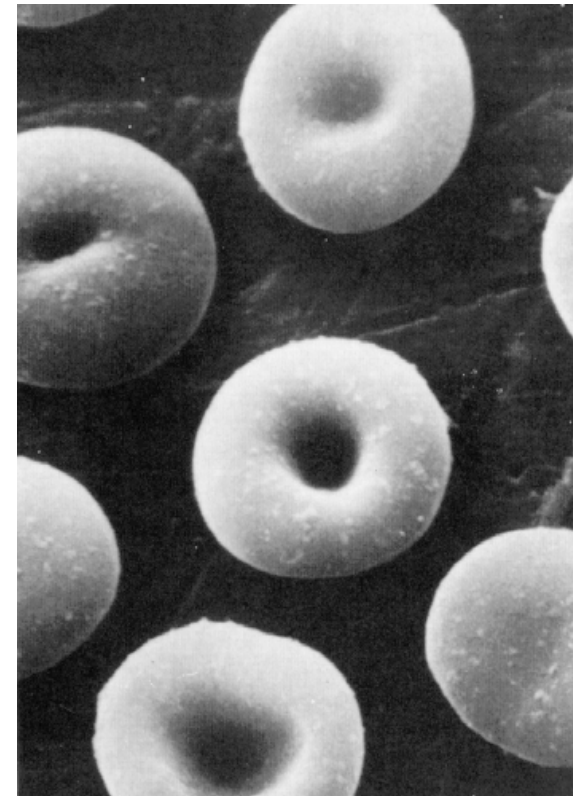




Circulatory physiology

- Suggested reading
 - Chapter 8
- Topics to be covered
 - Roles of **circulatory system**
 - Design of circulatory systems
 - Elements of circulatory systems
 - Pumps
 - Blood vessels
 - Control of **blood pressure and flow**
 - Adjustments for exercise



Roles of the circulatory system

- ☐ What animals need a circulatory system, and why?
- ☐ Once a circulatory system is in place, what else can it be used for?

Time to 95% equilibration of O₂ by diffusion

0.1 mm → 0.067 s



1 mm → 6.7 s



1 cm → 10.9 min



1 m → 78 days



□ Diffusion vs. convection

- **Size** (time $\propto d^2$) and **metabolic rate** are limiting factors
- **Diffusion** is always the final step in O_2 transport
- **Convection** is essential for
 - **Complex** organ systems
 - To support **high metabolic rates**
 - To achieve **large body mass**

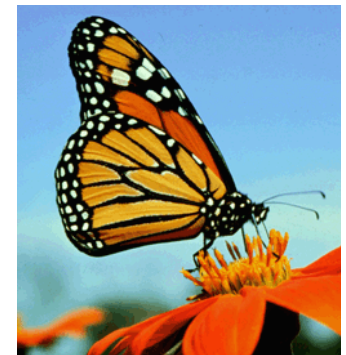
□ Circulatory system functions in

■ **Rapid mass transportation** of:

- respiratory gases (except insects)
- nutrients
- waste products
- hormones
- antibodies
- salts/acid-base equivalents
- heat

■ **Production of force**:

- Hydrostatic skeletons
- Wing expansion in insects
- Renal filtration and excretion in vertebrates (regulation of ECF volume)



Design of circulatory systems

□ Three essential components:

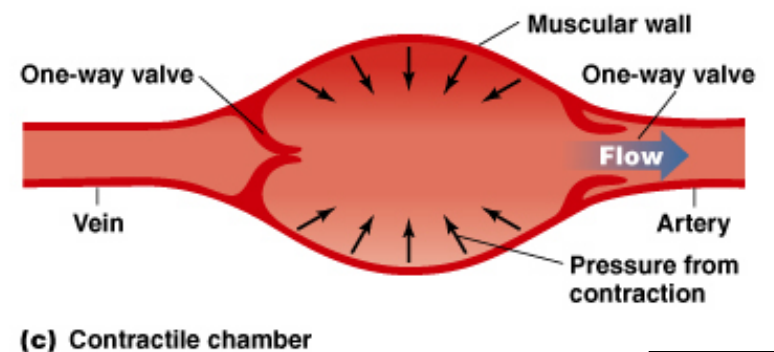
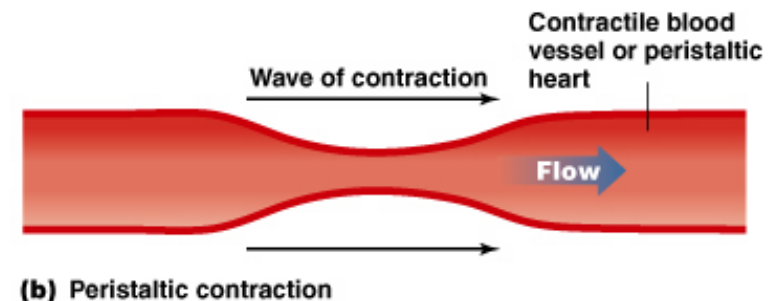
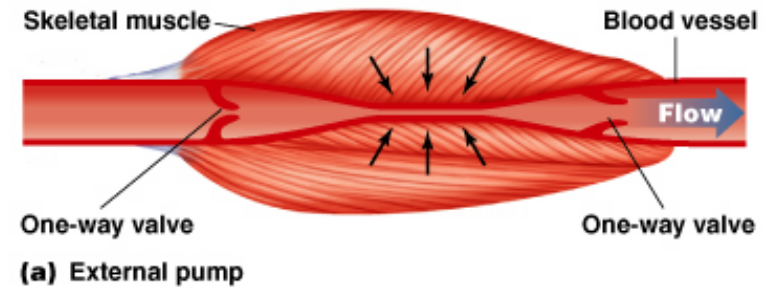
☰ (1) **Pump** (usually a heart):

- Positive vs. negative forces
- peristaltic pump
- chamber pump with contractile walls
- chamber pump driven by external forces

☰ (2) **Vascular system**

- arterial system
 - capillaries
 - venous system
- } Peripheral circulation

(3) **Circulating fluid**



□ **Two broad trends (with increases in metabolic rate):**

☰ ■ **Open** → **closed** systems

- Open system = incomplete system of vessels (invertebrates)
 - low blood pressure and blood flow
- Closed system (vertebrates, some invertebrates)
 - high blood pressure (resistance provided by vessels) and blood flow
 - exchange occurs across capillaries

☰ ■ **Undivided** → **divided** systems

- Separation of systemic and respiratory circulations (or oxygenated and deoxygenated blood)

■ **Advantages**

- improved ability to control velocity and distribution of blood flow
 - Allows increases in metabolic rate and body mass
- higher pressures achieved
 - enabled **evolution of glomerular kidney**

Open systems

■ Invertebrates

■ Haemolymph pumped by heart empties into sinuses or lacunae to bathe tissues directly

■ High haemolymph volume (~30% body weight)

■ Low pressure (typically <10 torr)

■ Limited capacity to alter velocity and distribution of blood flow → low max rate of O₂ uptake

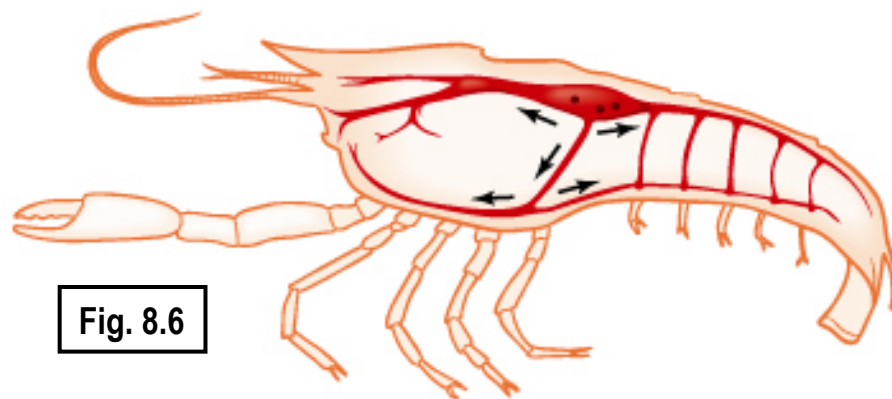
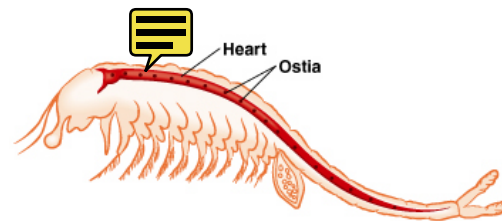


Fig. 8.6

Fig. 23.21, Hill et al. 2004

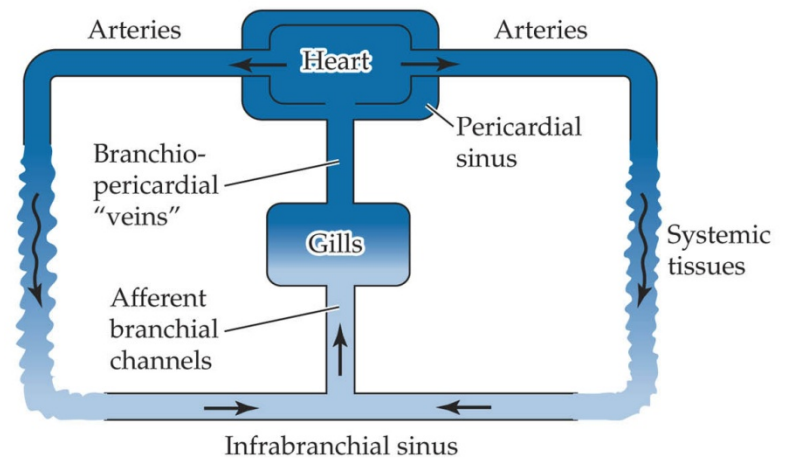
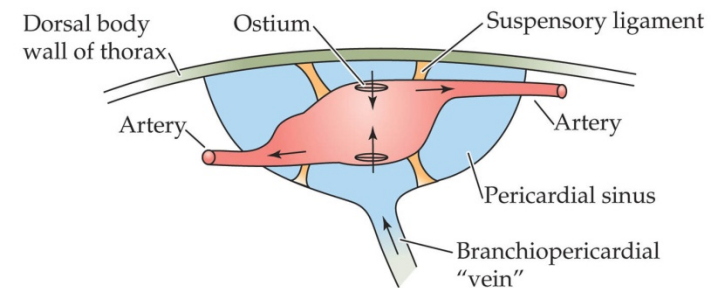
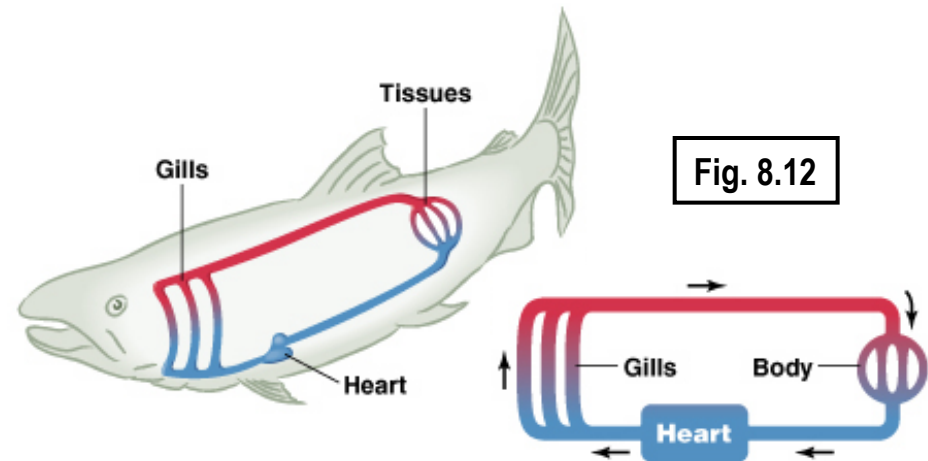
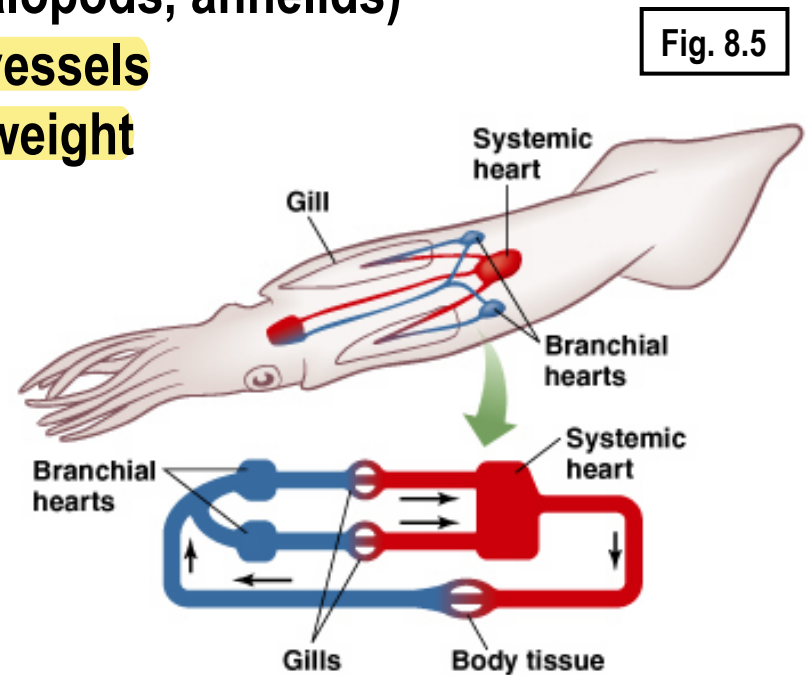


Fig. 23.22, Hill et al. 2004

Closed systems

- Vertebrates, some invertebrates (cephalopods, annelids)
- Blood flows in a **continuous circuit of vessels**
- Blood volume typically **5-10% of body weight**
 - ECF = **blood + interstitial fluid**
- High pressure system because blood vessels provide resistance
- Differential distribution of blood flow
- Exchange occurs across **capillary walls**
 - Plasma proteins
 - Requirement for lymphatic system



□ What is the defining characteristic of a closed system?

TABLE 23.2 Systemic circulatory function in two decapod crustaceans and two fish of similar body sizes

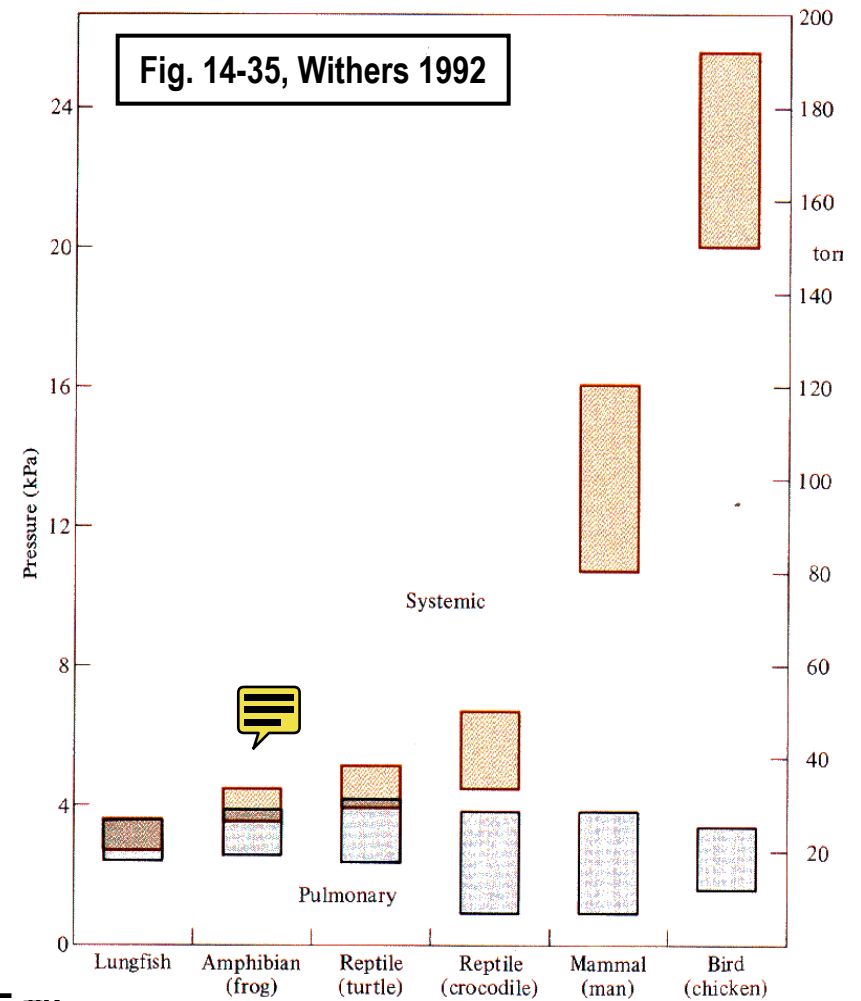
Characteristics of circulatory function	Spiny lobster (<i>Panulirus interruptus</i>)	Rock crab ^a (<i>Cancer productus</i>)	Starry flounder (<i>Platichthys stellatus</i>)	Rainbow trout (<i>Oncorhynchus mykiss</i>)
Principal features of circulatory function				
Rate of O ₂ delivery to tissues (mL O ₂ /kg·min) ^b	0.80	0.60	0.46	0.65
Rate of blood flow through systemic circuit (mL blood/kg·min) ^c	128–148	125	39	18
Pressure change to perfuse systemic circuit (mm Hg) ^d	14	3	16	22
Systemic resistance (pressure change divided by flow rate) ^e	0.1	0.03	0.4	1.2
Secondary information				
Heart rate (beats/min)	65	101	35	63
Stroke volume (mL/kg·stroke)	2.1	1.2	1.2	0.3
Blood pressure in major systemic arteries (mm Hg) ^d	35	10	18	26
Blood pressure in major systemic veins or venous sinuses (mm Hg) ^d	21	7	2	4
Blood oxygen-carrying capacity (vol %)	2.0	1.3	5.7	7.8
Temperature during studies (°C)	16	12–16	8–11	9–15
Body weight (g)	515	~370	684	~210

$\Delta P = QR$

□ Evolutionary trends in closed systems

■ With increasing O₂ uptake, see:

- Shift from water- to air-breathing
- Shift towards increasing blood pressure and flow
- Shift towards increasing separation of oxy and deoxy circulation



□ Evolutionary trends in closed systems

■ With increasing O₂ uptake, see:

- Shift from water- to air-breathing
- Shift towards increasing blood pressure and flow
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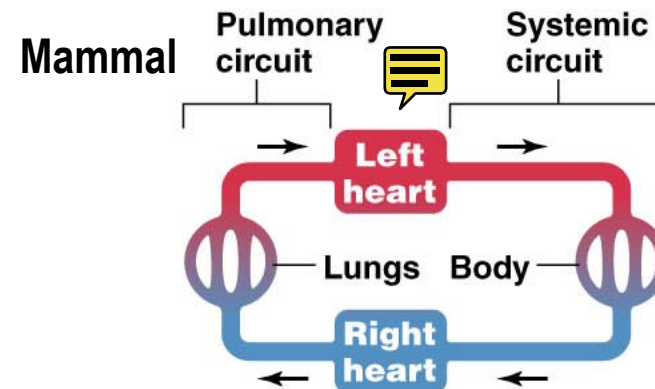
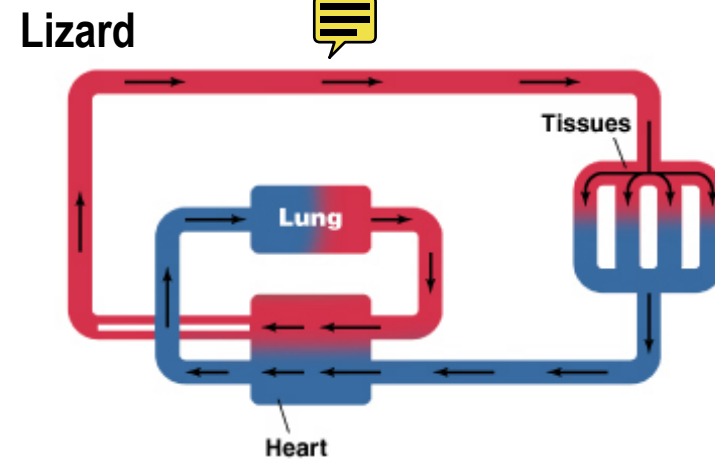
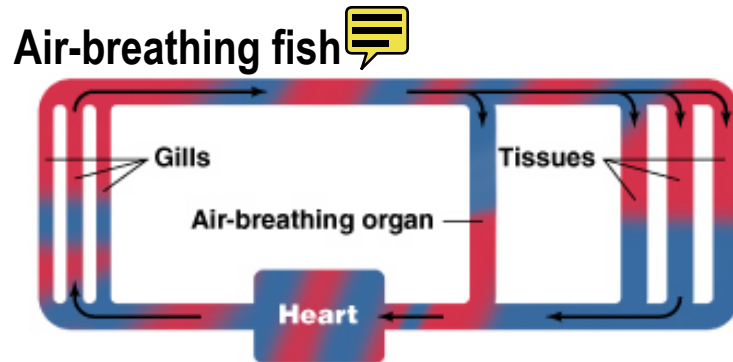
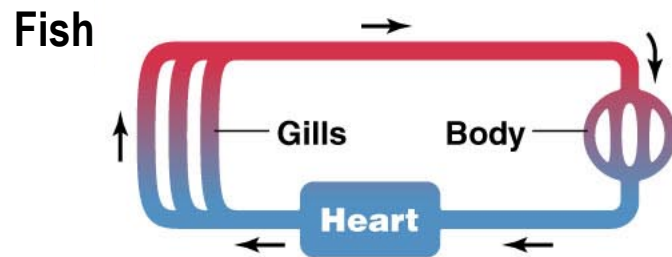


Fig. 8.12 (fish, mammal);
Fig. 9.11, 1st ed. (air-breathing fish, lizard)

Evolutionary trends in closed systems

With increasing O₂ uptake, see:

- Shift from water- to air-breathing
- Shift towards increasing blood pressure and flow
- Shift towards increasing separation of oxy and deoxy circulation

Air-breathing fish



Lizard

Mammal

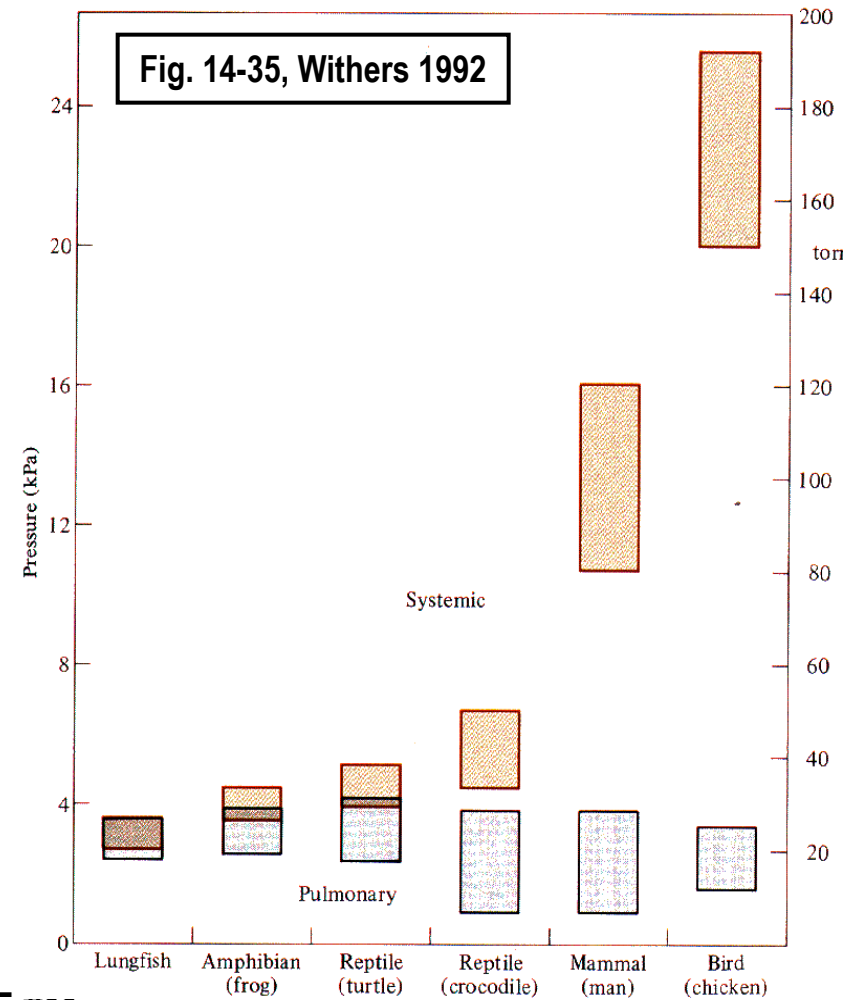
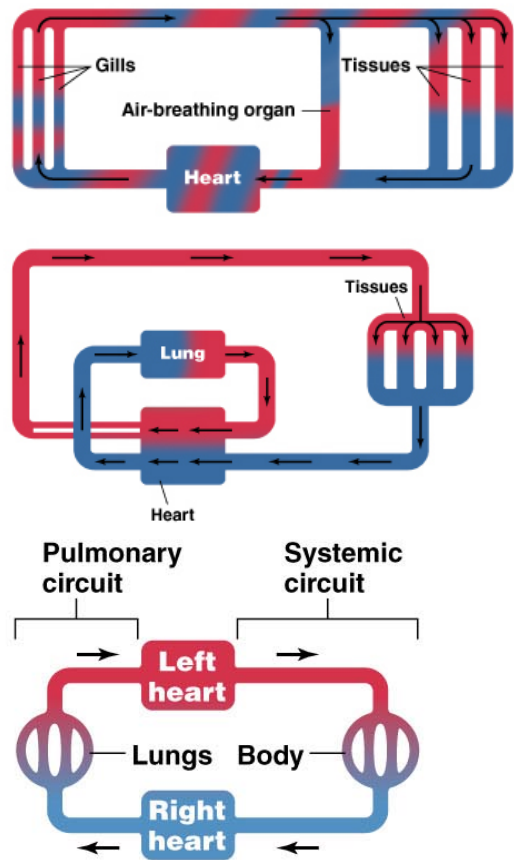
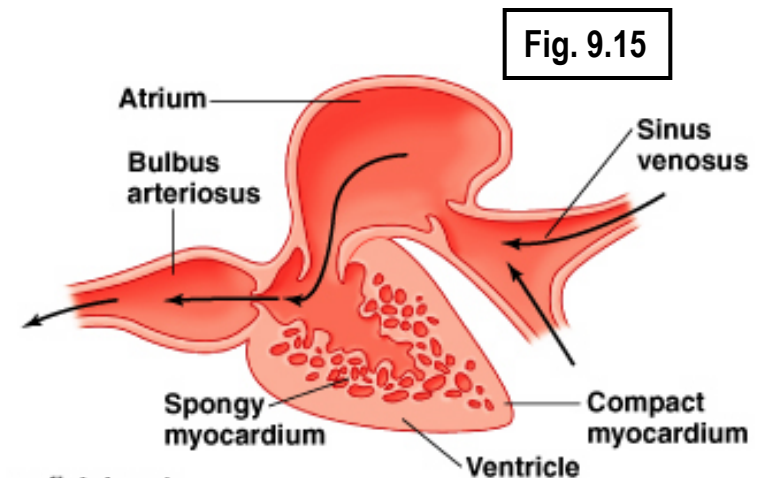
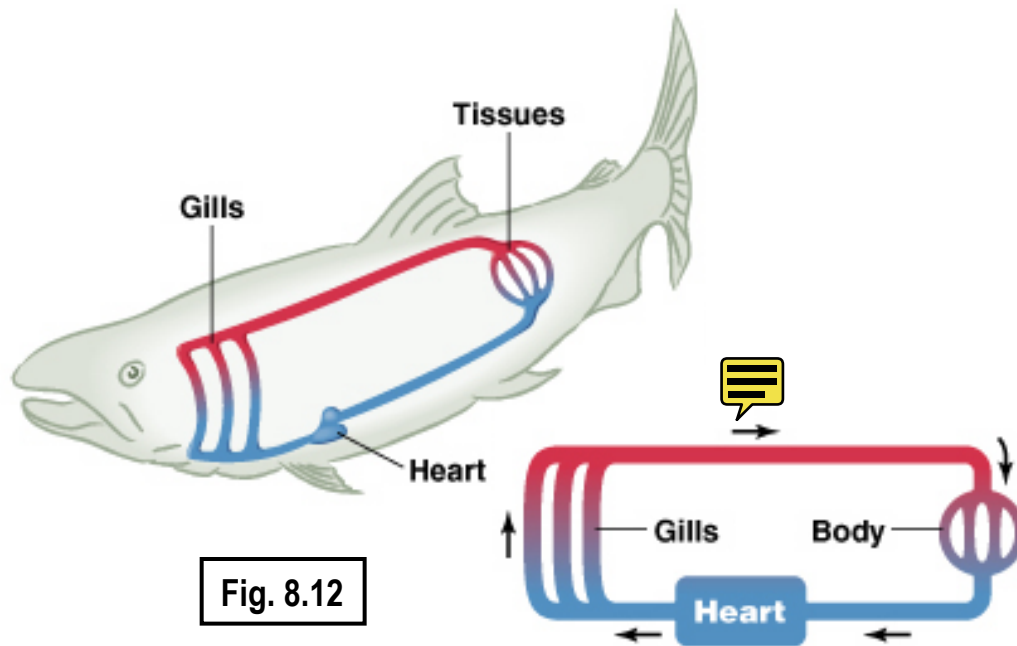


Fig. 8.12 (fish, mammal);
Fig. 9.11, 1st ed. (air-breathing fish, lizard)

Fish

- **4-chambered heart with chambers (sinus venosus, atrium, ventricle, bulbus or conus arteriosus) in series**
- **Gills between heart and systemic circulation in single circulation**
 - 2 resistance beds in series
 - Require relatively high pressure
 - Gills must be able to withstand high pressure



- **Birds/mammals**
 - Lungs cannot withstand high pressure but need high pressure to systemic circulation
 - Separation of systemic and pulmonary circulations
 - Two pairs of heart chambers in parallel
 - Atrium and ventricle
 - Allows different input pressures to separate circuits
 - Requires equal total blood flow through separate circuits

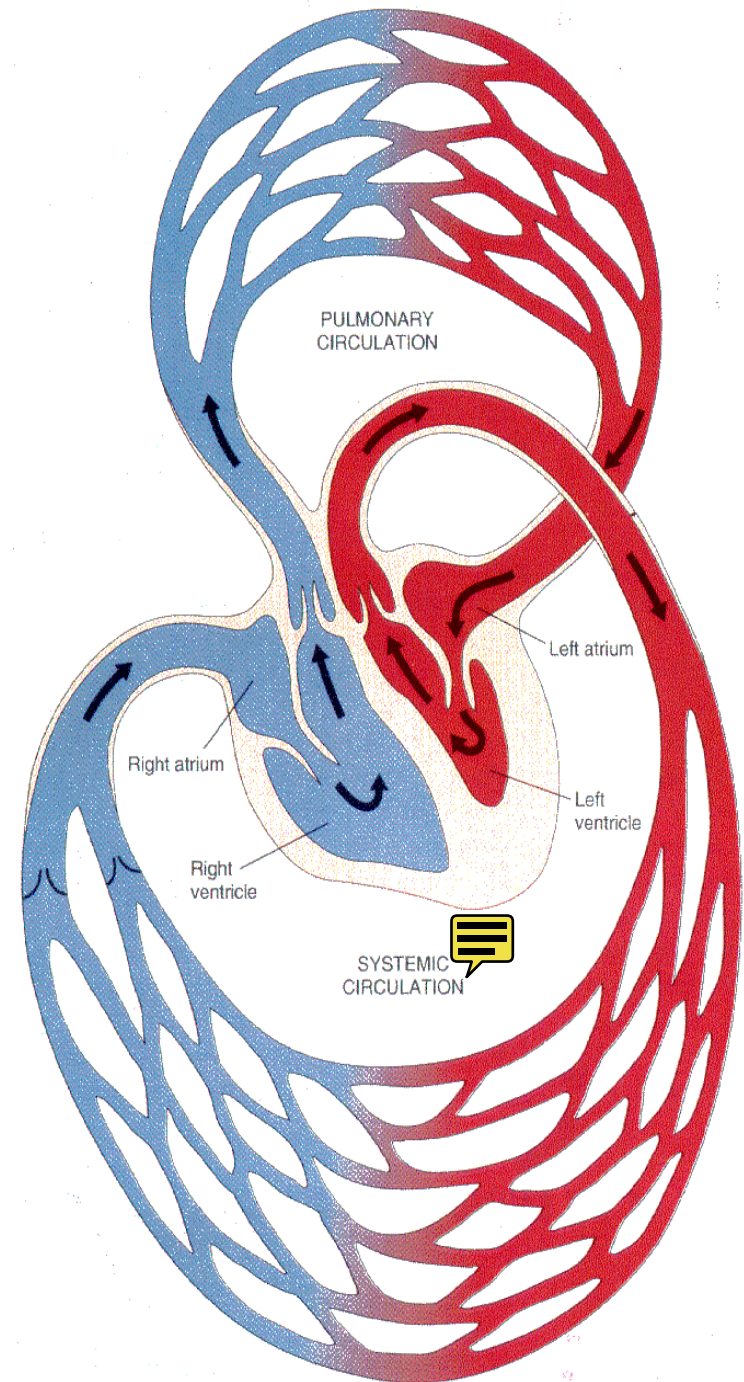


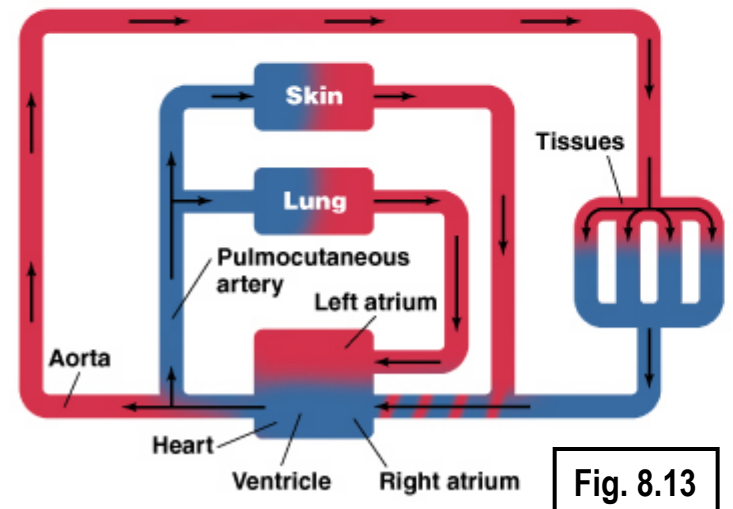
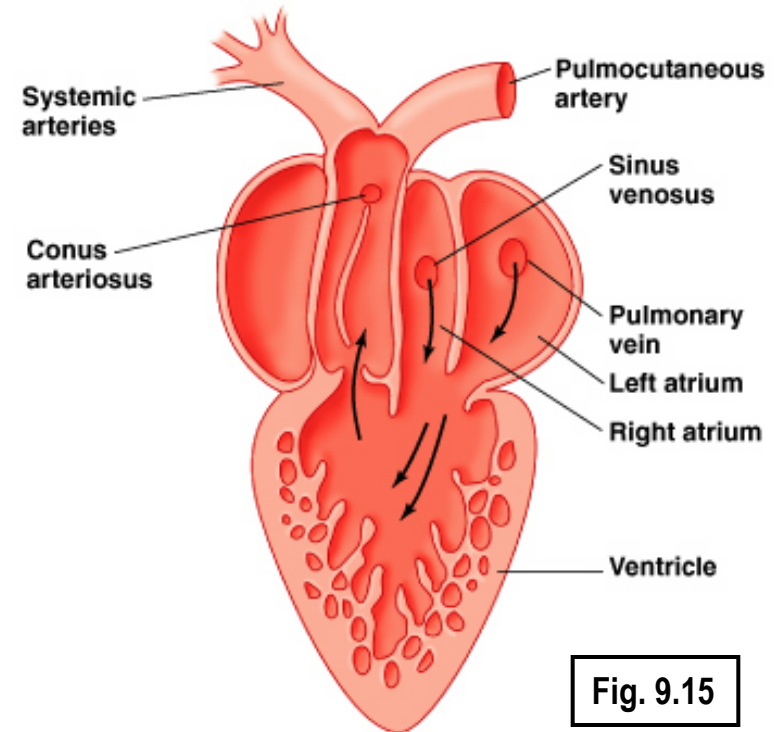
Fig. 14-8, Vander et al. 1994



□ Intermittent air-breathers

■ Amphibians and reptiles

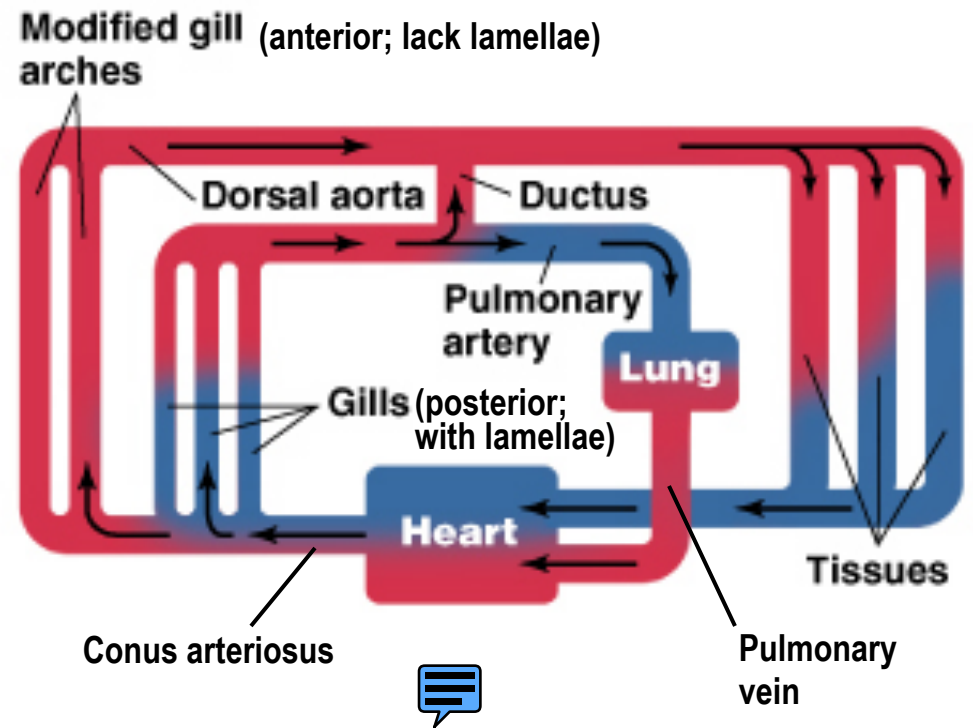
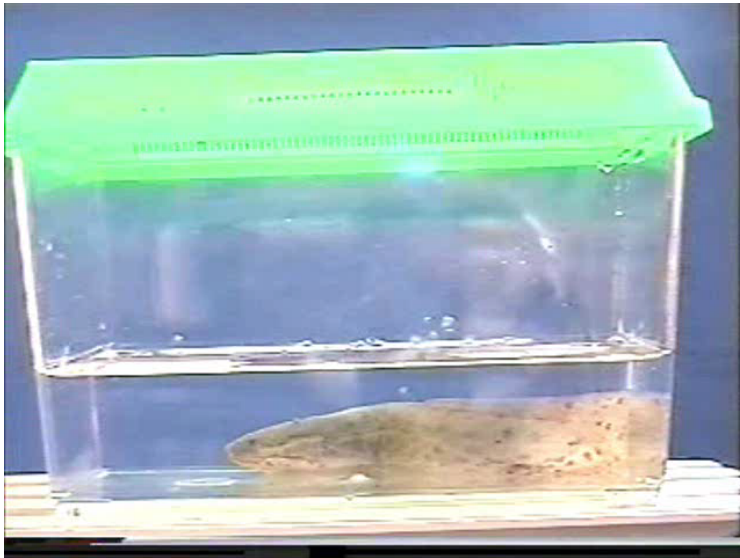
- Separate atria
- Variable degree of anatomical division in ventricle
- Selective distribution of blood flow by mechanisms that are poorly understood
- Same input pressure to pulmonary and systemic circulations
- Differential distribution of blood flow to lungs, skin, body can occur
- Advantage for intermittent breathing?





■ Lungfish

- Partial anatomic separation of conus arteriosus
- Oxy blood from lungs returned directly to heart and preferentially directed to anterior branchial arches to systemic tissues
- Deoxy blood from systemic tissues preferentially directed to posterior branchial arches for oxygenation at gills or lungs
 - Bypasses lung via ductus if lung not ventilated



Heart function

□ Structure (mammal)

■ 2 atria, 2 ventricles

- Right → pulmonary
- Left → systemic

■ Valves

- Atrioventricular
- Aortic and pulmonary valves

■ Cardiac muscle

- Strongly contractile cardiac muscle cells



- Sinoatrial (SA) and atrioventricular (AV) nodes
- Conducting system (atrioventricular bundle, Purkinje fibres)

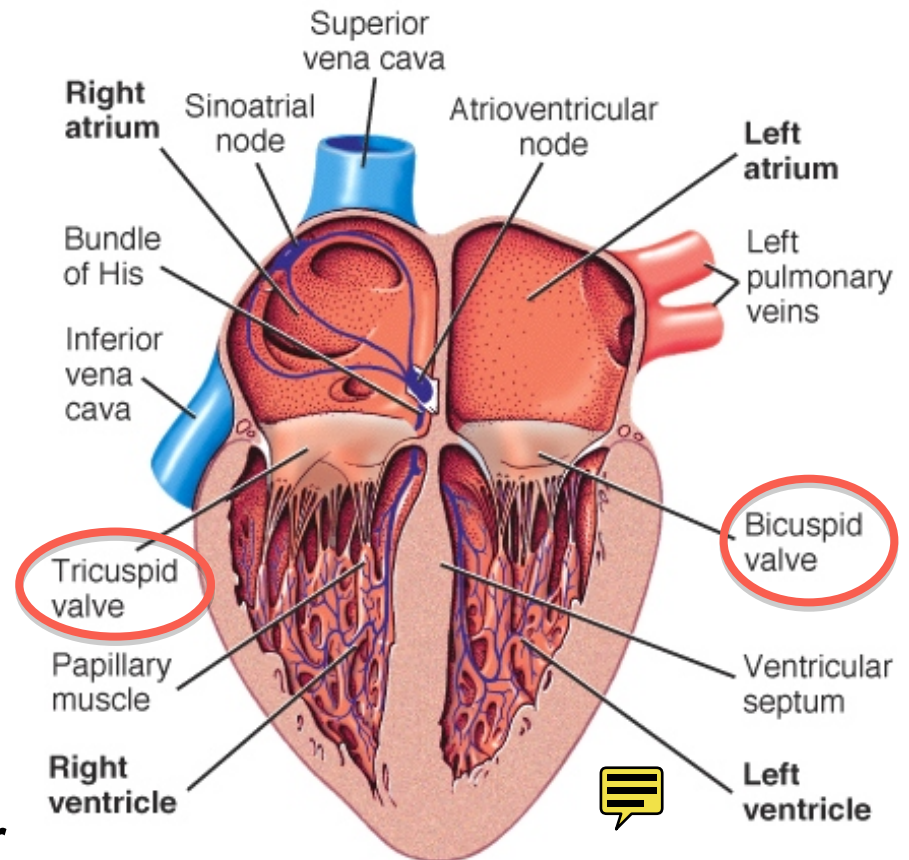


Fig. 12-4 Randall et al. 2002



□ Cardiac rhythm

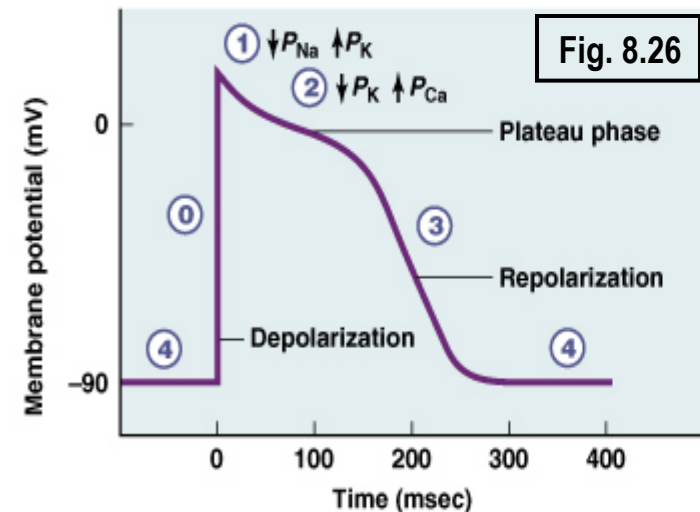
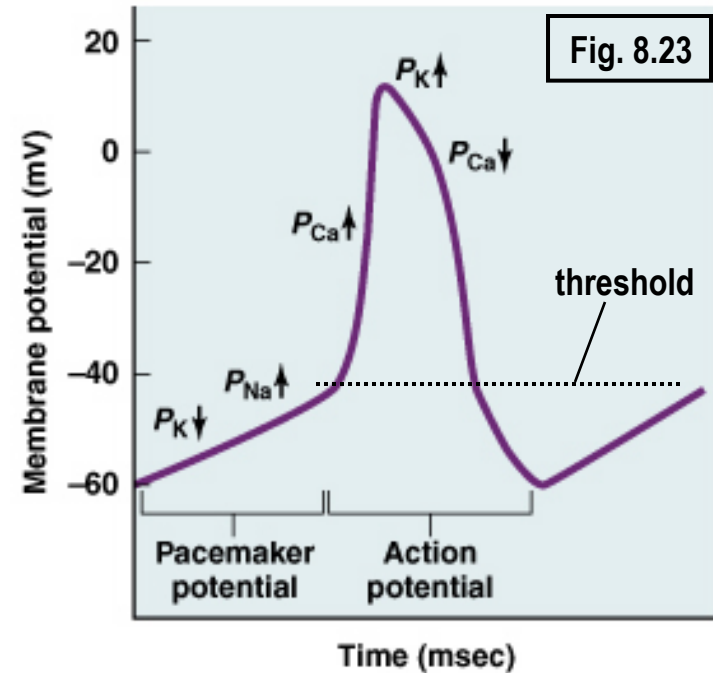
■ Electrical activity initiated by pacemaker region

- Neurogenic vs myogenic hearts
- Pacemaker (sinus venosus or SA node) contains cells with fastest intrinsic rate of activity.

■ V_m in pacemaker cells is never stable

- Slope \rightarrow rate
- 100 depolarisations/min
- Why? \rightarrow Na^+ leak (funny channels)

■ APs spread via gap junctions

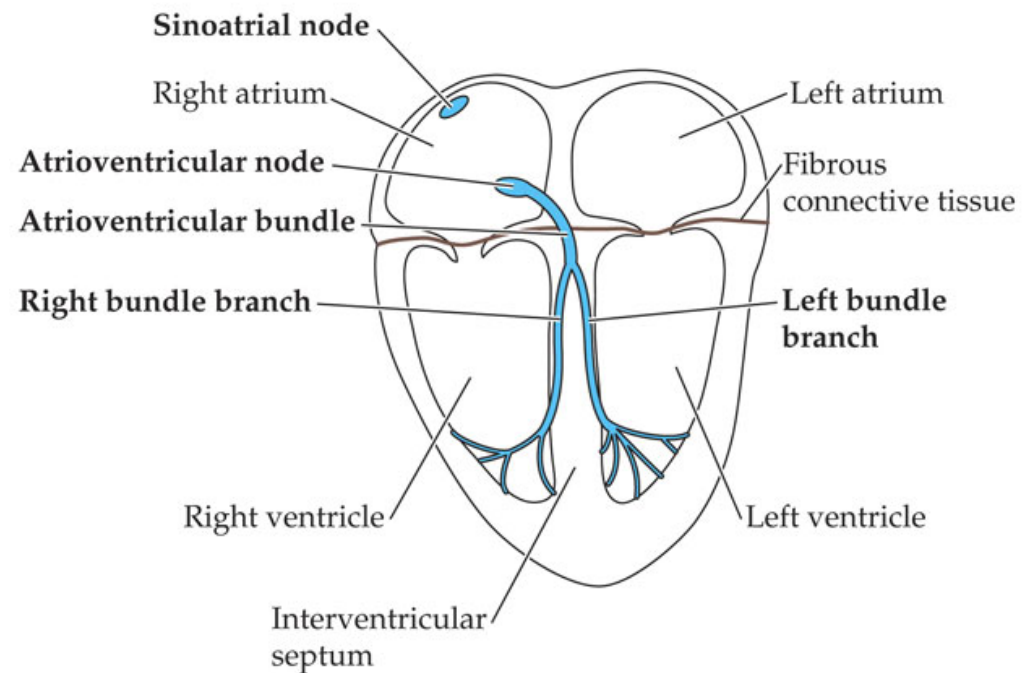




■ Transmission of excitation over the heart:

- Spreads from SA node over both atria at 0.8 m s^{-1} .
- Electrical connection to ventricles at AV node – slow conduction (0.1 m s^{-1})
 - Consequence?
 -
- Conduction through AV bundle, left and right bundles and Purkinje fibres fast at $4\text{-}5 \text{ m s}^{-1}$
 - Consequence?
 -

- What happens if the electrical connection between atria and ventricles is severed?



■ Electrocardiogram (ECG)

- Summation of membrane potential changes across all heart cells
- Normal mammalian ECG
 - P wave
 - QRS complex
 - T wave

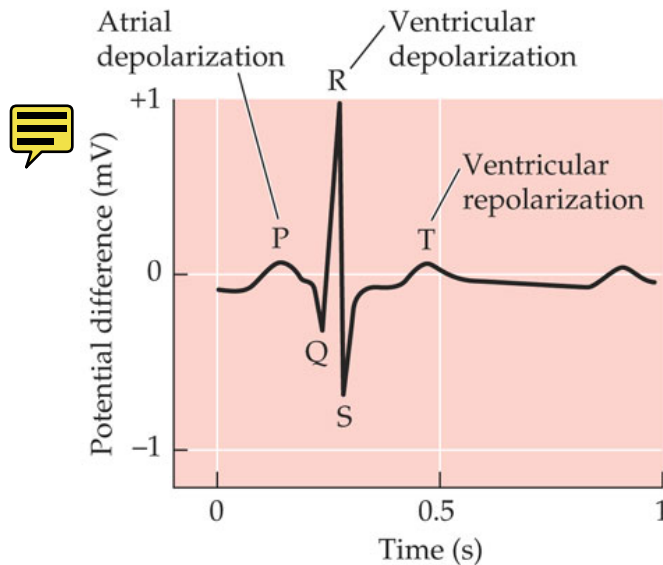


Fig. 23.6, Hill et al. 2004

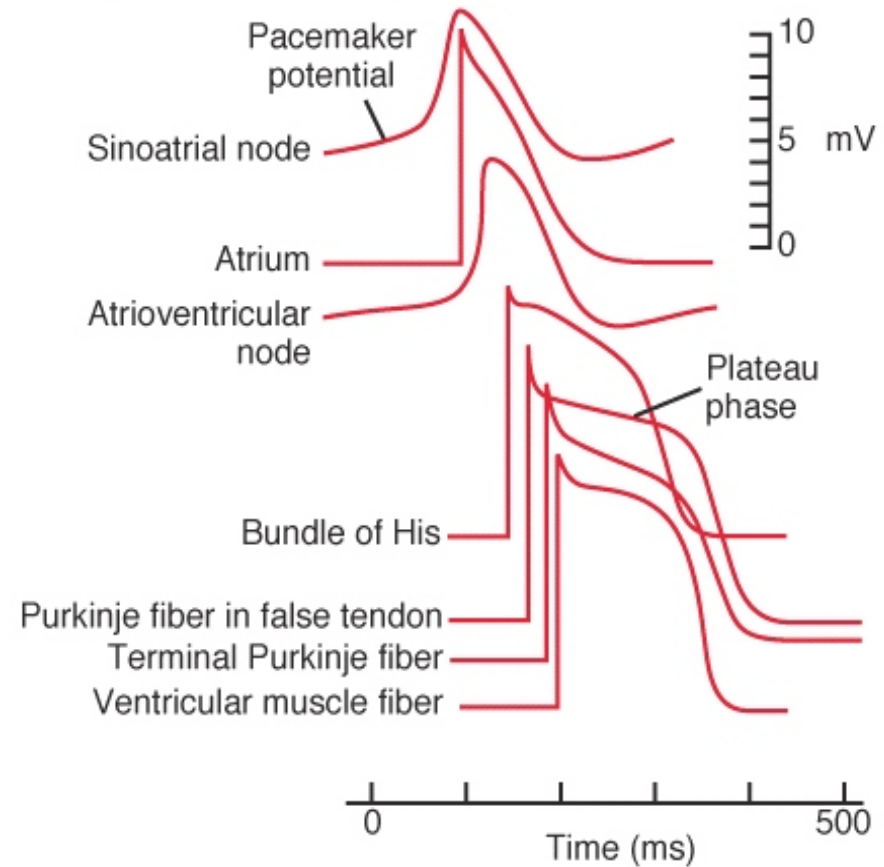


Fig. 12-8 Randall et al. 2002



□ The heart as a pump

- Systole vs diastole
- Contraction triggered by depolarization
- AP reflects:
 - Voltage-gated Na^+ channels open
 - Voltage-gated Ca^{2+} channels then open
 - Voltage-gated K^+ channels close (then open)
 - Note prolonged plateau phase and refractory period – significance?
- Ca^{2+} entry + Ca^{2+} -induced Ca^{2+} release activate the contractile apparatus

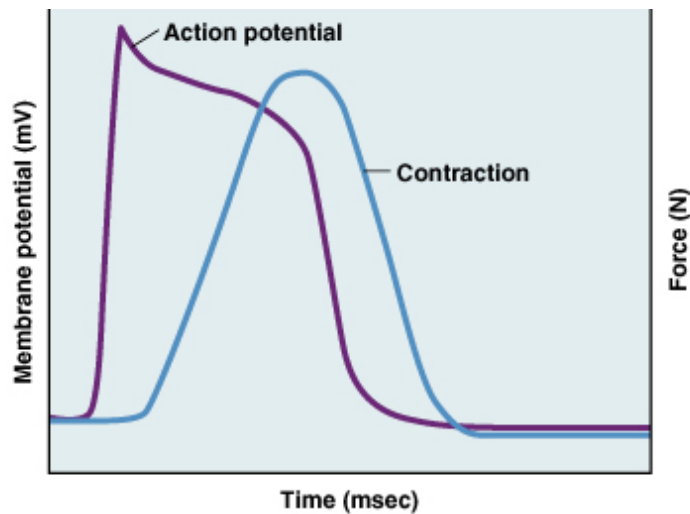


Fig. 5.24

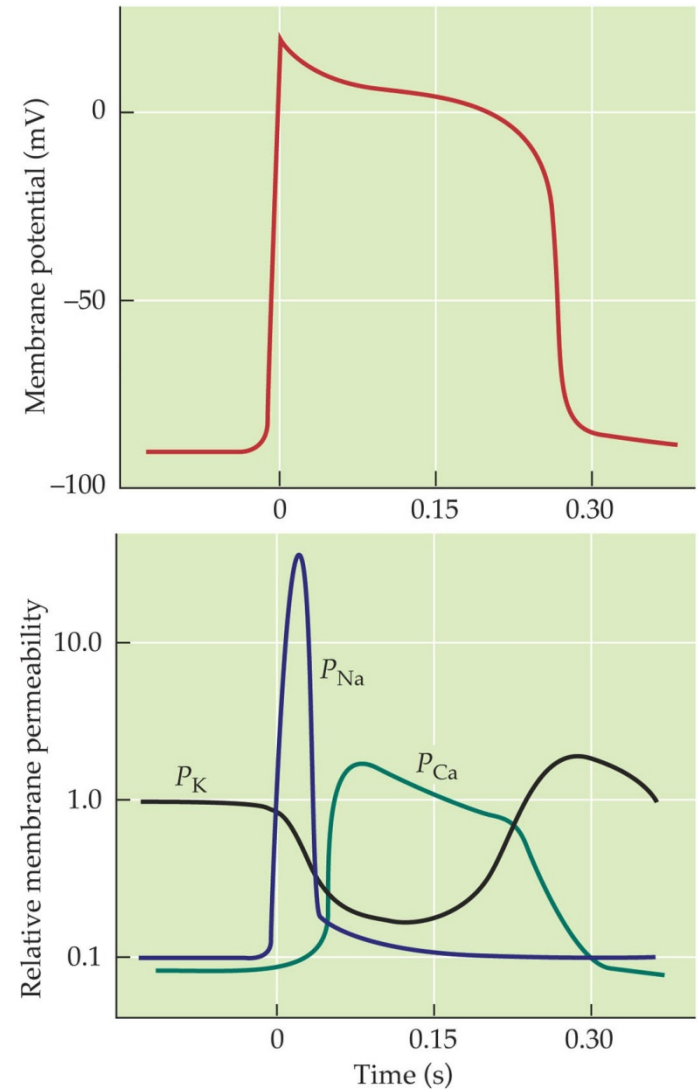


Fig. 11-21, Hill et al. 2004




■ **Stroke volume (SV) = volume ejected in a single heart beat**

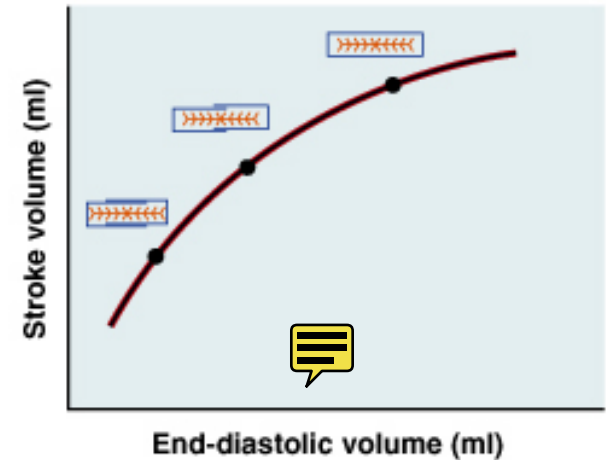
- End-diastolic volume – end-systolic volume
- End-diastolic volume determined by venous filling pressure
- Atrial contraction increases ventricular volume by ~20-30%

■ **To adjust SV (inotropic effects)**

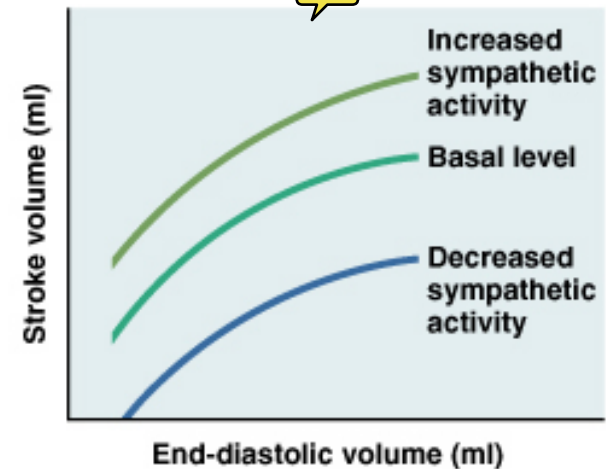
- Increase filling (greater venous return) → more forceful contraction
- Frank-Starling relationship
 - SV proportional to diastolic filling
 - Stretch produces more forceful contraction
 - Family of curves – role of **neural or humoral factors**

■ **Cardiac output (Q or Vb) = SV x HR**

(~5 L min⁻¹ in a 70-kg human or ~25 mL kg⁻¹ min⁻¹ in )



(a) Frank-Starling effect



(b) Effects of sympathetic activity on the Frank-Starling effect

■ To adjust HR (chronotropic effects)

- Parasympathetic innervation
 - ACh increases K^+ conductance of pacemaker cells
 - **Negative** chronotropic effect
 - vagal tone
- Sympathetic innervation and catecholamines
 - Increase Na^+ and Ca^{2+} conductance
 - **Positive** chronotropic effect

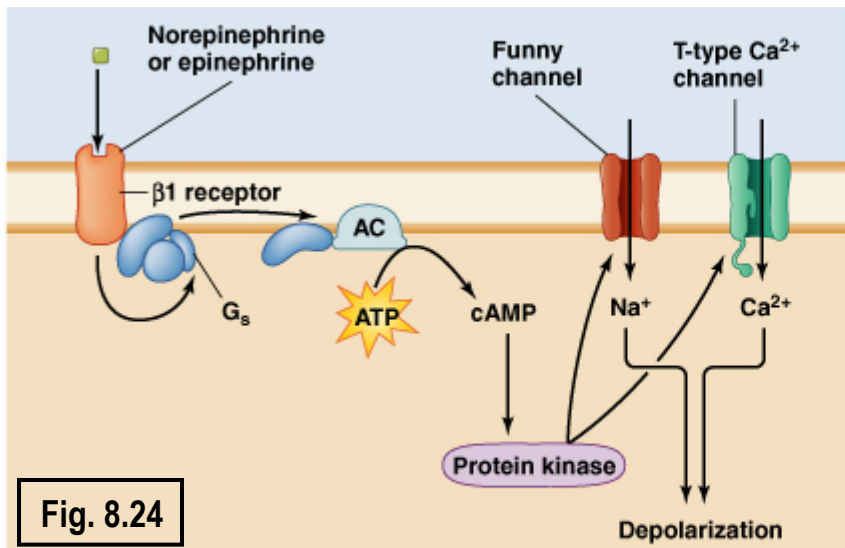
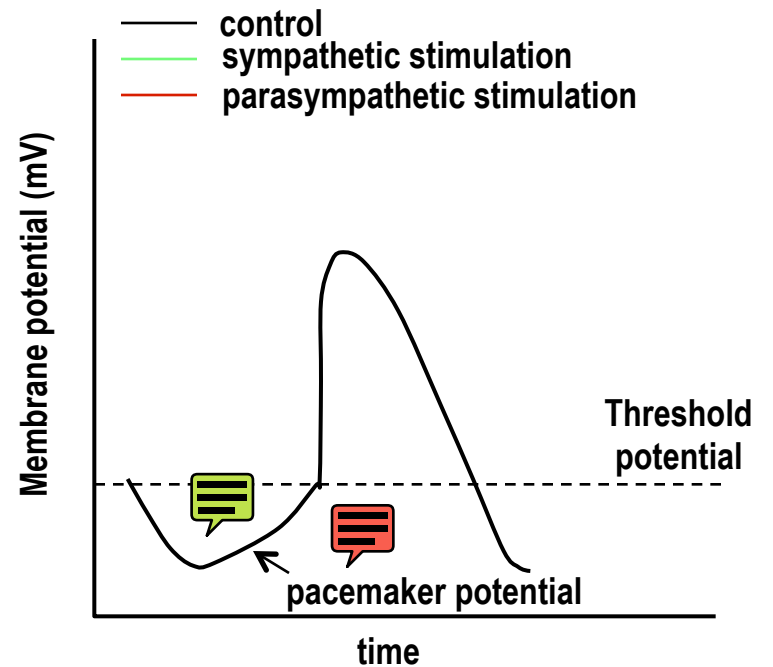


Fig. 8.24

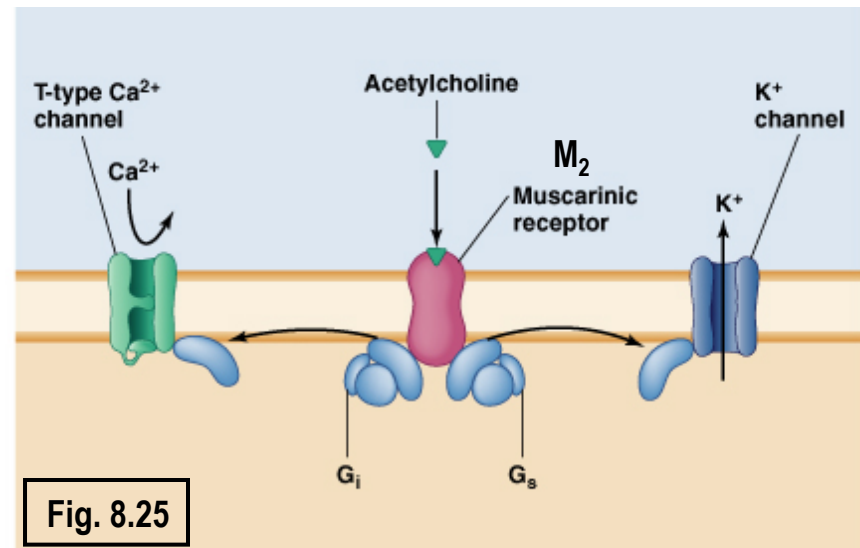


Fig. 8.25

□ Practise makes perfect...

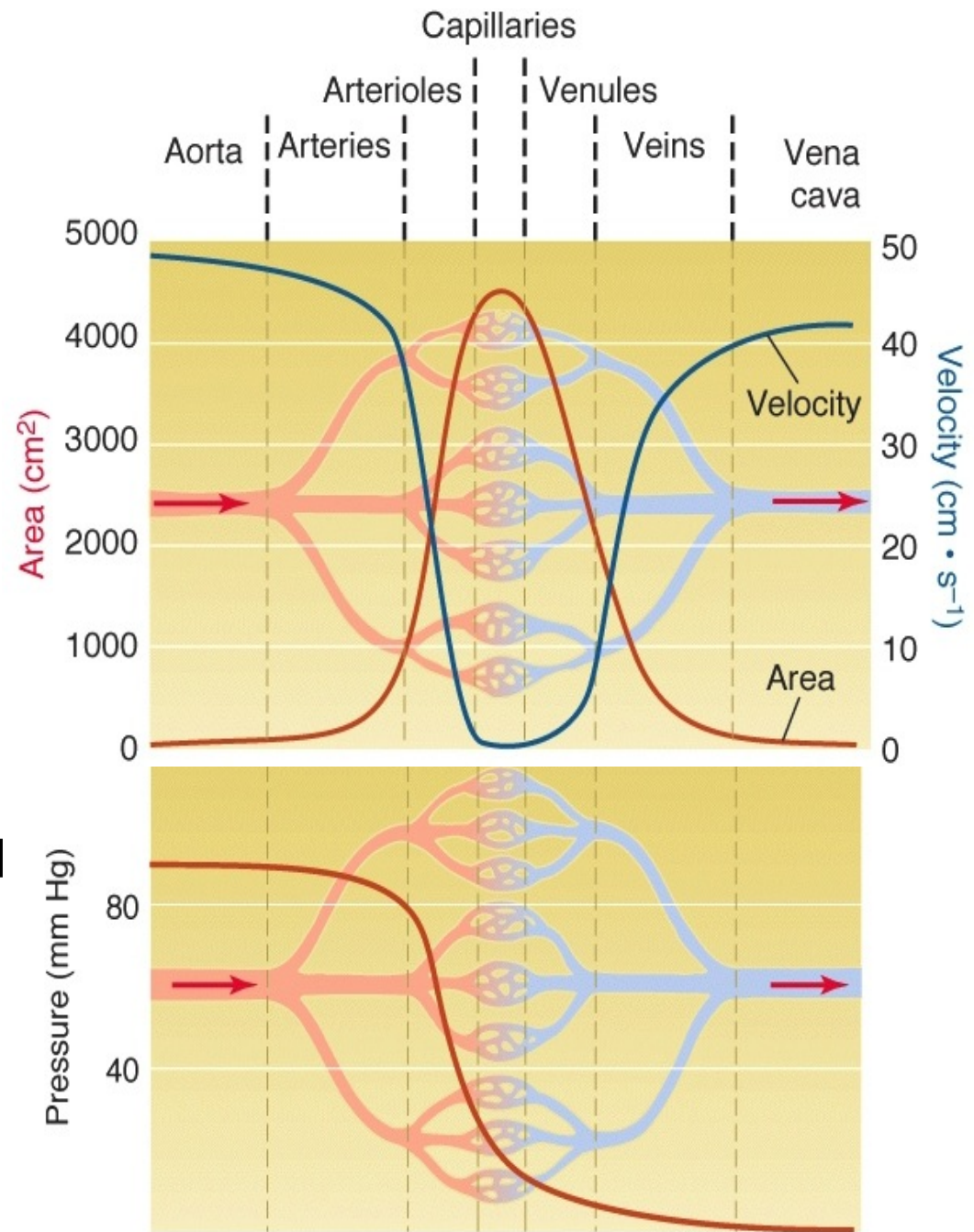
- Determine **your** SV assuming that $Q = 5 \text{ L min}^{-1}$.
- What does **your** current HR suggest about activity in the sympathetic vs parasympathetic branches of your ANS?
- How might an increase in HR affect SV?





Blood vessels

- **3 types of vessels on the basis of anatomy**
 - **arteries, capillaries, veins**
 - **All have endothelial cell lining**
 - **Arteries & veins have additional layers of connective tissue (elastic and collagenous fibres) and smooth muscle**
 - **Progressive sub-division**
 - X-sectional area
 - Flow and velocity
- **On the basis of function?**



□ Haemodynamic considerations

■ Pressure, resistance and flow

- Ohm's Law: $V=IR$
- Analogous relationship for circulatory system:
 $\Delta P=QR$
 - $\Delta P = V$ (driving force)
 - $R = R$
 - $Q = I$ (current or **blood flow**)




- $R \propto L\eta/r^4$

- $r =$ radius
- $\eta =$ viscosity
- $L =$ length

- **Poiseuille's equation**

$$Q = \left(\frac{\pi}{8} \right) \left(\frac{\Delta P r^4}{L \eta} \right)$$

Practise...

- If ΔP falls to half its normal value and R is unchanged, what happens to Q ? 
- If R doubles but Q is unchanged, what happens to ΔP ? 
- If R doubles while Q is halved, what happens to ΔP ? 

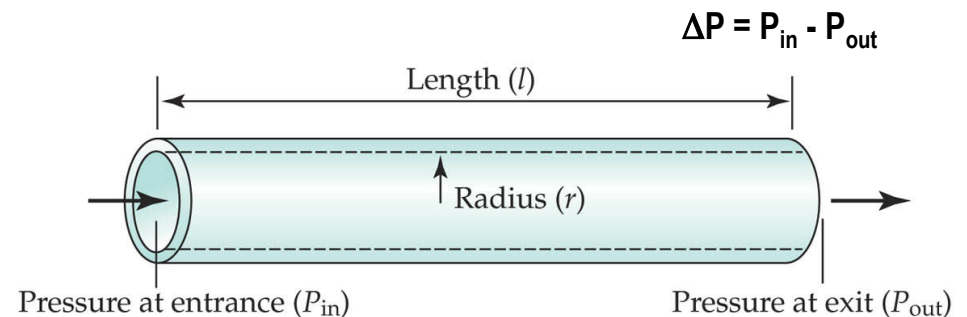


Fig. 23.9, Hill et al. 2004

■ Practise makes perfect...

- How does doubling the length of a straw and the viscosity of the fluid affect the difficulty (resistance) of sipping the fluid through the straw?
- To maintain a constant intake of fluid under these conditions, how must pressure change?
- If the radius of a blood vessel is halved, the pressure difference across the vessel must increase OR decrease (select one) by a factor of _____ to avoid a change in blood flow.

■ Assumptions of Poiseuille's equation

● Laminar flow

- Force required to slide adjacent layers past each other
- Viscosity = resistance to sliding (plasma ~1.8 x water, blood ~3-4x water)
- Turbulent flow = irregular, random, noisy
- Fahraeus-Lindqvist effect → rbc's accumulate in centre of bloodstream, reducing apparent viscosity (and resistance) for small blood vessels

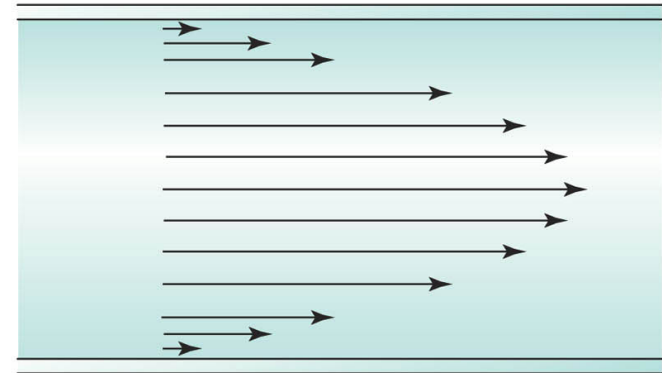


Fig. 23.9, Hill et al. 2004

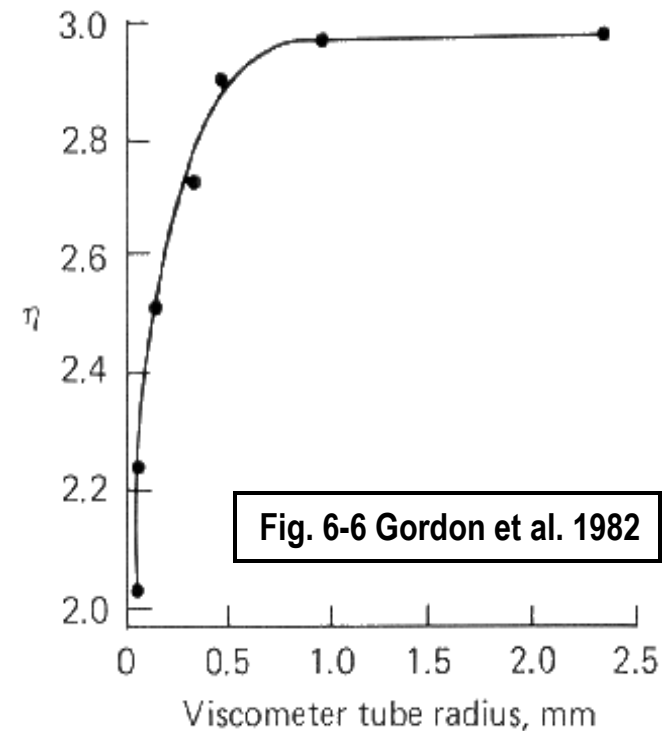
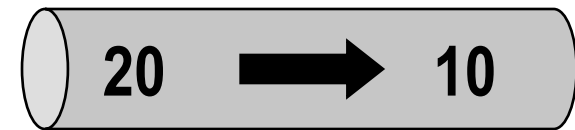


Fig. 6-6 Gordon et al. 1982



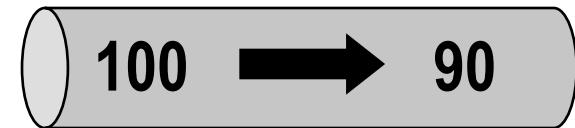
- **Straight, rigid tubes**

- **Blood vessels are not rigid tubes** → **elastic fibres** in walls allow distension
- So, **increasing pressure increases r...** and **flow rates are higher at higher absolute pressures**
- **Compliance = $\Delta\text{volume}/\Delta\text{pressure}$**
- **High distensibility** → high compliance
- **Large volume changes with little change in pressure**
- **Venous system has higher compliance** → volume reservoir
- **Arterial system** → pressure reservoir



$$\Delta P = 10$$

Which has higher **Q**?





□ Blood vessels by function

(1) “Windkessel vessels”

- Aorta, large arteries
- Large r so low resistance, low pressure drop → conduits
- Elastic walls → damp pressure oscillations and maintain continuous flow
- Thick walled to withstand high pressures (Laplace’s Law → wall tension = radius x pressure across wall)

Fig. 19-2, Rhoades & Pflanzler 1992

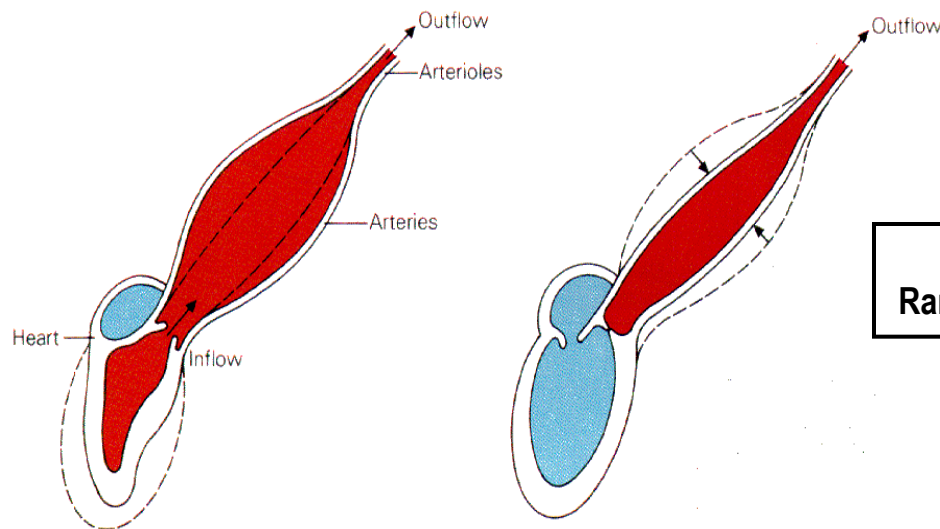
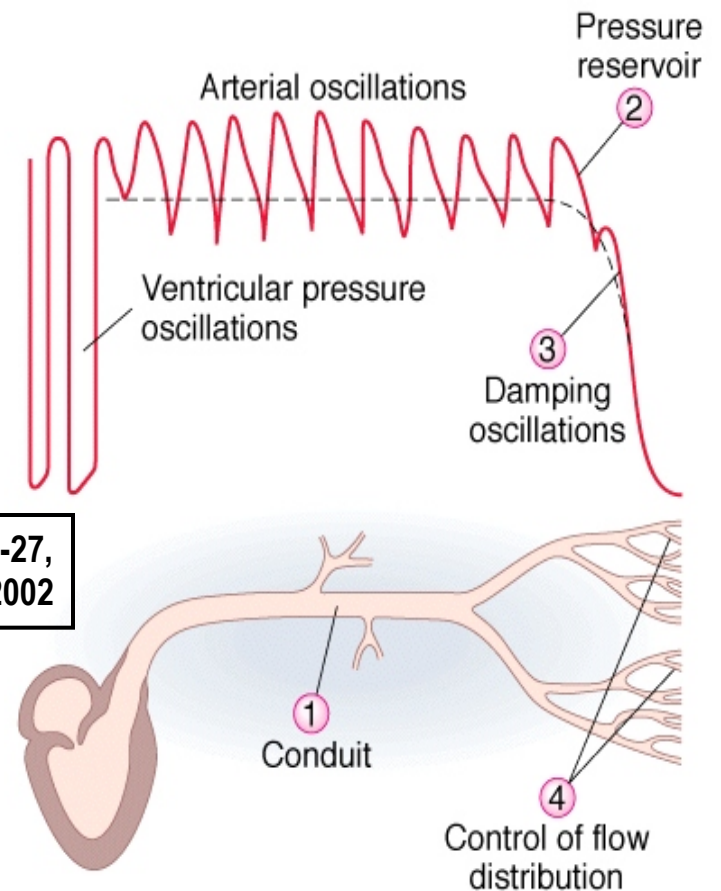


Fig. 12-27, Randall et al. 2002





(2) Pre-capillary resistance vessels

- **Smallest arteries, arterioles**
- **Small r so highest resistance** → **greatest pressure drop**
- **Muscular walls** to control resistance and therefore
 - Control over regional blood flow
 - Control over blood pressure
- **Sympathetic nervous system, hormones, local chemical agents, metabolites**

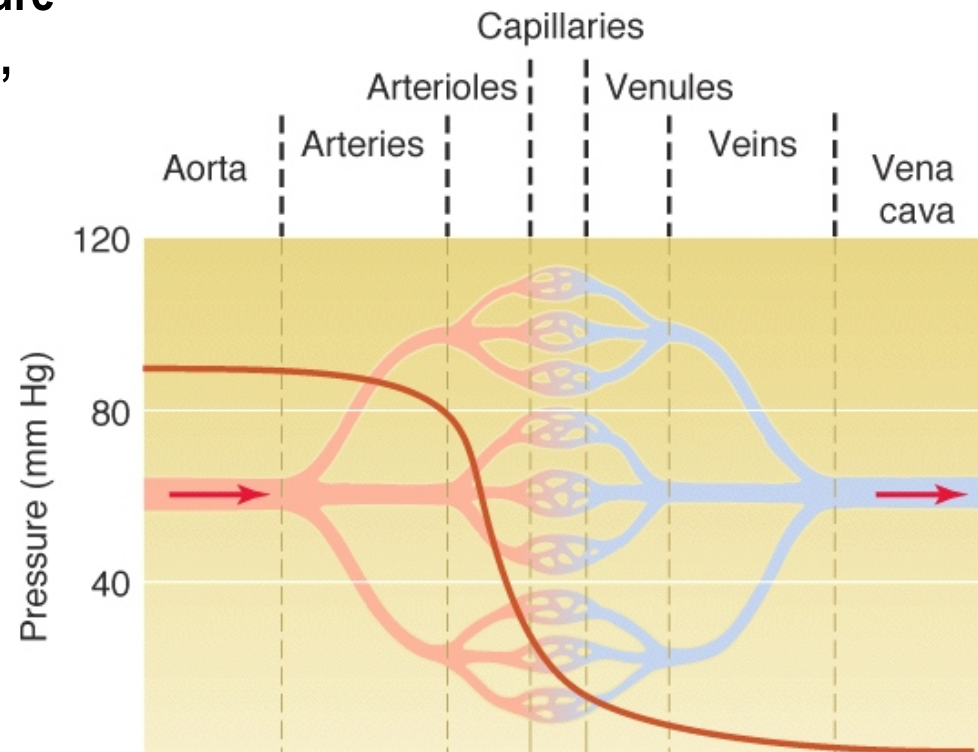


Fig. 12-25, Randall et al. 2002



(3) Pre-capillary sphincters

- Determine **capillary exchange area within tissue**
- Local chemical factors, metabolites

(4) Capillaries

- Thin-walled vessels → transfer site
- **Low velocity blood flow, long transit time (1-3 s)**

(5) Post-capillary resistance vessels

- Venules and small veins
- r can be adjusted → adjust resistance and hence affects pressure → enables adjustment of pressure across capillary beds

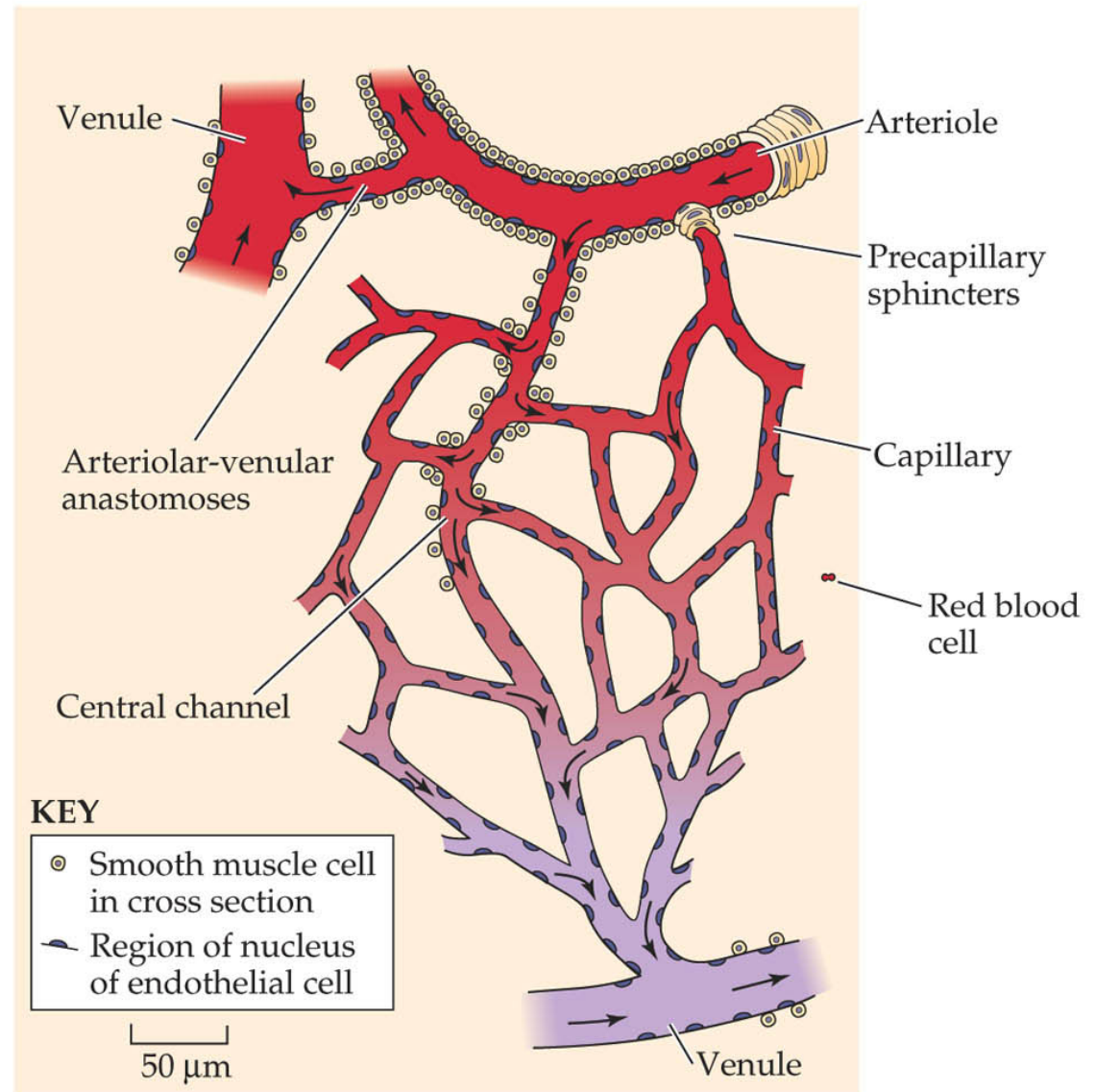
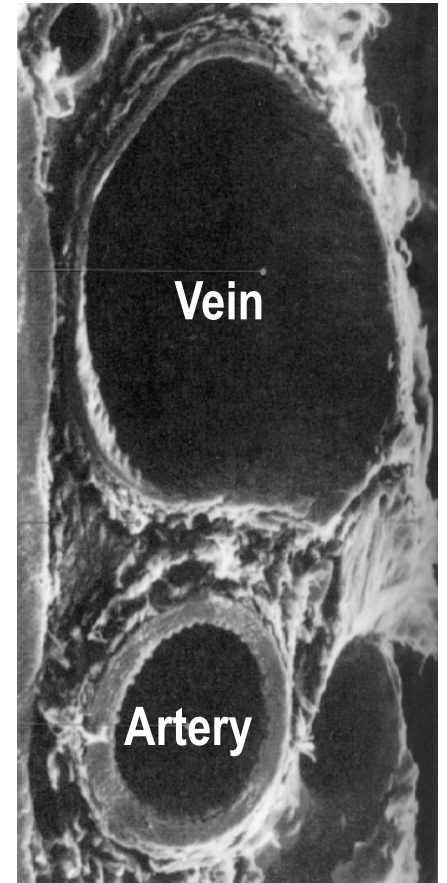


Fig. 23.11, Hill et al. 2004

(6) Capacitance vessels

- Veins
- Compliant walls → volume reservoir (~50% of total blood volume)
- Smooth muscle; sympathetic innervation
- Major influence on **cardiac output** through venous return
- e.g. Blood donation – loss of blood from venous reservoir associated with vasoconstriction to reduce volume. Little pressure change, so little effect on venous return.
- e.g. Standing perfectly still for too long!





□ Capillary function

■ Structure

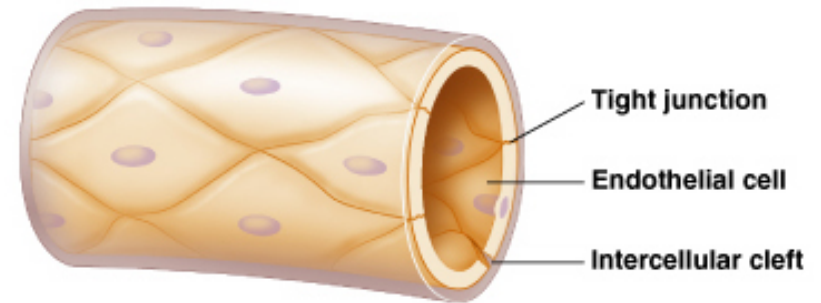
- ~1 mm long, 3-10 μm diameter
- Endothelial cells, basement membrane
- Extensive network, high surface area

■ Functions

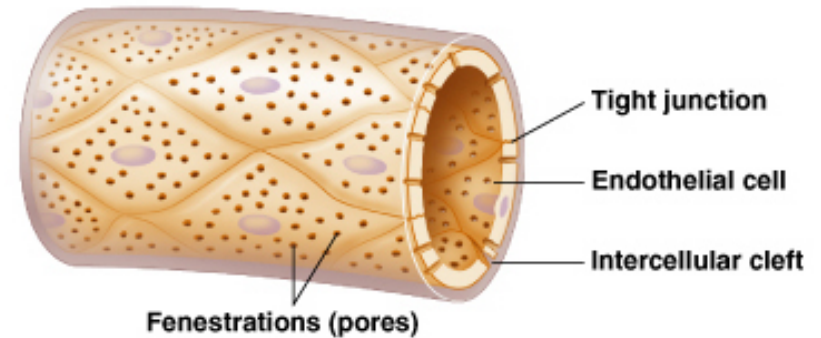
- Gas, nutrient and waste exchange
- Fluid exchange (balance)

■ Exchange by diffusion

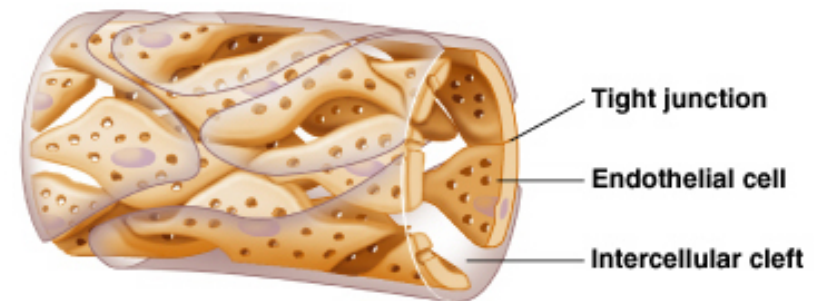
- Fick equation: Amount transferred = gradient · permeability · SA/T
- Concentration or partial pressure gradients
- Permeability
 - Lipid soluble vs lipid insoluble substances
 - Capillaries vary in permeability
- Transit time



(a) Continuous capillary



(b) Fenestrated capillary

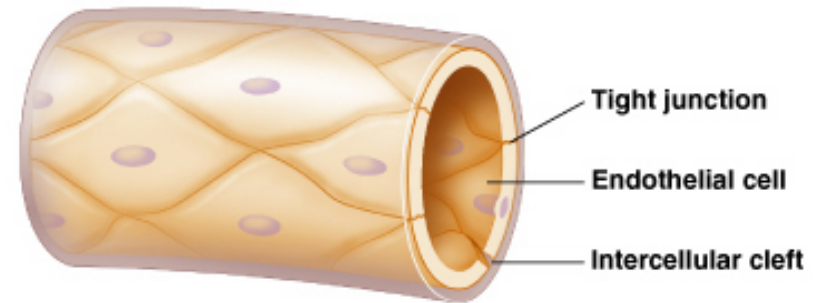


(c) Sinusoidal capillary

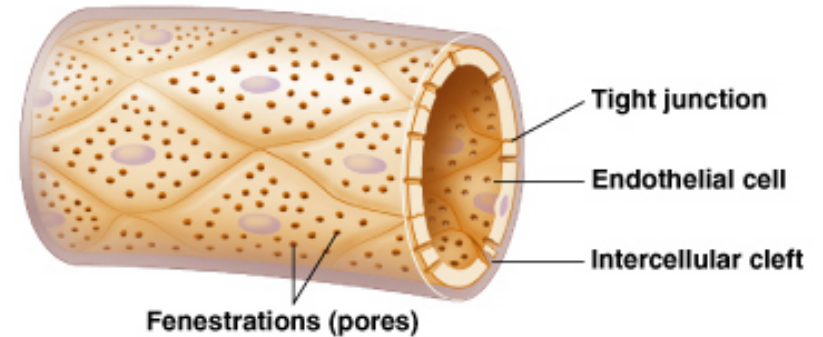


■ Match capillary characteristics with tissue function to predict what type of capillary will be found in different tissues...

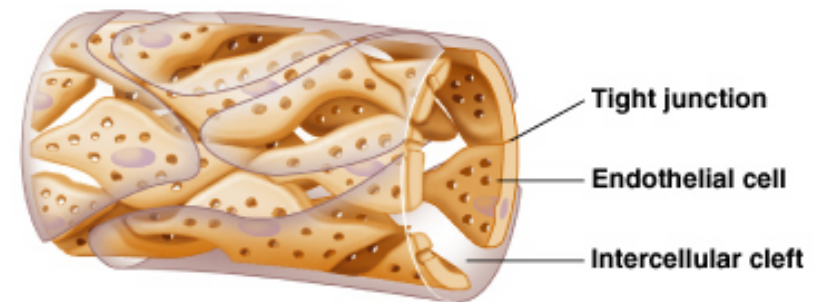
- Gut
- Nervous tissue, brain
- Lungs
- Muscle
- Kidney
- Liver



(a) Continuous capillary



(b) Fenestrated capillary

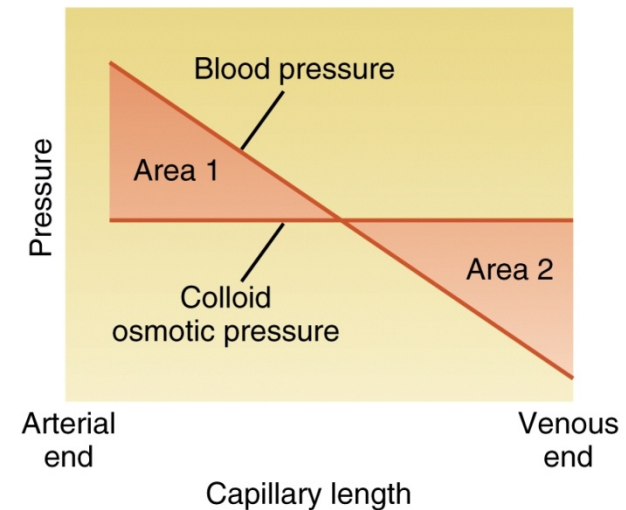
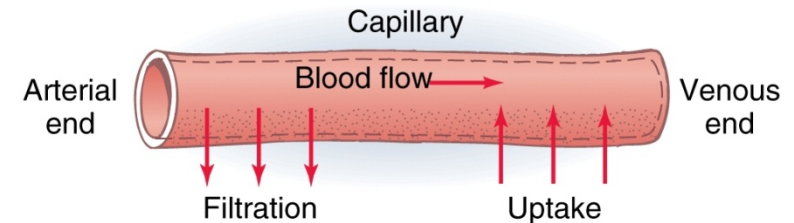
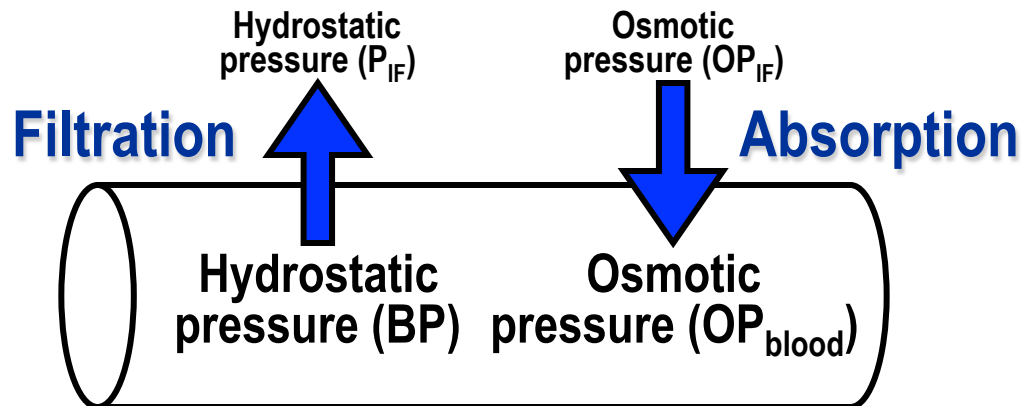


(c) Sinusoidal capillary



■ Fluid exchange

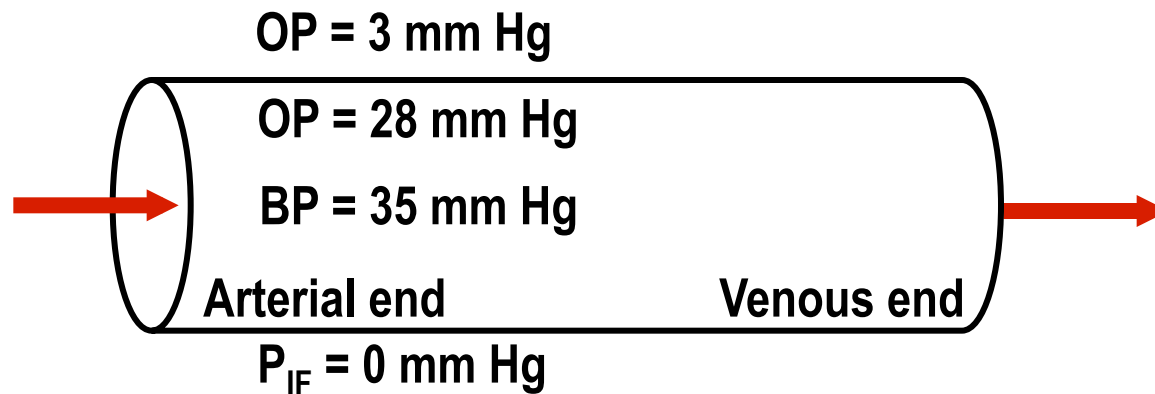
- Convective exchange of fluids to maintain **fluid balance**
- Driven by **hydrostatic and osmotic pressure gradients**
 - Hydrostatic pressure: capillary $>$ interstitial fluid \rightarrow filtration force
 - Colloid osmotic pressure: plasma $>$ interstitial fluid \rightarrow absorption force
 - Plasma proteins (albumin)
 - Net filtration pressure = $(BP - P_{IF}) - (OP_{\text{blood}} - OP_{IF})$
- Starling-Landis hypothesis
 - Arterial vs venous end of capillary
 - net fluid loss and need for lymphatic system





● Practise...

- Net filtration pressure?
- Assuming that interstitial fluid values and OP_{blood} remain constant, what must BP fall to at venous end to prevent net loss of fluid?





■ Lymphatic system

- Lymph capillaries
 - Highly permeable walls
 - Diffusion
- How does fluid move?
- Functions
 - Return plasma proteins to circulation
 - Drain extra fluid
- Failure, e.g. filariasis?
 - Oedema
 - Other causes of oedema

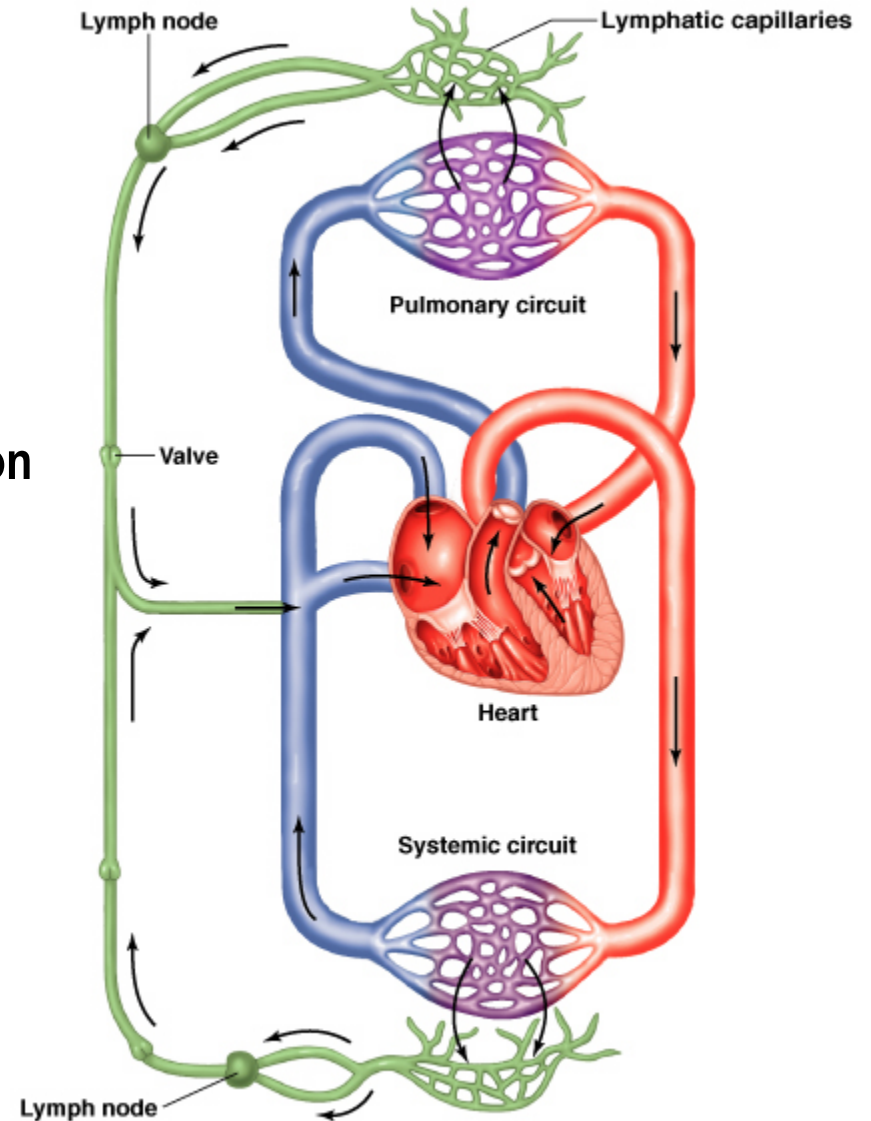


Fig. 8.41



Control of regional circulation

- Capillary blood flow to an organ reflects metabolism
 - Priority system: brain, heart & lungs/gills vs. gut, liver, muscles
- Definitions
 - Ischemia Example: Raynaud's syndrome
 - Hyperemia
 - Active hyperemia
 - Reactive hyperemia
- Control mechanisms
 - local, neural and hormonal
 - arterioles vs. pre-capillary sphincters

Cold-induced ischemia
Rewarming – reactive hyperemia



back



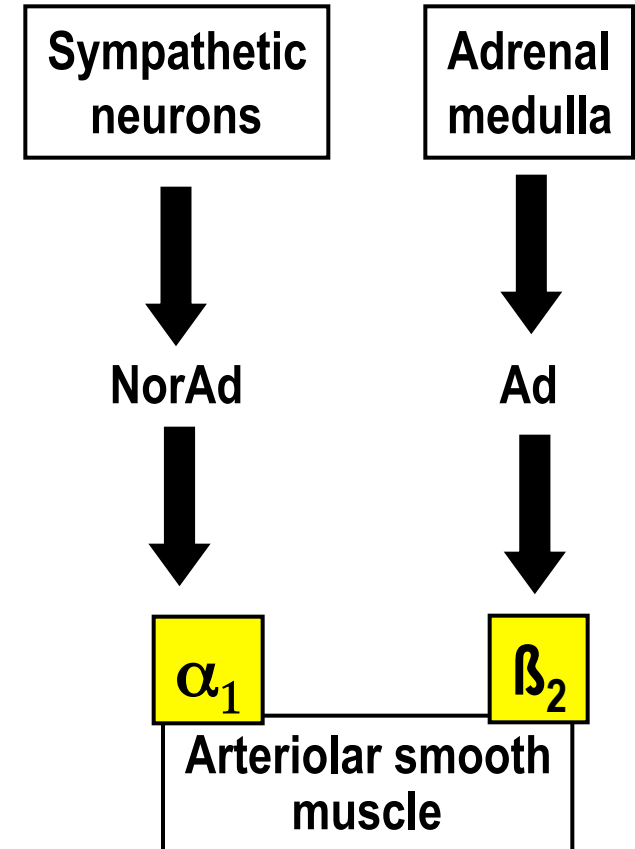
□ Neural and hormonal mechanisms

■ Sympathetic nerves (adrenergic fibres) → release noradrenaline

- α_1 -adrenergic receptors
- vasoconstrictor tone
 - \uparrow sympathetic stimulation → vasoconstriction
 - \downarrow sympathetic stimulation → vasodilation
- viscera
- Brain, heart, lungs/gills lack α -adrenoreceptors

■ Circulating catecholamines (adrenaline)

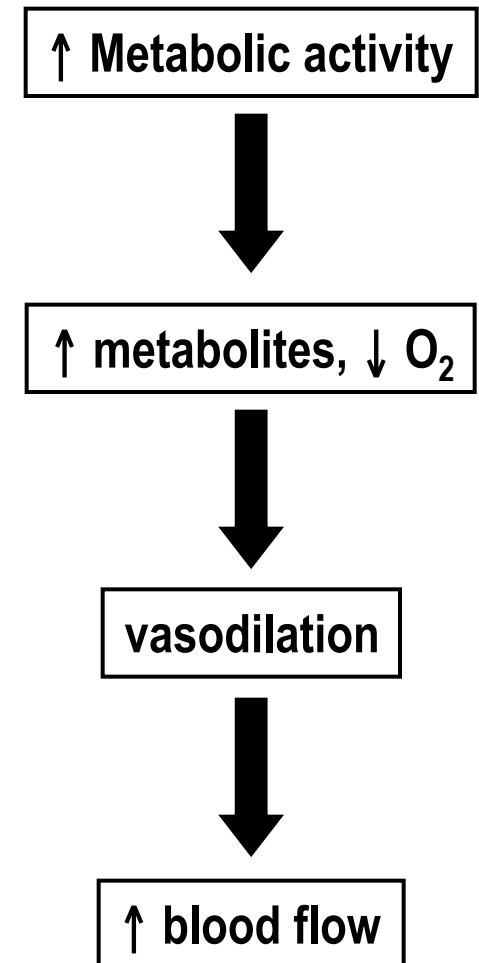
- β_2 -adrenoreceptors
- Vasodilation
- Skeletal muscle



☰ Local control mechanisms

- Arterioles vs. pre-capillary sphincters
- Heat
- Compounds produced by endothelial cells (e.g. nitric oxide)
- Inflammatory mediators (e.g. histamine)
- Metabolic control
 - Most active tissues → vasodilation → elevated blood flow (active hyperemia)
 - Independent of nerves or hormones
 - Metabolic activity: ↓ O₂, ↑ CO₂, ↑ [H⁺] (↓ pH), ↑ adenosine (from ATP), ↑ heat, ↑ K⁺
 - Highly developed in muscle
 - O₂ → systemic vs pulmonary capillaries
 - [Raynaud's?](#)

Active hyperemia

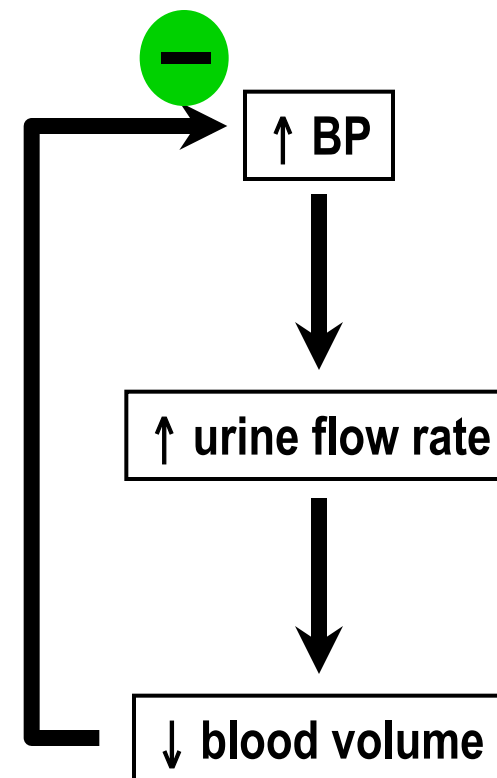




Control of blood pressure

- **Control of blood pressure**
 - Maintenance of blood flow to brain & heart, and then other tissues
 - Maintenance of tissue volume and composition
- **Chronic mechanisms**
 - Based on adjustment of blood volume *via* control of fluid loss in urine
 - Requires hours to days

Chronic control of arterial blood pressure



□ Acute mechanisms

- Based on neural reflex arcs; act in seconds to minutes.

- $\Delta P = QR$

- ΔP = arterial pressure - right atrial pressure \approx arterial pressure
- Q = cardiac output
- R = total peripheral resistance

- $Q = SV \cdot HR$

- In mammals, heart rate adjusted

- Total peripheral resistance

- Vasoconstriction or vasodilation
- Arterioles vs venous system

- Therefore, blood pressure is regulated by controlling heart rate (Q) and the diameter of arterioles (R)



Neural reflex arcs

Peripheral sensory receptors and afferent pathways

- Baroreceptors

- Respond to pressure as stretch of vessel wall
- Located in carotid sinus & aortic arch

Cardiovascular centre in medulla of CNS

Efferent output via ANS to effector organs

- Heart
- Smooth muscle of blood vessel walls
 - Vasomotor tone (tonic activity)

Feedback loops

- \uparrow blood pressure \rightarrow \uparrow baroreceptor firing \rightarrow integration in CNS \rightarrow response \rightarrow \downarrow blood pressure

Fig. 14-59, Vander et al. 1994

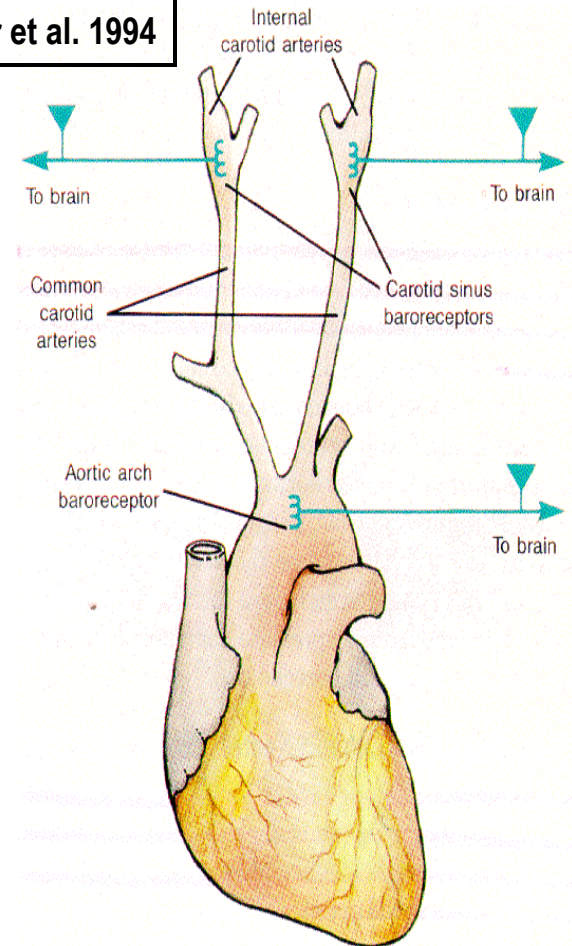
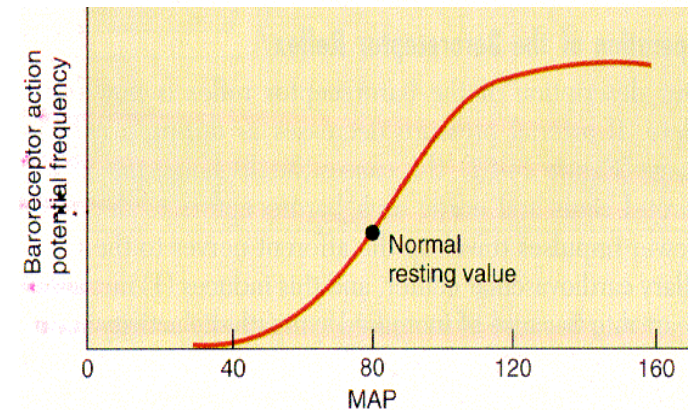
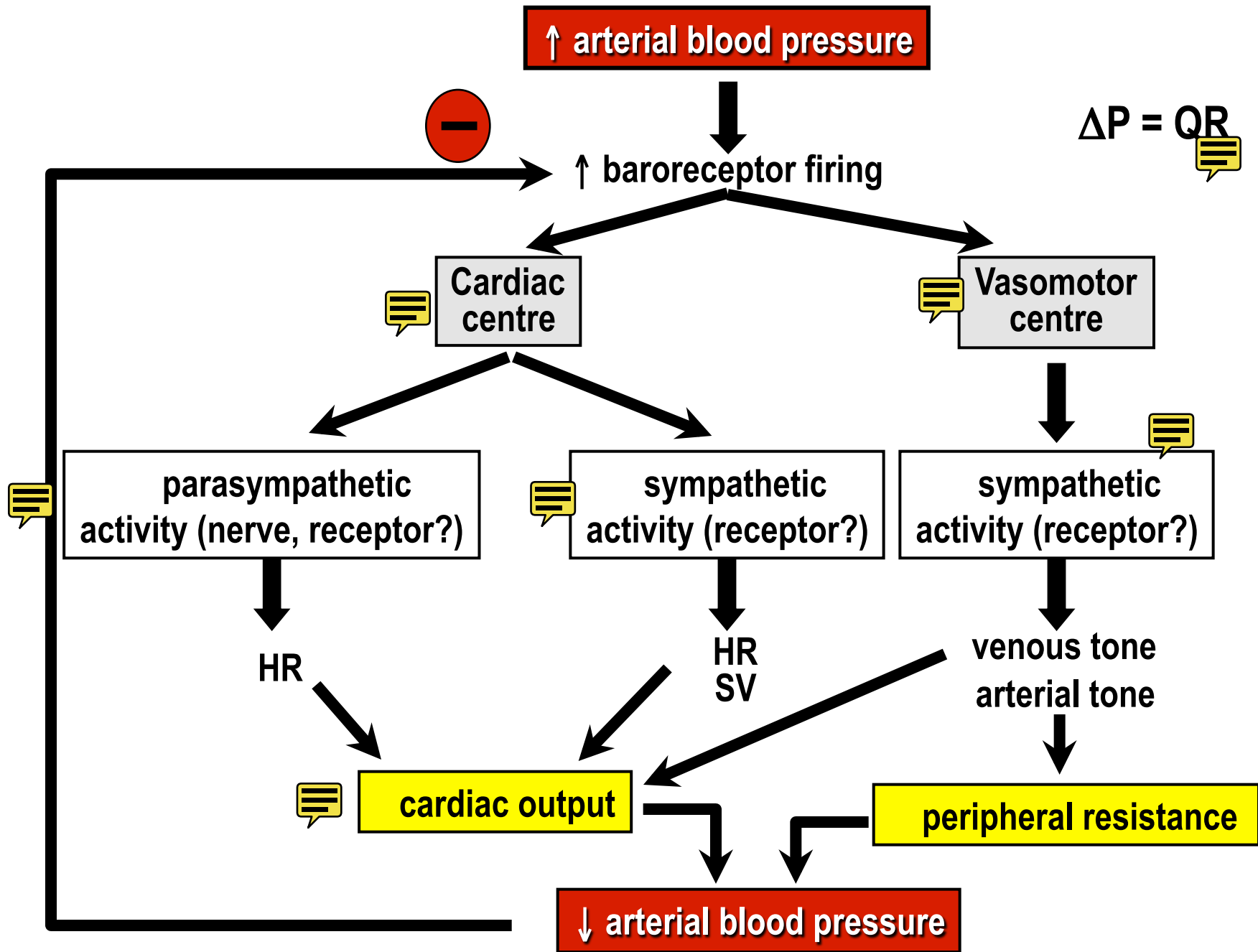


Fig. 14-60, Vander et al. 1994







Example: circulatory responses to exercise

□ Exercise

- ↑ O₂ consumption (5-10x)
- ↑ heat dissipation
- ↑ blood flow (up to 7x)
- Redistribution of blood flow
- Only small changes in arterial blood pressure → How?

$$\Delta P = QR$$

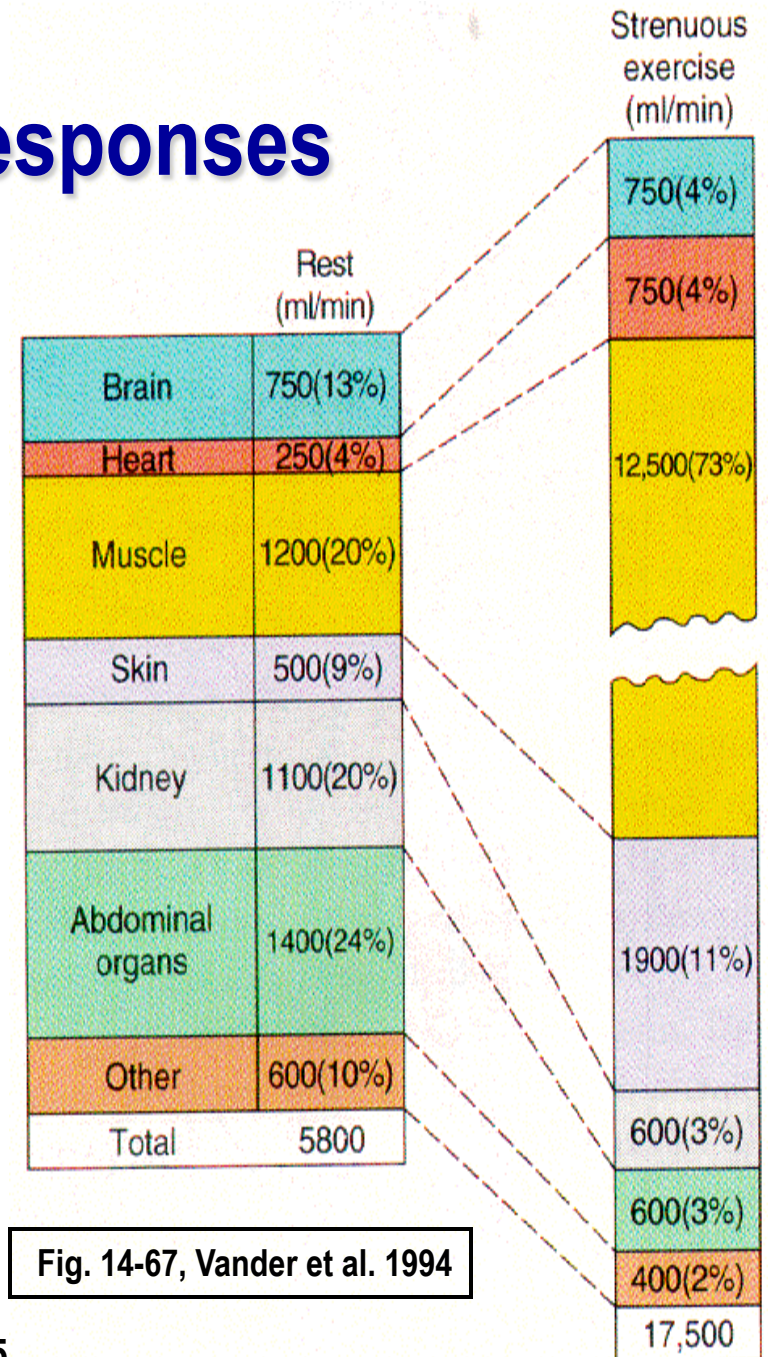


Fig. 14-67, Vander et al. 1994

□ Circulatory responses:

(1) Hyperemia in exercising muscles

- Sympathetic **cholinergic** stimulation → anticipatory increase in blood flow
- Active hyperemia in response to local metabolic changes

(2) Increased cardiac output

- ↑ sympathetic activity: +ve inotropic & +ve chronotropic effects and venous vasoconstriction (*i.e.* ↑ venous return)
- ↑ venous return due to skeletal muscle pump

(3) Peripheral vasoconstriction

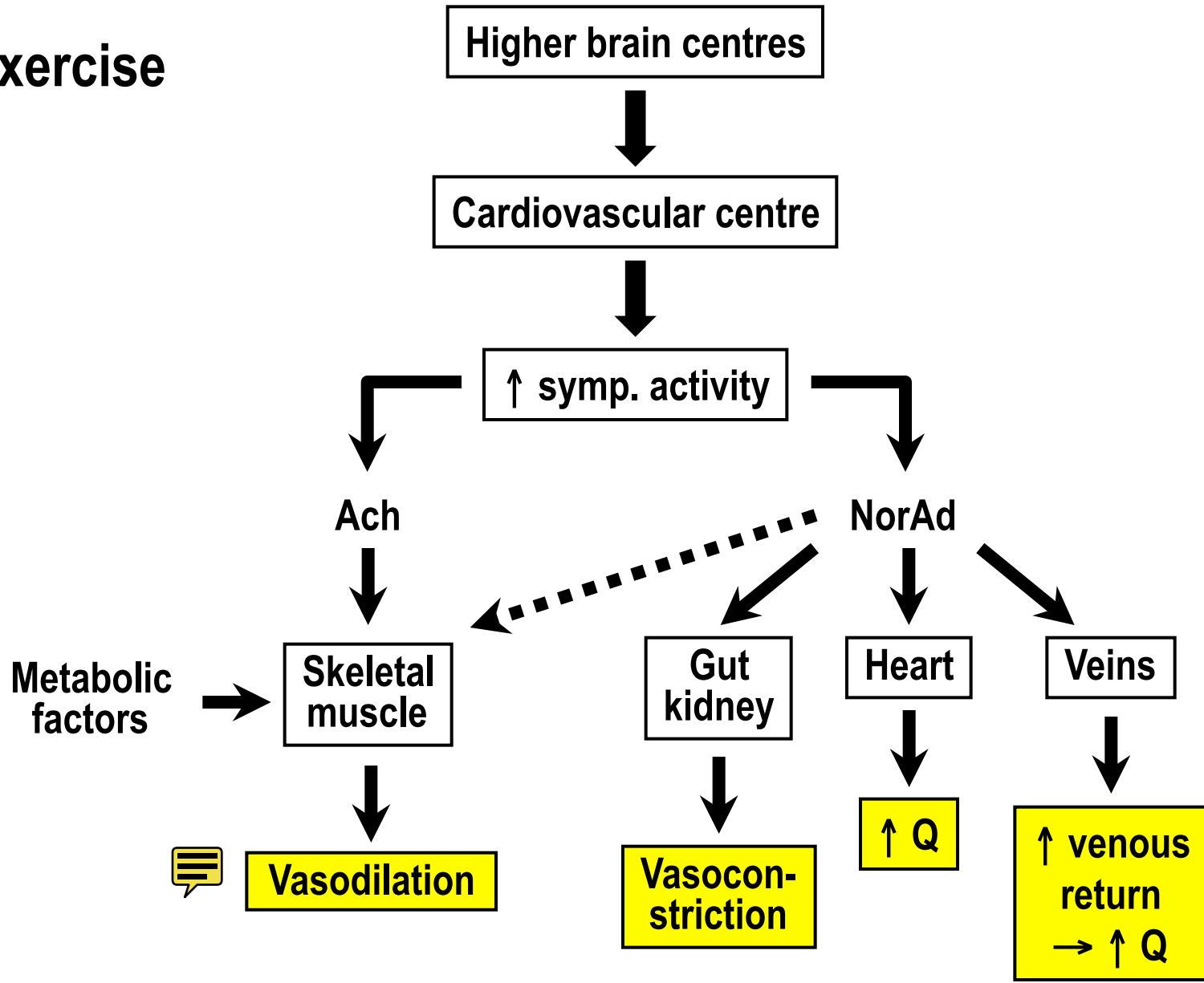
- Reduced blood flow to gut, kidney etc *via* sympathetic stimulation of α_1 -adrenoreceptors

■ Constant systemic blood pressure:

- ↓ total peripheral resistance (muscle vasodilation > vasoconstriction elsewhere) but ↑ cardiac output

$$\Delta P = QR$$

Exercise



REVIEW and/or BACKGROUND

- Cardiac muscle (Ch. 5)
 - **Striated** muscle fibres
 - Joined end-to-end
 - intercalated discs
 - **gap junctions**
 - Functional syncytium
 - All-or-none contraction pattern
 - **Autonomic nervous system (ANS)** innervation

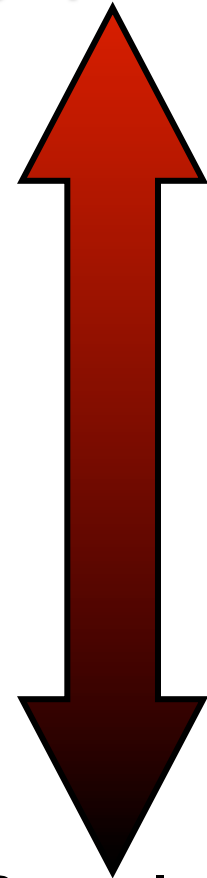


Fig. 17.19, Hill et al 2004

REVIEW and/or BACKGROUND

- Autonomic Nervous System (Ch. 7 pp 324-332)
 - Innervates smooth muscle, cardiac muscle and glands
 - Two divisions differing in anatomy, pharmacology and physiology
 - Normally have **dual** (both divisions), **antagonistic** (opposite effects) and **reciprocal** (one increases, the other decreases) innervation
 - Sympathetic
 - Dominates during stress
 - Sympathetic chain ganglia close to spinal cord provide for mass activation
 - Noradrenaline released at effector organ interacts with adrenergic receptors (α_1 , β_1 , β_2)
 - Parasympathetic
 - Vegetative or housekeeping functions
 - Acetylcholine released at effector organ interacts with muscarinic cholinergic receptors

ALARM!
(sympathetic)



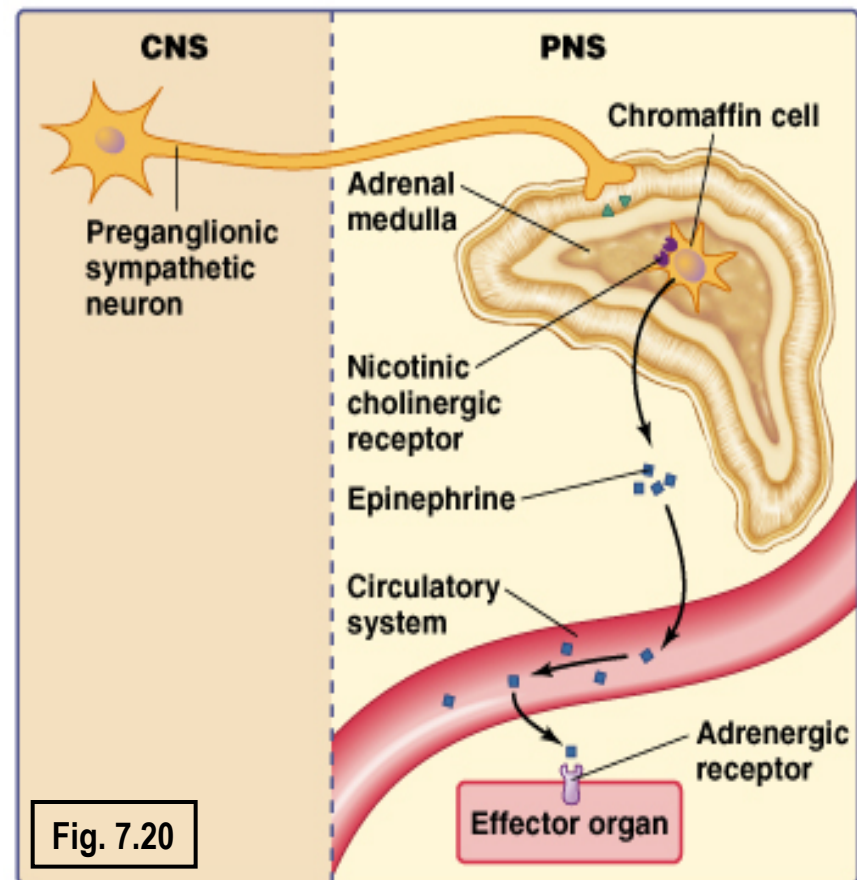
Deep sleep
(parasympathetic)

back

REVIEW and/or BACKGROUND

■ Circulating catecholamines

- Chromaffin cells - sympathetic postganglionic neurons without axons
- Neurotransmitter released into blood (noradrenaline, adrenaline → catecholamine hormones)
- Chromaffin cells located
 - Adrenal medulla – mammals
 - Adrenal gland – birds, reptiles
 - Associated with kidney tissue – amphibians, fish



back

REVIEW and/or BACKGROUND

□ Reflex arcs in the vertebrate NS

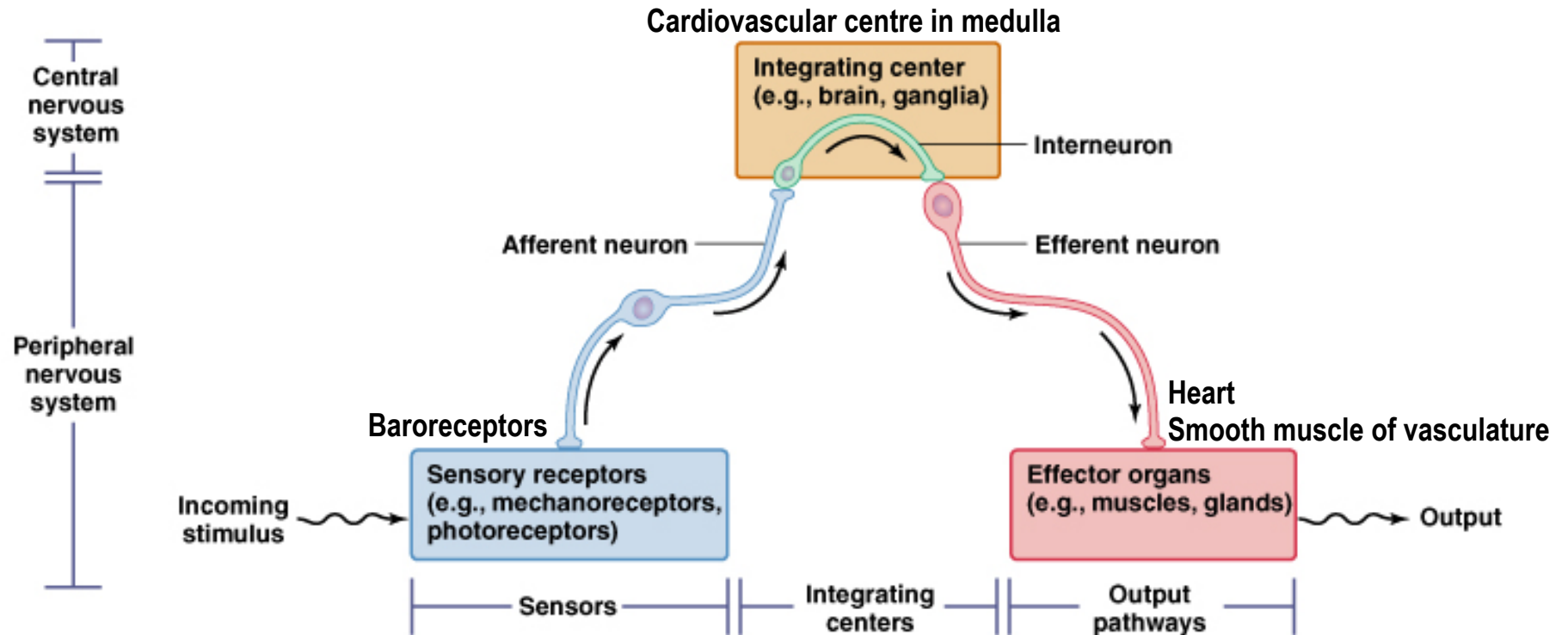


Fig. 7.1