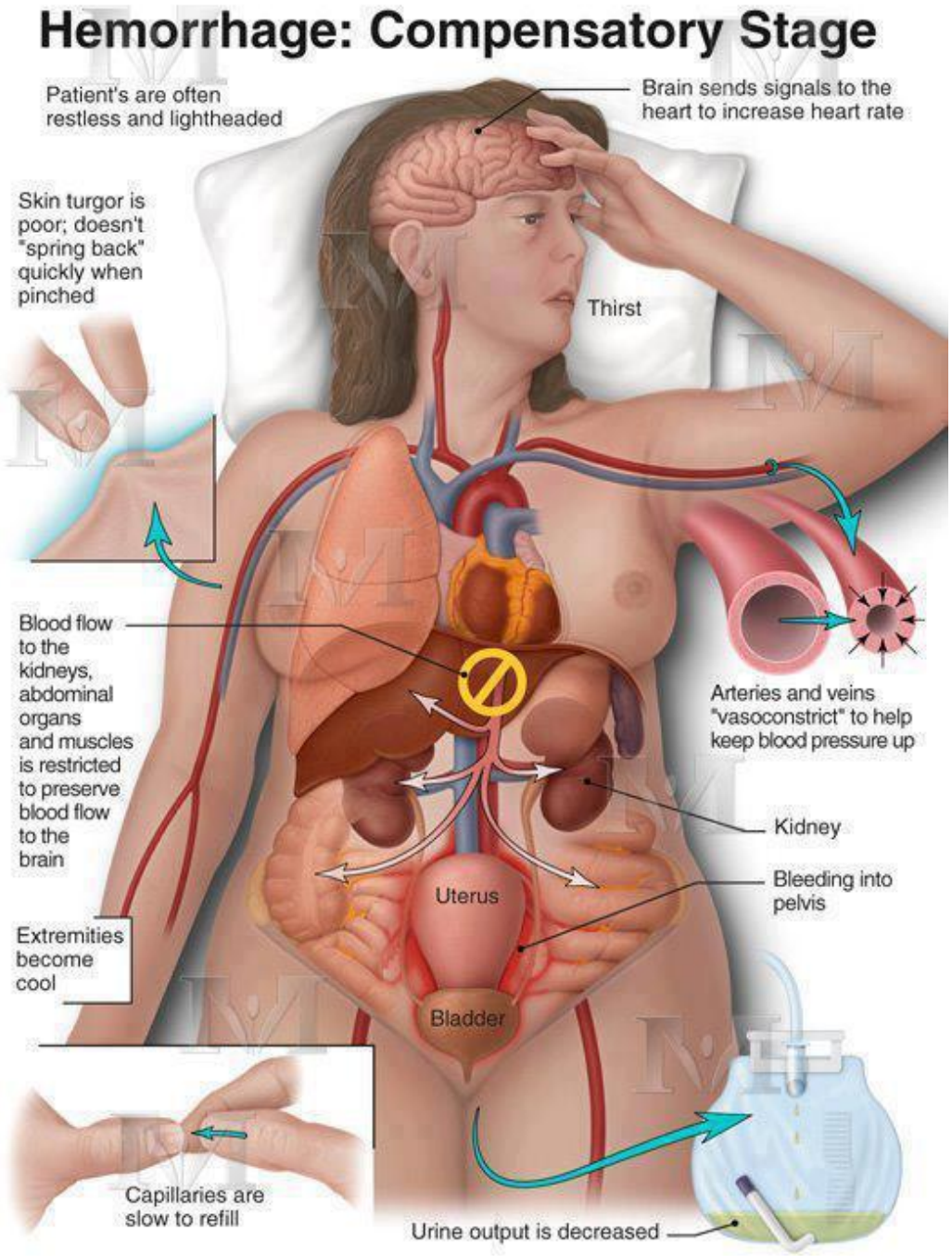

Begin
Hemorrhage
(see Fig. 12–52)
↓ Arterial pressure
↓ Firing by arterial baroreceptors
BRR
↓ Parasympathetic discharge to heart
↑ Sympathetic discharge to heart
↑ Sympathetic discharge to veins
↑ Sympathetic discharge to arterioles
SA node
↑ Heart rate
Veins
↑ Constriction
Arterioles
↑ Constriction
↑ 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 and Blood Flow

Baroreceptor reflex

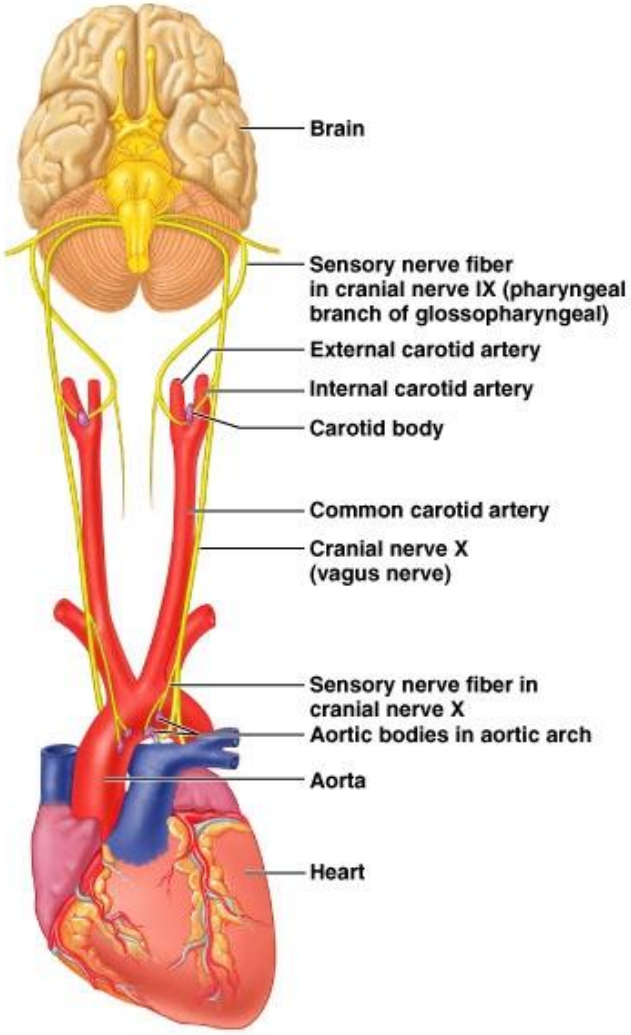


- **GI tract**
  - *--Increased resistance*
  - *--Decreased blood flow*
- **Brain**
  - *--Vasculature not subject of extrinsic control*
  - *--No change in resistance*
  - *--Blood diverted from GI tract to brain*


Hemorrhage: Compensatory Stage
Patient's are often restless and lightheaded
Brain sends signals to the heart to increase heart rate
Skin turgor is poor; doesn't "spring back" quickly when pinched
Thirst
Blood flow to the kidneys, abdominal organs and muscles is restricted to preserve blood flow to the brain
Arteries and veins "vasoconstrict" to help keep blood pressure up
Kidney
Uterus
Bleeding into pelvis
Extremities become cool
Bladder
Capillaries are slow to refill
Urine output is decreased

Neural Regulation of Blood Pressure

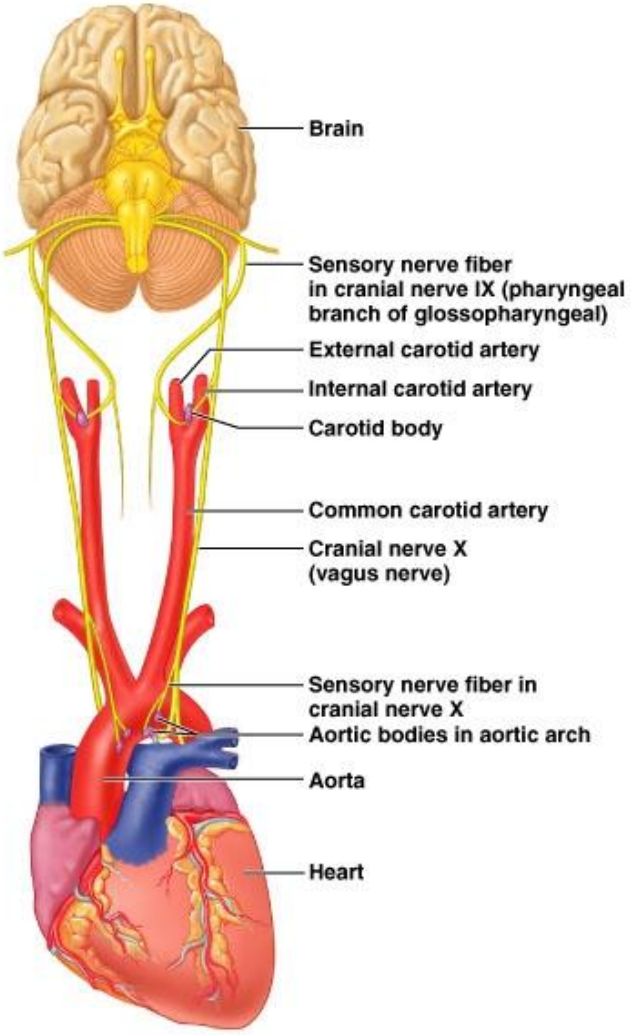
2. Chemoreceptor Reflexes



- Receptors located close to baroreceptors of carotid sinus (**carotid bodies**) and aortic arch (**aortic bodies**)
- Detect **hypoxia (low O_2), hypercapnia (high CO_2), acidosis (high H^+)** and send signals to CV
- CV ***increases*** ***sympathetic stimulation*** to arterioles and veins, producing vasoconstriction and an ***increase in blood pressure***
- Receptors also provide input to ***respiratory center*** to adjust breathing rate (***increased ventilation***)

Neural Regulation of Blood Pressure

2. Chemoreceptor Reflexes



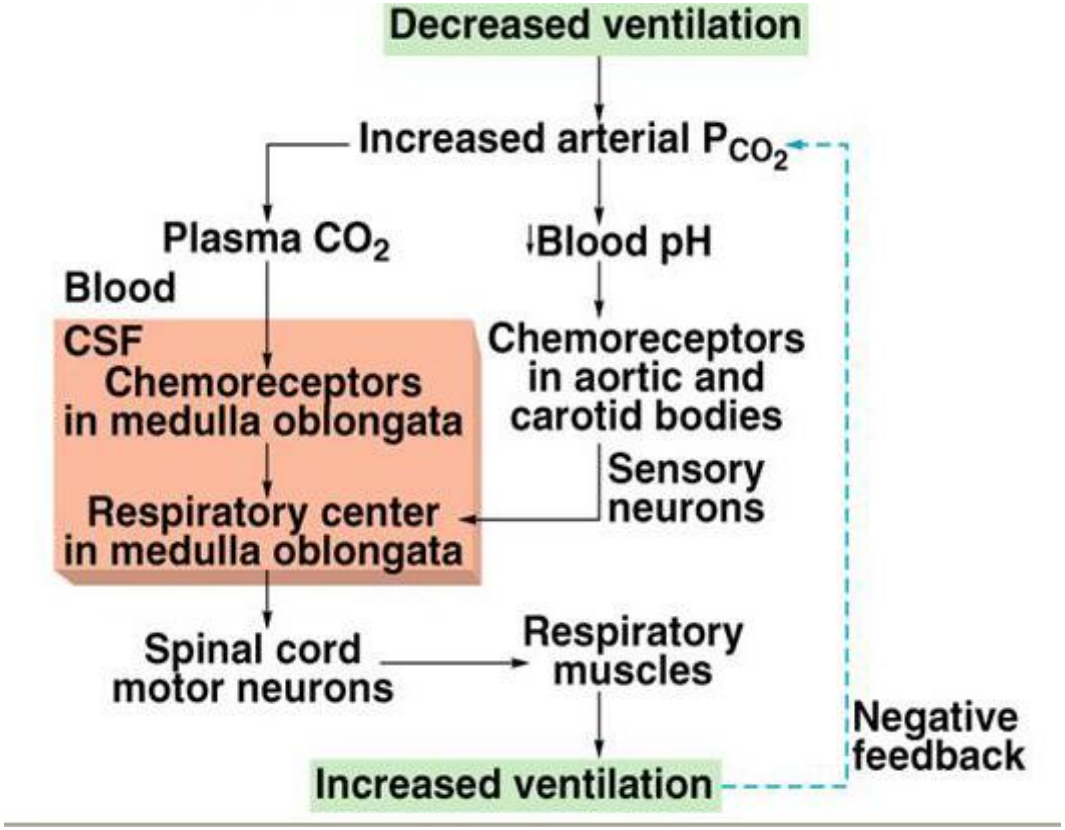


表 11-17　壓力感受器反射與化學感受器反射的比較

比較項目	壓力感受器反射	化學感受器反射
感受刺激	血壓搏動性變化比非搏動性變化更敏感	缺 O_2、CO_2 ↑、H^+ ↑
感受器	頸動脈竇、主動脈弓壓力感受器	頸動脈體、主動脈體化學感受器
中樞作用	心迷走中樞緊張性增強 心交感中樞緊張性減弱 交感性血管收縮中樞緊張性減弱	心迷走中樞緊張性減弱 心交感中樞緊張性增強 交感性血管收縮中樞緊張性增強 呼吸中樞緊張性增強
總合作用	血壓↓	呼吸↑，血壓↑
特性	平時經常發生作用（當血壓在 60~180 mmHg 時），頸動脈竇比主動脈弓更敏感，屬負迴饋機制	平時不發生調節作用，在缺氧、CO_2 ↑、酸中毒或嚴重失血時發生作用
生理意義	經常監視血壓波動，對維持正常血壓的相對穩定有重要作用	移緩濟急（首先確保心腦血液供應）的應急反應

Neural Regulation of Blood Pressure

3. Right Atrial Reflexes (Bainbridge reflex)

- Atrial reflex is an ***increase in heart rate*** due to an increase in central venous pressure
- Increased blood volume is detected by ***stretch receptors*** located in both **atria at the venoatrial junctions**
- This reflex and the ***baroreceptor reflex*** act antagonistically to control heart rate
- The BRR acts to increase heart rate when blood pressure drops. When blood volume is increased, the ***Bainbridge reflex*** is dominant; when blood volume is decreased (BP drops), the ***BRR*** is dominant
- Bainbridge reflex is involved in ***Respiratory Sinus Arrhythmia***

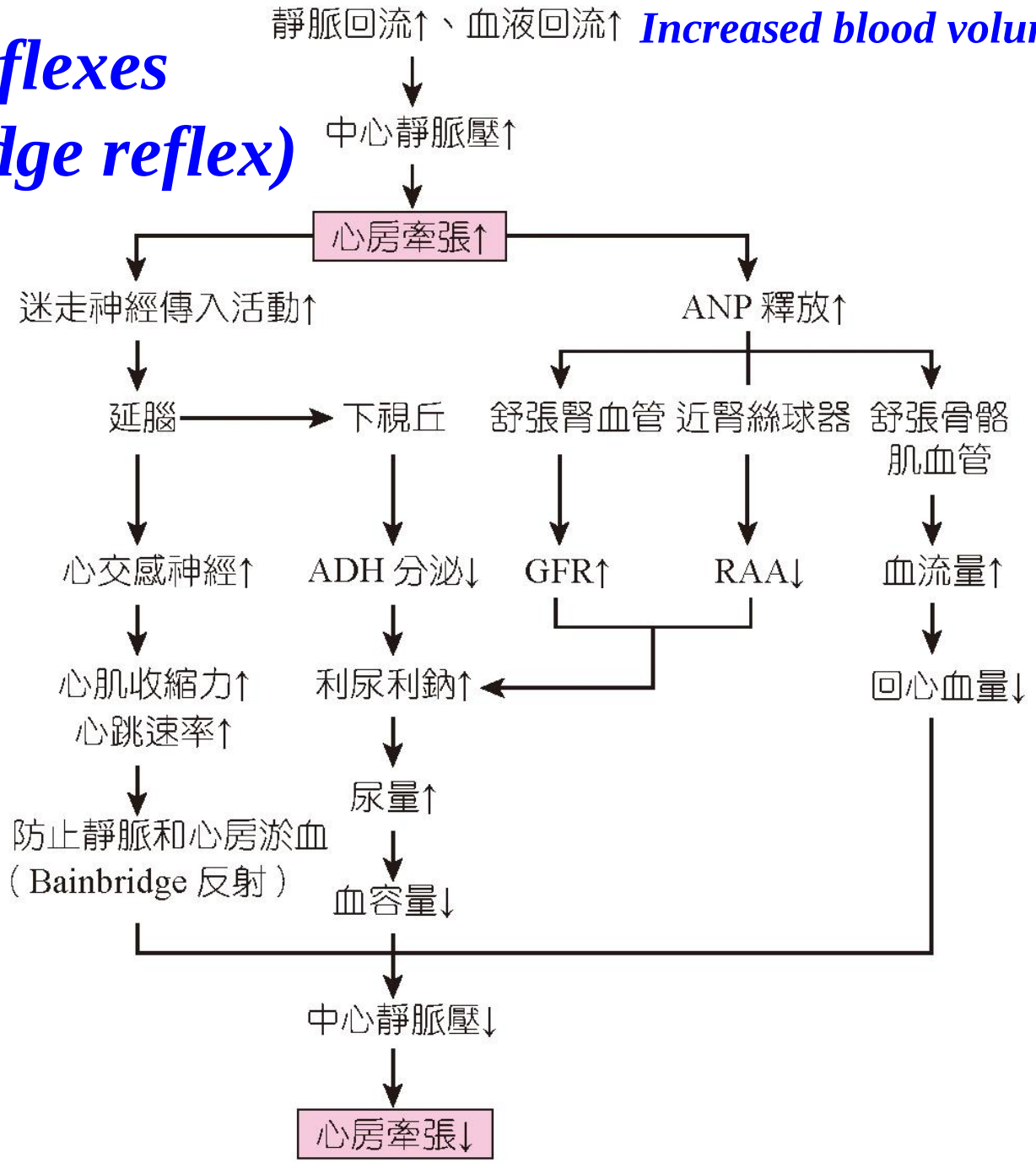
--During inspiration

↑ Sympathetic activity → ↑ HR (Bainbridge reflex)

--During expiration

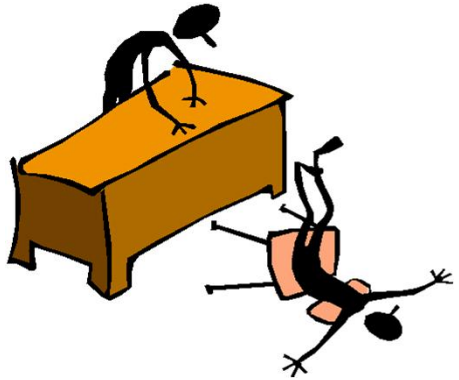
↑ Parasympathetic activity → ↓ HR

Atrial Reflexes (Bainbridge reflex)



Clinical Application: 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



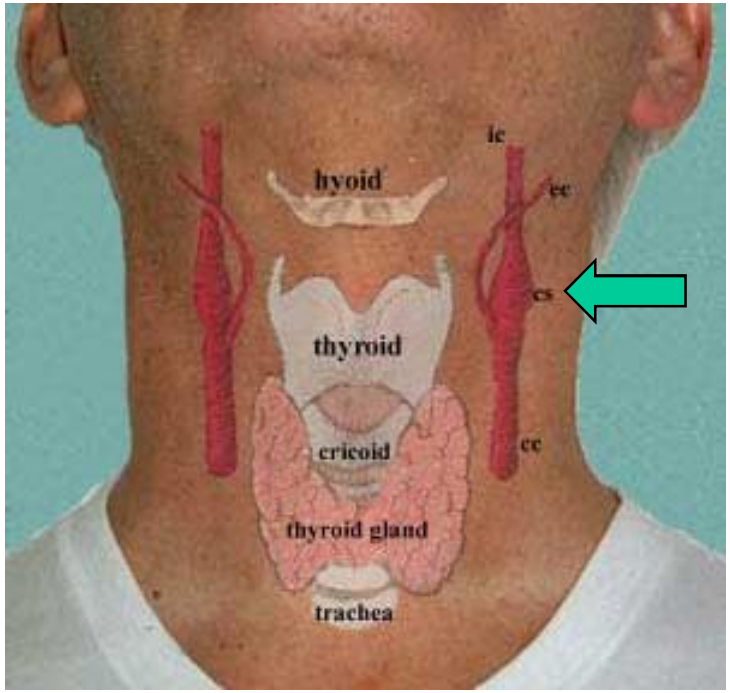
- **Causes**
  - --**Vasodepressor syncope** = sudden emotional stress
  - --**Situational syncope** = pressure stress of coughing, defecation, or urination (vagal stimulation)
  - --**Drug-induced syncope** = antihypertensives, diuretics, vasodilators and tranquilizers
  - --**Orthostatic hypotension** = decrease in BP upon standing

Clinical Application: Orthostatic Hypotension

- **Orthostatic (postural) hypotension** is defined as a drop in systolic blood pressure of **>20 mmHg within 2 minutes** of standing
- Changing from a lying position to standing **loses about 700 ml** of blood from the thorax, with a decrease in systolic blood pressure .The overall effect is an insufficient blood perfusion in the upper part of the body

Syncope due to orthostatic hypotension	
Primary autonomic failure ***BRR sensitivity↓***	Pure autonomic failure, multiple system atrophy Parkinsons disease with autonomic failure Lew Body dementia
Secondary autonomic failure	Diabetes, amyloidosis, spinal cord injuries **Atherosclerosis**
Drug induced orthostatic hypotension	Diuretics, vasodilators, tricyclic antidepressants
Volume depletion	Diarrhoea, vomiting

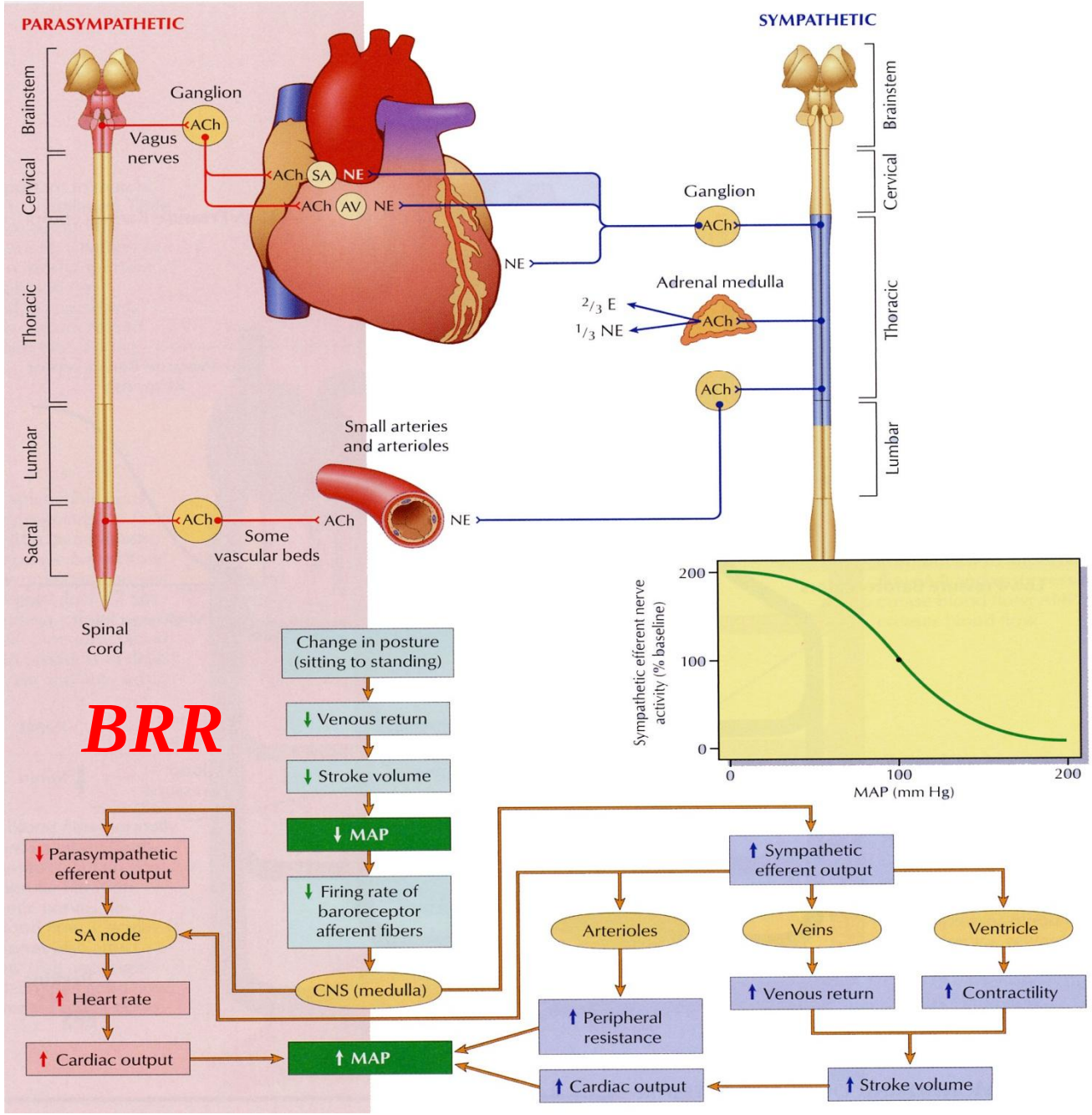
Clinical Application: Superventricular Tachycardia



- If **vagal maneuvers** are not effective, used ***Adenosine***, an ultra short acting ***AV nodal blocking agent*** via the ***A1 receptor***

- **Carotid sinus massage** can ***slow heart rate*** in paroxysmal superventricular tachycardia (PSVT)
- Stimulation (careful neck massage) over ***the carotid sinus*** lowers heart rate
  - --PSVT: tachycardia originating from the **atria** due to ***re-entry***
- Anything that puts pressure on carotid sinus
  - --***Tight collar or hyperextension of the neck***
  - --May slow heart rate & cause carotid sinus ***syncope or fainting***

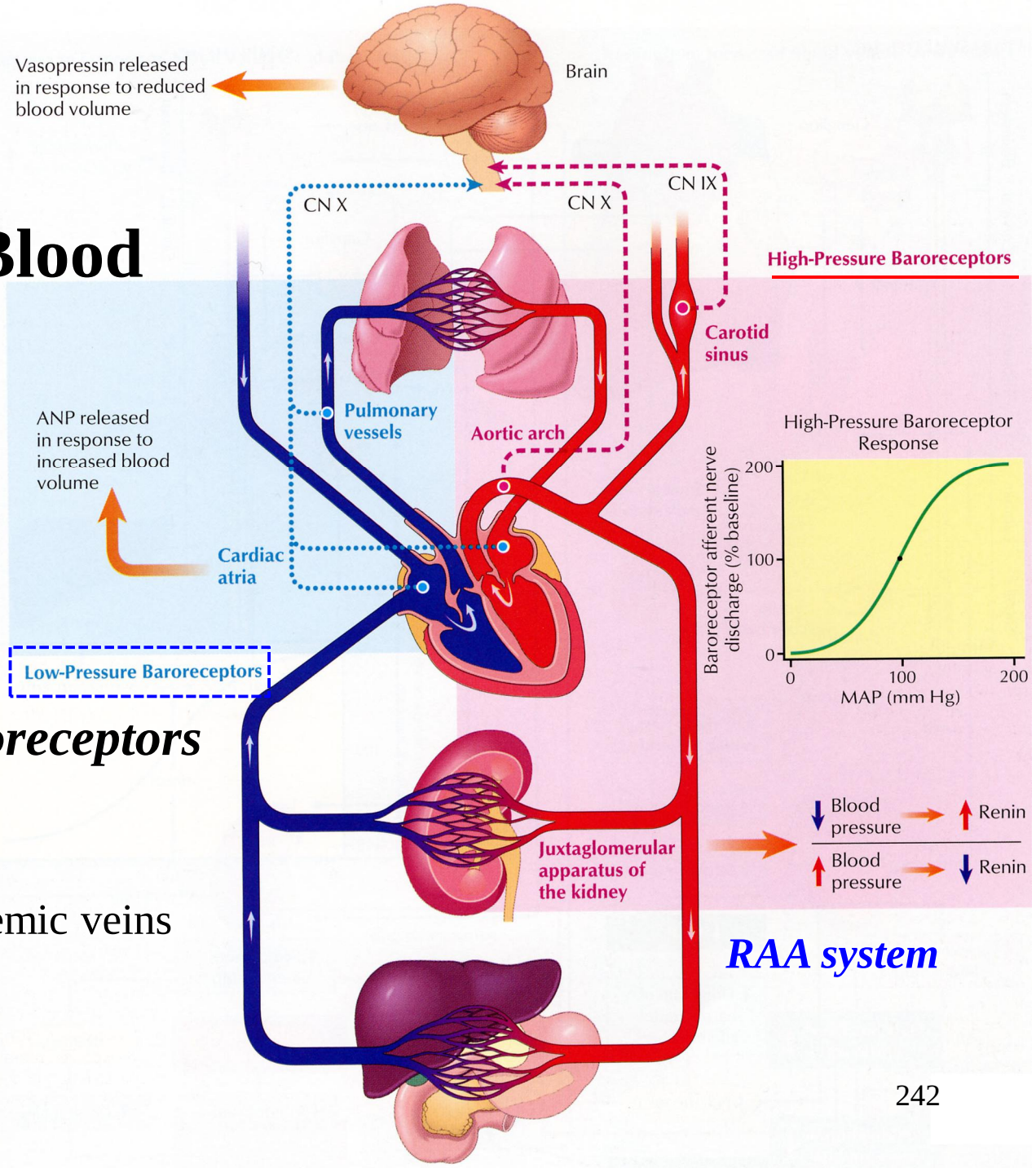
Short-Term Regulation of BP



Hormonal Regulation of Blood Pressure

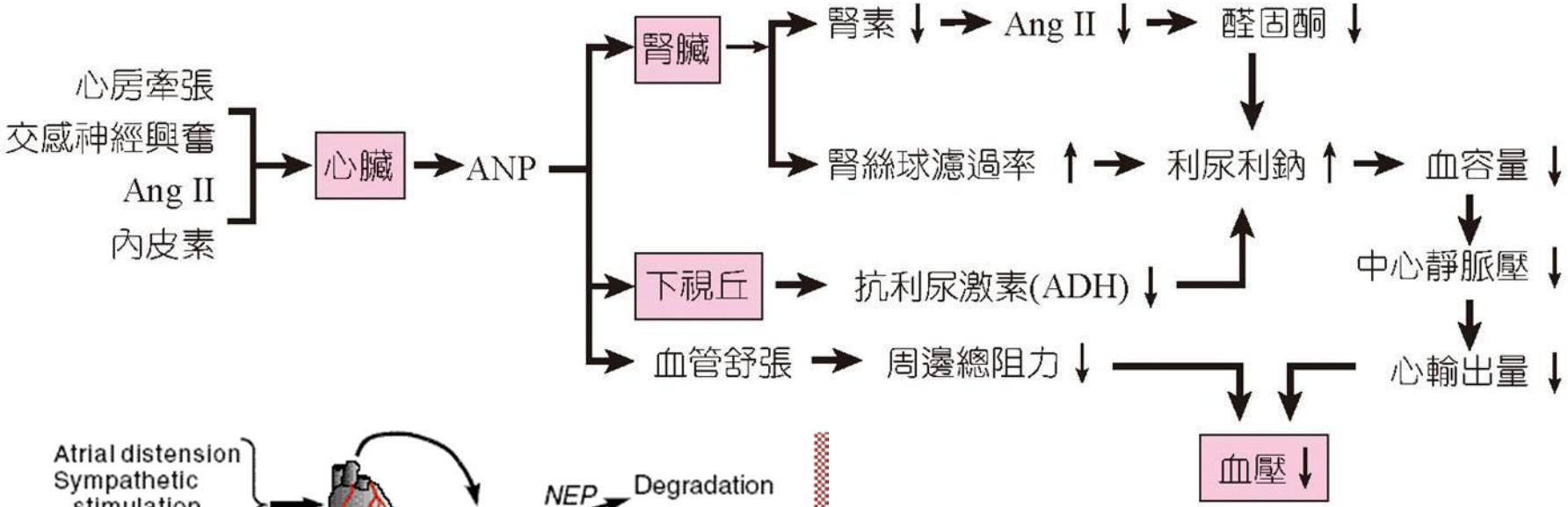
- **Renin-angiotensin-aldosterone (RAA) system**
  - --Decrease in BP or decreased blood flow to kidney
  - --Release of renin/results in formation angiotensin II
    - Systemic vasoconstriction
    - Causes release aldosterone (H_2O & Na^+ reabsorption)
- **Epinephrine & norepinephrine**
  - --Increases 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

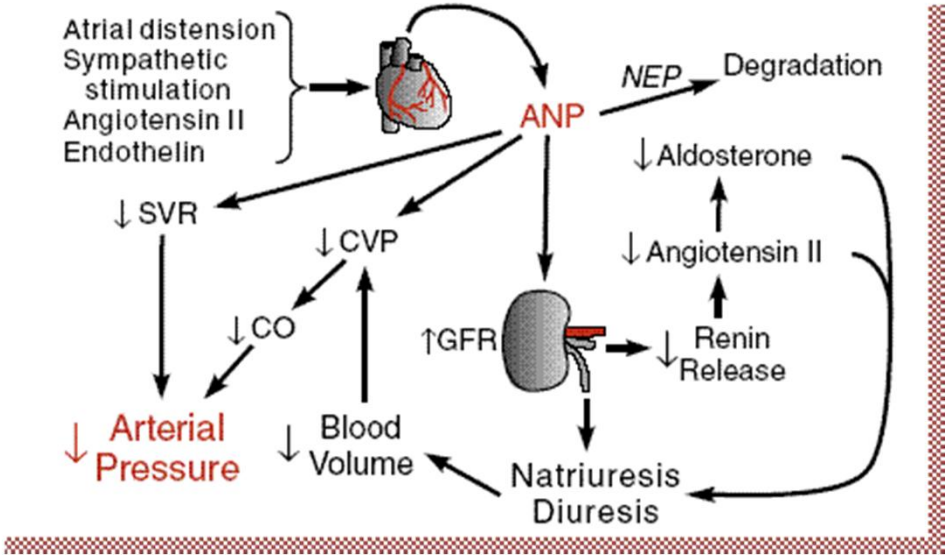
Hormonal Regulation of Blood Pressure



- ***Low-pressure baroreceptors***
  = volume receptors
- ***Location***
  --Walls of large systemic veins
  --Walls of the atria

Atrial natriuretic peptide (ANP)





Hormonal Regulation of Blood Pressure

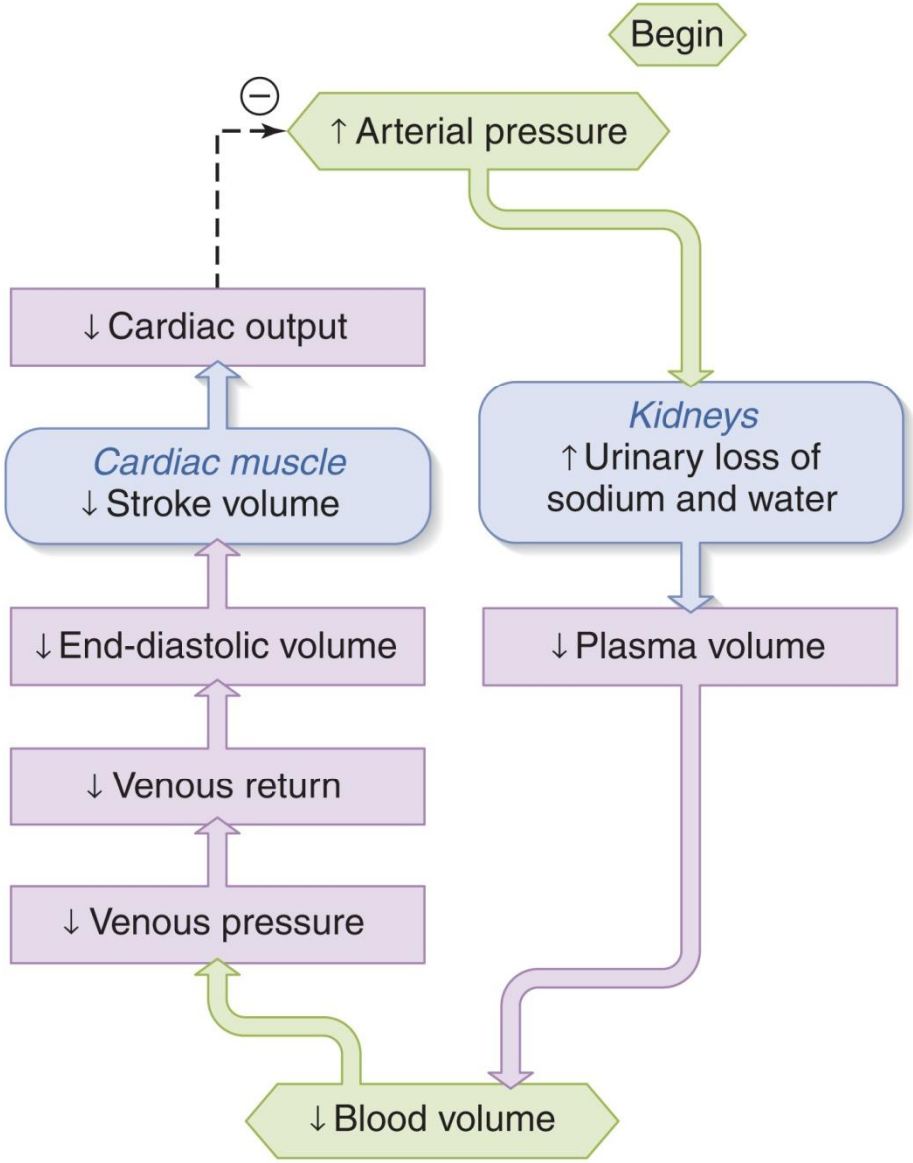
FACTOR INFLUENCING BLOOD PRESSURE	HORMONE	EFFECT ON BLOOD PRESSURE
CARDIAC OUTPUT		
Increased heart rate and contractility	Norepinephrine Epinephrine	Increase
SYSTEMIC VASCULAR RESISTANCE		
Vasoconstriction	Angiotensin II	Increase
	Antidiuretic hormone (vasopressin)	
	Norepinephrine*	
	Epinephrine†	
Vasodilation	Atrial natriuretic peptide	Decrease
	Epinephrine†	
	Nitric oxide	
BLOOD VOLUME		
Blood volume increase	Aldosterone Antidiuretic hormone	Increase
Blood volume decrease	Atrial natriuretic peptide	Decrease

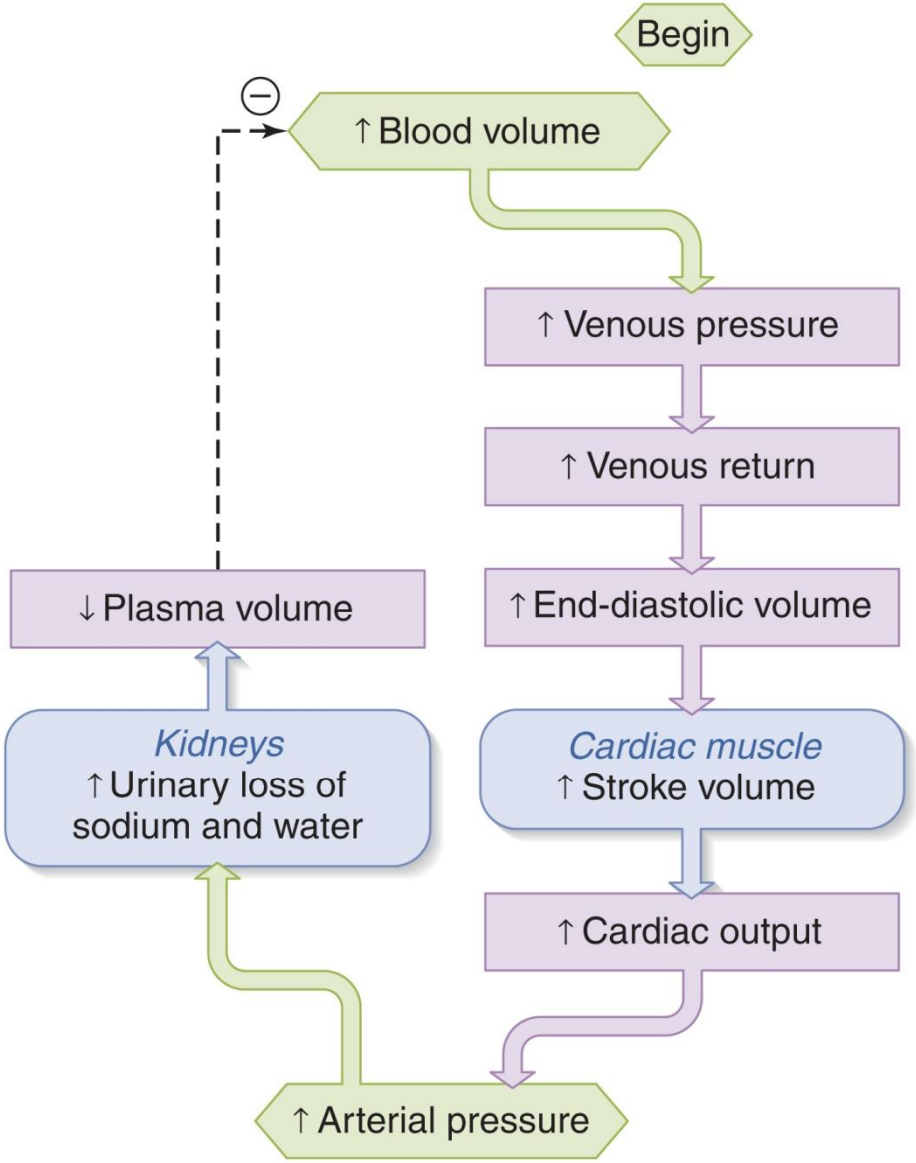
*Acts at α_1 receptors in arterioles of abdomen and skin.

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

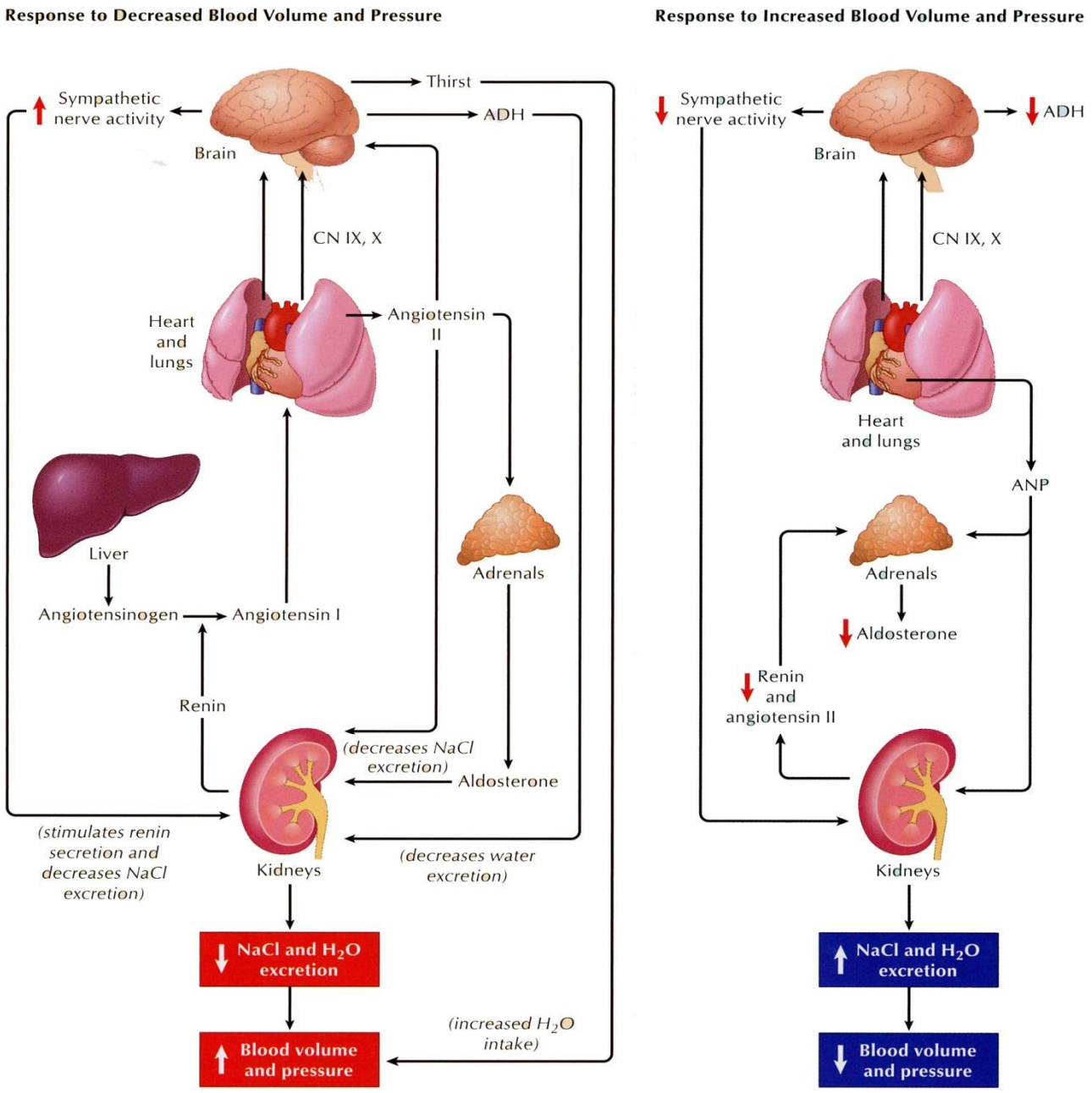
Long-Term Regulation of BP

Blood Volume vs. Blood Pressure





Long-Term Regulation of BP



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 O_2
  - --Pulmonary vessels constrict in response to low levels of O_2

Clinical Application: Hypertension

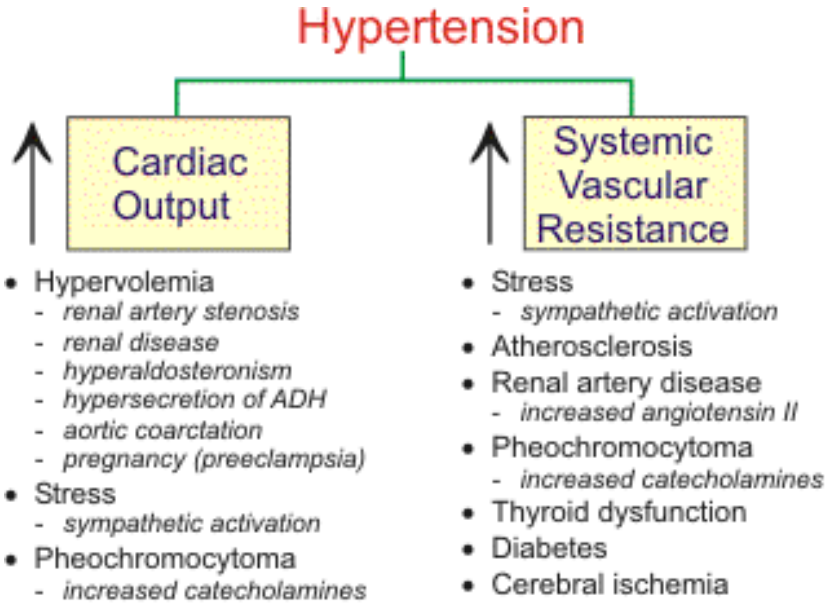
- Hypertension (not a disease) is ***chronically elevated blood pressure***. It is usually a ***"silent" killer*** because most people don't know that they have it until it has caused significant damage

- Prolonged hypertension is the major cause of ***heart failure, renal failure, stroke, and vascular disease***

Table 14.9 | Possible Causes of Secondary Hypertension

System Involved	Examples	Mechanisms
Kidneys	Kidney disease	Decreased urine formation
	Renal artery disease	Secretion of vasoactive chemicals
Endocrine	Excess catecholamines (tumor of adrenal medulla)	Increased cardiac output and total peripheral resistance
	Excess aldosterone (Conn's syndrome)	Excess salt and water retention by the kidneys
Nervous	Increased intracranial pressure	Activation of sympathoadrenal system
	Damage to vasomotor center	Activation of sympathoadrenal system
Cardiovascular	Complete heart block; patent ductus arteriosus	Increased stroke volume
	Arteriosclerosis of aorta; coarctation of aorta	Decreased distensibility of aorta

Clinical Application: Hypertension



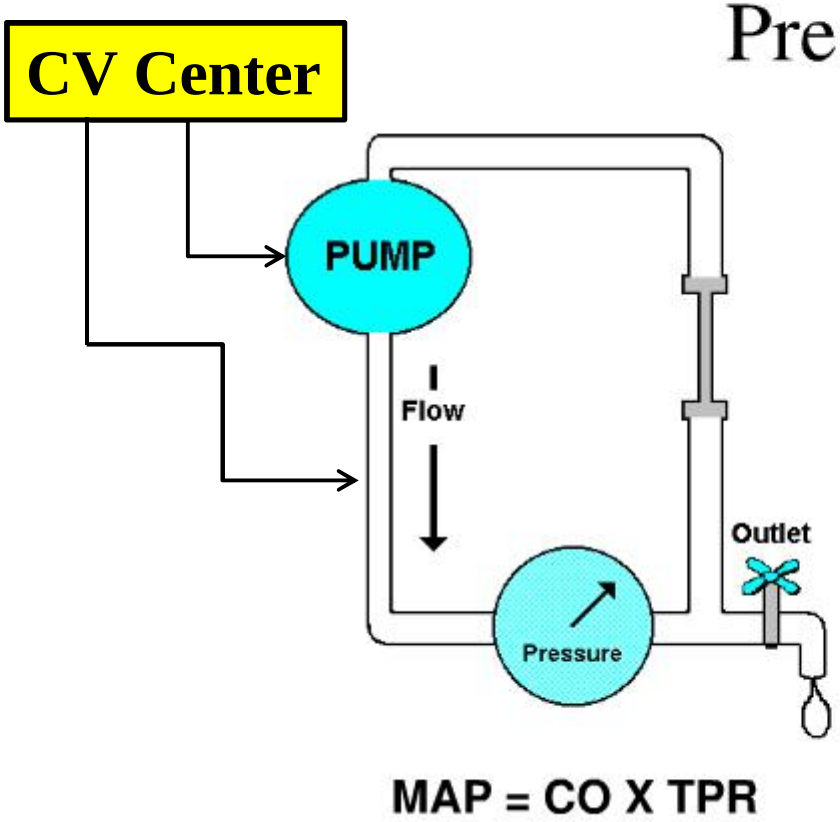
Drugs Commonly Linked to Hypertension

Class	Drugs	Mechanism
Sympathomimetic agents	Amphetamines (dextroamphetamine, methamphetamine, methylphenidate); phenylpropanolamine, ephedrine, pseudoephedrine	Cause dose-related increases in blood pressure; CNS stimulant
NSAIDs and COX-2 inhibitors	Ibuprofen, diclofenac, celecoxib	Block COX-1 and COX-2 enzymes, which leads to a reduction in prostaglandin formation; cause dose-related increases in sodium and water retention
Corticosteroids	Prednisone, fludrocortisone, hydrocortisone	Cause sodium retention, resulting in dose-related fluid retention
CNS stimulants	Caffeine	Stimulant effect
Estrogens and progestins	Oral contraceptives, ERT/HRT	Estrogen stimulates the hepatic production of the renin substrate angiotensinogen; both appear to contribute in a dose-dependent fashion
Dietary supplements	Ginseng, natural licorice, yohimbine	Mild stimulant effect; increase arterial pressure
SNRIs	Venlafaxine, sibutramine	Increase levels of norepinephrine and the subsequent potentiation of noradrenergic neurotransmission
Immunosuppressants	Cyclosporine, tacrolimus	Increase prostaglandin synthesis and decrease water, sodium, and potassium excretion

CNS: central nervous system; NSAID: nonsteroidal anti-inflammatory drug; COX: cyclooxygenase; ERT/HRT: estrogen replacement therapy/hormone replacement therapy; SNRI: serotonin-norepinephrine reuptake inhibitor.

Clinical Application: Hypertension

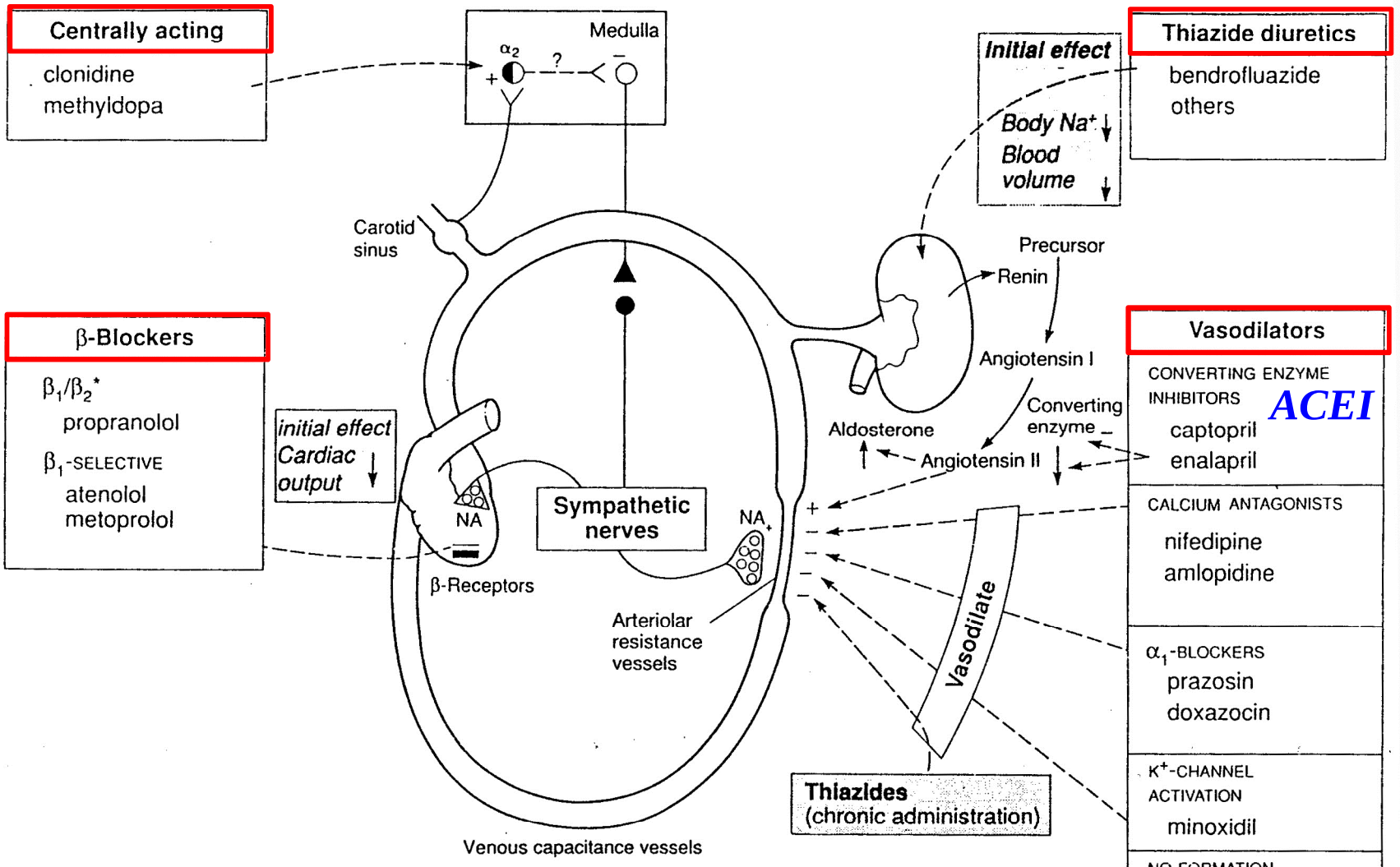
Ways of Lowering Blood Pressure



- Reduce cardiac output (ß-blockers, Ca^{2+} channel blockers)
- Reduce plasma volume (diuretics)
- Reduce peripheral vascular resistance (vasodilators)

Drugs used in hypertension

Central Sympatholytics

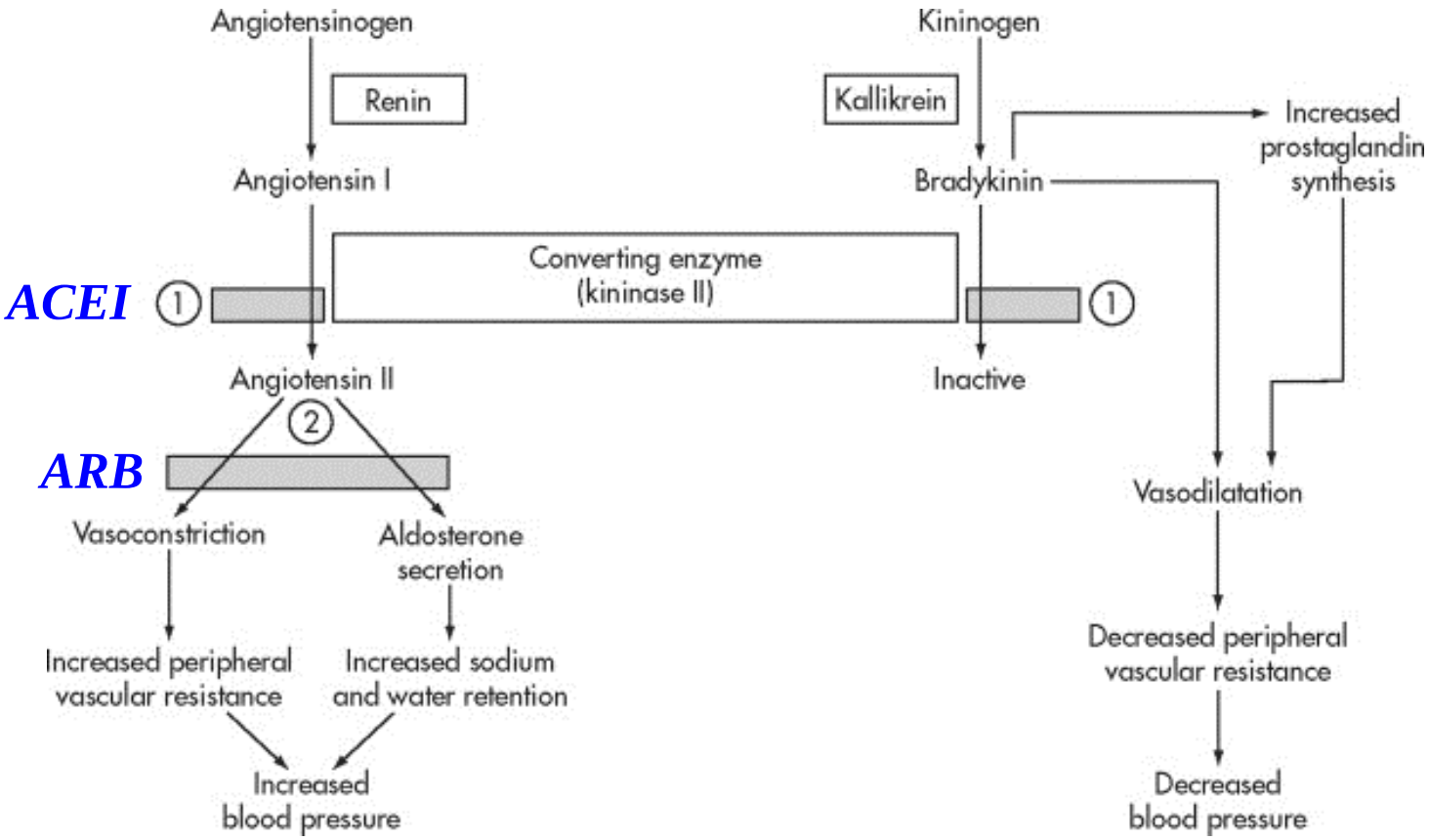


➢ ***Angiotensin Receptor Blocker (ARB)***

= ***AT1 receptor antagonists***

Hypertension Treatment

ACEI vs. ARB



Antihypertensive Drugs

Category of Drugs	Examples	Mechanisms
Diuretics	Thiazide; furosemide	Increase volume of urine excreted, thus lowering blood volume
Sympathoadrenal system inhibitors	Clonidine; alpha-methyldopa	Act to decrease sympathoadrenal stimulation by bonding to α_2-adrenergic receptors in the brain
	Guanethidine; reserpine	Deplete norepinephrine from sympathetic nerve endings
	Atenolol	Blocks beta-adrenergic receptors, decreasing cardiac output and/or renin secretion
	Phentolamine	Blocks alpha-adrenergic receptors, decreasing sympathetic vasoconstriction
Direct vasodilators	Hydralazine; minoxidil sodium nitroprusside	Cause vasodilation by acting directly on vascular smooth muscle
Calcium channel blockers	Verapamil; diltiazem	Inhibit diffusion of Ca^{2+} into vascular smooth muscle cells, causing vasodilation and reduced peripheral resistance
Angiotensin-converting enzyme (ACE) inhibitors	Captopril; enalapril	Inhibit the conversion of angiotensin I into angiotensin II
Angiotensin II–receptor antagonists	Losartan	Blocks the binding of angiotensin II to its receptor

- ***Angiotensin Receptor Blocker (ARB)***
  = ***AT1 receptor antagonists***

Clinical Application: Shock

- ***Shock*** is an ***inadequate cardiac output (inadequate perfusion)*** to match oxygen usage in the tissues
- As a result, cells forced to switch to ***anaerobic respiration, lactic acid builds up, and cells and tissues become damaged & die (blood volume drops by 10-20% or BP does not rise sufficiently)***

Table 14.11 | Signs of Shock

	Early Sign	Late Sign
Blood pressure	Decreased pulse pressure	Decreased systolic pressure
	Increased diastolic pressure	
Urine	Decreased Na^+ concentration	Decreased volume
	Increased osmolality	
Blood pH	Increased pH (alkalosis) due to hyperventilation	Decreased pH (acidosis) due to "metabolic" acids
Effects of poor tissue perfusion	Slight restlessness; occasionally warm, dry skin	Cold, clammy skin; "cloudy" senses

- ***Signs and symptoms:*** clammy, cool, pale skin; tachycardia; weak, rapid pulse; sweating; hypotension (systemic pressure < 90 mm Hg); altered mental status; decreased urinary output; thirst; and acidosis

Types of Shock

- ***Hypovolemic shock*** is due to loss of blood or body fluids (hemorrhage, sweating, diarrhea or extensive burns)

  --Venous return to heart declines & output decreases

- ***Cardiogenic shock*** is caused by damage to pumping action of the heart (MI, ischemia, valve problems, cardiac failure or arrhythmias)
- ***Vascular shock*** causing drop inappropriate vasodilation--anaphylatic shock (histamine↑), septic shock or neurogenic shock (head trauma, spinal cord injury or anesthesis)
- ***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***

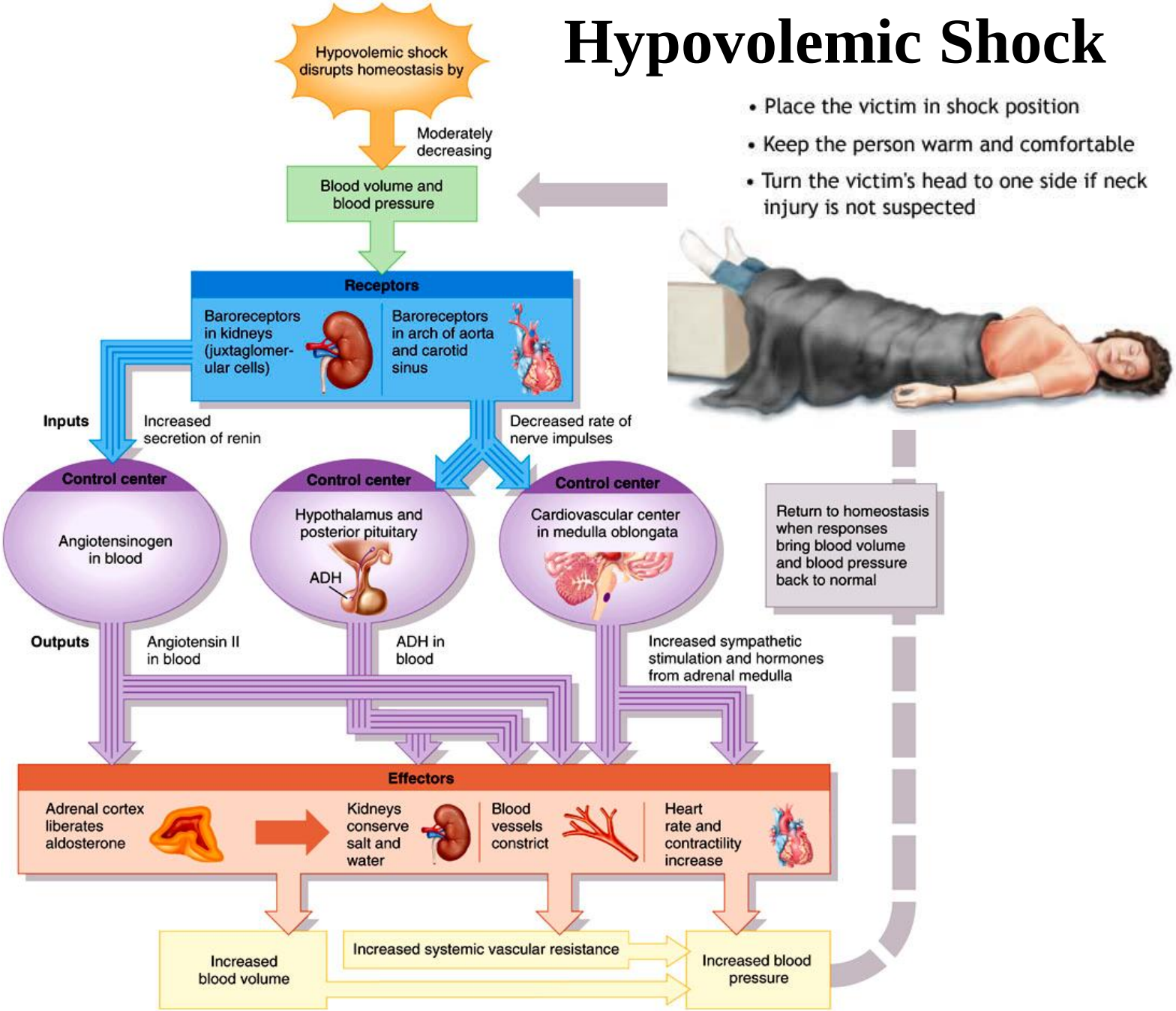
Homeostatic Responses to Shock

- **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***

Table 14.12 | Cardiovascular Reflexes That Help to Compensate for Circulatory Shock

Organ(s)	Compensatory Mechanisms
Heart	Sympathoadrenal stimulation produces increased cardiac rate and increased stroke volume due to "positive inotropic effect" on myocardial contractility
Digestive tract and skin	Decreased blood flow due to vasoconstriction as a result of sympathetic nerve stimulation (alpha-adrenergic effect)
Kidneys	Decreased urine production as a result of sympathetic-nerve-induced constriction of renal arterioles; increased salt and water retention due to increased plasma levels of aldosterone and antidiuretic hormone (ADH)

Hypovolemic Shock

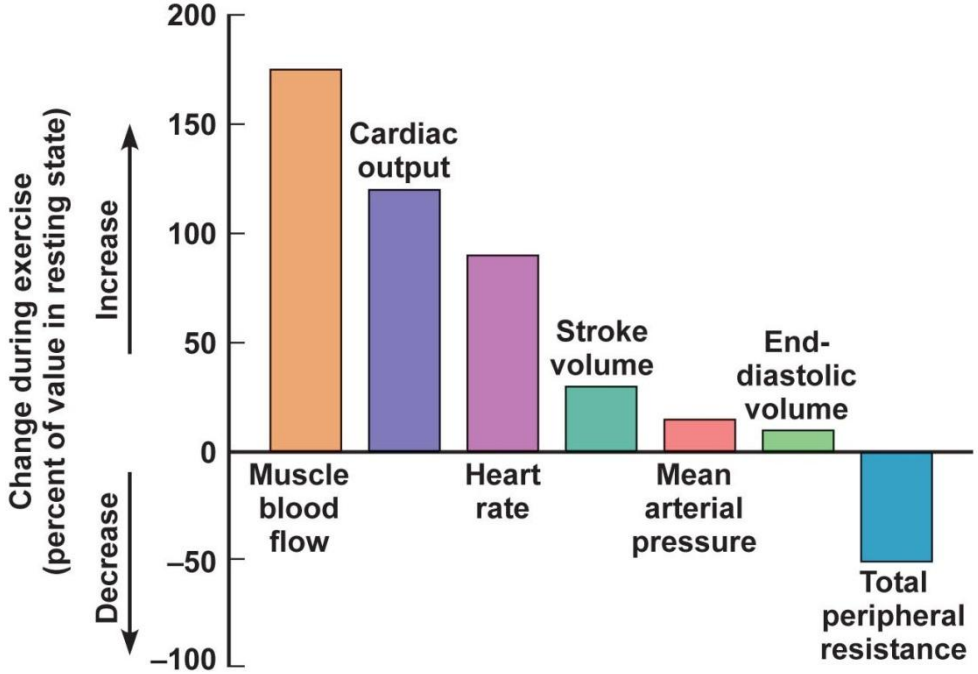


- Place the victim in shock position
- Keep the person warm and comfortable
- Turn the victim's head to one side if neck injury is not suspected

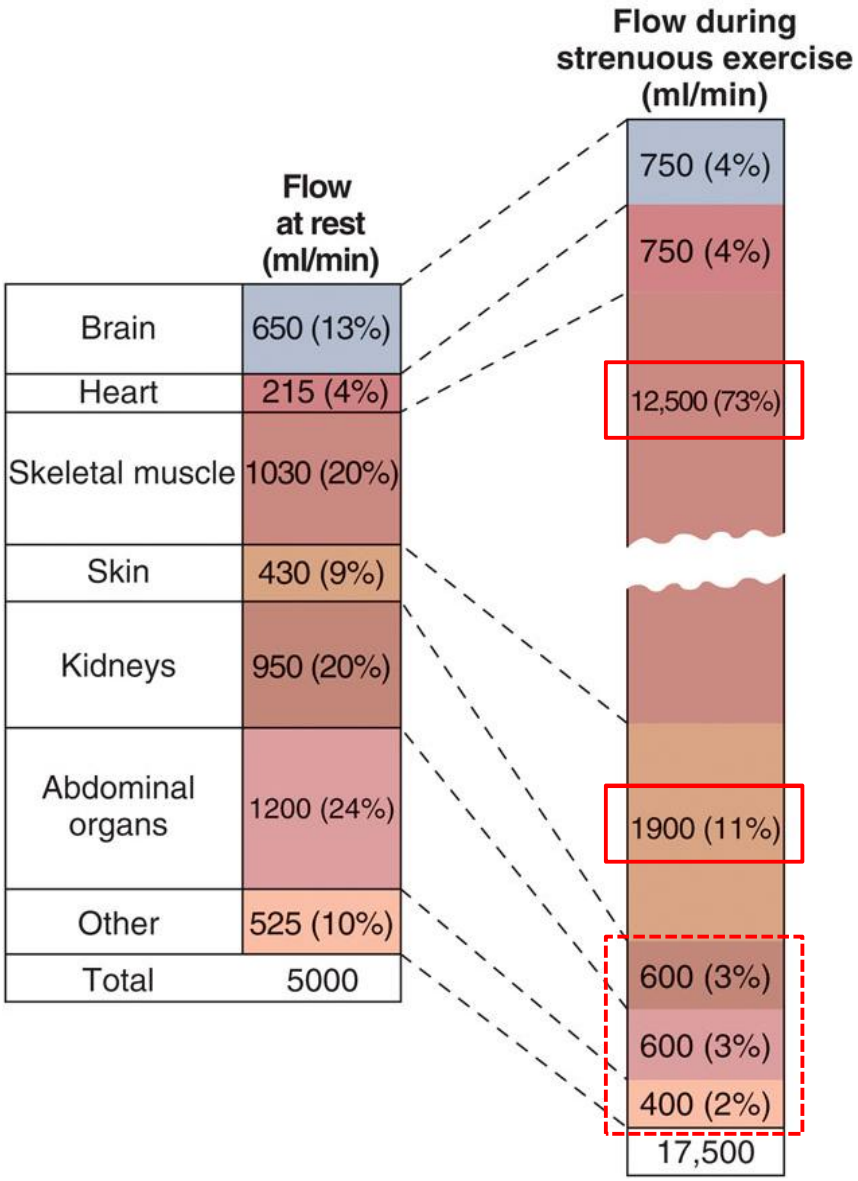
Cardiovascular Adaptation to Exercise

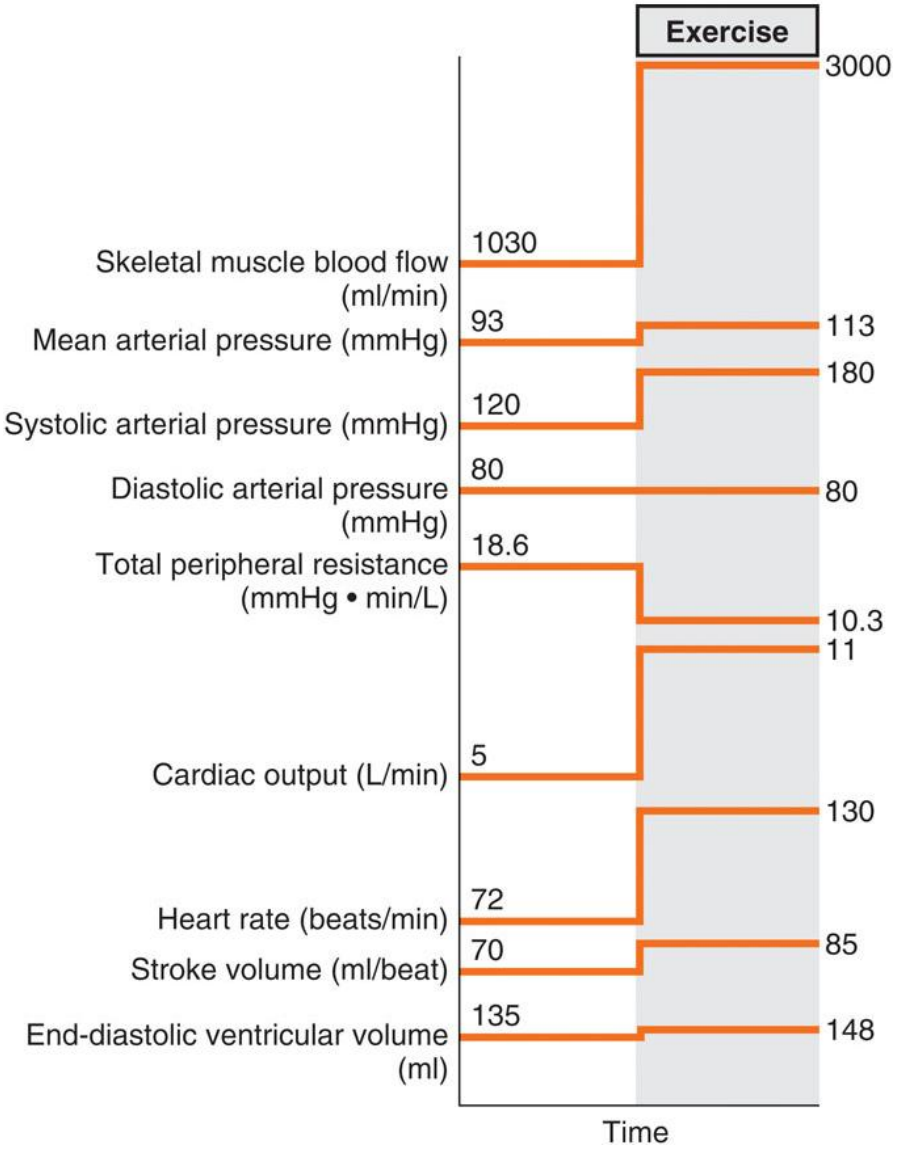
Table 14.5 | Changes in Skeletal Muscle Blood Flow Under Conditions of Rest and Exercise

Condition	Blood Flow (ml/min)	Mechanism
Rest	1,000	High adrenergic sympathetic stimulation of vascular alpha receptors, causing vasoconstriction
Beginning exercise	Increased	Dilation of arterioles in skeletal muscles due to cholinergic sympathetic nerve activity and stimulation of beta-adrenergic receptors by the hormone epinephrine
Heavy exercise	20,000	Fall in alpha-adrenergic activity Increased cholinergic sympathetic activity Increased metabolic rate of exercising muscles, producing intrinsic vasodilation

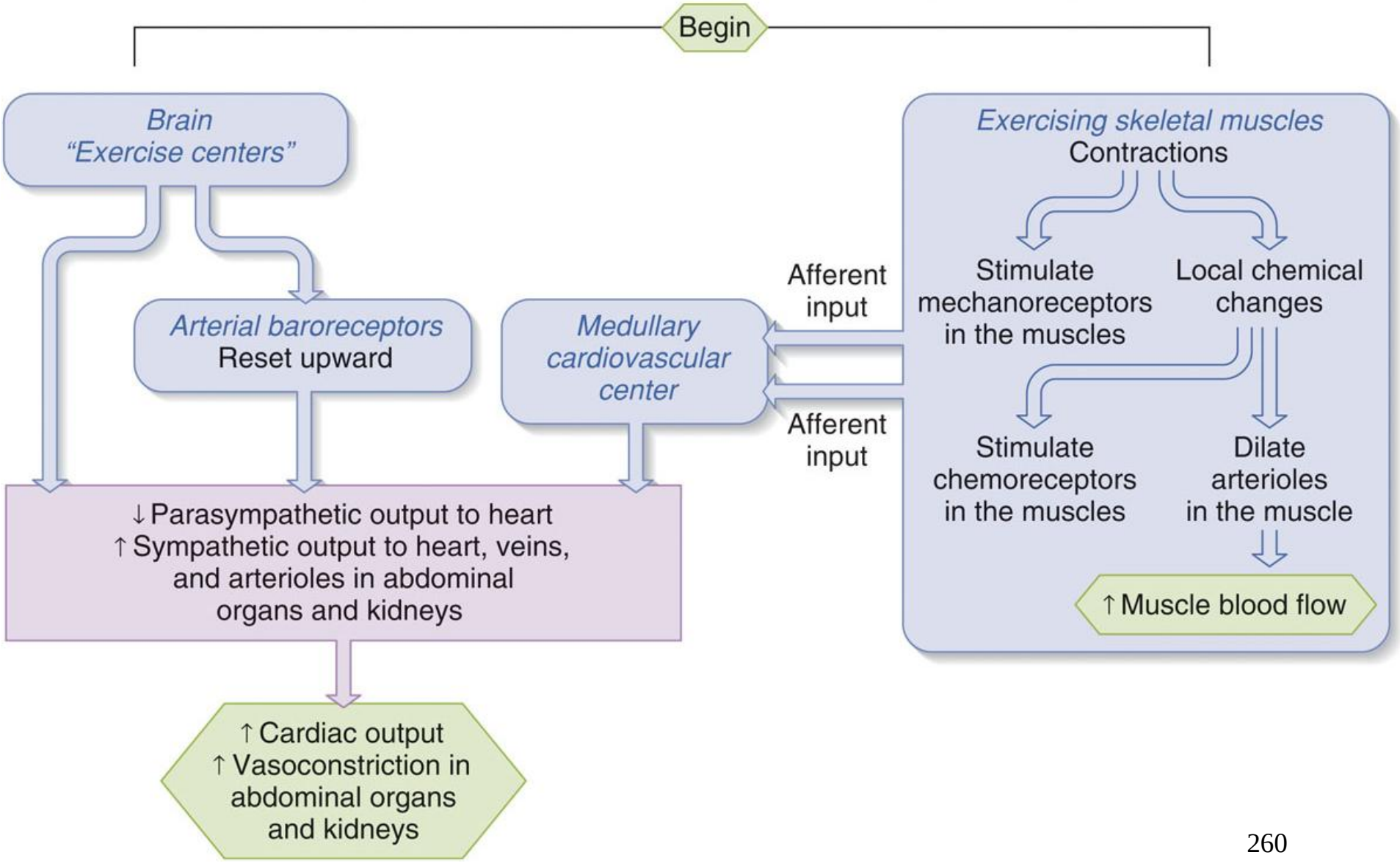


Cardiovascular Adaptation to Exercise





Cardiovascular Adaptation to Exercise

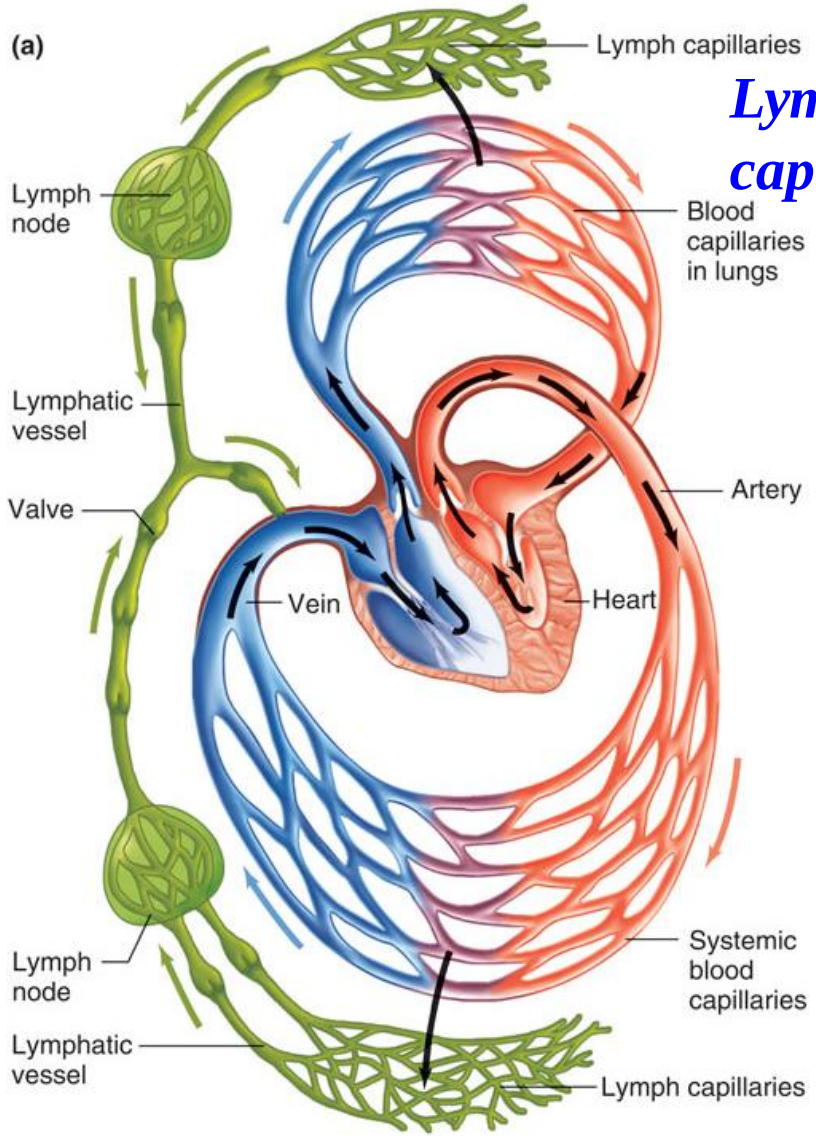


Cardiovascular Changes During Exercise

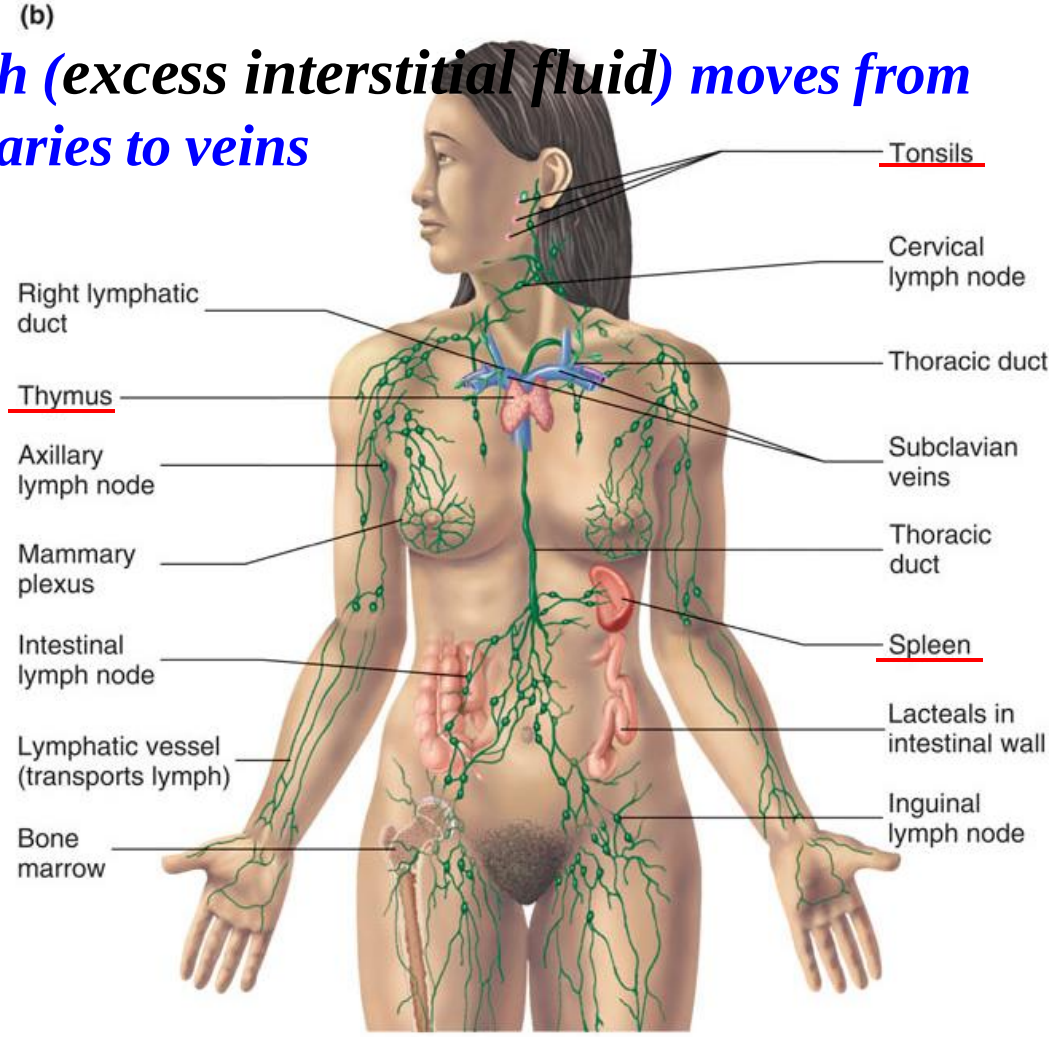
Variable	Change	Explanation
Cardiac output	Increases	Heart rate and stroke volume both increase, the former to a much greater extent.
Heart rate	Increases	Sympathetic nerve activity to the SA node increases, and parasympathetic nerve activity decreases.
Stroke volume	Increases	Contractility increases 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 reflexively 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

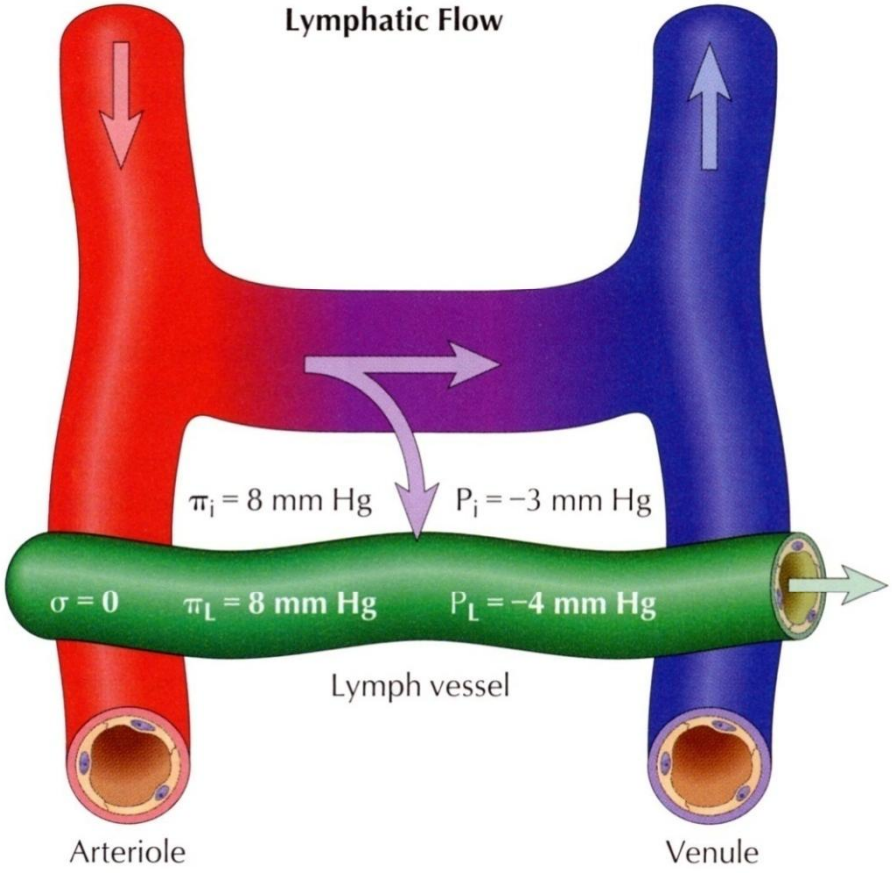
Lymphatic vessels + lymphatic tissue (node & organ)

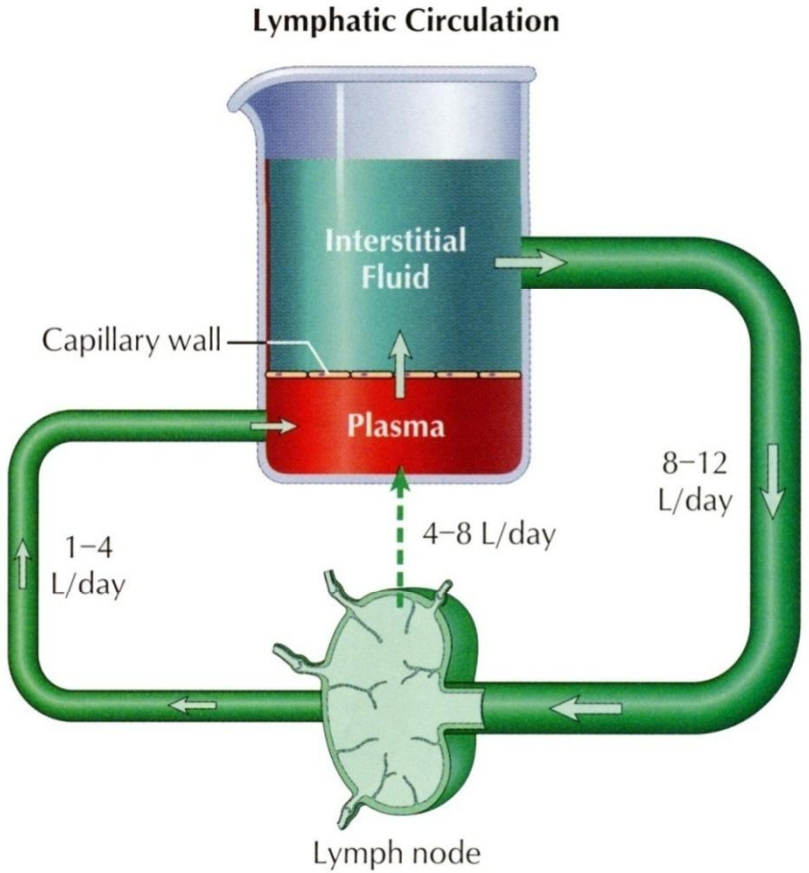


Lymph (excess interstitial fluid) moves from capillaries to veins



Lymphatic Circulation





- **Lymphatic vessels** involved in ***returning excess filtrate to circulation***
- **Lymph nodes** where the lymph is provide ***a proliferation site for lymphocytes*** and ***cleaned and examined by immune cells (phagocytes & lymphocytes) for pathogens (part of immune system)***
- **Swollen glands (lymphedema)*= lymph nodes become swollen and painful***

成功的祕訣

日本人把“不倒翁” 稱為“永遠向上的小法師”

因為重心在下面，所以無論你怎樣推它，

只要一鬆手，它就會馬上彈起來

不怕失敗每當我們跌倒時都能爬起來

正是因為不斷地接受磨難，人才能變得更加堅強

“人生成功的祕訣只有那些在奮鬥中尚未成功的人才知道”

——格林斯