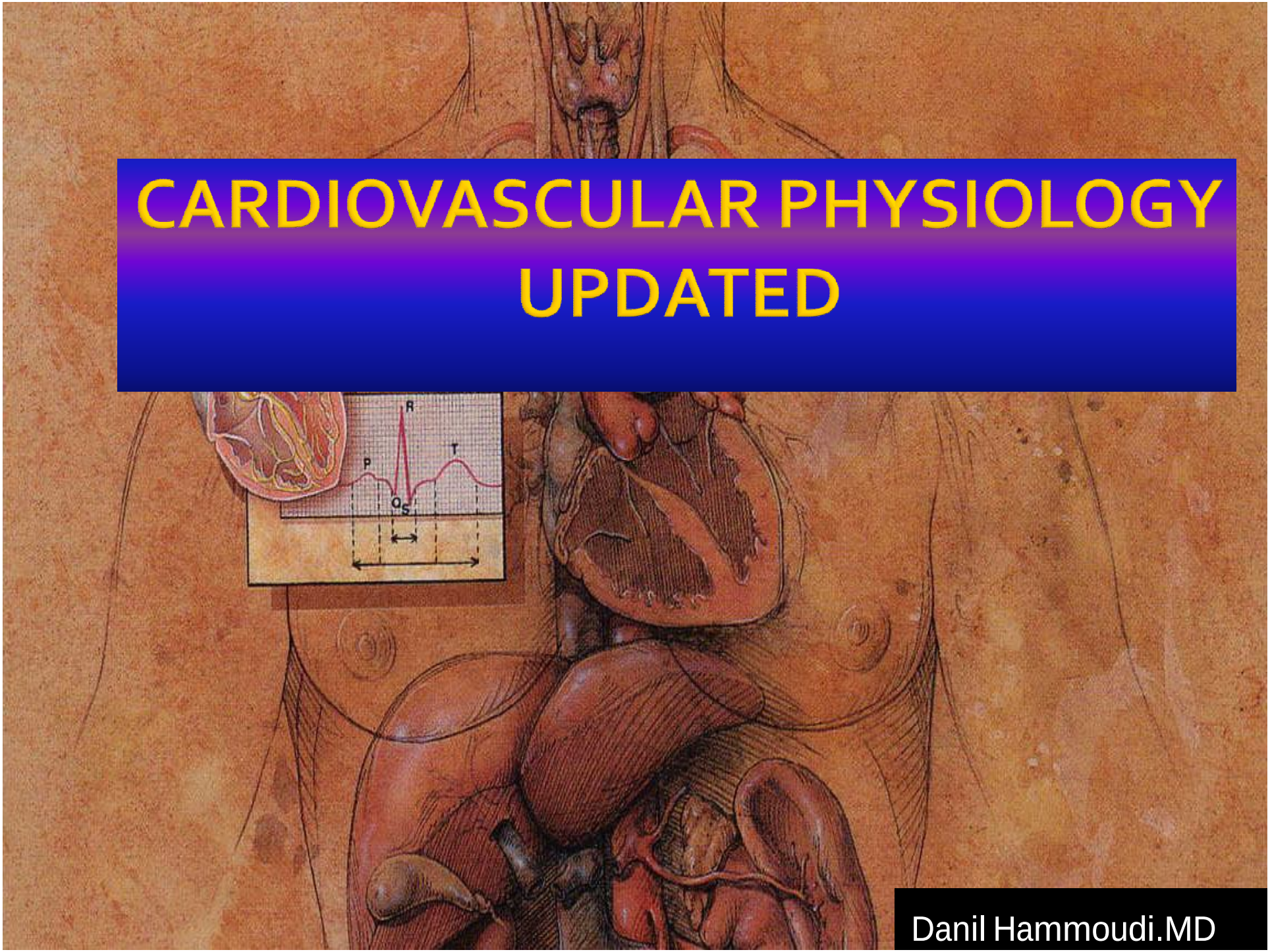
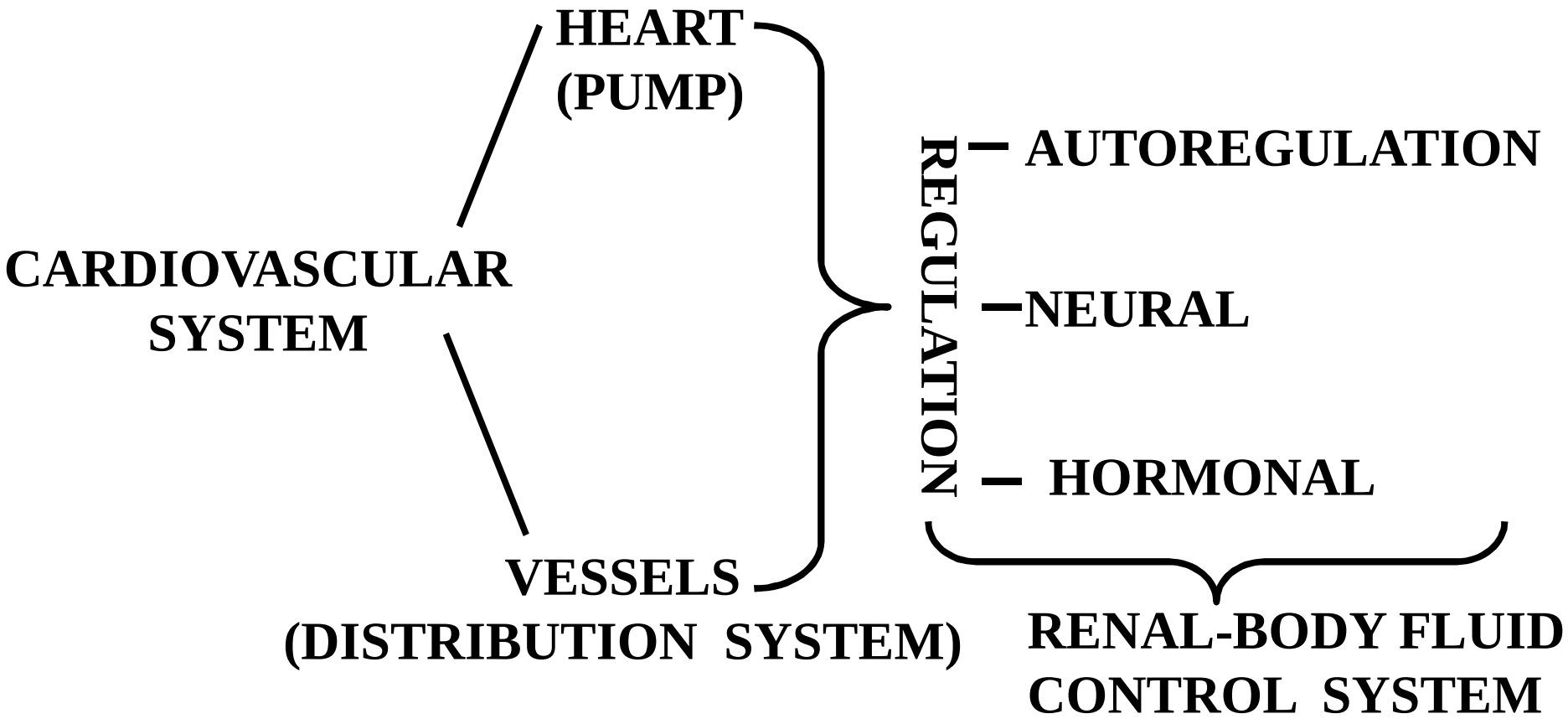
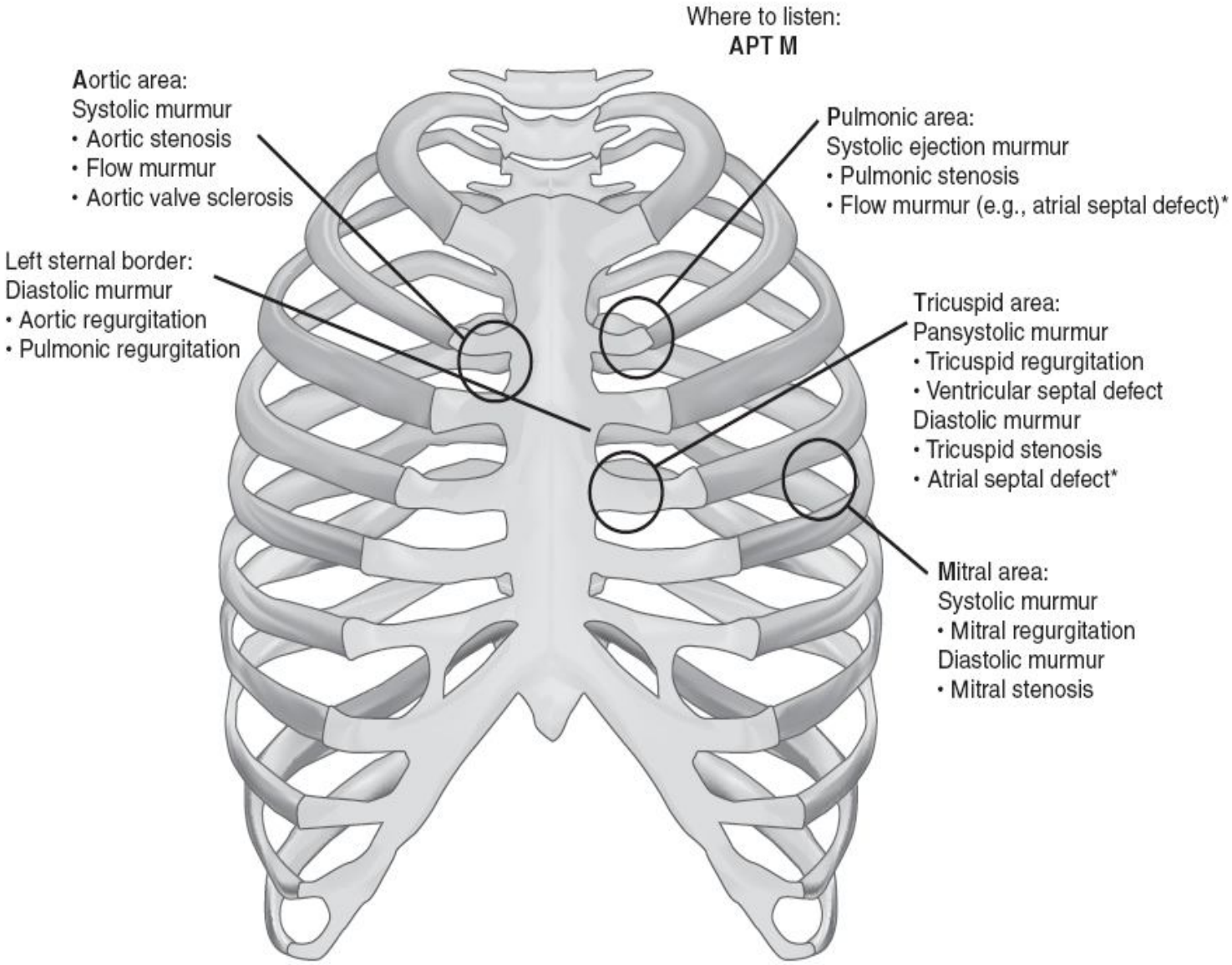
CARDIOVASCULAR PHYSIOLOGY UPDATED



Danil Hammoudi.MD


HEART
(PUMP)
CARDIOVASCULAR
SYSTEM
VESSELS
(DISTRIBUTION SYSTEM)
REGULATION
AUTOREGULATION
NEURAL
HORMONAL
RENAL-BODY FLUID
CONTROL SYSTEM

Auscultation of the heart



*ASD commonly presents with a pulmonary flow murmur (↑ flow through pulmonary valve) and a diastolic rumble (↑ flow across tricuspid). The murmur later progresses to a louder diastolic murmur of pulmonic regurgitation from dilatation of the pulmonary artery.

Coronary Blood Flow

- coronary blood flow: 250 ml/min
- 5% of resting cardiac output
- 60-80 ml blood/100g tissue/min
- entirely during diastole
  ~ aortic diastolic pressure minus LVDP
  ~ duration of diastole
- pressure < 150 mmHg
- oxygenated by superb membrane oxygenator-"the lungs"

Cerebral Blood Flow

- Cerebral blood flow: 750 ml/min
- 15% of resting cardiac output
- 50-55 ml blood/100g tissue/min

Heart HORMONES

Natriuretic Peptides

In response to a rise in blood pressure, the heart releases two peptides:
•**A-type Natriuretic Peptide** (ANP)
This hormone of 28 amino acids is released from stretched **atria** (hence the "A").
•**B-type Natriuretic Peptide** (BNP)

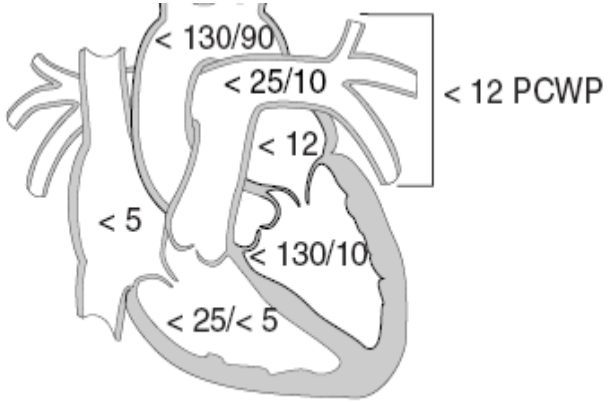
This hormone is released from the **ventricles**. (It was first discovered in brain tissue; hence the "B".)

Both hormones lower blood pressure by
•relaxing arterioles
•inhibiting the secretion of **renin** and **aldosterone**
•inhibiting the reabsorption of sodium ions by the kidneys.

The latter two effects reduce the reabsorption of water by the kidneys. So the volume of urine increases as does the amount of sodium excreted in it. The net effect of these actions is to reduce blood pressure by reducing the volume of blood in the circulatory system.

These effects give ANP and BNP their name (natrium = sodium; uresis = urinate).

Normal pressures



PCWP—pulmonary capillary wedge pressure (in mmHg) is a good approximation of left atrial pressure.

Measured with Swan-Ganz catheter.

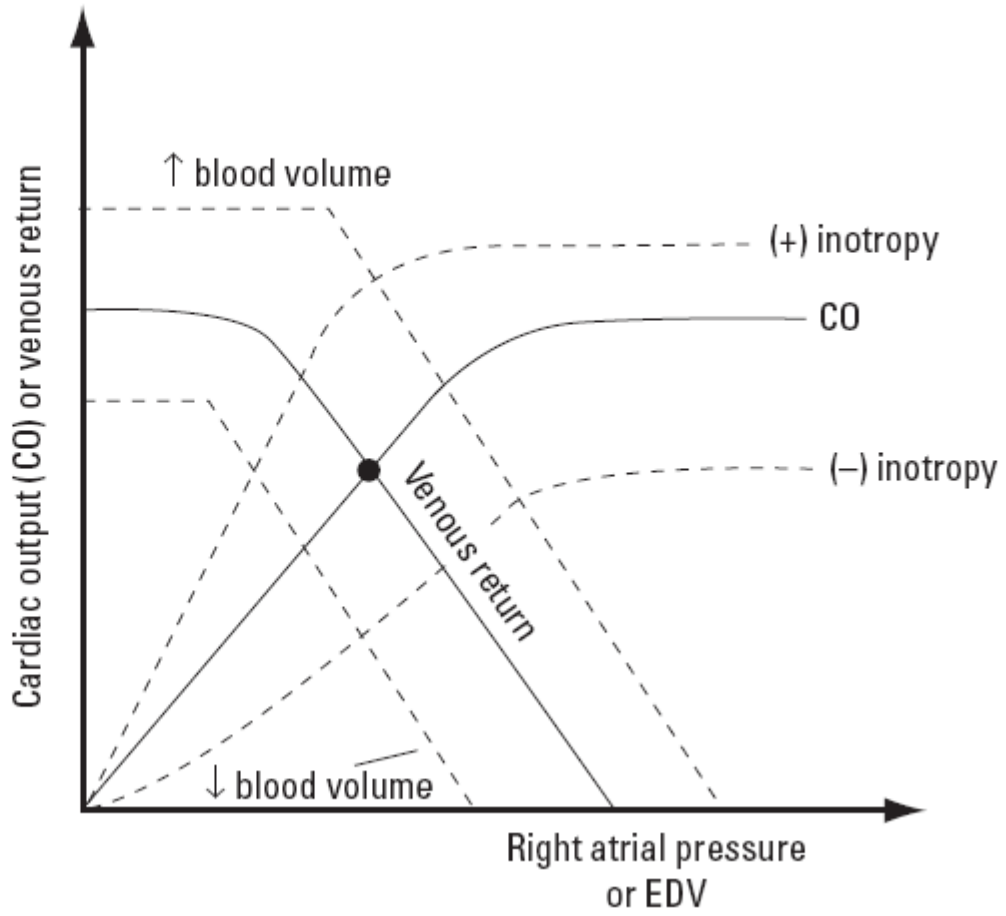
Cardiac myocyte physiology

Cardiac muscle contraction is dependent on extracellular calcium, which enters the cells during plateau of action potential and stimulates calcium release from the cardiac muscle sarcoplasmic reticulum (calcium-induced calcium release).

In contrast to skeletal muscle:

1. Cardiac muscle action potential has a plateau, which is due to Ca^{2+} influx
2. Cardiac nodal cells spontaneously depolarize, resulting in automaticity
3. Cardiac myocytes are electrically coupled to each other by gap junctions

Cardiac and vascular function curves



Differences Between Skeletal and Cardiac Muscle Physiology

- Action Potential
  - Cardiac: Action potentials conducted from cell to cell.
  - Skeletal, action potential conducted along length of single fiber
- Rate of Action Potential Propagation
  - Slow in cardiac muscle because of gap junctions and small diameter of fibers.
  - Faster in skeletal muscle due to larger diameter fibers.
- Calcium release
  - Calcium-induced calcium release (CICR) in cardiac
    - Movement of extracellular Ca^{2+} through plasma membrane and T tubules into sarcoplasm stimulates release of Ca^{2+} from sarcoplasmic reticulum
  - Action potential in T-tubule stimulates Ca^{++} release from sarco-plasmic reticulum

Cardiac Muscle Contraction

- Heart muscle:
  - Is stimulated by nerves and is self-excitable (automaticity)
  - Contracts as a unit
  - Has a long (250 ms) absolute refractory period
- Cardiac muscle contraction is similar to skeletal muscle contraction

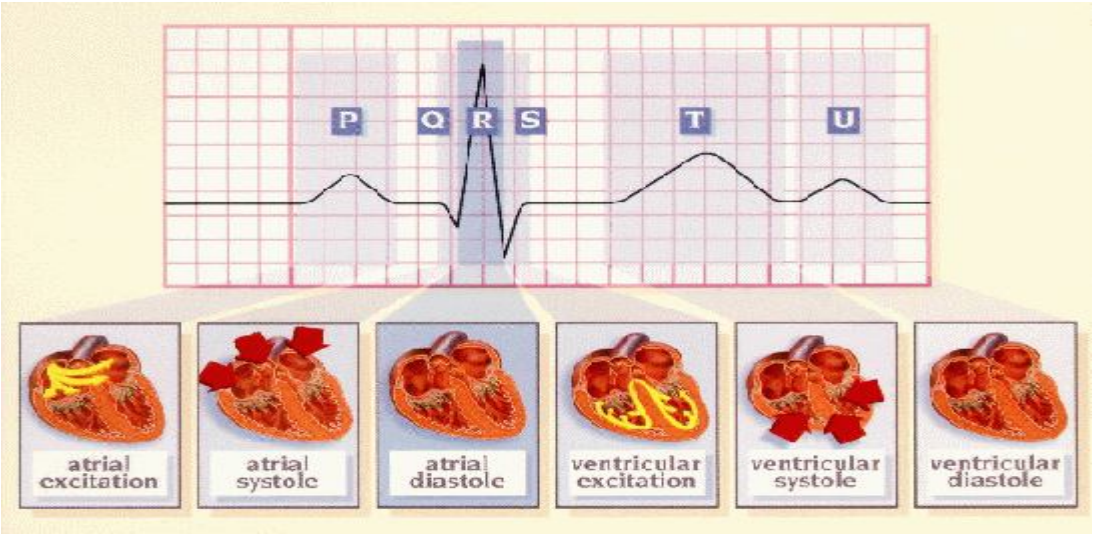
pacemaker can funciton for many years without interruption

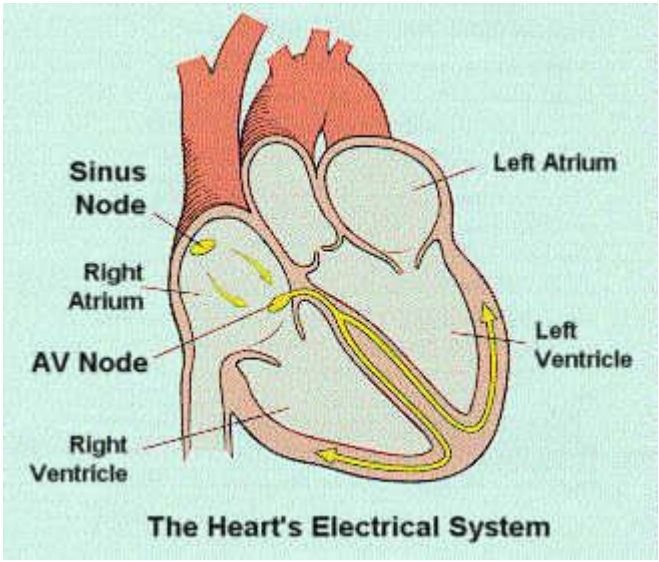
Ach (**from ParaSym terminals** of **vagus nerve Xth cranial nerve**) =➔slows HR by increasing K+ conductance & reducing Ca2+ conductance of pacemaker cells

norepinephrine (Sym NS) accelerates pacemake potential = increasing HR

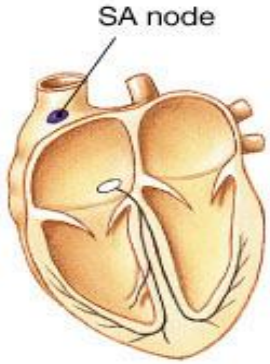
Heart Physiology: Intrinsic Conduction System

- **Autorhythmic cells:**
  - Initiate action potentials
  - Have unstable resting potentials called pacemaker potentials
  - Use calcium influx (rather than sodium) for rising phase of the action potential



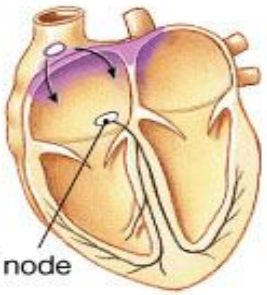


Impulse Conduction through the Heart



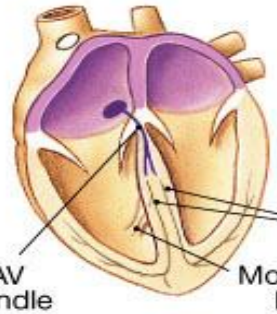
STEP 1:
SA node activity and atrial activation begin.

Time = 0



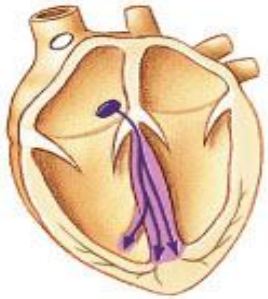
STEP 2:
Stimulus spreads across the atrial surfaces and reaches the AV node.

Elapsed time = 50 msec



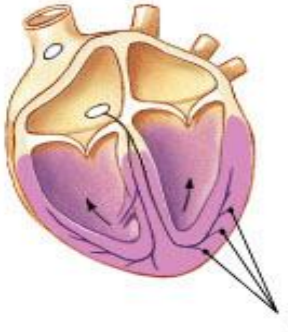
STEP 3:
There is a 100-msec delay at the AV node. Atrial contraction begins.

Elapsed time = 150 msec



STEP 4:
The impulse travels along the interventricular septum within the AV bundle and the bundle branches to the Purkinje fibers and, via the moderator band, to the papillary muscles of the right ventricle.

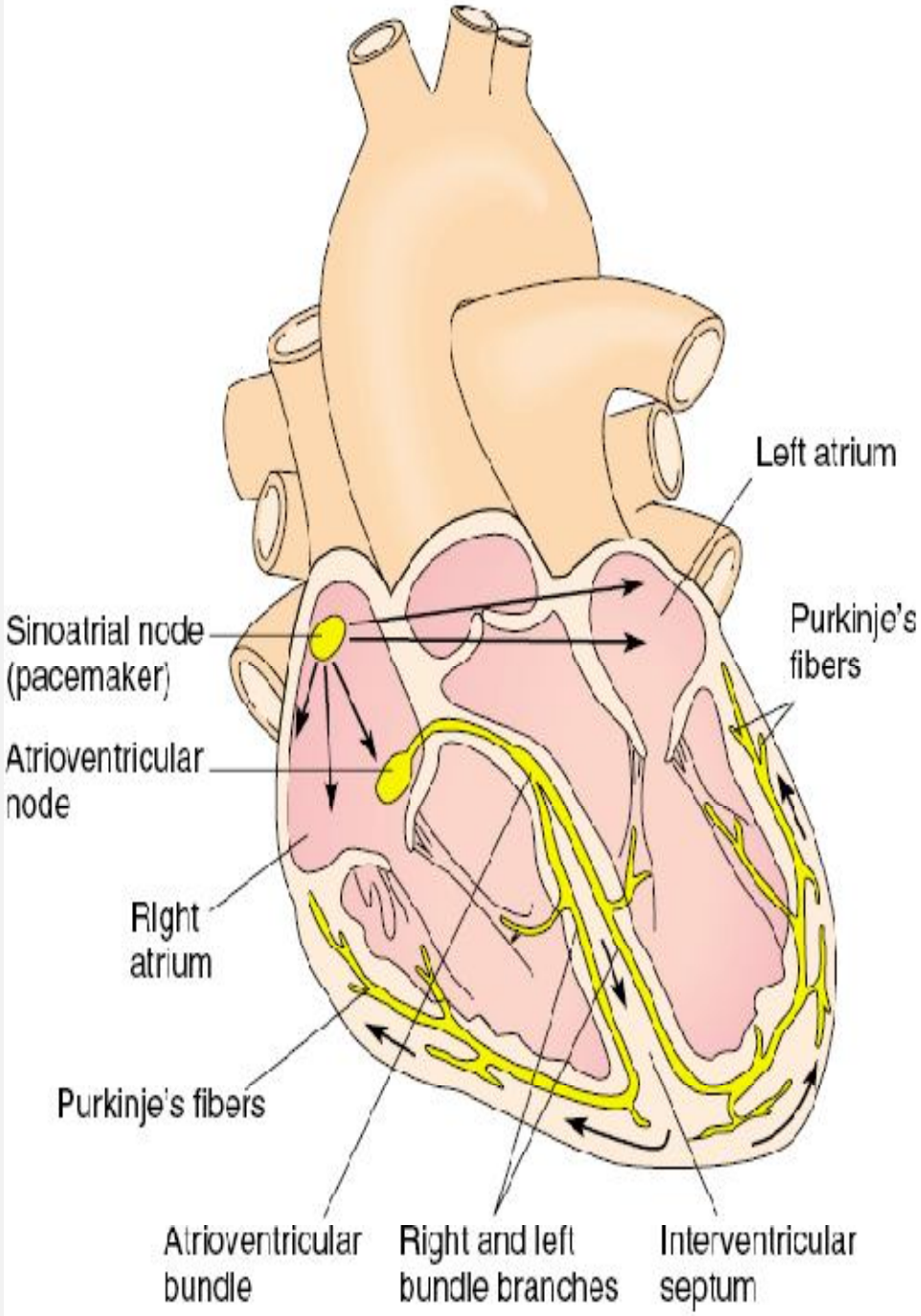
Elapsed time = 175 msec



STEP 5:
The impulse is distributed by Purkinje fibers and relayed throughout the ventricular myocardium. Atrial contraction is completed, and ventricular contraction begins.

Elapsed time = 225 msec

- Action potentials (electrical impulses) in the heart originate in specialized cardiac muscle cells called autorhythmic cells.
- These cells are self-excitable, able to generate an action potential without external stimulation by nerve cells.
- The autorhythmic cells serve as a pacemaker to initiate the cardiac cycle (pumping cycle of the heart) and provide a conduction system to coordinate the contraction of muscle cells throughout the heart.



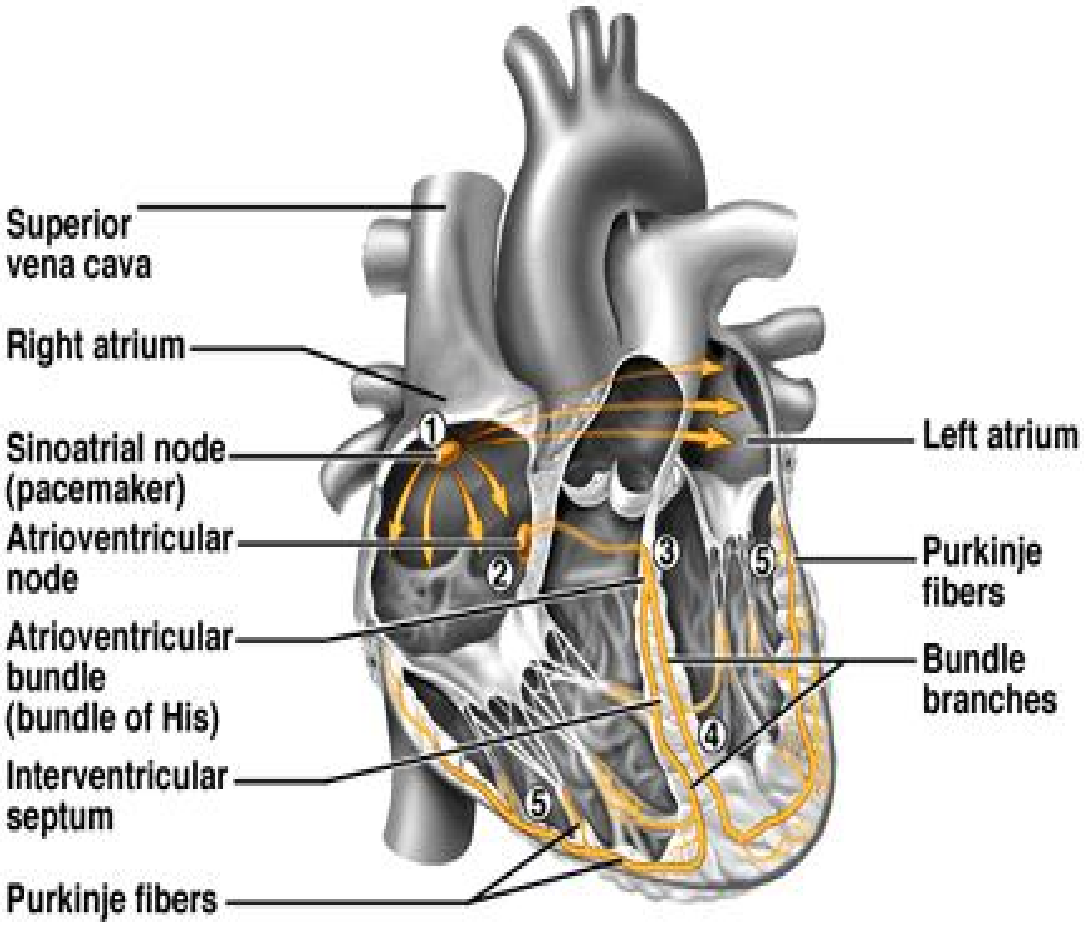
The autorhythmic cells are concentrated in the following areas.

•**The sinoatrial (SA) node**, located in the upper wall of the right atrium, initiates the cardiac cycle by generating an action potential that spreads through both atria through the gap junctions of the cardiac muscle fibers.

•**The atrioventricular (AV) node**, located near the lower region of the interatrial septum, receives the action potential generated by the SA node. A slight delay of the electrical transmission occurs here, allowing the atria to fully contract before the action potential is passed on to the ventricles.

•**The atrioventricular (AV) bundle (bundle of His)** receives the action potential from the AV node and transmits the impulse to the ventricles by way of the right and left bundle branches. Except for the AV bundle, which provides the only electrical connection, the atria are electrically insulated from the ventricles.

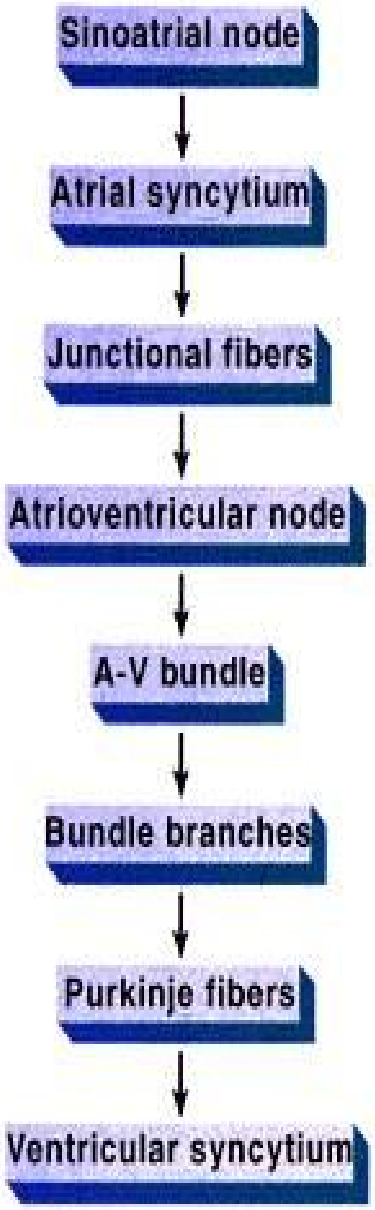
•**The Purkinje fibers** are large-diameter fibers that conduct the action potential from the interventricular septum, down to the apex, and then upward through the ventricles.



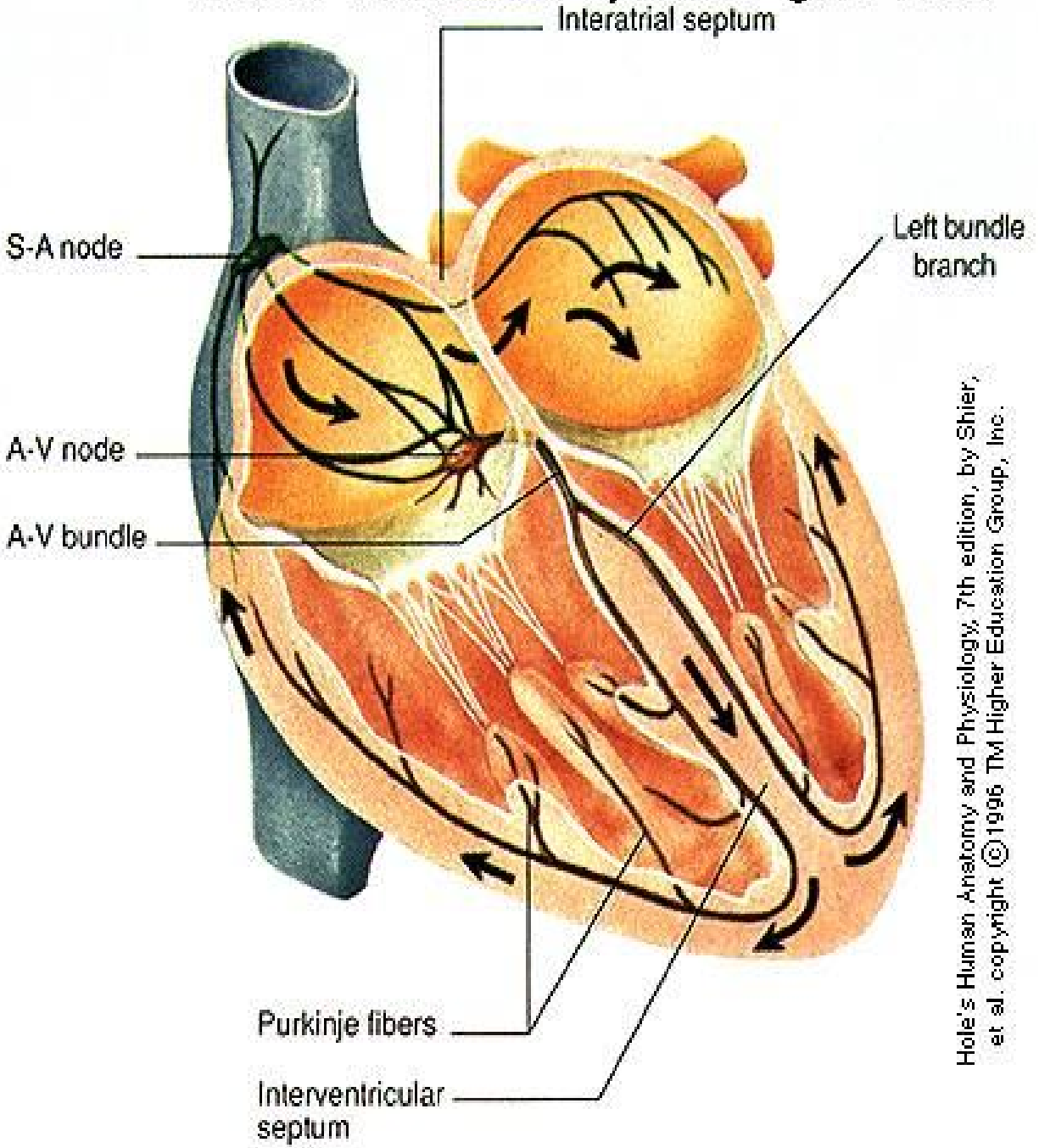
PACEMAKERS (in order of their inherent rhythm)

- Sino-atrial (SA) node
- Atrio-ventricular (AV) node
- Bundle of His
- Bundle branches
- Purkinje fibers

Cardiac Conduction System
Figure 15.20



Cardiac Conduction System. Figure 15.19



CONDUCTION SYSTEM

Sequence of excitation

1. sinoatrial (SA) node - spreads to both atria
   - 90 - 100 action potentials per minute
2. atrioventricular (AV) node
   - 40 -50 action potentials per minute
3. atrioventricular (AV) bundle (bundle of His)
   - 20-40 action potentials per minute
4. right & left bundle branches
   - in the interventricular septum
5. Purkinje fibers
   - conduction myofibers

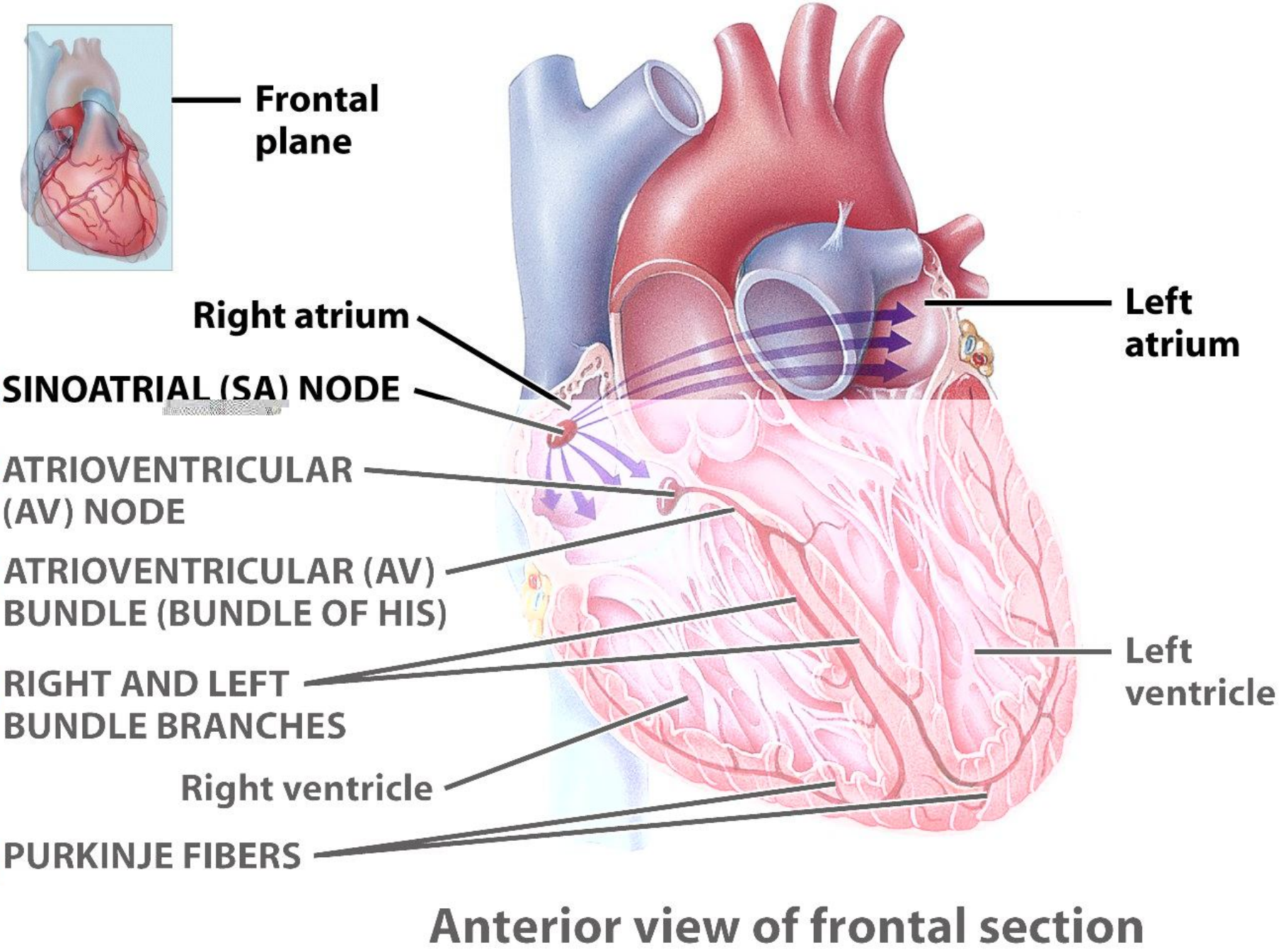
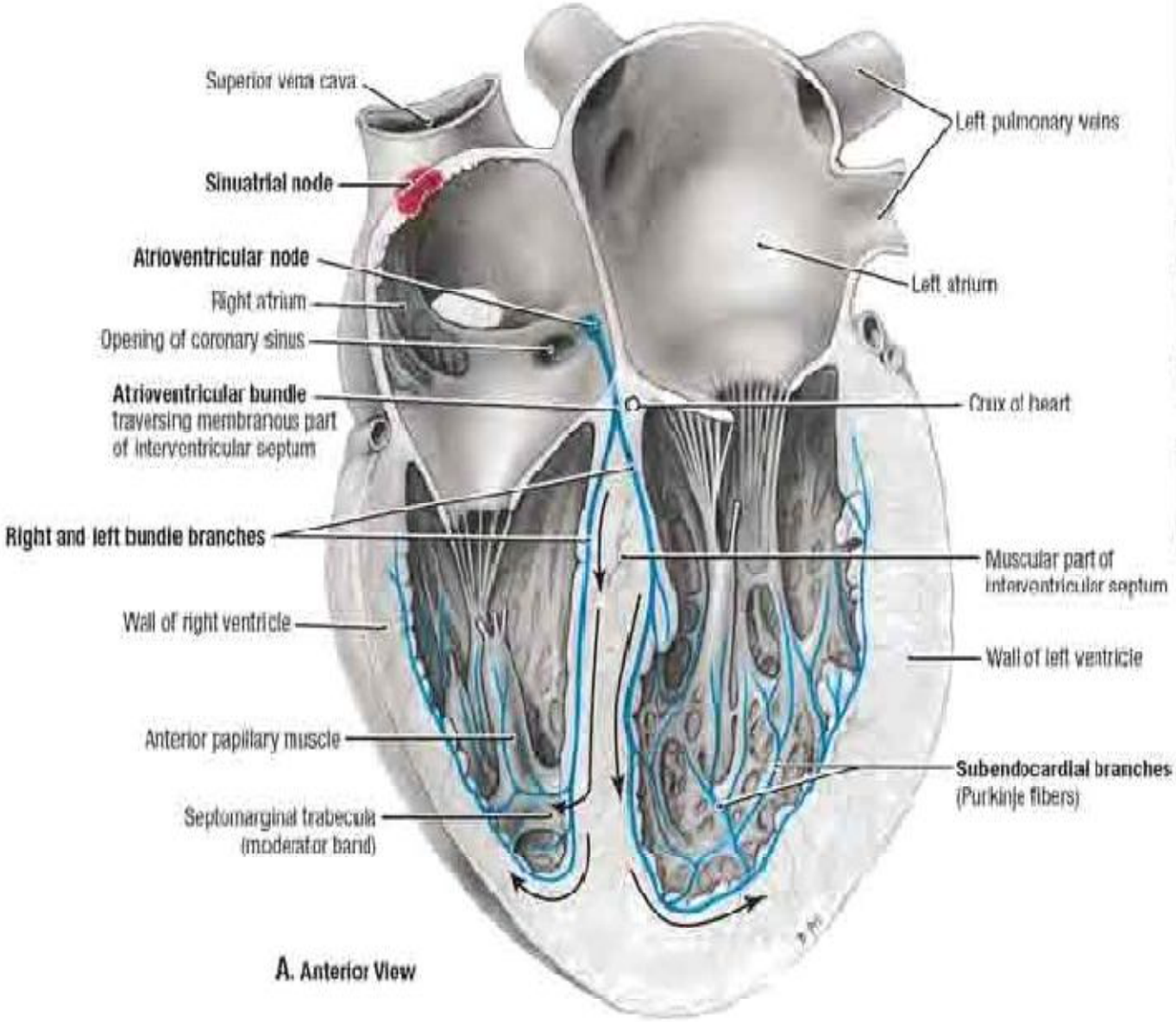
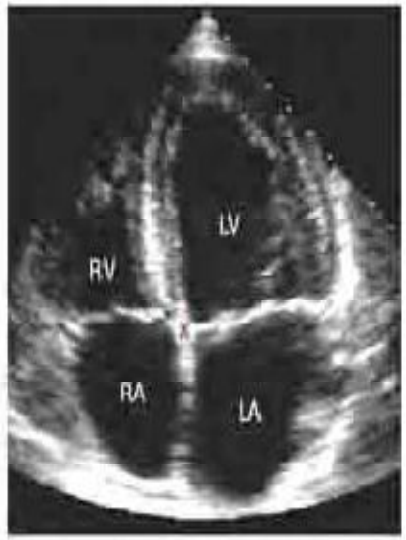


Figure 19-8 Anatomy and Physiology: From Science to Life



A. Anterior View

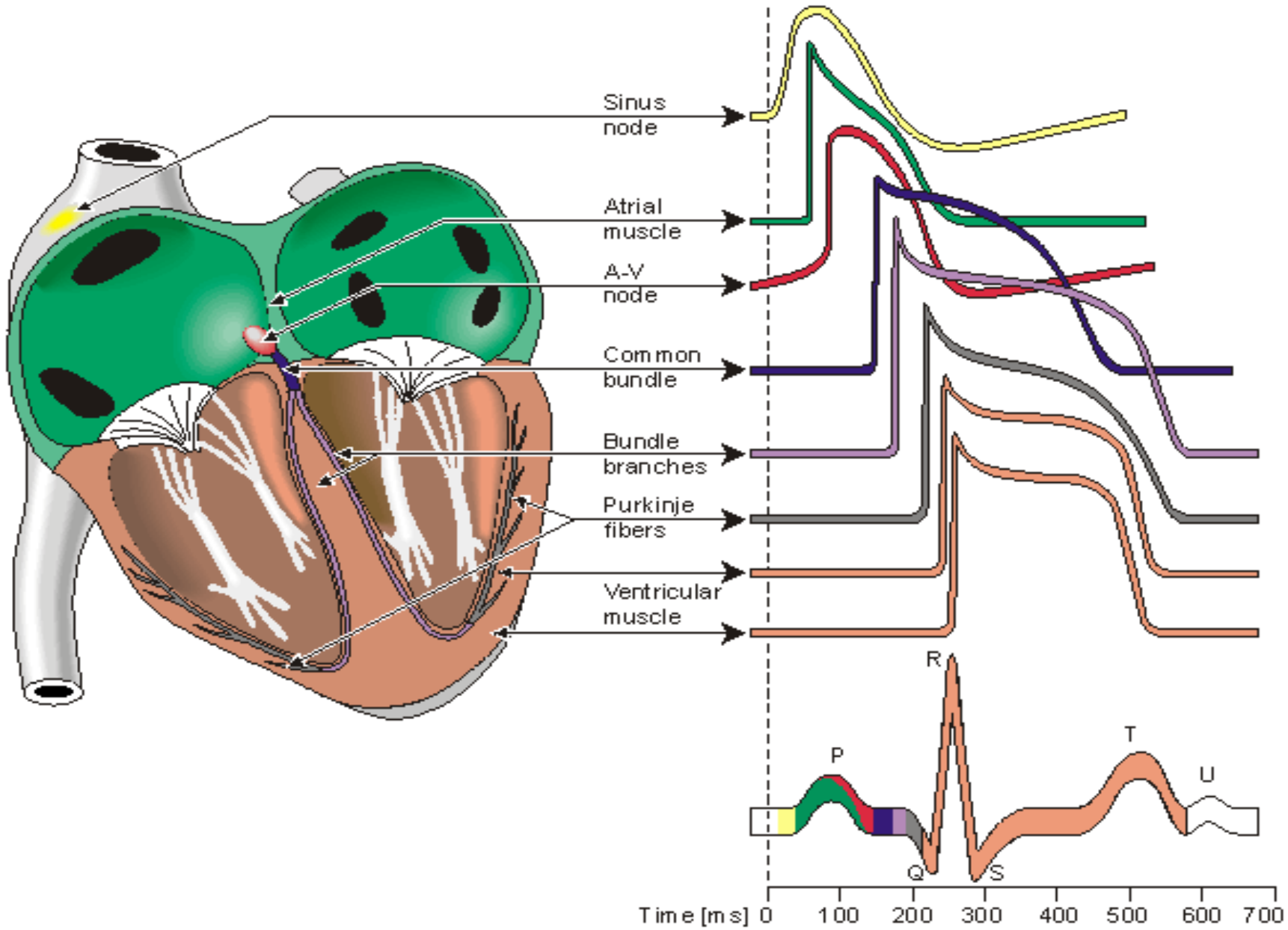


B. Echocardiogram,
Apical Four-chamber View

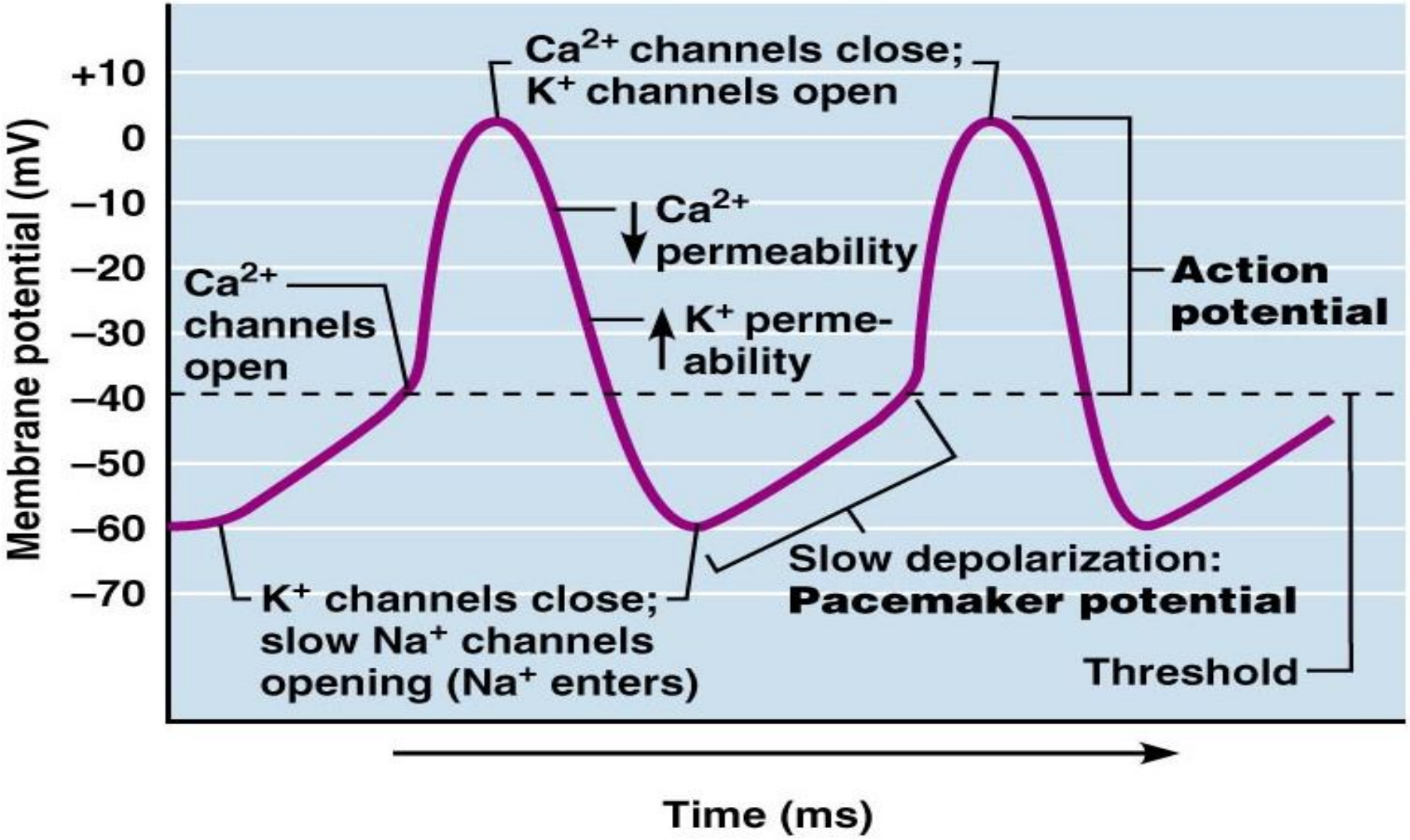
RV	Right ventricle	LV	Left ventricle
	x Crux of heart		
RA	Right atrium	LA	Left atrium

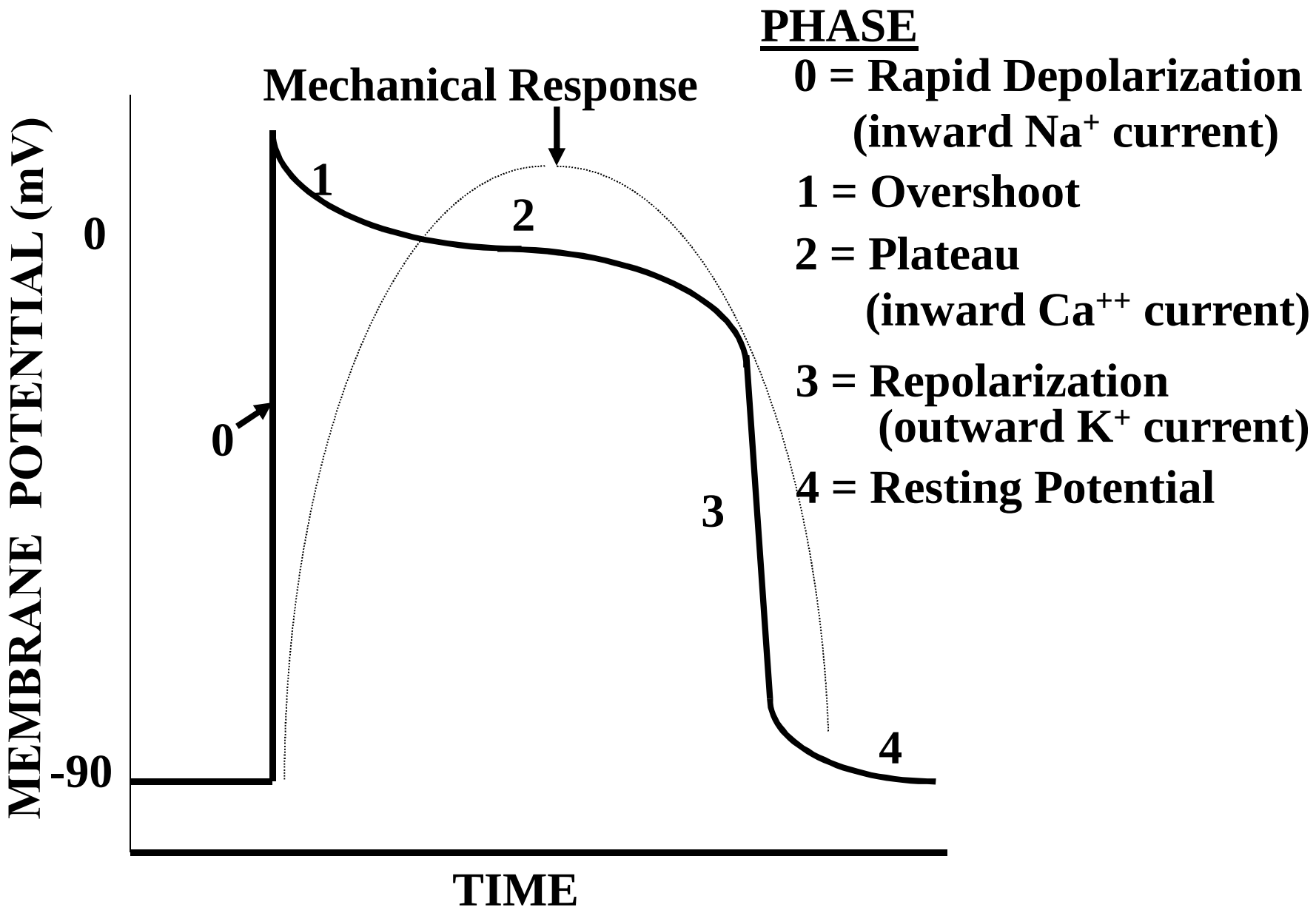
Depolarization of SA Node

- SA node - no stable resting membrane potential
- Pacemaker potential
  - gradual depolarization *from -60 mV*, slow influx of Na^+
- Action potential
  - occurs at threshold of *-40 mV*
  - depolarizing phase *to 0 mV*
    - fast Ca^{2+} channels open, (Ca^{2+} in)
  - repolarizing phase
    - K^+ channels open, (K^+ out)
    - *at -60 mV* K^+ channels close, pacemaker potential starts over
- Each depolarization creates one heartbeat
  - SA node at rest fires at 0.8 sec, about 75 bpm

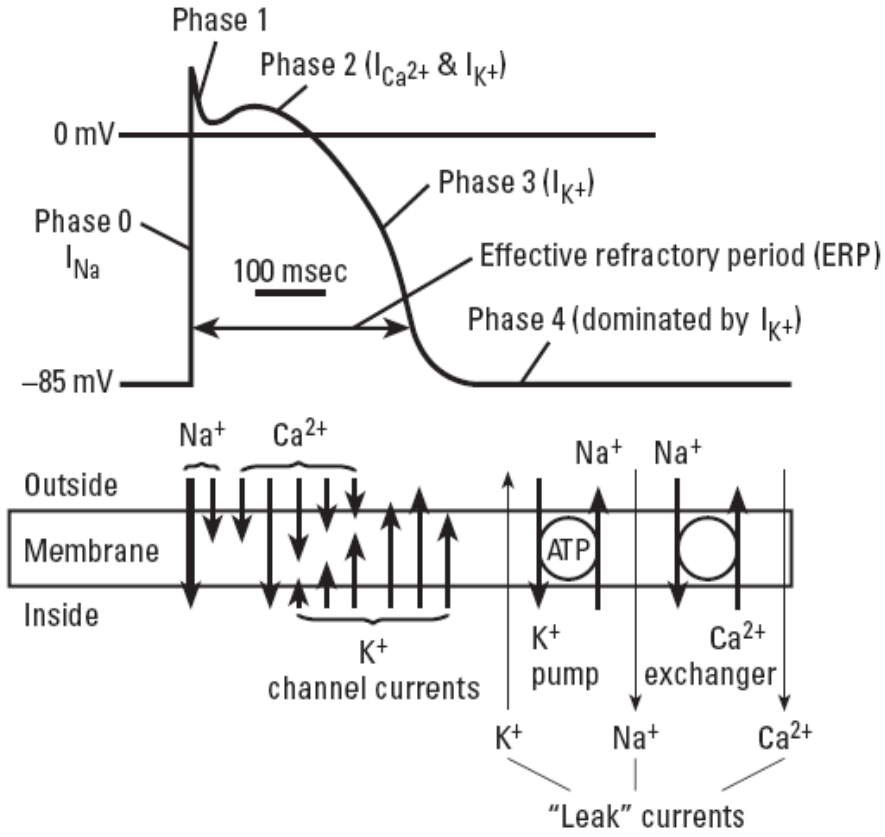

Sinus node
Atrial muscle
A-V node
Common bundle
Bundle branches
Purkinje fibers
Ventricular muscle
R
P
T
U
Q
S
Time [ms]
0
100
200
300
400
500
600
700

Pacemaker and Action Potentials of the Heart




Mechanical Response
MEMBRANE POTENTIAL (mV)
0
-90
1
2
0
3
4
TIME
PHASE
0 = Rapid Depolarization
(inward Na+ current)
1 = Overshoot
2 = Plateau
(inward Ca++ current)
3 = Repolarization
(outward K+ current)
4 = Resting Potential

Ventricular action potential



Occurs in atrial and ventricular myocytes and Purkinje fibers.

Phase 0 = rapid upstroke—voltage-gated Na^+ channels open.

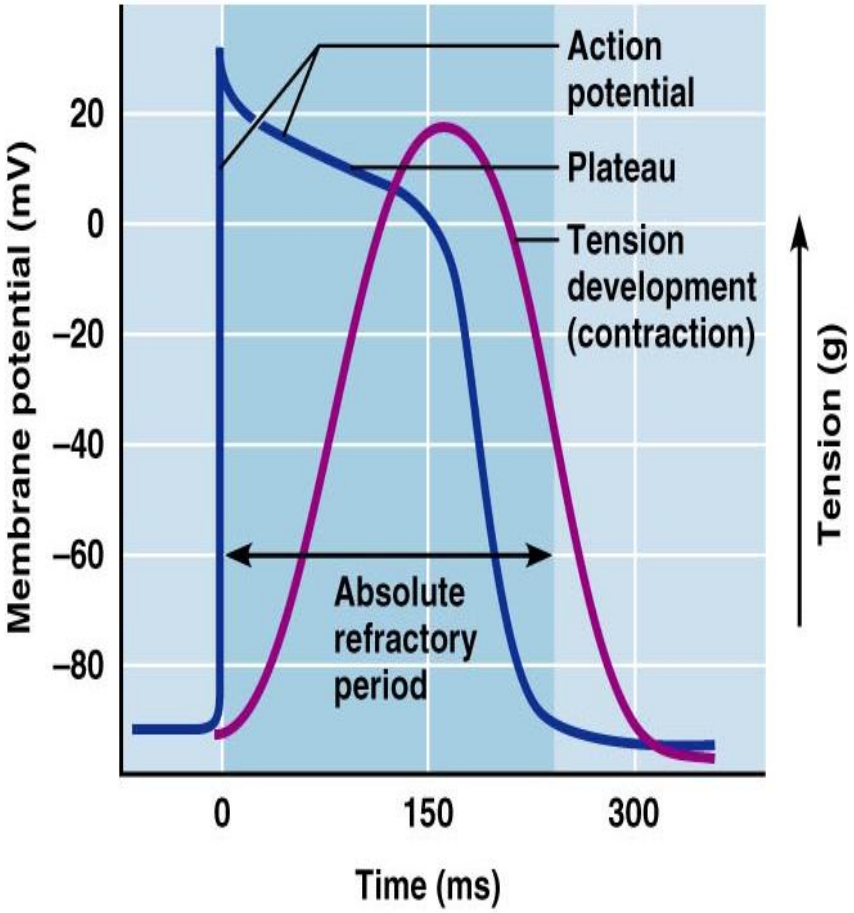
Phase 1 = initial repolarization—inactivation of voltage-gated Na^+ channels. Voltage-gated K^+ channels begin to open.

Phase 2 = plateau—Ca^{2+} influx through voltage-gated Ca^{2+} channels balances K^+ efflux. Ca^{2+} influx triggers Ca^{2+} release from sarcoplasmic reticulum and myocyte contraction.

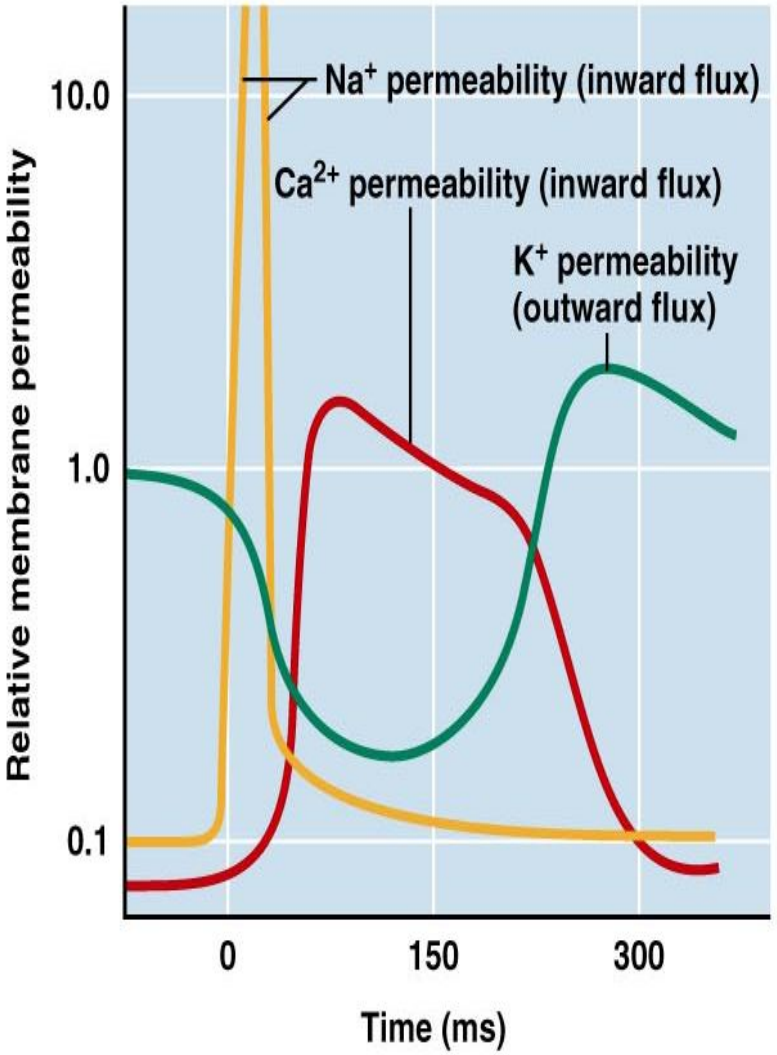
Phase 3 = rapid repolarization—massive K^+ efflux due to opening of voltage-gated slow K^+ channels and closure of voltage-gated Ca^{2+} channels.

Phase 4 = resting potential—high K^+ permeability through K^+ channels.

Cardiac Membrane Potential

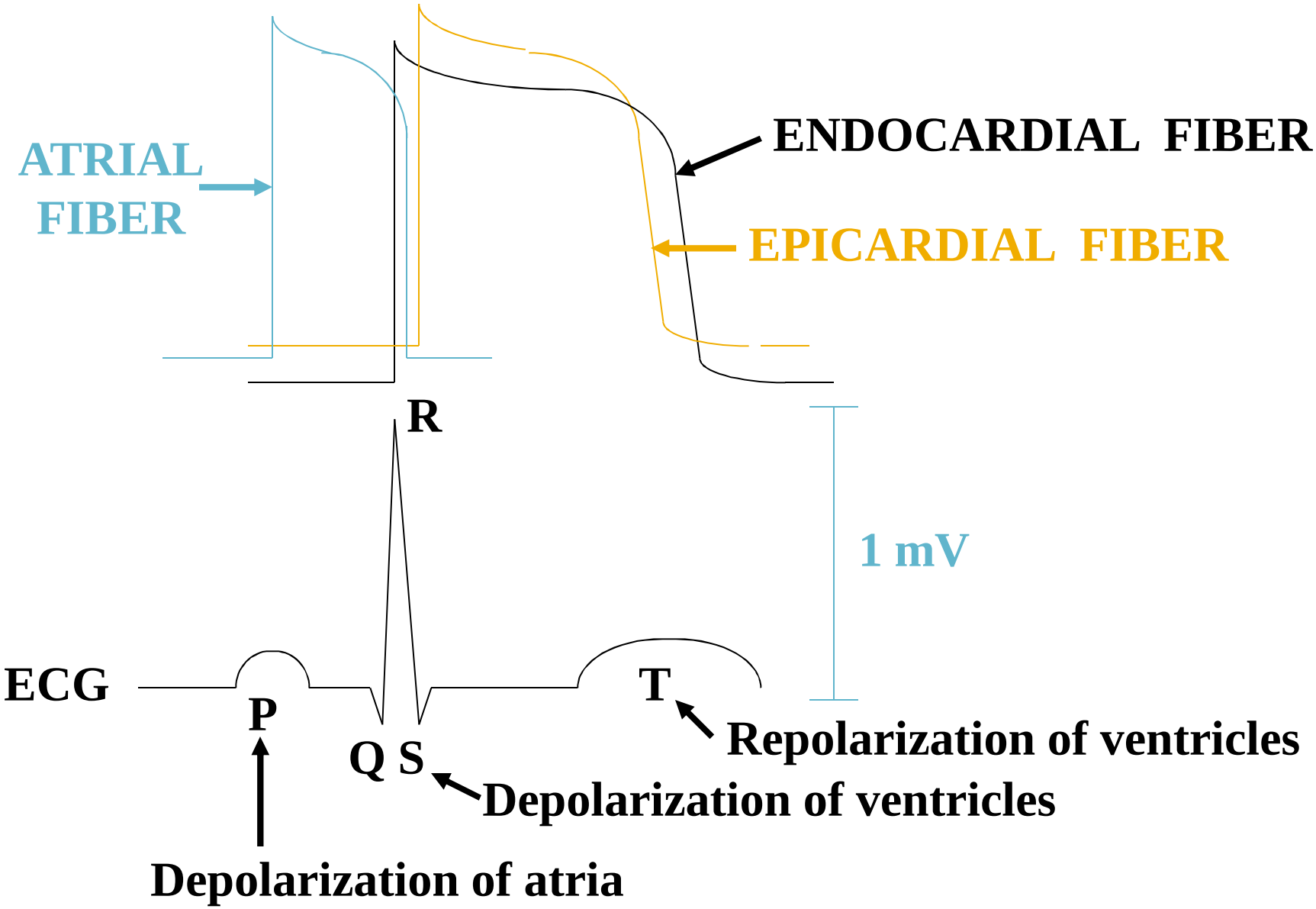


(a)

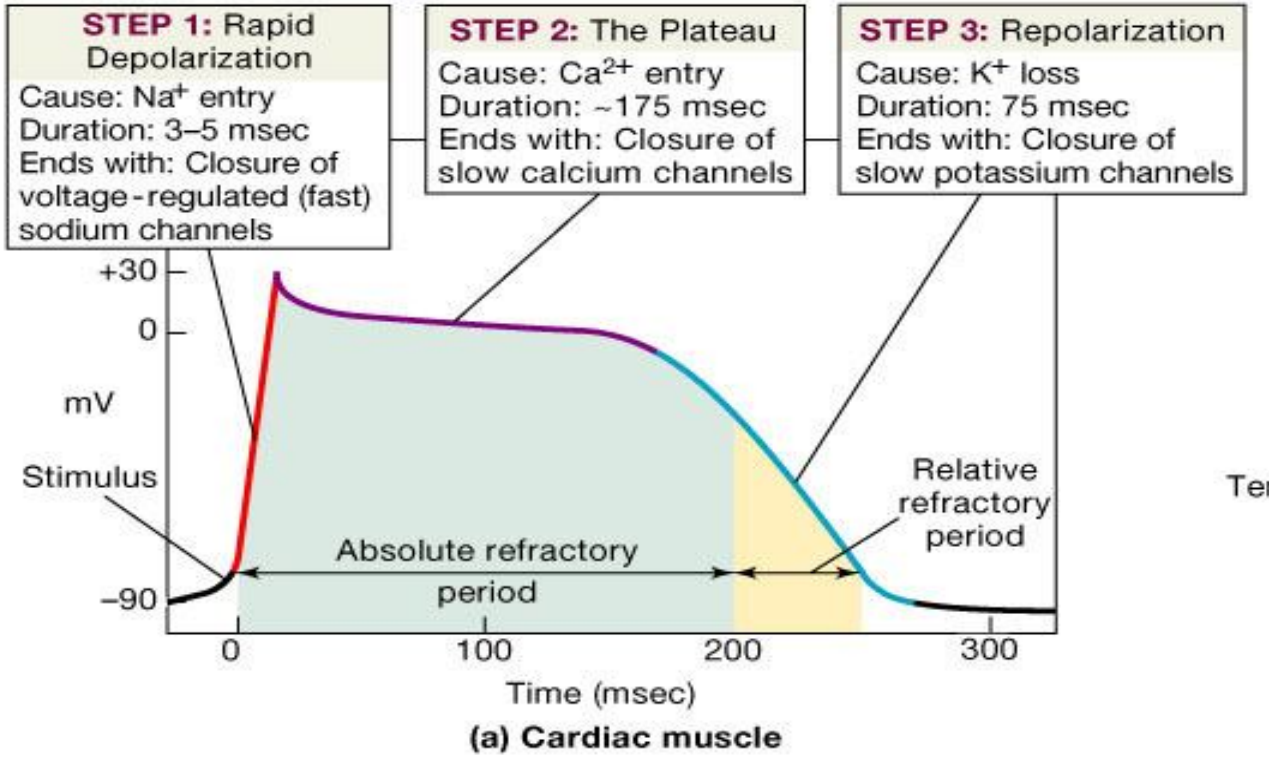


(b)

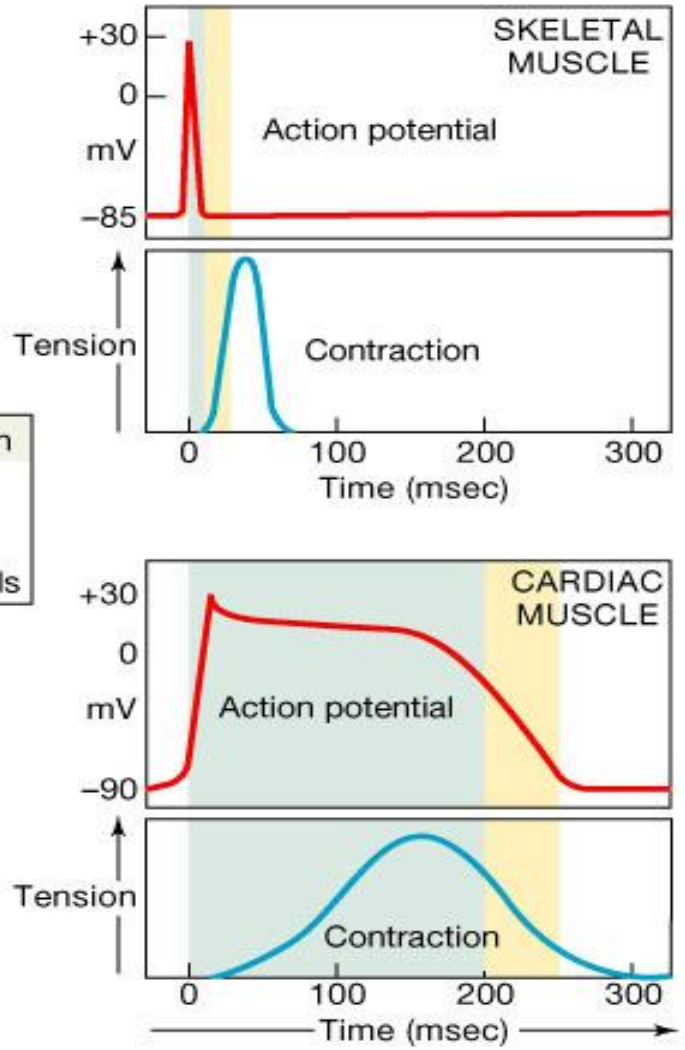
SINGLE VENTRICULAR ACTION POTENTIAL



The Action Potential in Skeletal and Cardiac Muscle



(a) Cardiac muscle



(b)

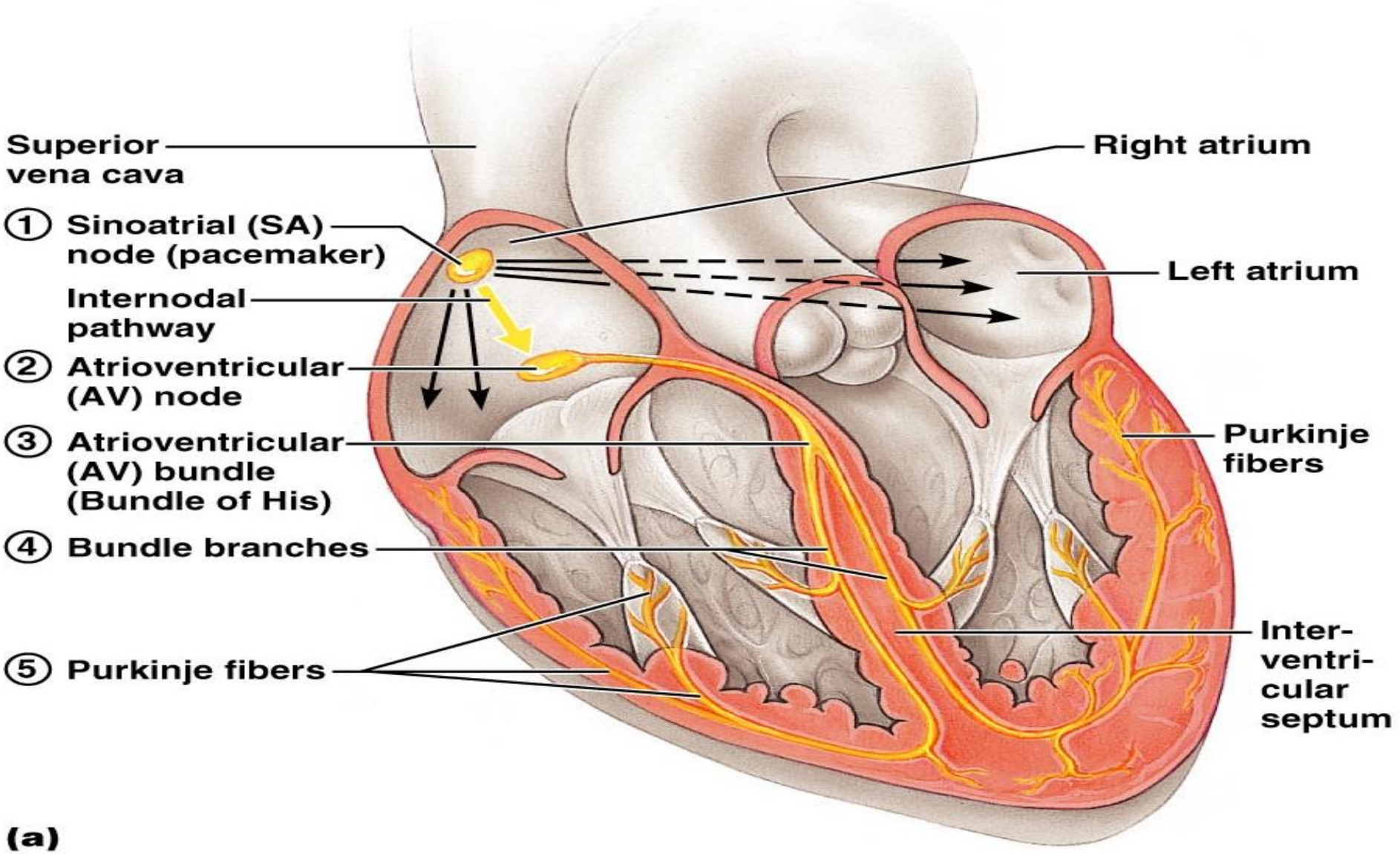
Heart Physiology: Sequence of Excitation

- Sinoatrial (SA) node generates impulses about 75 times/minute
- Atrioventricular (AV) node delays the impulse approximately 0.1 second
- Impulse passes from atria to ventricles via the atrioventricular bundle (bundle of His)

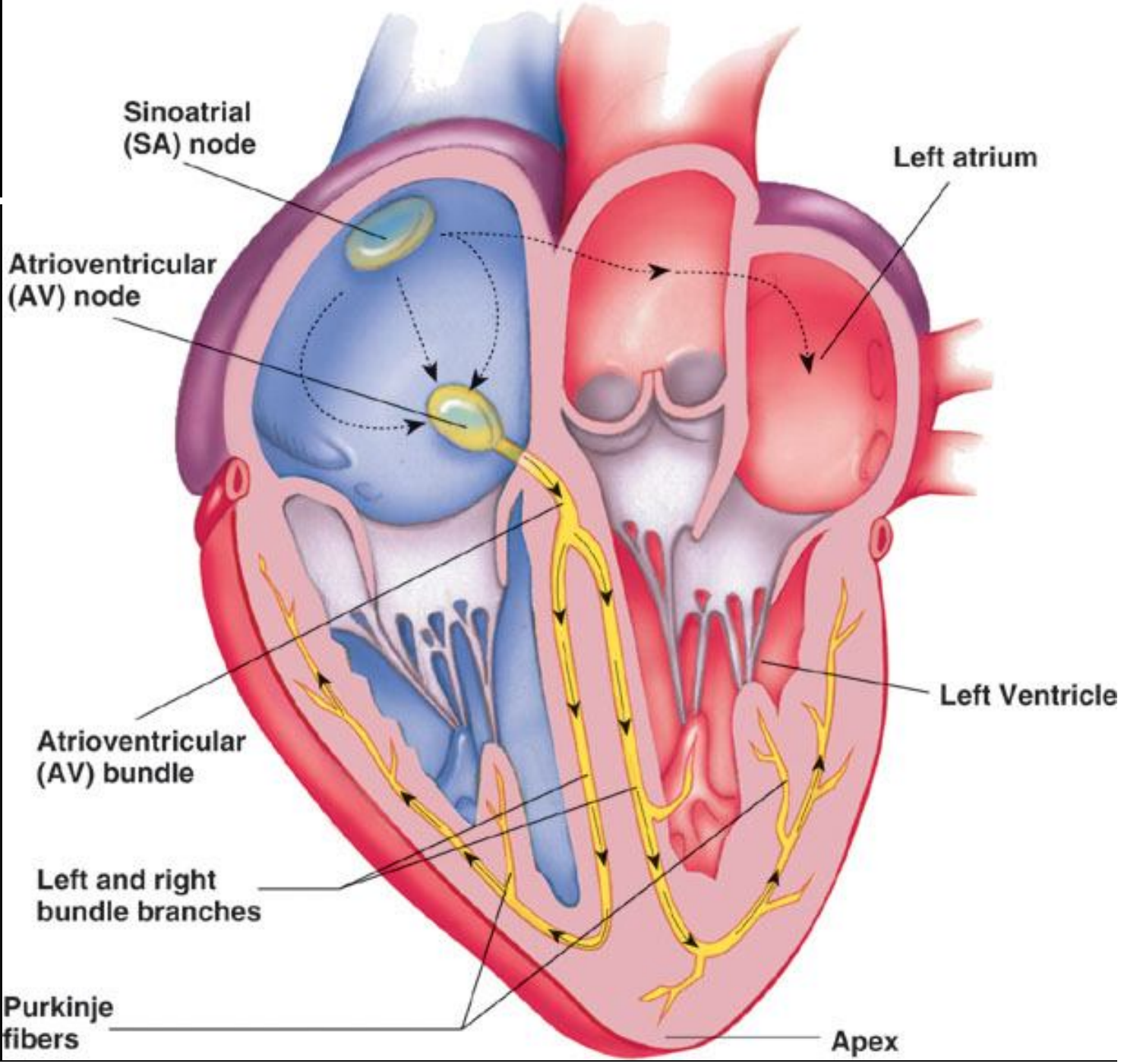
Heart Physiology: Sequence of Excitation

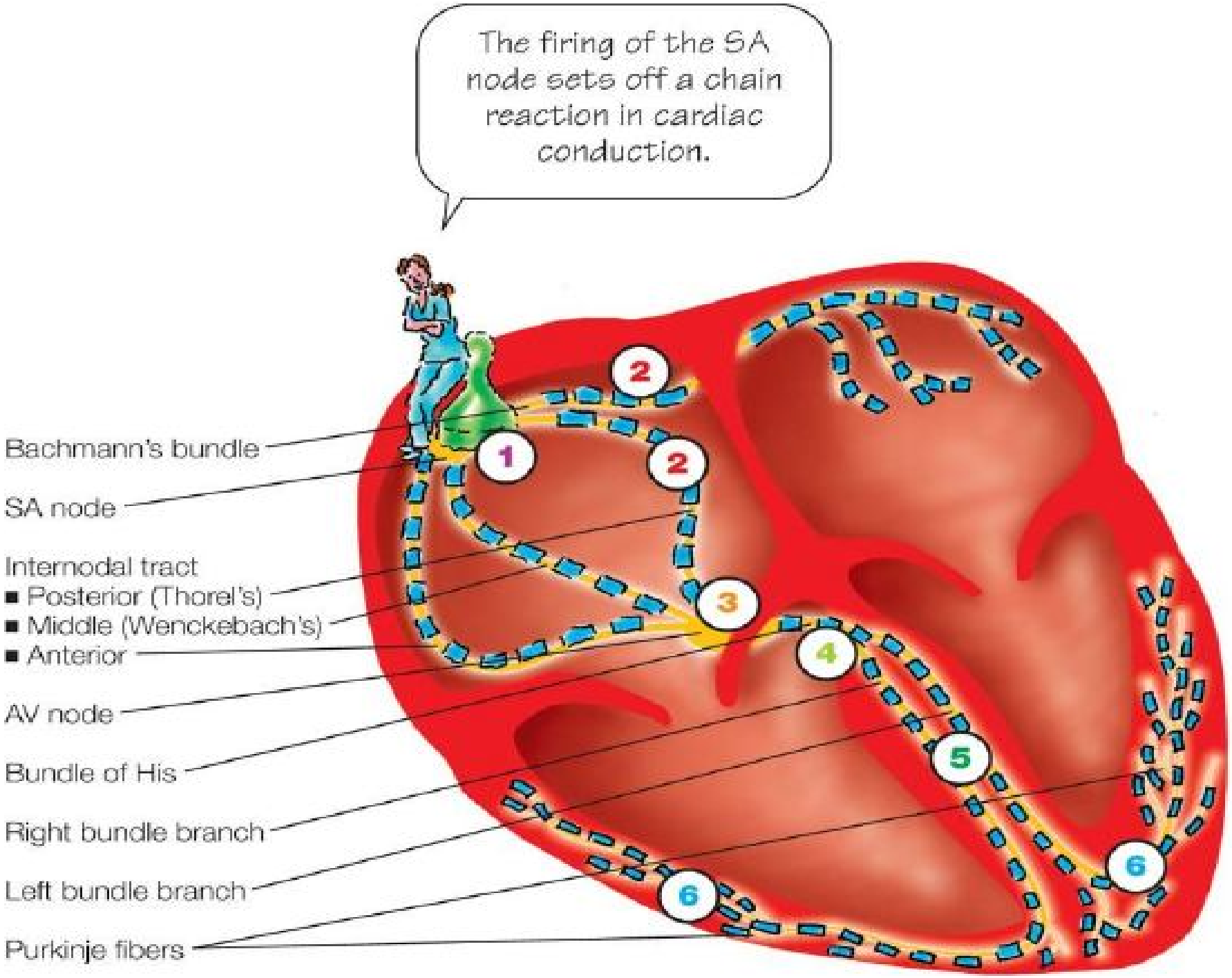
- AV bundle splits into two pathways in the interventricular septum (bundle branches)
  - Bundle branches carry the impulse toward the apex of the heart
  - Purkinje fibers carry the impulse to the heart apex and ventricular walls

Cardiac Intrinsic Conduction



Conducting System of Heart




The firing of the SA node sets off a chain reaction in cardiac conduction.
Bachmann's bundle
SA node
Internodal tract
■ Posterior (Thorel's)
■ Middle (Wenckebach's)
■ Anterior
AV node
Bundle of His
Right bundle branch
Left bundle branch
Purkinje fibers
1
2
2
3
4
5
6
6

Heart Excitation Related to ECG

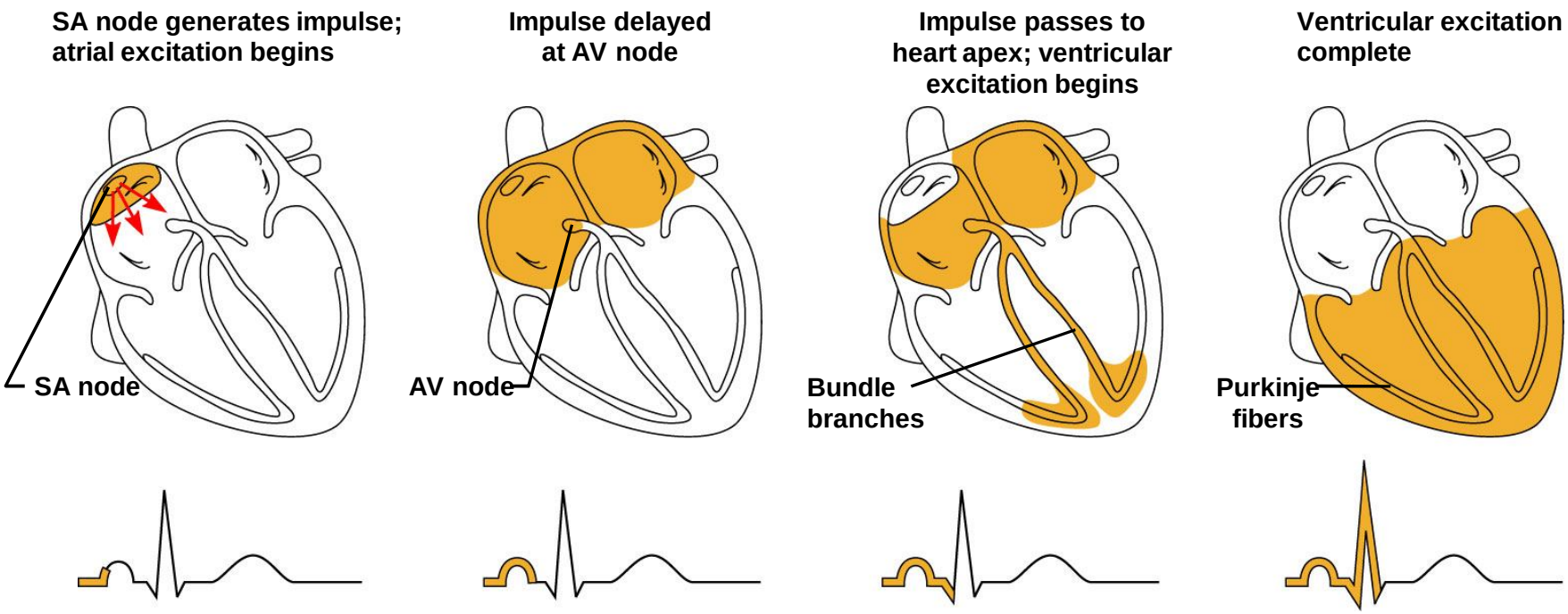
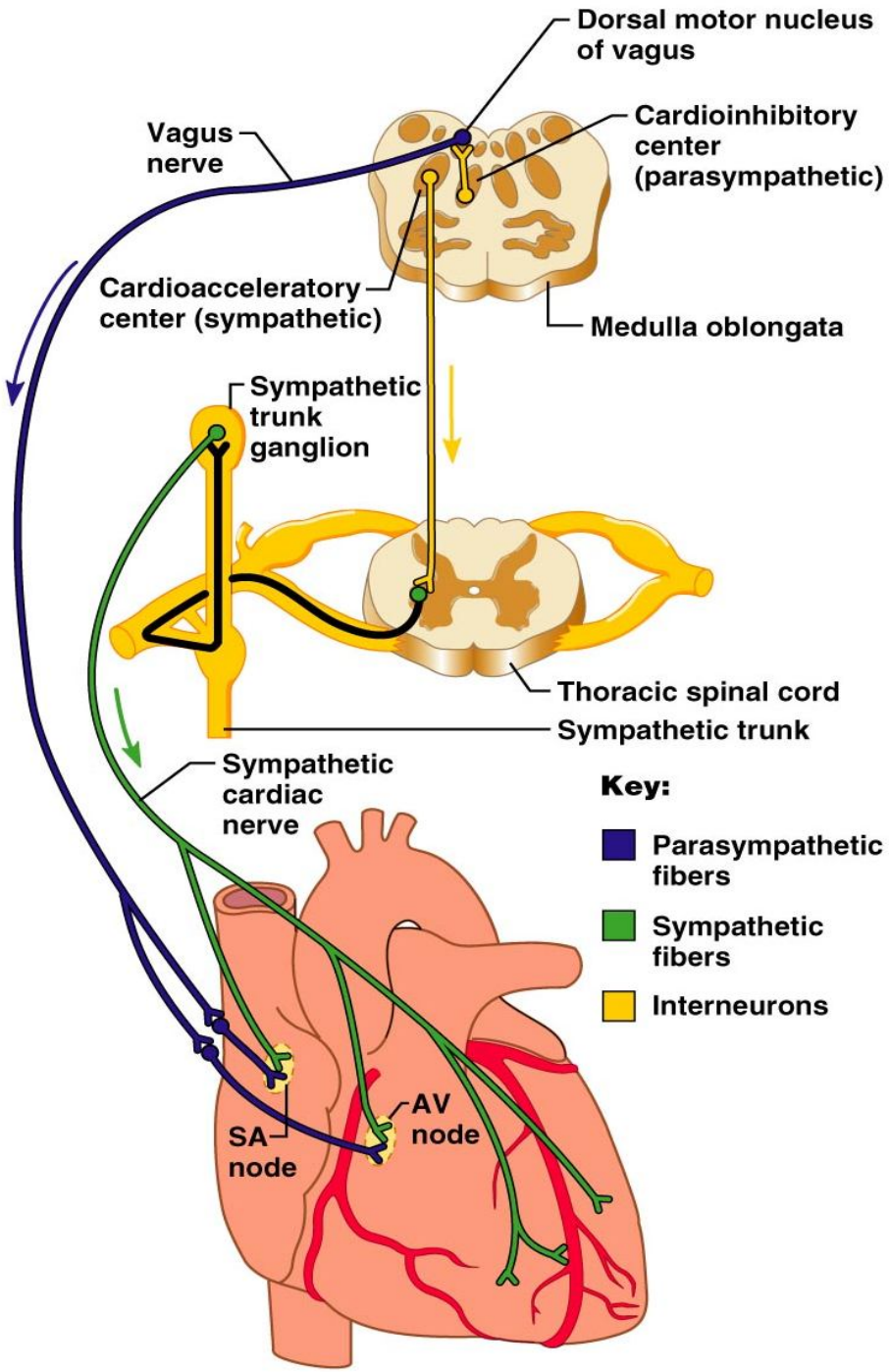


Figure 18.17

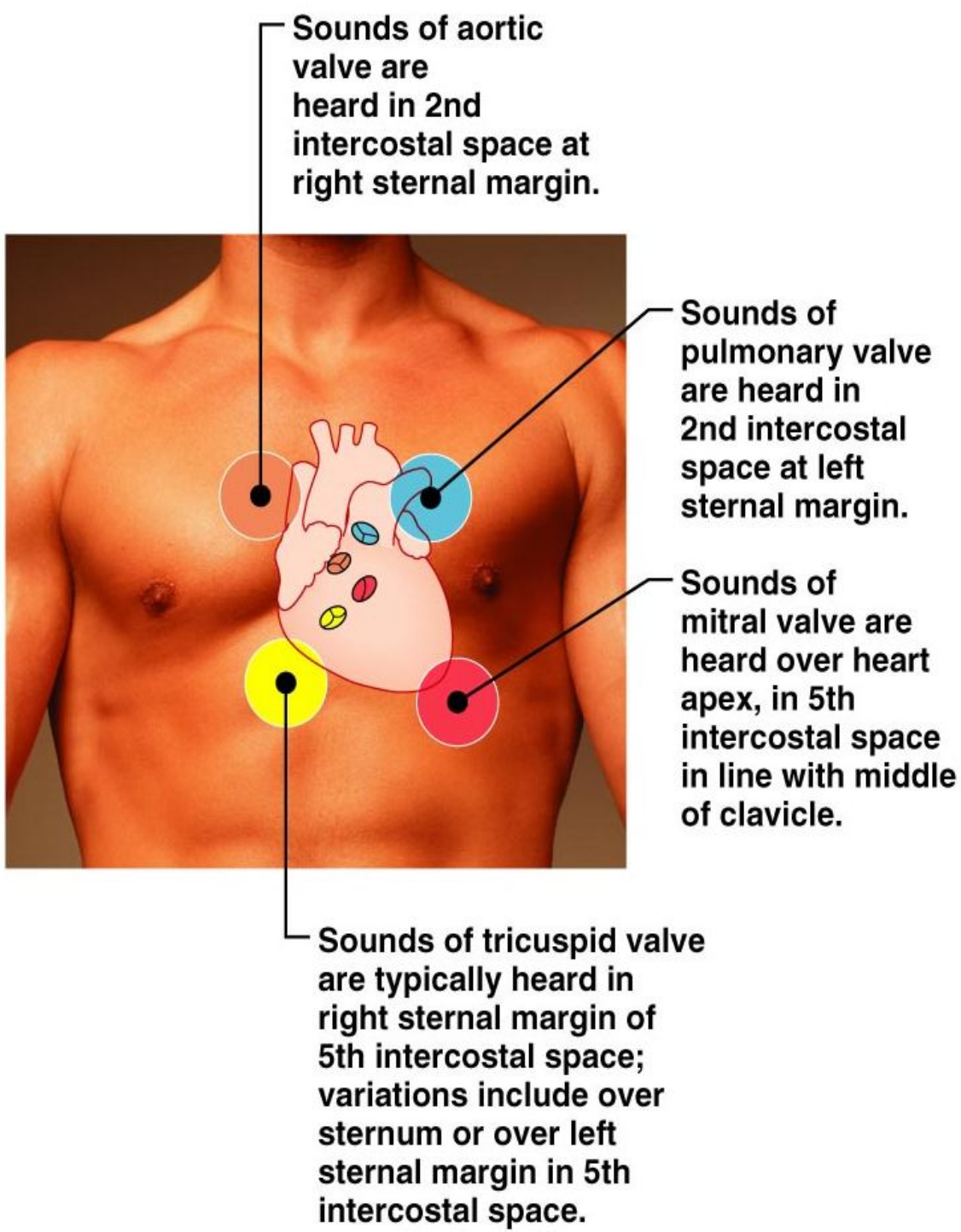
Extrinsic Innervation of the Heart

- Heart is stimulated by the sympathetic cardioacceleratory center
- Heart is inhibited by the parasympathetic cardioinhibitory center



Base the heart physiology

- Automaticity
- Excitability
- Conductivity
- Contractility

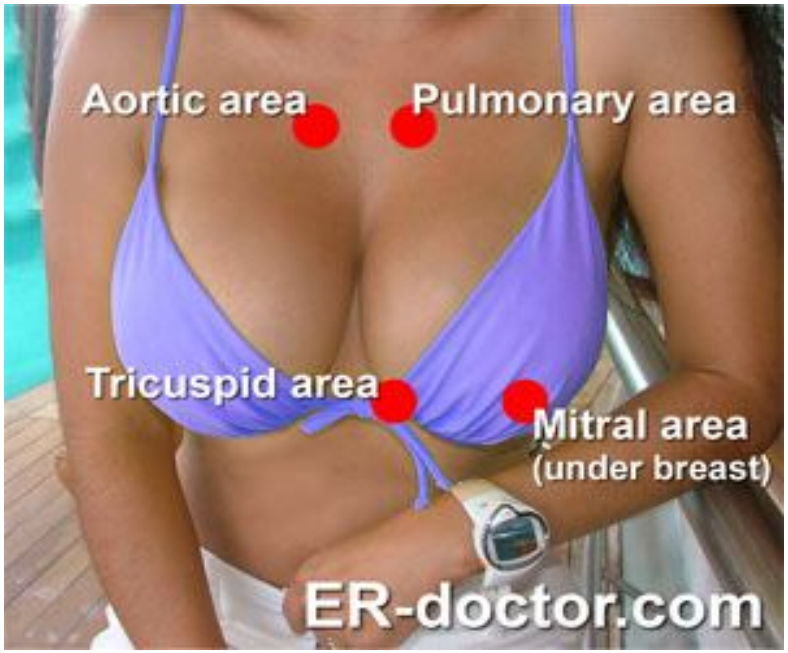


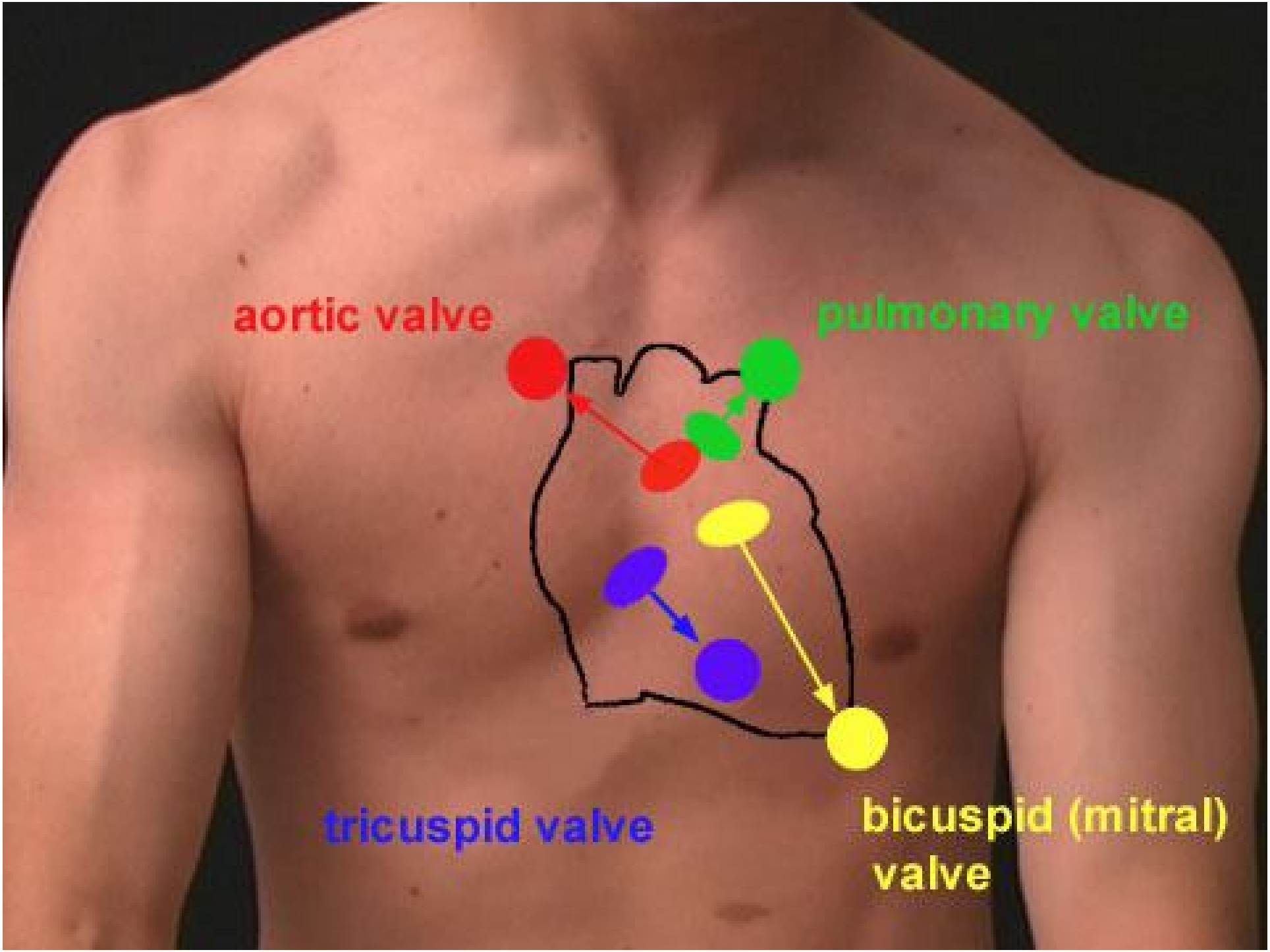
Heart Sounds

S4

S1 = Mitral,Tricuspid then pulmonary artery valve,aortic valve

S2= Aortic ,Pulmunary valve then tricuspid mitral




aortic valve
pulmonary valve
tricuspid valve
bicuspid (mitral) valve

Heart sounds

- Right side lower pressure open first , closed second
- Left side higher pressure open second , closed first.

- Unless Eisenmenger syndrome , everything is reversed [condition that affects blood flow from the heart to the lungs in some babies who have structural problems of the heart]

BREATH IN AND OUT

- BREATH IN[INHALE] =➔RIGHT SIDE OF HEART LOUDER [SPLIT]
- BREATH OUT [EXHALE]LEFT SIDE OF THE HEART

Effects of inhalation/expiration

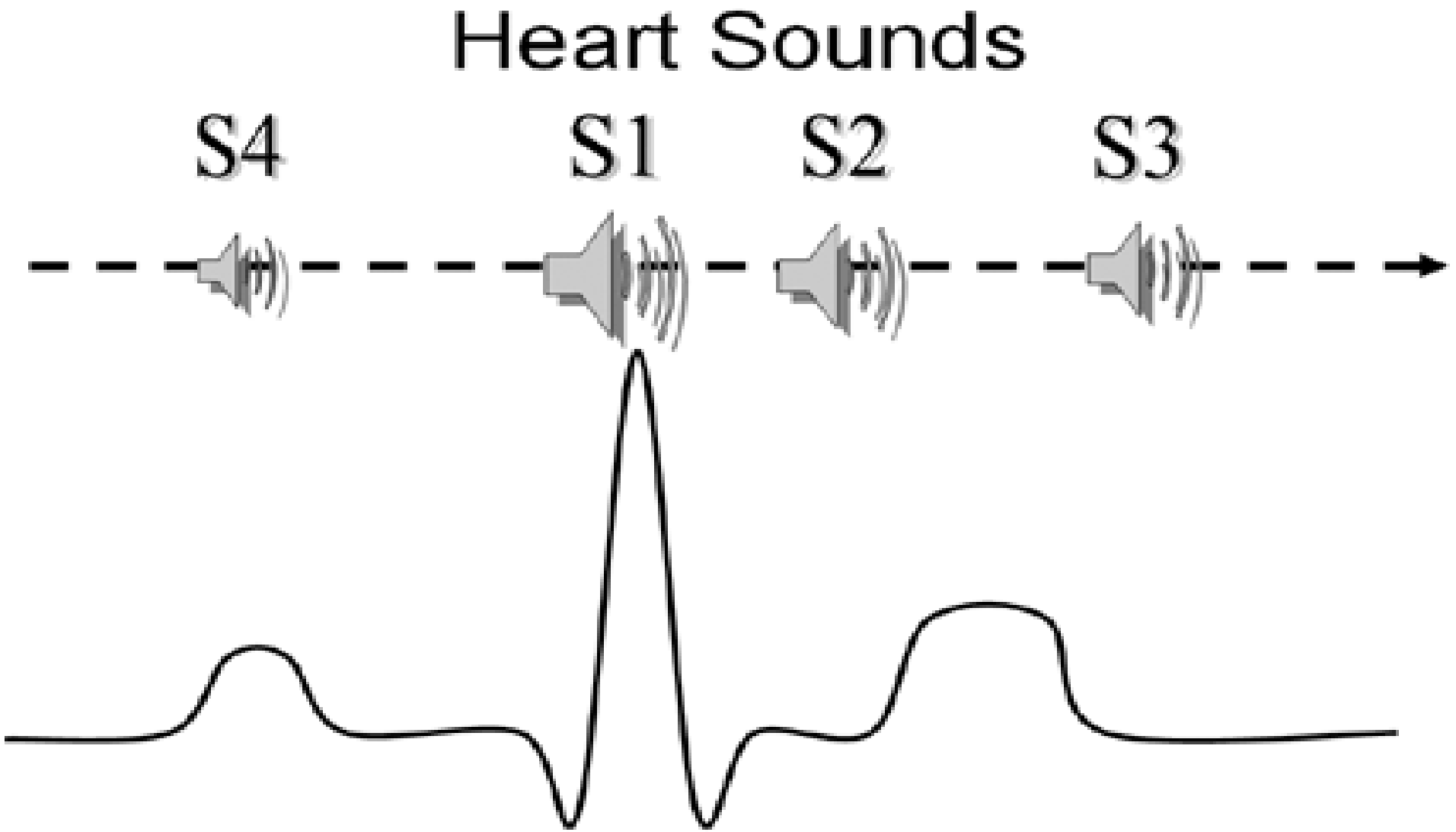
•**Inhalation** pressure causes an **increase in the venous blood return to the right side of the heart.**
Therefore, *right-sided murmurs generally increase in intensity with inspiration*.
The increased volume of blood entering the right sided chambers of the heart restricts the amount of blood entering the left sided chambers of the heart. This causes left-sided murmurs to generally decrease in intensity during inspiration.

Expiration, the opposite hemodynamic changes occur.
This means that left-sided murmurs generally increase in intensity with expiration.
Having the patient lie supine and raising their legs up to a 45 degree angle facilitates an increase in venous return to the right side of the heart producing effects similar to inhalation-increased blood flow.

Heart Sounds

- Heart sounds are not caused by opening of the valves
- Heart sounds (lub-dup) are associated with closing of heart valves
  - First sound occurs as AV valves close and signifies beginning of systole
  - Second sound occurs when SL valves close at the beginning of ventricular diastole

S_1, forms the "lub" of "lub-dub" **S_2**, forms the "dub" of "lub-dub"



S1, S2, S3 sound like "Ken-tuck-y" (lub-dub-dub)

Normal Heart Sounds

Area	Location		Abnormality
Aortic	2nd ICS R sternal border		Aortic Stenosis S2 is loudest here
Pulmonic	2nd ICS L sternal border		Pulmonary stenosis or regurgitation
Tricuspid	L lower sternal border		Tricuspid stenosis
Mitral	5th ICS		Mitral stenosis or regurgitation S1 is loudest here

S1:
The S1 sound is normally the first heart sound heard.
The S1 is best heard in the *mitral area*, and corresponds to closure of the mitral and tricuspid (AV) valves.
A normal S1 is low-pitched and of longer duration than S2.

S2:
The S2 sound is normally the second sound heard.
The S2 is best heard over the *aortic area*, and corresponds to closure of the pulmonic and aortic valves.
A normal S2 is higher-pitched and of shorter duration than S1.

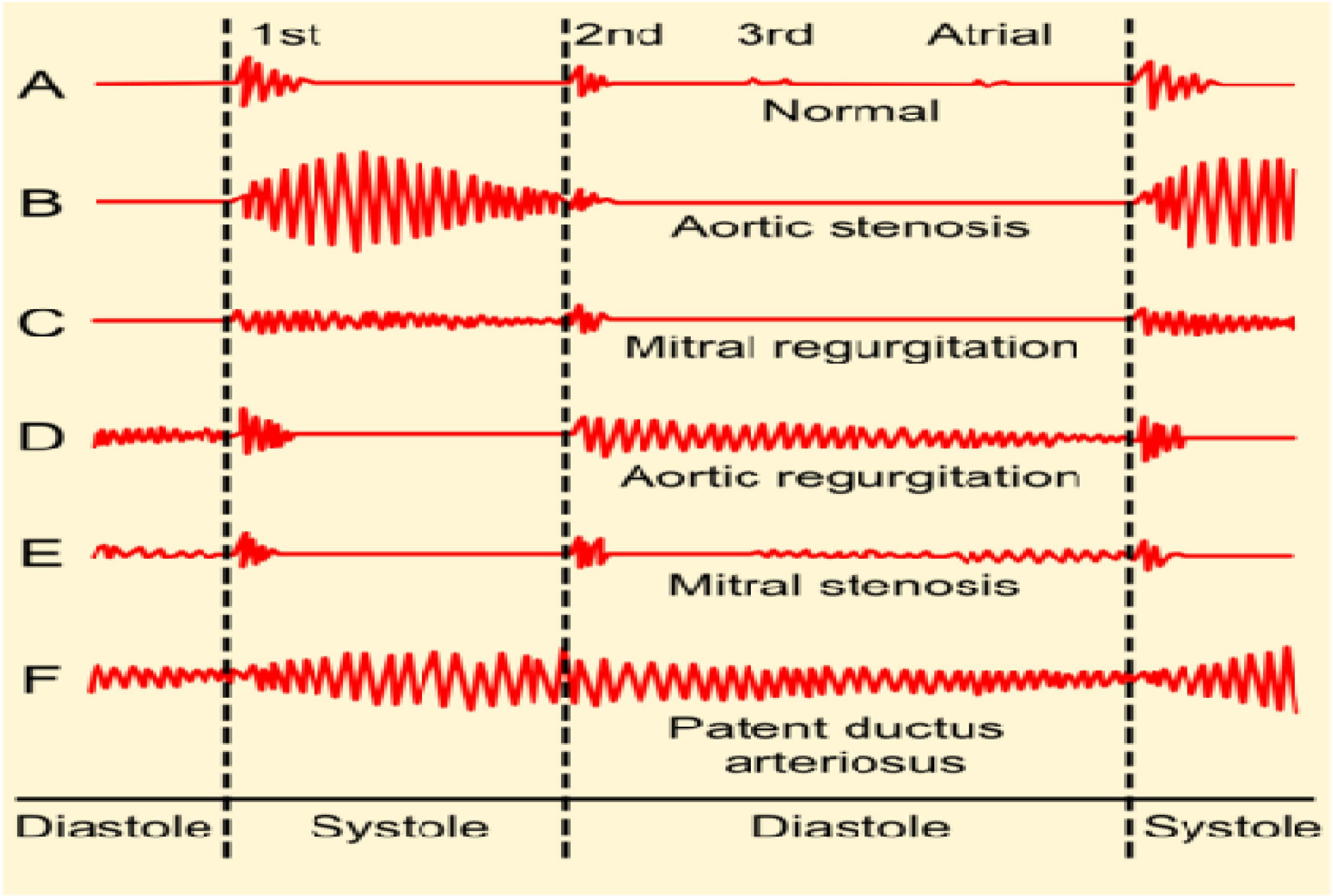
The flow from the ventricles is more forceful than the flow from the atria. Therefore, S2 will normally be the louder sound.

Abnormal Heart Sounds

S3:
The S3 sound is heard immediately following S2, and is **normal in children and adolescents, but usually disappears after age 30**.
When heard in adults, an **S3 is called a "gallop"** and **indicates left ventricular failure.**

S4:
The S4 sound is heard immediately before the S1, and may be **present in infants and children.**
The S4 is produced with decreased compliance of the ventricle and may indicate **myocardial infarction or shock.**

Gradations of Murmurs	(Defined based on use of an acoustic, not a high-fidelity amplified electronic stethoscope)
Grade	**Description**
Grade 1	Very faint, heard only after listener has "tuned in"; may not be heard in all positions. Only heard if the patient "bears down" or performs the Valsalva maneuver.
Grade 2	Quiet, but heard immediately after placing the stethoscope on the chest.
Grade 3	Moderately loud.
Grade 4	Loud, with palpable thrill (i.e., a tremor or vibration felt on palpation)
Grade 5	Very loud, with thrill. May be heard when stethoscope is partly off the chest.
Grade 6	Very loud, with thrill. May be heard with stethoscope entirely off the chest.



Phonocardiograms from normal and abnormal heart sounds

Cardiac Cycle

Cardiac Cycle: the **electrical, pressure and volume changes** that occur in a functional heart between successive heart beats.

- Phase of the cardiac cycle when myocardium is relaxed is termed ***diastole***.
- Phase of the cardiac cycle when the myocardium contracts is termed ***systole***.
  - ***Atrial systole***: when atria contract.
  - ***Ventricular systole***: when ventricles contract.

Mechanical Events of the Cardiac Cycle

1. **Ventricular Filling Period** [ventricular diastole, atrial systole]
2. **Isovolumetric Contraction Period** [ventricular systole]
3. **Ventricular Ejection Period** [ventricular systole]
4. **Isovolumetric Relaxation Period** [ventricular diastole]

Phases of the Cardiac Cycle

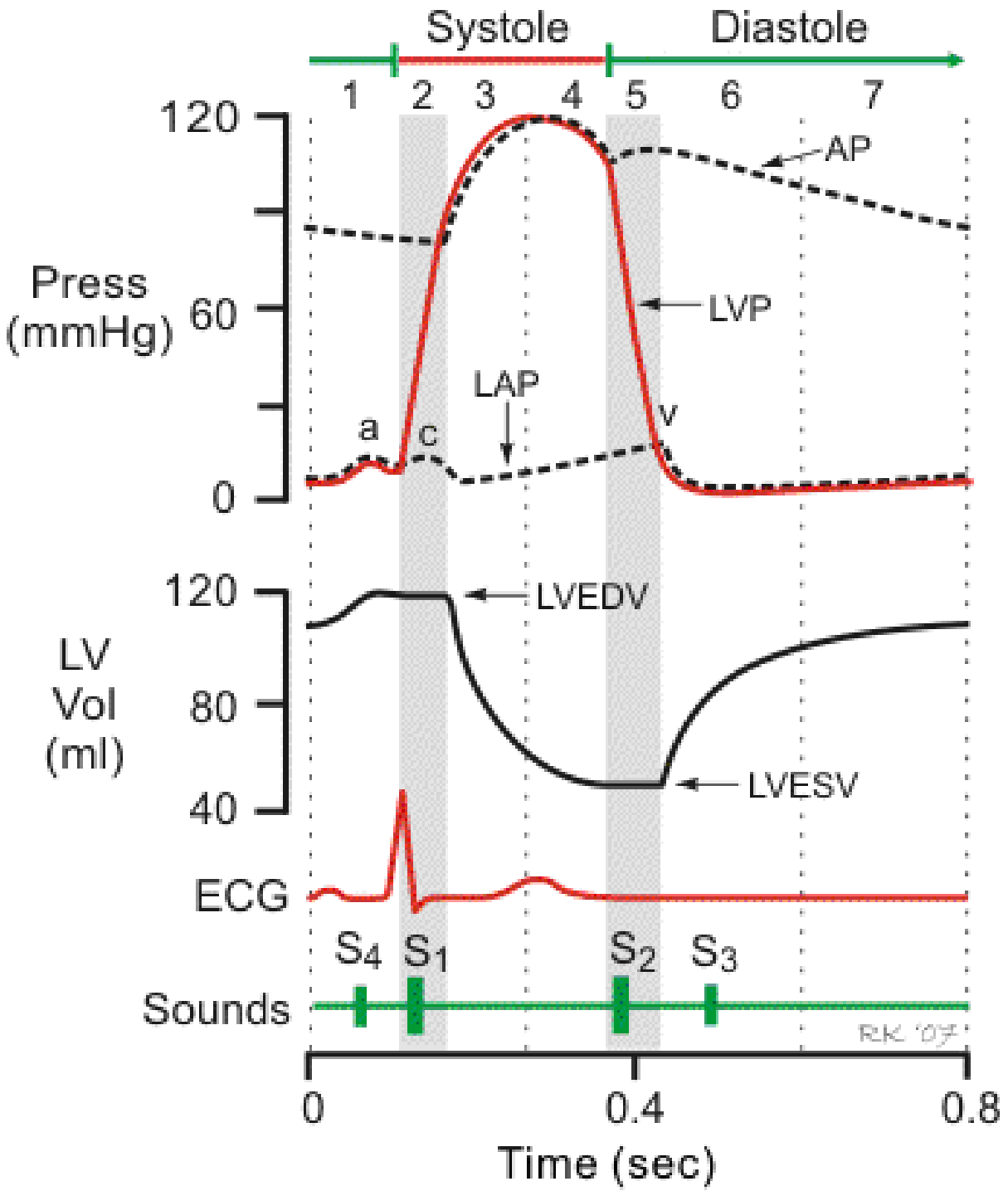
- Ventricular filling – mid-to-late diastole
  - Heart blood pressure is low as blood enters atria and flows into ventricles
  - AV valves are open, then atrial systole occurs

Phases of the Cardiac Cycle

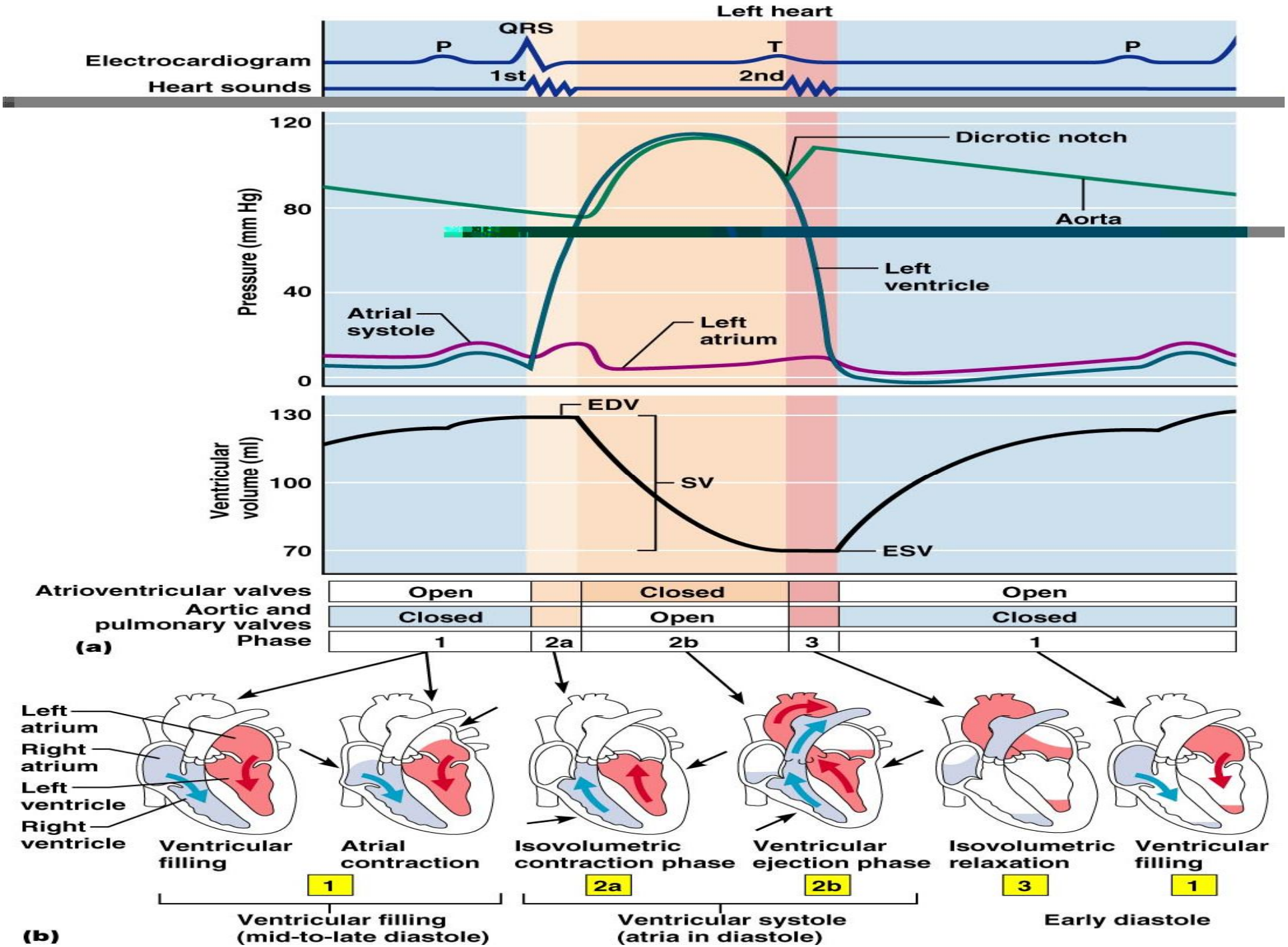
- Ventricular systole
  - Atria relax
  - Rising ventricular pressure results in closing of AV valves
  - Isovolumetric contraction phase
  - Ventricular ejection phase opens semilunar valves

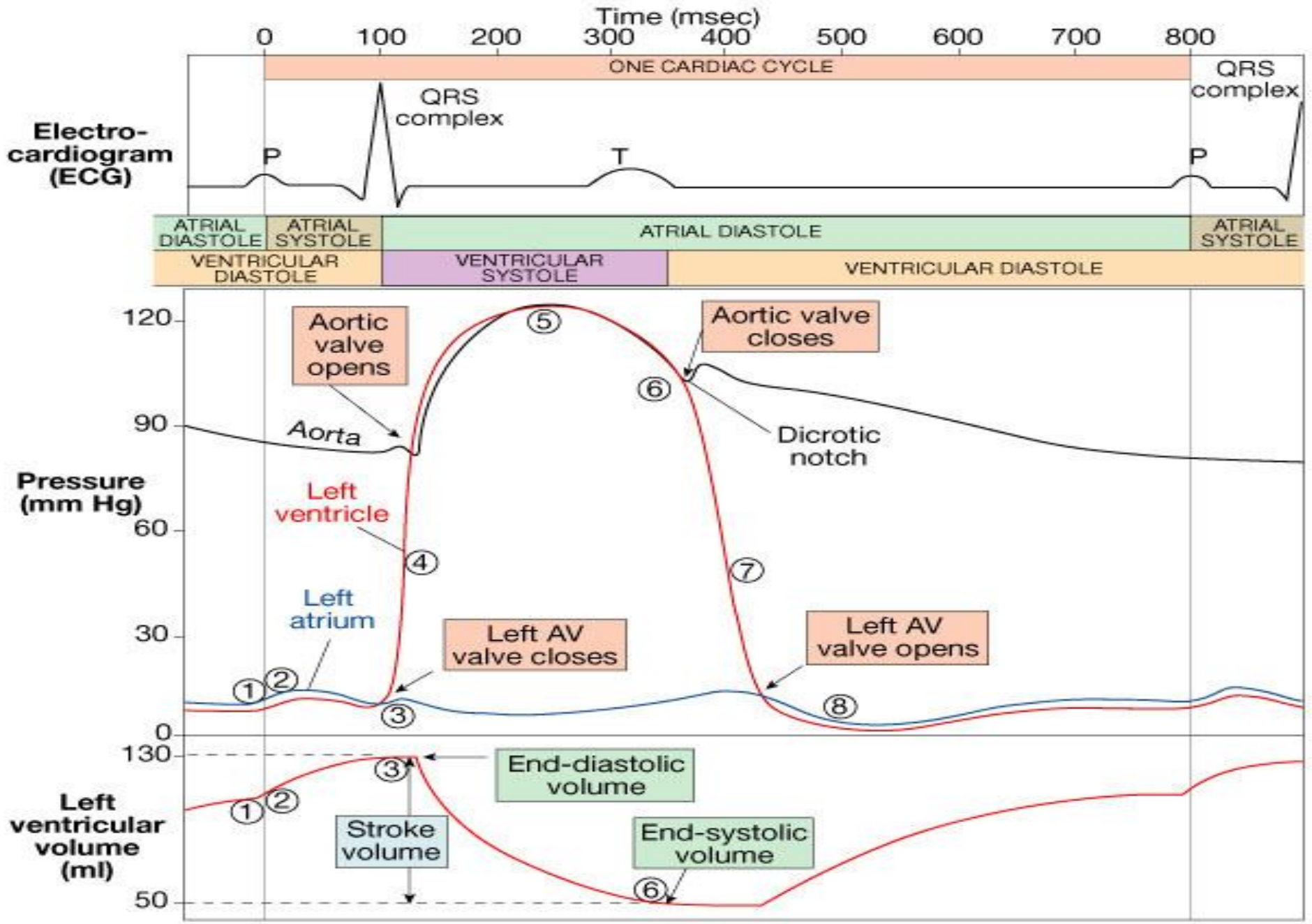
Phases of the Cardiac Cycle

- Isovolumetric relaxation – early diastole
  - Ventricles relax
  - Backflow of blood in aorta and pulmonary trunk closes semilunar valves
- Dicrotic notch – brief rise in aortic pressure caused by backflow of blood rebounding off semilunar valves



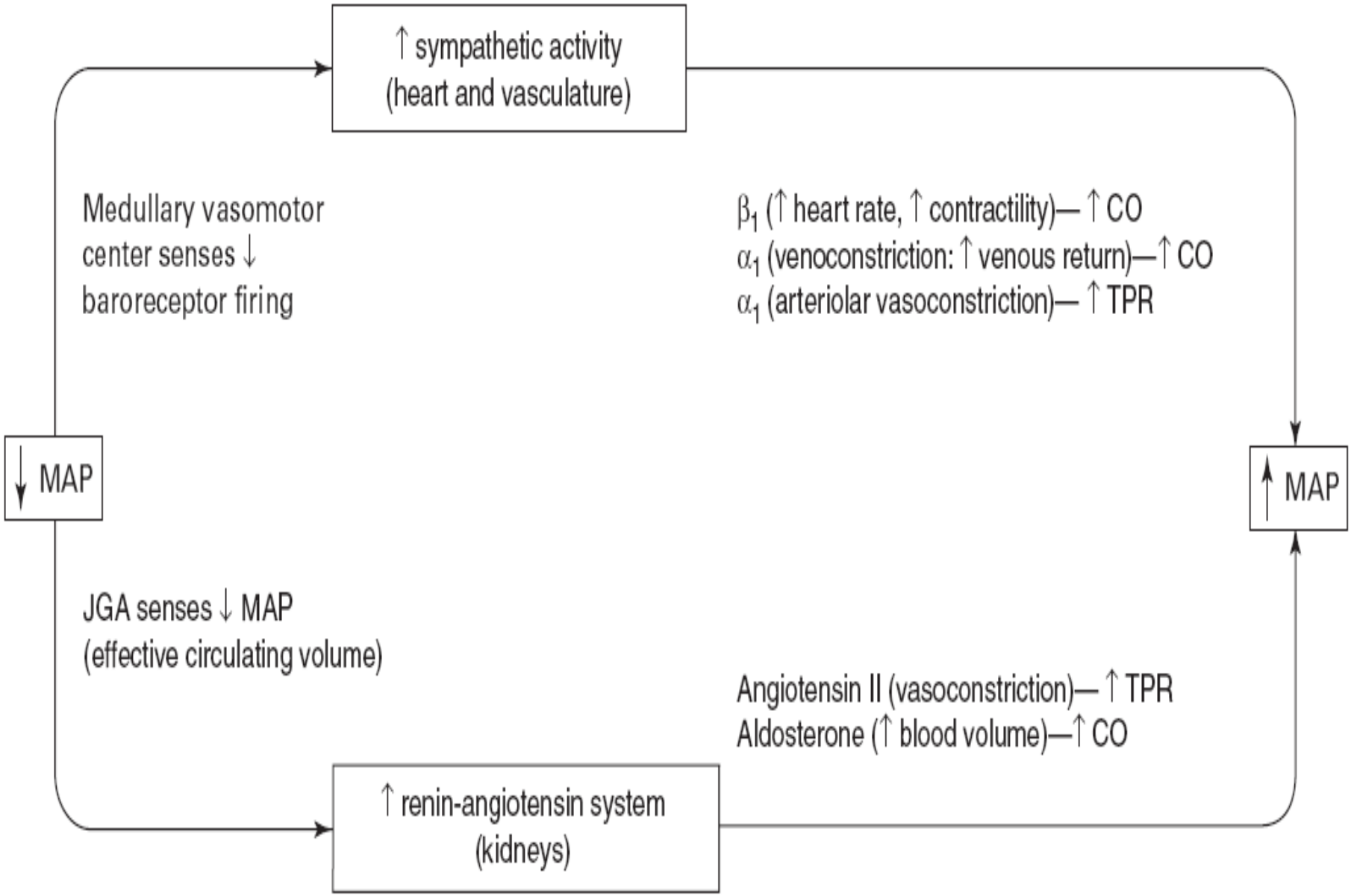
- Phase 1 - Atrial Contraction
- Phase 2 - Isovolumetric Contraction
- Phase 3 - Rapid Ejection
- Phase 4 - Reduced Ejection
- Phase 5 - Isovolumetric Relaxation
- Phase 6 - Rapid Filling
- Phase 7 - Reduced Filling


Left heart
Electrocardiogram
Heart sounds
QRS
P
T
P
1st
2nd
120
80
40
0
Pressure (mm Hg)
Dicrotic notch
Aorta
Left ventricle
Atrial systole
Left atrium
130
100
70
Ventricular volume (ml)
EDV
SV
ESV
Atrioventricular valves
Aortic and pulmonary valves
Phase
Open
Closed
Closed
Open
Open
Closed
1
2a
2b
3
1
(a)
Left atrium
Right atrium
Left ventricle
Right ventricle
Ventricular filling
Atrial contraction
Isovolumetric contraction phase
Ventricular ejection phase
Isovolumetric relaxation
Ventricular filling
1
2a
2b
3
1
Ventricular filling (mid-to-late diastole)
Ventricular systole (atria in diastole)
Early diastole
(b)



Pressure and Volume Relationships in the Cardiac Cycle

Control of mean arterial pressure



Cardiac output (CO)

Cardiac output (CO) = (stroke volume) × (heart rate).

Fick principle:

$$CO = \frac{\text{rate of } O_2 \text{ consumption}}{\text{arterial } O_2 \text{ content} - \text{venous } O_2 \text{ content}}$$

$$\text{Mean arterial pressure} = \begin{pmatrix}\text{cardiac}\\ \text{output}\end{pmatrix} \times \begin{pmatrix}\text{total peripheral}\\ \text{resistance}\end{pmatrix}$$

MAP = ⅔ diastolic pressure + ⅓ systolic pressure.

Pulse pressure = systolic pressure – diastolic pressure.

Pulse pressure is proportion to stroke volume.

$$SV = \frac{CO}{HR} = EDV - ESV$$

During exercise, CO ↑ initially as a result of an ↑ in SV. After prolonged exercise, CO ↑ as a result of an ↑ in HR.

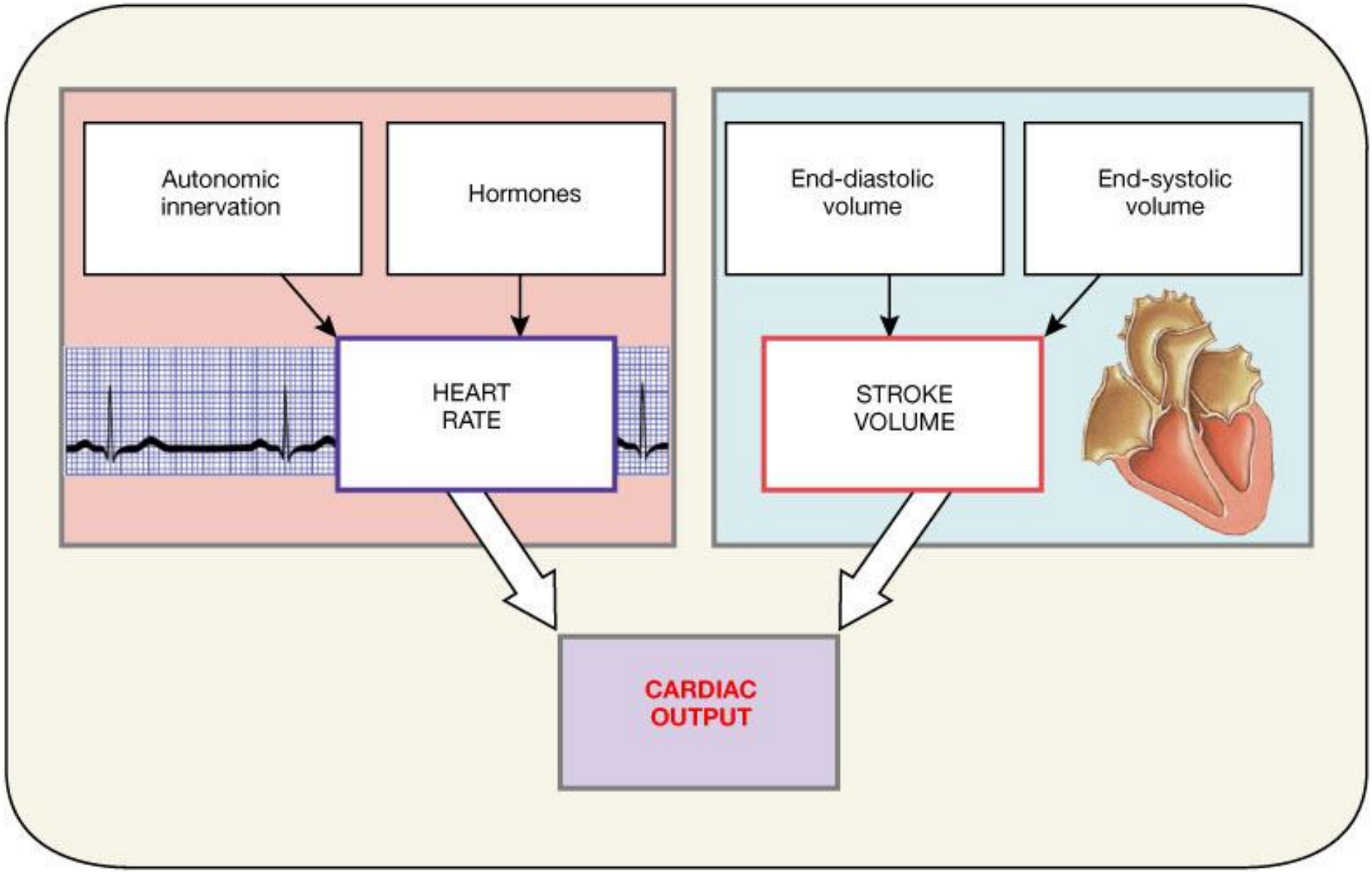
If HR is too high, diastolic filling is incomplete and CO ↓ (e.g., ventricular tachycardia).

Cardiac Output (CO) and Reserve

- CO is the amount of blood pumped by each ventricle in one minute
- CO is the product of heart rate (HR) and stroke volume (SV)
- HR is the number of heart beats per minute
- SV is the amount of blood pumped out by a ventricle with each beat
- Cardiac reserve is the difference between resting and maximal CO

- Cardiac Output CO is the amount of blood pumped by each ventricle in one minute
- CO is the product of heart rate (HR) and stroke volume (SV)
- HR is the number of heart beats per minute
- SV is the amount of blood pumped out by a ventricle with each beat
  - SV = EDV - ESV
  - EDV = amount of blood collected in a ventricle during diastole
  - ESV = amount of blood remaining in a ventricle after contraction
- Ejection Fraction (EF) = Stroke Volume / End Diastolic Volume
- Example of Cardiac Output
  - CO (ml/min) = HR (75 beats/min) x SV (70 ml/beat)
  - CO = _____

Factors Affecting Cardiac Output



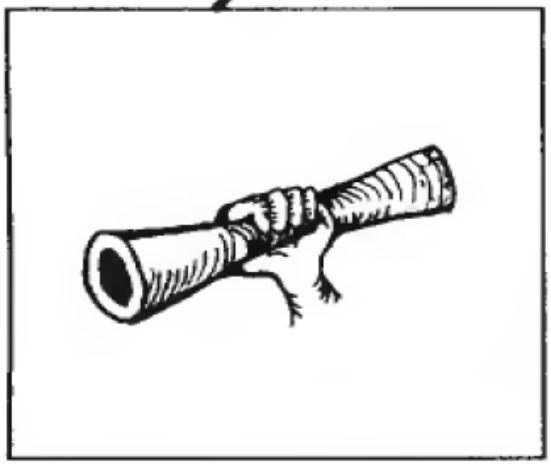
Factors Affecting Stroke Output

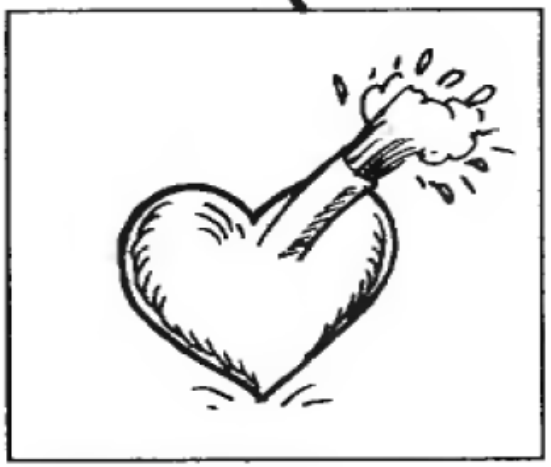
- Preload - amount ventricles are stretched by contained blood
- Contractility - cardiac cell contractile force due to factors other than EDV
  - Increase in contractility comes from:
    - Increased sympathetic stimuli
    - Certain hormones
    - Ca2+ and some drugs
  - **Agents/factors that decrease contractility:**
    - Acidosis
    - Increased extracellular K+
    - Calcium channel blockers
- **Afterload** -back pressure exerted by blood in the large arteries leaving the heart
- **Frank-Starling Law of the Heart**
  - Preload, or degree of stretch, of cardiac muscle cells before they contract is the critical factor controlling stroke volume
  - Slow heartbeat and exercise increase venous return to the heart, increasing SV

Frank-Starling Law of the Heart

- Preload, or degree of stretch, of cardiac muscle cells before they contract is the critical **factor controlling stroke volume;**
- **↑EDV leads to ↑stretch of myocard.**
  - **↑preload → ↑stretch of muscle → ↑force of contraction → ↑SV**
  - Unlike skeletal fibers, cardiac fibers contract MORE FORCEFULLY when stretched thus ejecting MORE BLOOD (↑SV)
  - If SV is increased, then ESV is decreased!!
- Slow heartbeat and exercise increase venous return (VR) to the heart, increasing SV
  - VR changes in response to blood volume, skeletal muscle activity, alterations in cardiac output
  - **↑VR → ↑EDV and ↓in VR → ↓ in EDV**
  - **Any ↓ in EDV → ↓ in SV**
- Blood loss and extremely rapid heartbeat decrease SV

↑ BLOOD PRESSURE





↑ PERIPHERAL RESISTANCE

- ↑Vasoconstriction
  - ↑ADH
  - ↑Renin/Angiotensin/Aldosterone
  - ↑Sympathetic stimulation of
    - α1 receptors (blood vessels)
    - β1 receptors (kidney glomerular cells)
  - Autoregulatory mechanisms
  - ↑Vascular reactivity
  - ↓Nitric oxide
- ↑Blood viscosity
- ↓Blood vessel elasticity

↑ CARDIAC OUTPUT

- ↑Blood volume
  - ↑Sodium intake
    - Osmotic effect on water retention
    - ↑Osmolality causes thirst
    - ↑Osmolality stimulates ADH secretion
  - ↑Aldosterone
  - ↓ANF
  - ↑ADH
  - ↑Water intake
  - ↓Water output
- ↑Sympathetic stimulation
- ↓Parasympathetic stimulation
- Starling's Law

LOCATION AND EFFECTS OF STIMULATION OF ADRENERGIC RECEPTORS

ALPHA-1 RECEPTORS

Arterioles and Veins:
constriction (epinephrine and norepinephrine)

Glands:
↓ secretions

Eye:
constriction of radial muscle

Intestine:
↓ motility

ALPHA-2 RECEPTORS

CNS Postsynaptic Terminals:
↓ sympathetic outflow from brain

CNS Presynaptic Terminals:
norepinephrine release

Beta Islet Cells of Pancreas:
↓ secretion

BETA-1 RECEPTORS

Heart:
↑ heart rate (SA node)
↑ contractility
↑ conduction velocity
↑ automaticity

Kidney:
↑ renin secretion

BETA-2 RECEPTORS

Trachea and Bronchioles:
dilation

Pregnant/nonpregnant Uterus:
relaxation

Arterioles (no beta-2 receptors in skin or brain):
dilation (epinephrine)

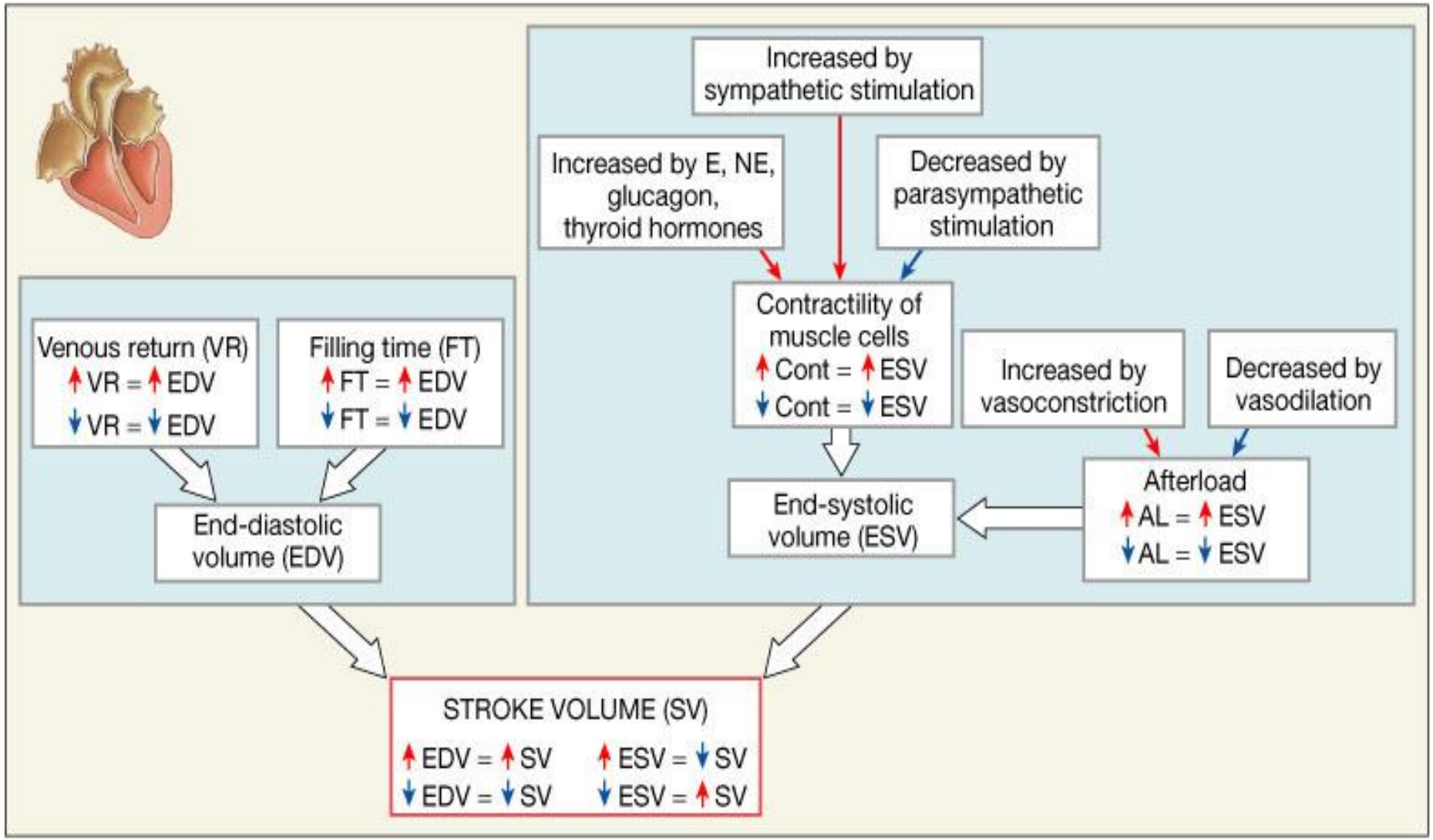
Cardiac Output: Example

- CO (ml/min) = HR (75 beats/min) x SV (70 ml/beat)
- CO = 5250 ml/min (5.25 L/min)

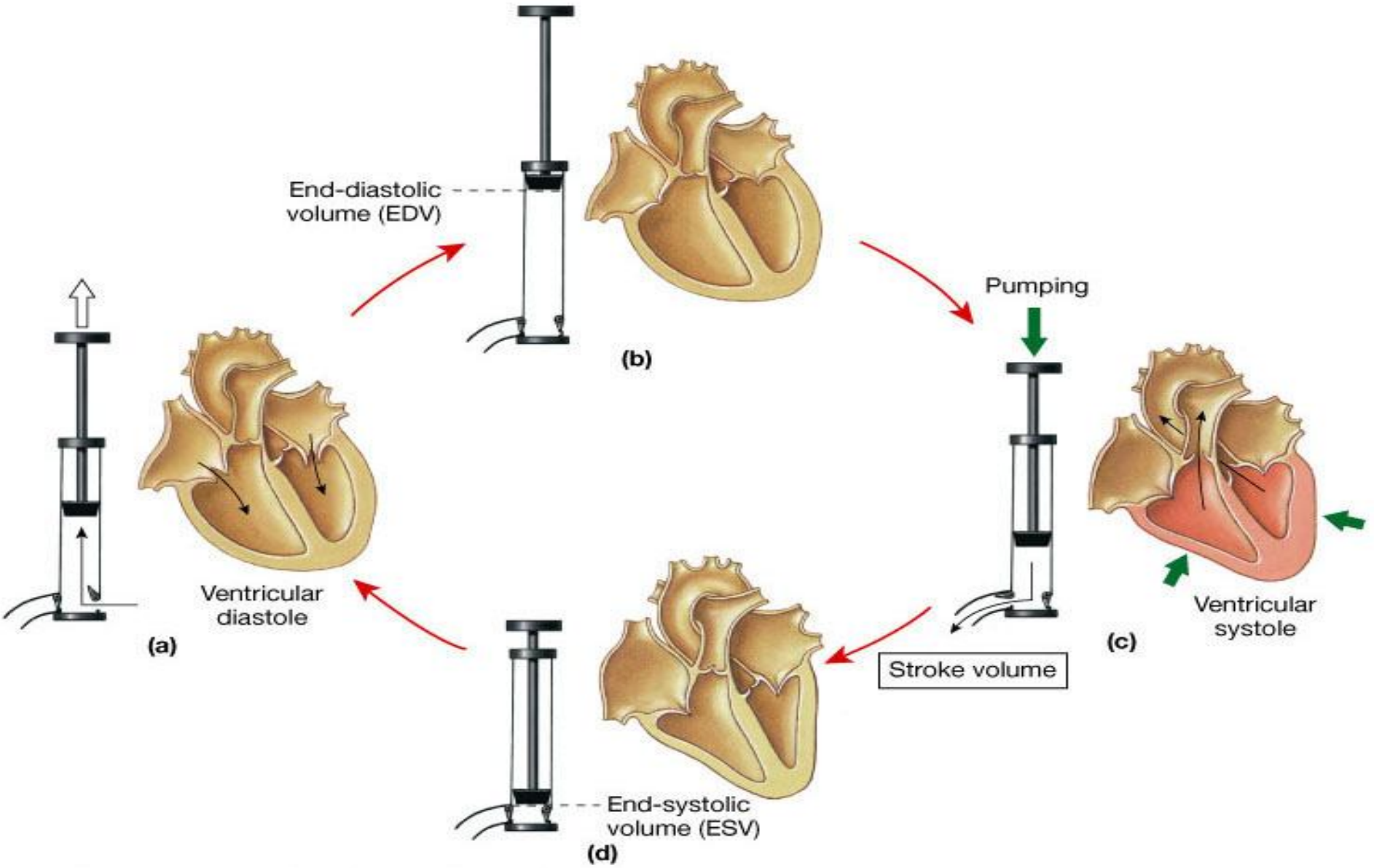
Regulation of Stroke Volume

- SV = end diastolic volume (EDV) minus end systolic volume (ESV)
- EDV = amount of blood collected in a ventricle during diastole
- ESV = amount of blood remaining in a ventricle after contraction

Factors Affecting Stroke Volume



A Simple Model of Stroke Volume



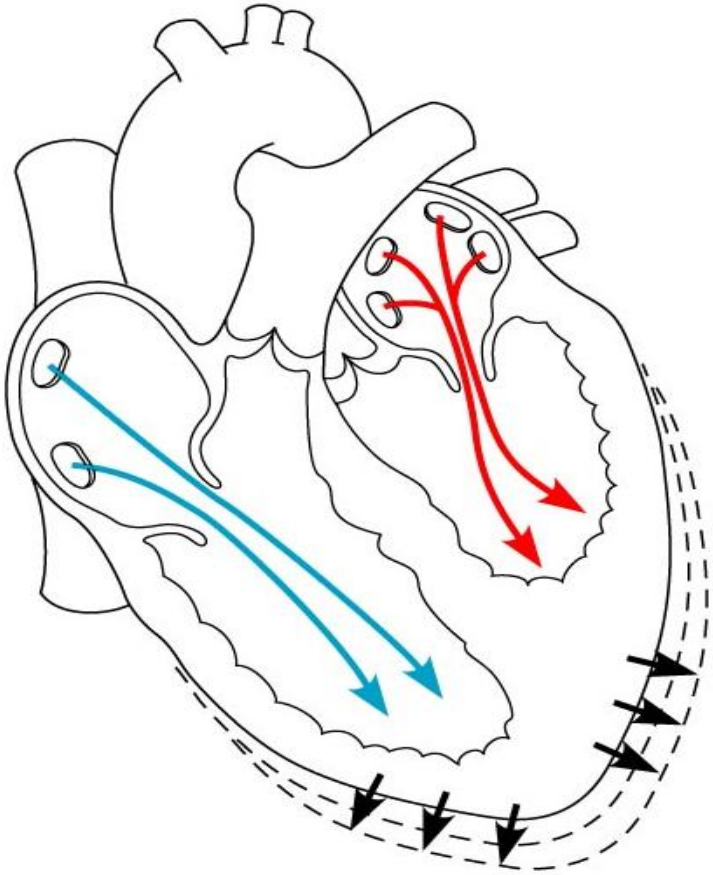
Factors Affecting Stroke Volume

- Preload – amount ventricles are stretched by contained blood
- Contractility – cardiac cell contractile force due to factors other than EDV
- Afterload – back pressure exerted by blood in the large arteries leaving the heart

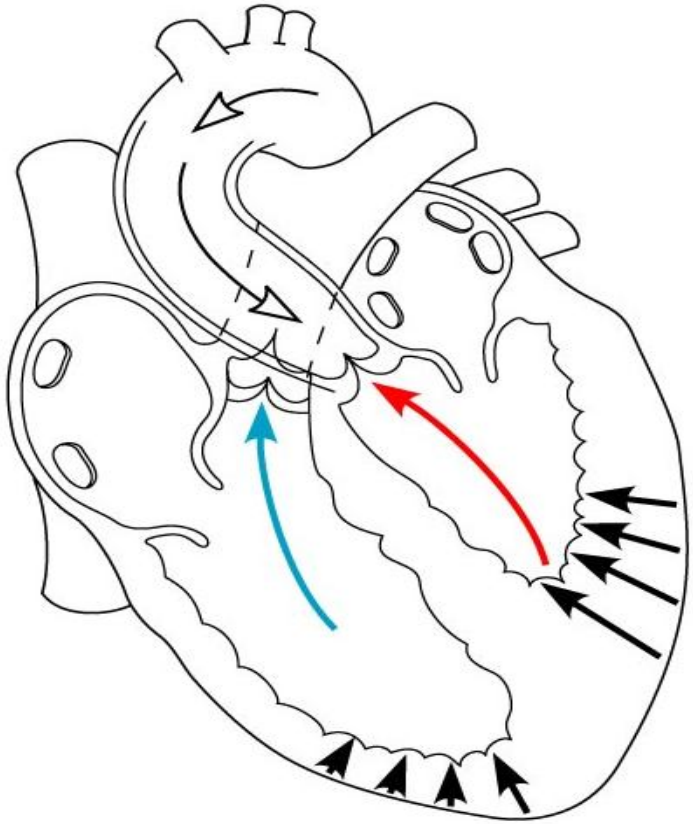
Frank-Starling Law of the Heart

- Preload, or degree of stretch, of cardiac muscle cells before they contract is the critical factor controlling stroke volume
- Slow heartbeat and exercise increase venous return to the heart, increasing SV
- Blood loss and extremely rapid heartbeat decrease SV

Preload and Afterload



(a) Preload



(b) Afterload

Figure 18.21

Cardiac output variables

Stroke Volume affected by Contractility, Afterload, and Preload. ↑ SV when ↑ preload, ↓ afterload, or ↑ contractility.

Contractility (and SV) ↑ with:

1. Catecholamines (↑ activity of Ca^{2+} pump in sarcoplasmic reticulum)
2. ↑ intracellular calcium
3. ↓ extracellular sodium
4. Digitalis (↑ intracellular Na^+, resulting in ↑ Ca^{2+})

Contractility (and SV) ↓ with:

1. β_1 blockade
2. Heart failure
3. Acidosis
4. Hypoxia/hypercapnea
5. Non-dihydropyridine Ca^{2+} channel blockers

SV CAP.

SV ↑ in anxiety, exercise, and pregnancy.

A failing heart has ↓ SV.

Myocardial O_2 demand is ↑ by:

1. ↑ afterload (∝ arterial pressure)
2. ↑ contractility
3. ↑ heart rate
4. ↑ heart size (↑ wall tension)

Preload and afterload

Preload = ventricular EDV.

Afterload = mean arterial pressure (proportional to peripheral resistance).

Venodilators (e.g., nitroglycerin) ↓ preload.

Vasodilators (e.g., hydralazine) ↓ afterload.

Preload ↑ with exercise (slightly), ↑ blood volume (overtransfusion), and excitement (sympathetics). Preload pumps up the heart.

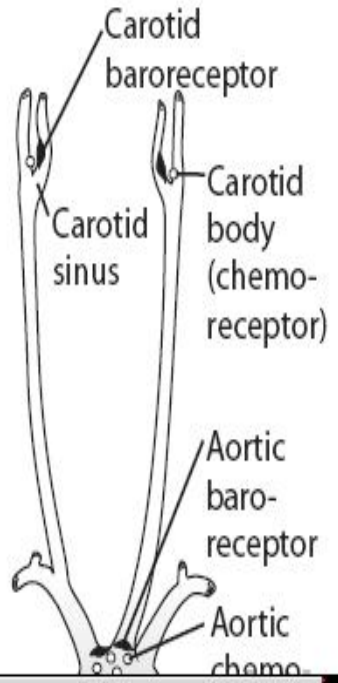
Extrinsic Factors Influencing Stroke Volume

- Contractility is the increase in contractile strength, independent of stretch and EDV
- Increase in contractility comes from:
  - Increased sympathetic stimuli
  - Certain hormones
  - Ca^{2+} and some drugs

Extrinsic Factors Influencing Stroke Volume

- Agents/factors that decrease contractility include:
  - Acidosis
  - Increased extracellular K^+
  - Calcium channel blockers

Baroreceptors and chemoreceptors



Receptors:

1. Aortic arch transmits via vagus nerve to medulla (responds only to ↑ BP)
2. Carotid sinus transmits via glossopharyngeal nerve to medulla (responds to ↓ and ↑ in BP).

Baroreceptors:

1. Hypotension—↓ arterial pressure → ↓ stretch → ↓ afferent baroreceptor firing → ↑ efferent sympathetic firing and ↓ efferent parasympathetic stimulation → vasoconstriction, ↑ HR, ↑ contractility, ↑ BP. Important in the response to severe hemorrhage.
2. Carotid massage—↑ pressure on carotid artery → ↑ stretch → ↑ afferent baroreceptor firing → ↓ HR

Heart Contractility and Norepinephrine

- Sympathetic stimulation releases norepinephrine and initiates a cyclic AMP second-messenger system

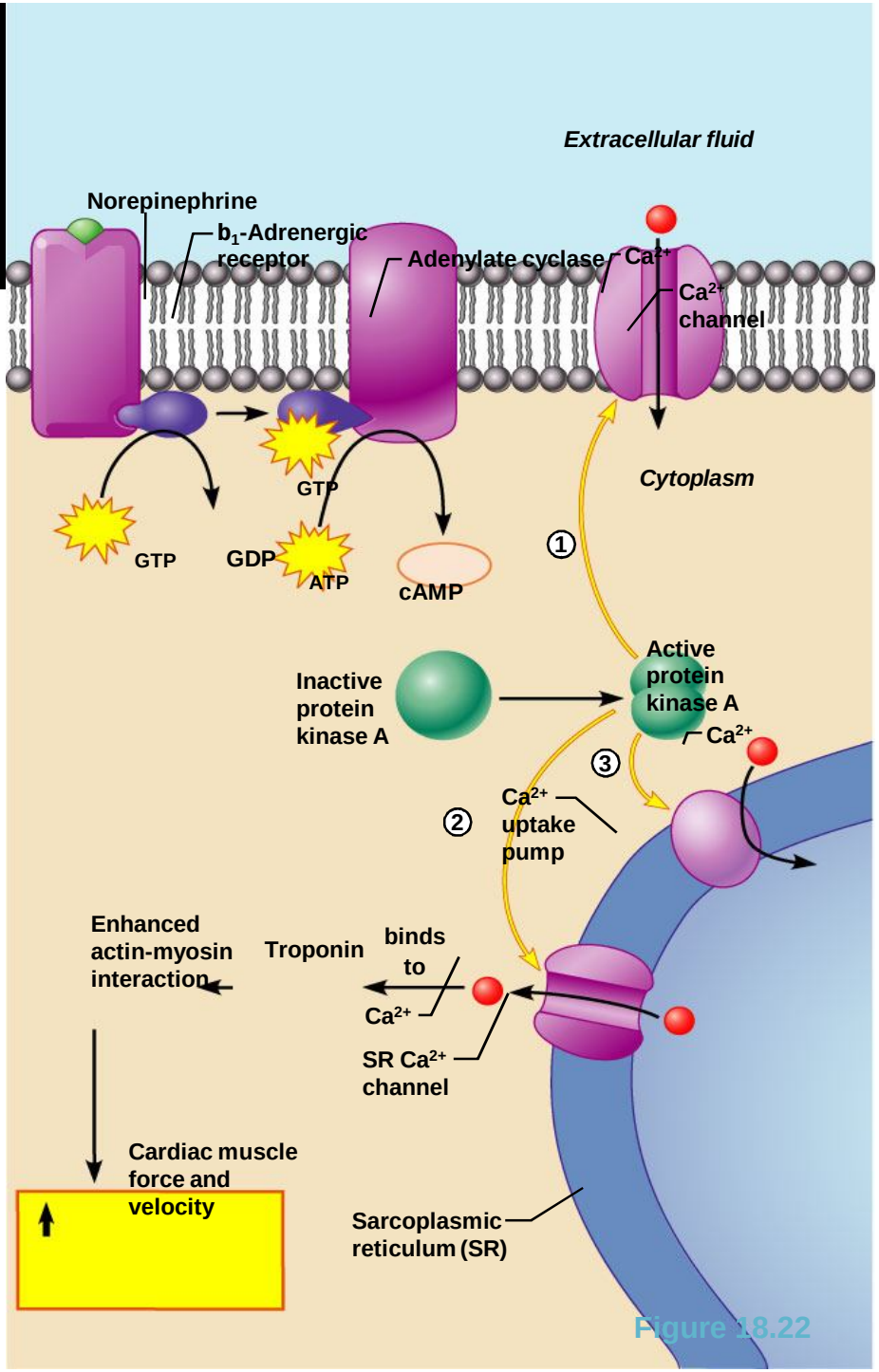


Figure 18.22

Regulation of Heart Rate

- Positive chronotropic factors increase heart rate
- Negative chronotropic factors decrease heart rate

Regulation of Heart Rate: Autonomic Nervous System

- Sympathetic nervous system (SNS) stimulation is activated by stress, anxiety, excitement, or exercise
- Parasympathetic nervous system (PNS) stimulation is mediated by acetylcholine and opposes the SNS
- PNS dominates the autonomic stimulation, slowing heart rate and causing vagal tone

Atrial (Bainbridge) Reflex

- Atrial (Bainbridge) reflex – a sympathetic reflex initiated by increased blood in the atria
  - Causes stimulation of the SA node
  - Stimulates baroreceptors in the atria, causing increased SNS stimulation

Chemical Regulation of the Heart

- The hormones epinephrine and thyroxine increase heart rate
- Intra- and extracellular ion concentrations must be maintained for normal heart function

Factors Involved in Regulation of Cardiac Output

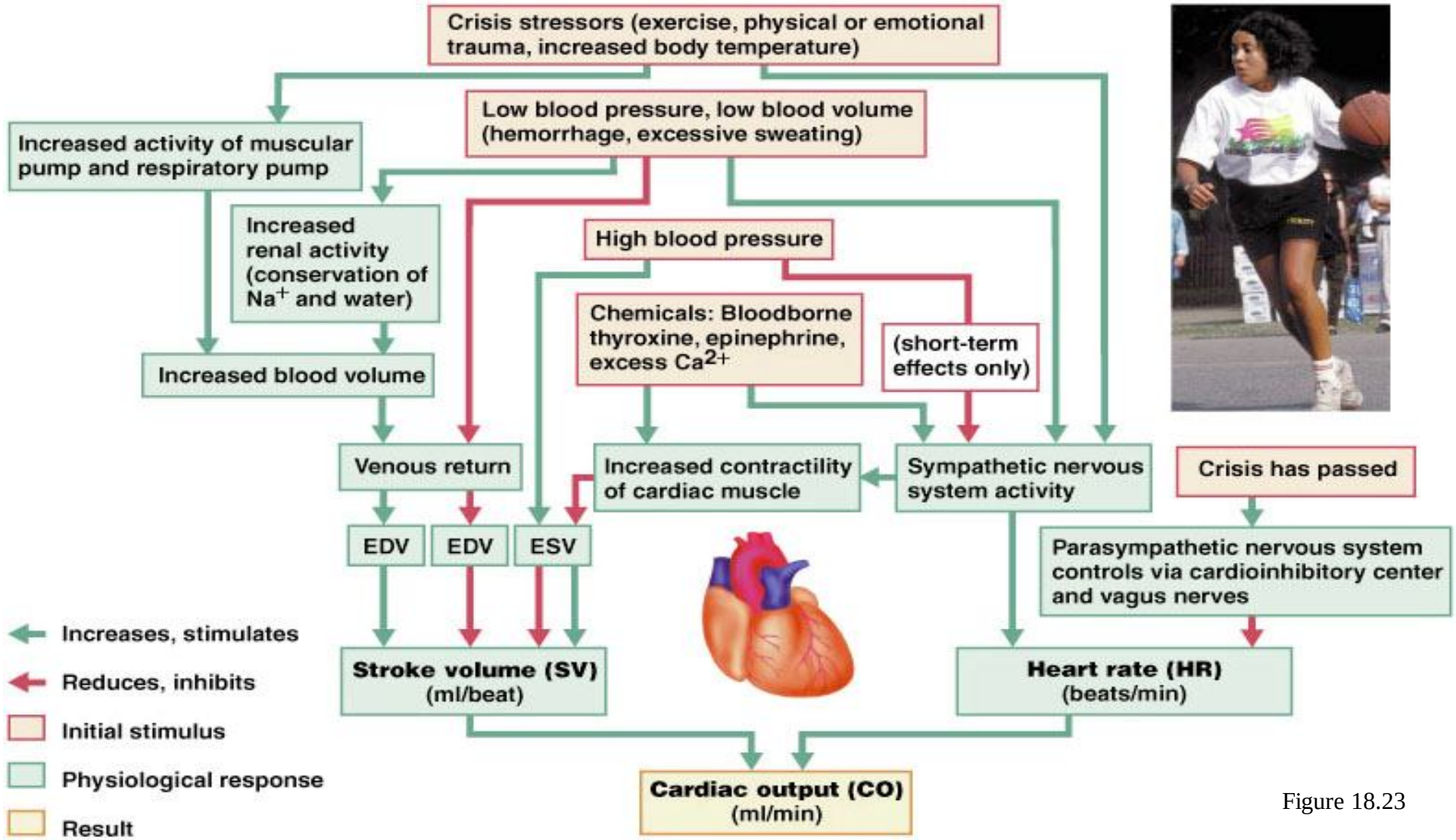


Figure 18.23

Circulation through organs

Liver	Largest share of systemic cardiac output.
Kidney	Highest blood flow per gram of tissue.
Heart	Large arteriovenous O_2 difference. ↑ O_2 demand is met by ↑ coronary blood flow, not by ↑ extraction of O_2.

Autoregulation

Organ	Factors determining autoregulation
Heart	Local metabolites—O_2, adenosine, NO
Brain	Local metabolites—CO_2 (pH)
Kidneys	Myogenic and tubuloglomerular feedback
Lungs	Hypoxia causes vasoconstriction
Skeletal muscle	Local metabolites—lactate, adenosine, K^+
Skin	Sympathetic stimulation most important mechanism—temperature control

Note: the pulmonary vasculature is unique in that hypoxia causes vasoconstriction. In other organs, hypoxia causes vasodilation.

Regulation of blood circulation

Mechanisms of regulation:

- **Local**
  - Humoral (chemical) – O_2, CO_2, H^+
  - Nervous
  - Enzymatic and hormonal
- **General**
  - **Fast** = short-term (regulate blood pressure)
  - **Slow** = long-term (regulate blood volume) – several days

Local chemical regulatory mechanisms

- The most obvious in the heart and the brain
- **Goal:** autonomic regulation of resistance by organ based on its metabolic needs
- **Principal:** accumulation of products of metabolism (CO_2, H^+, lactacid) or consumption of substances necessary for proper function (O_2) directly affects smooth muscles of vessels and induce **vasodilatation**

Local nervous regulatory mechanisms

- The most obvious in the skin and mucous
- **Goal:** central regulation of blood distribution
- **Principal:** Autonomic nervous system
  - **Sympaticus**
    - **Vasoconstriction** – activation of **α** receptors in vessels- noradrenalin (glands, GIT, skin, mucous, kidneys, other inner organs)
    - **Vasodilatation** – activation of **β** receptors in vessels – adrenalin (heart, brain, skeletal muscles)
  - **Parasympaticus** - Acetylcholin
    - **Vasoconstriction** – heart
    - **Vasodilatation** – salivatory glands, GIT, external genitals

Local enzymatic and hormonal regulatory mechanisms

- **Kinin ↑ = vasodilatation**
  - Cells of GIT glands contain **kallikrein** – changes kininogen to kinin → kallidin → **bradykinin** (vasodilatation)
  - **Kinins** are any of various structurally related polypeptides, such as bradykinin and kallikrein, that act locally to induce vasodilation and contraction of smooth muscle.
  - A role in inflammation, blood pressure control, coagulation and pain.
- **Hormones of adrenal medula:** adrenalin (vasodilatation), noradrenalin (vasoconstriction)

General fast (short-term) regulatory mechanisms (1)

- **Nervous autonomic reflexes**
  - **Baroreflex**
    - glomus caroticum, glomus aorticum
    - Afferentation: IX and X spinal nerve
    - Centre: medulla oblongata, nucleus tractus solitarii
    - Efferentation: X spinal nerve, sympatetic fibres
    - Effector: heart (atriums), vessels
    - Effect: After acute increase of blood pressure – activation of receptors – decrease of blood pressure (vasodilatation, decrease of effect of sympaticus)

General fast (short-term) regulatory mechanisms (2)

- **Receptors in the heart**
  - **Reflex of atrial receptors – mechano- and volumoreceptors** – activated by increased blood flow through the heart
    - A receptors – sensitive to ↑ of wall tension after systole of atriums
    - B receptors – sensitive to ↑ of wall tension after systole of ventricles
  - **Ventricular receptors** – mechano- and chemical receptors - activated in pathological cases
    - Hypoxia of myocardium → decrease of heart rate (Bezold-Jarisch reflex) → protection of myocardium of larger damage

General fast (short-term) regulatory mechanisms (3)

- **Humoral mechanisms**
  - **Adrenalin** – β receptors → vasodilatation → ↓ peripheral resistance → blood from skin and GIT to skeletal muscles, heart and brain → ↑ **minute heart volume**
  - **Noradrenalin** – α receptors → vasoconstriction → ↑ **blood pressure**
  - **Renin-angiotensin** – activated by ↓ pressure in vas afferens

General slow (long-term) regulatory mechanisms

Regulatory mechanisms of water and electrolytes exchanges

- **Regulation of total blood volume by kidneys**
  - When ↑ blood pressure → ↑ of filtration pressure in glomeruli → ↑ production of urine → ↓ volume of circulating blood → ↓ blood pressure
- **Increase of ADH (vasopressin)**
  - ↑ ADH → ↑ of the permeability of collecting ductus for the water → water is reabsorbed → ↑ volume of circulating blood → ↑ blood pressure
- **Increase of Aldosterone**
  - ↑ aldosterone → ↑ reabsorbtion Na^+ and water → ↓ volume of urine → ↑ volume of circulating blood → ↑ blood pressure

Intracardial regulatory mechanisms (1)

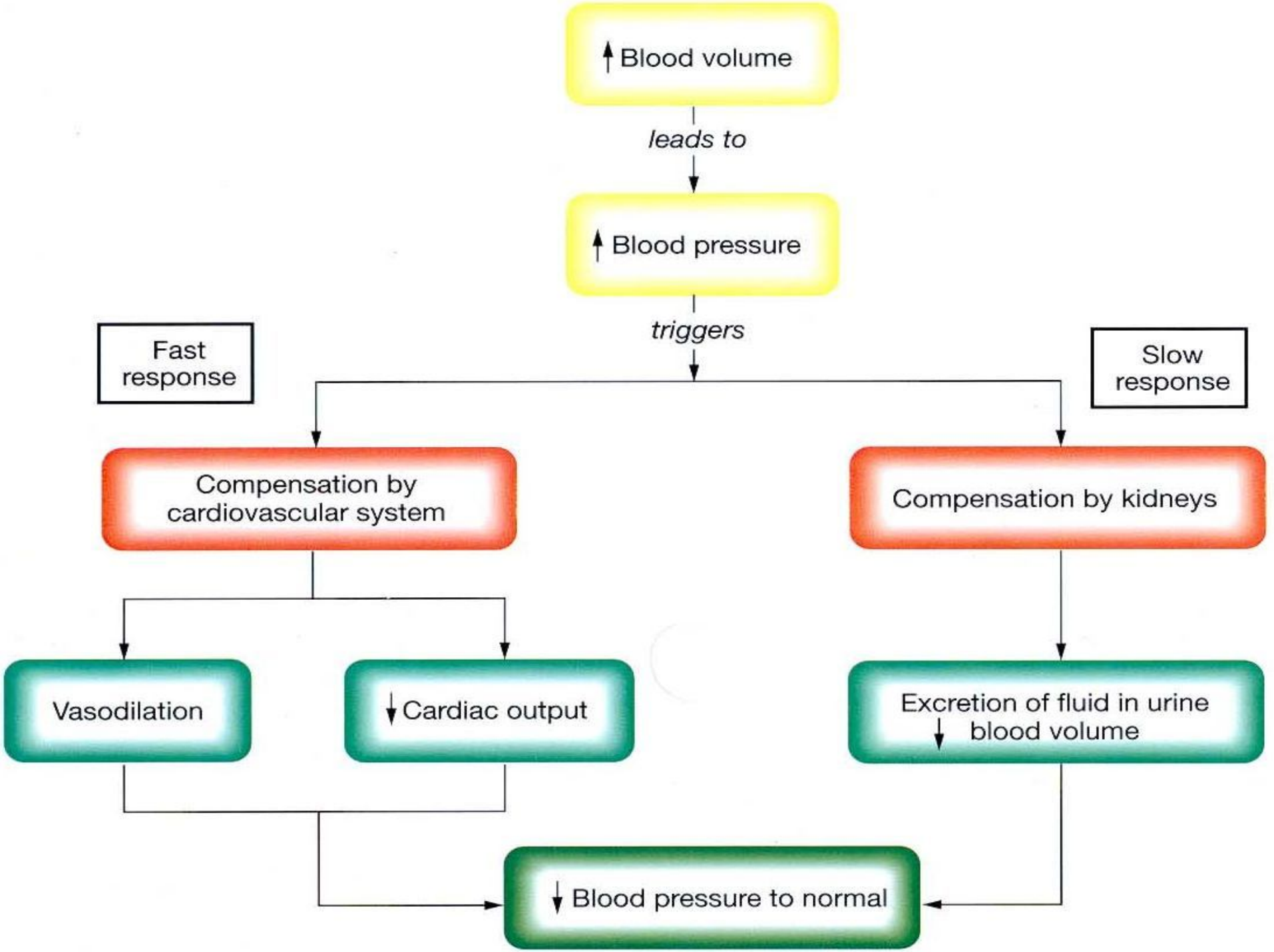
- **Frank-Starling's law** = initial length of the fibers is determined by the degree of diastolic filling of the heart, and the pressure developed in the ventricle is proportionate to the total tension developed.
- The developed tension increases as the diastolic volume increases until it reaches a maximum, then tends to decrease.

Intracardial regulatory mechanisms (2)

- **Ionotropic effect of heart rhythm**
  - ↑ heart frequency → ↑ amount of Ca^{2+} that goes into heart cells → ↑ Ca^{2+} available for tubules of sarkoplasmatic reticulum → ↑ Ca^{2+} that is freed by each contraction → **↑ strength of contraction**

Extracardial regulatory mechanisms

- **Cardiomotoric centers**
  - **Inhibition** – ncl. Ambiguus (beginning of n. vagus in medulla oblongata)
  - **Excitation** - Th1-3 beginning of sympathetic fibres
- **Vasomotoric centers**
  - In **brain stem** (medulla oblongata, Pons Varoli)
  - In the **hypothalamus** (controls activity of vasomotoric centers in brain stem)
  - Brain **cortex** – control both the hypothalamus and the brain stem


↑ Blood volume
leads to
↑ Blood pressure
triggers
Fast response
Slow response
Compensation by cardiovascular system
Compensation by kidneys
Vasodilation
↓ Cardiac output
Excretion of fluid in urine
↓ blood volume
↓ Blood pressure to normal

Resistance, pressure, flow

$\Delta P = Q \times R$

Similar to Ohm's law: $\Delta V = IR$.

$$\text{Resistance} = \frac{\text{driving pressure } (\Delta P)}{\text{flow } (Q)} = \frac{8\eta \text{ (viscosity)} \times \text{length}}{\pi r^4}$$

Viscosity depends mostly on hematocrit.

Viscosity ↑ in:

1. Polycythemia
2. Hyperproteinemic states (e.g., multiple myeloma)
3. Hereditary spherocytosis

Resistance is directly proportional to viscosity and inversely proportional to the radius to the 4th power.

Arterioles account for most of total peripheral resistance → regulate capillary flow.

Ejection fraction (EF)

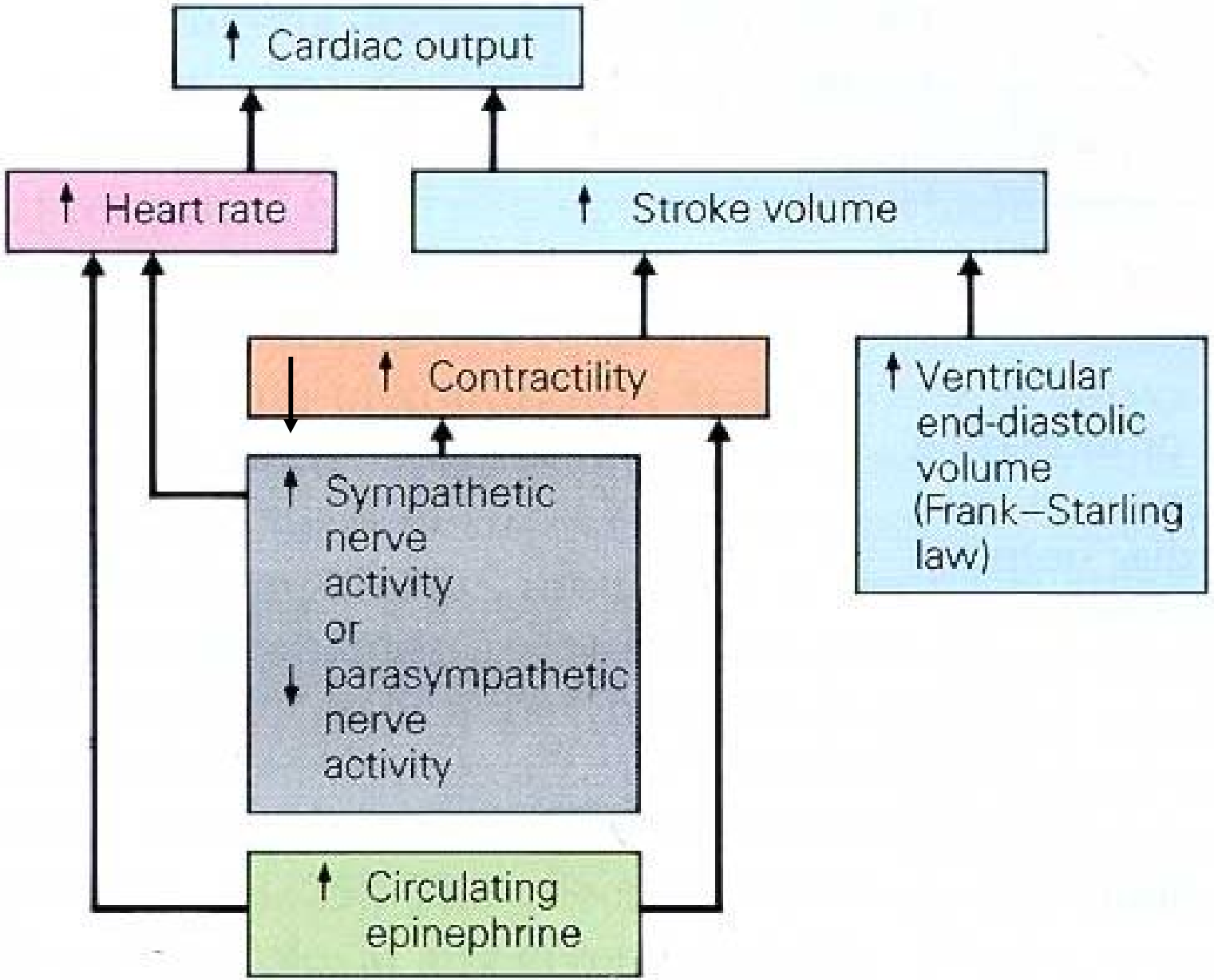
$$EF = \frac{SV}{EDV} = \frac{EDV - ESV}{EDV}$$

EF is an index of ventricular contractility.

EF is normally ≥ 55%.

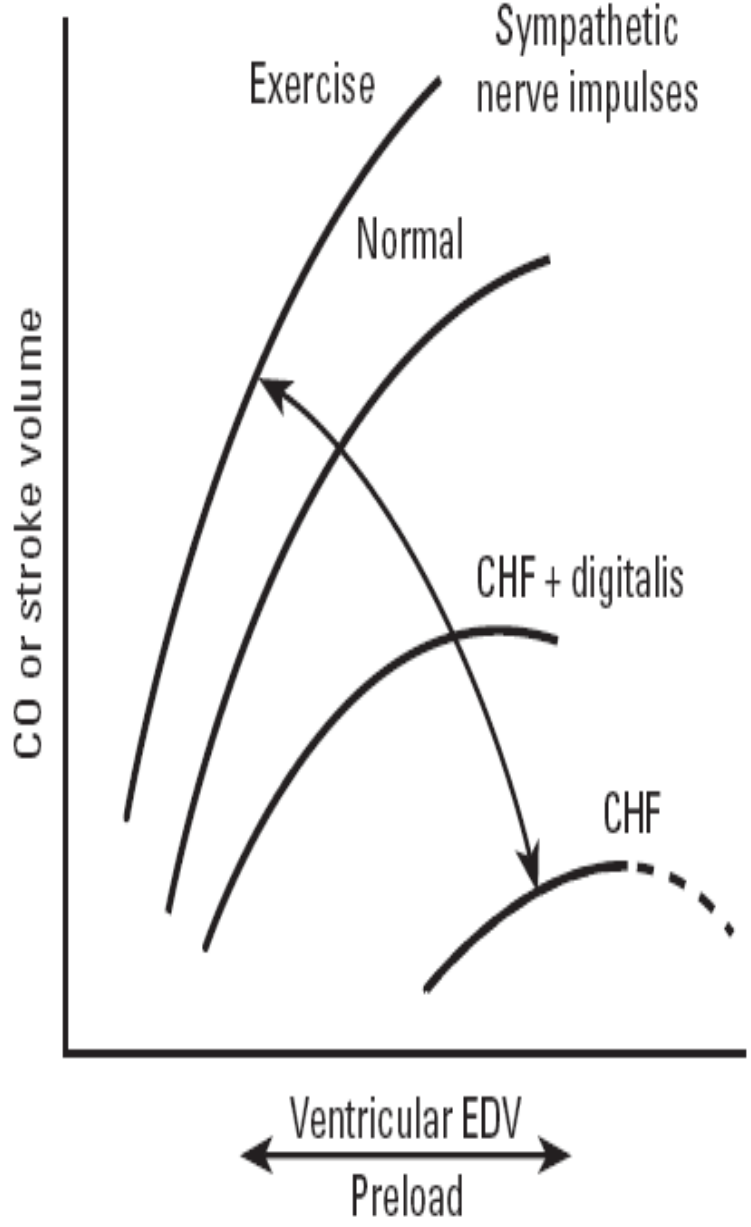
Control of the Heart

Summary of mechanisms that affect cardiac output.



Starling curve

Force of contraction is proportional to initial length of cardiac muscle fiber (preload).



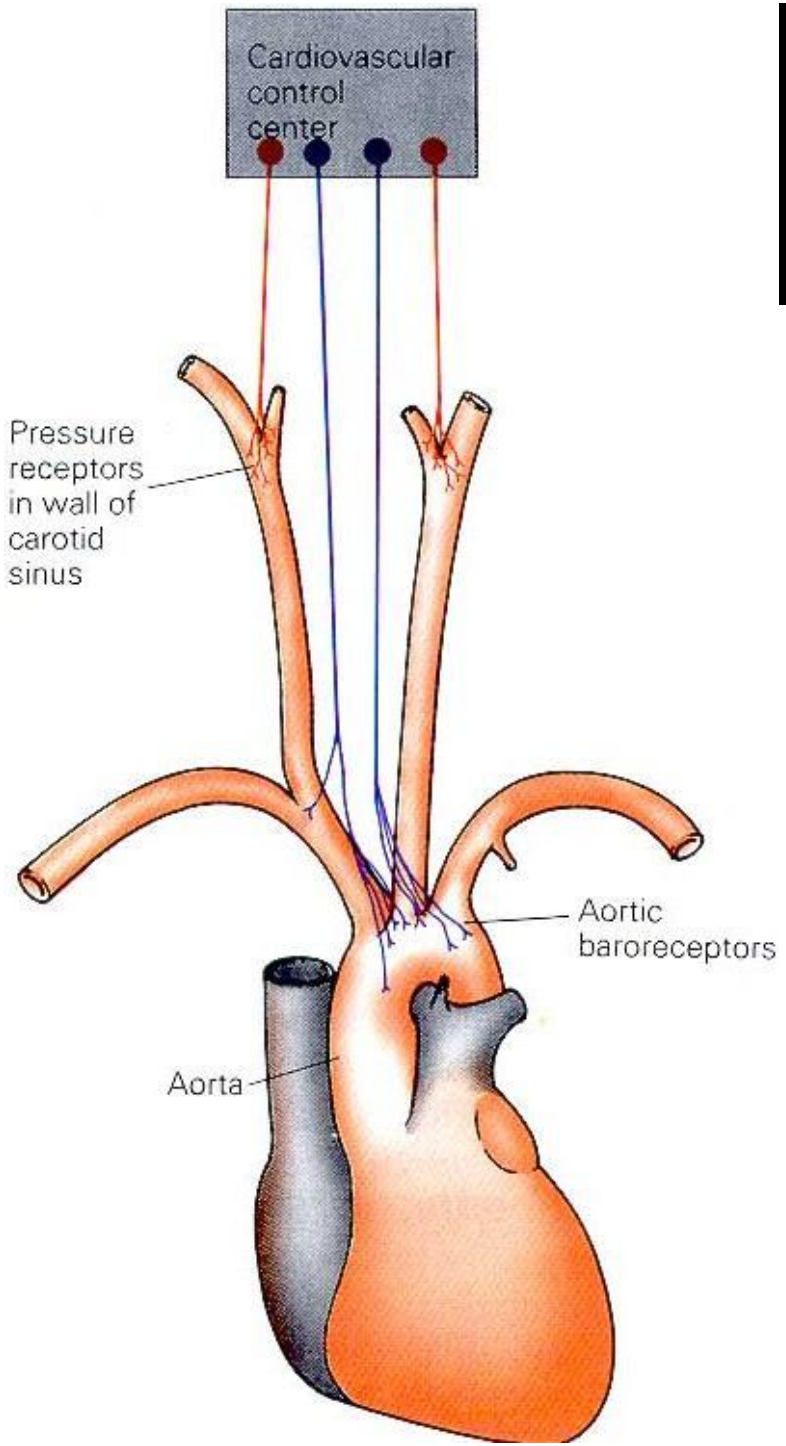
CONTRACTILE STATE OF MYOCARDIUM

⊕	⊖
Circulating catecholamines	Pharmacologic depressants
Digitalis	Loss of myocardium (MI)
Sympathetic stimulation	

Factors Controlling Blood Pressure

- ↑ Peripheral resistance → ↑ mean arterial pressure
- ↑Cardiac output → ↑ mean arterial pressure
- ↑Stroke volume → ↑ pulse pressure
- ↓ Arterial compliance → ↑pulse pressure
- ↑Heart Rate → ↓pulse pressure
- ↑Blood Volume → ↑ arterial & venous

The Baroreceptor Reflex



Changes in central arterial pressure are detected by baroreceptors (pressure receptors) in the carotid and aortic arteries. These receptors provide information to the cardiovascular centres in the hind brain.

Carotid baroreceptors are located in the carotid sinus at the branch of the carotid artery.
Aortic baroreceptors are less sensitive than carotid pressure receptors.

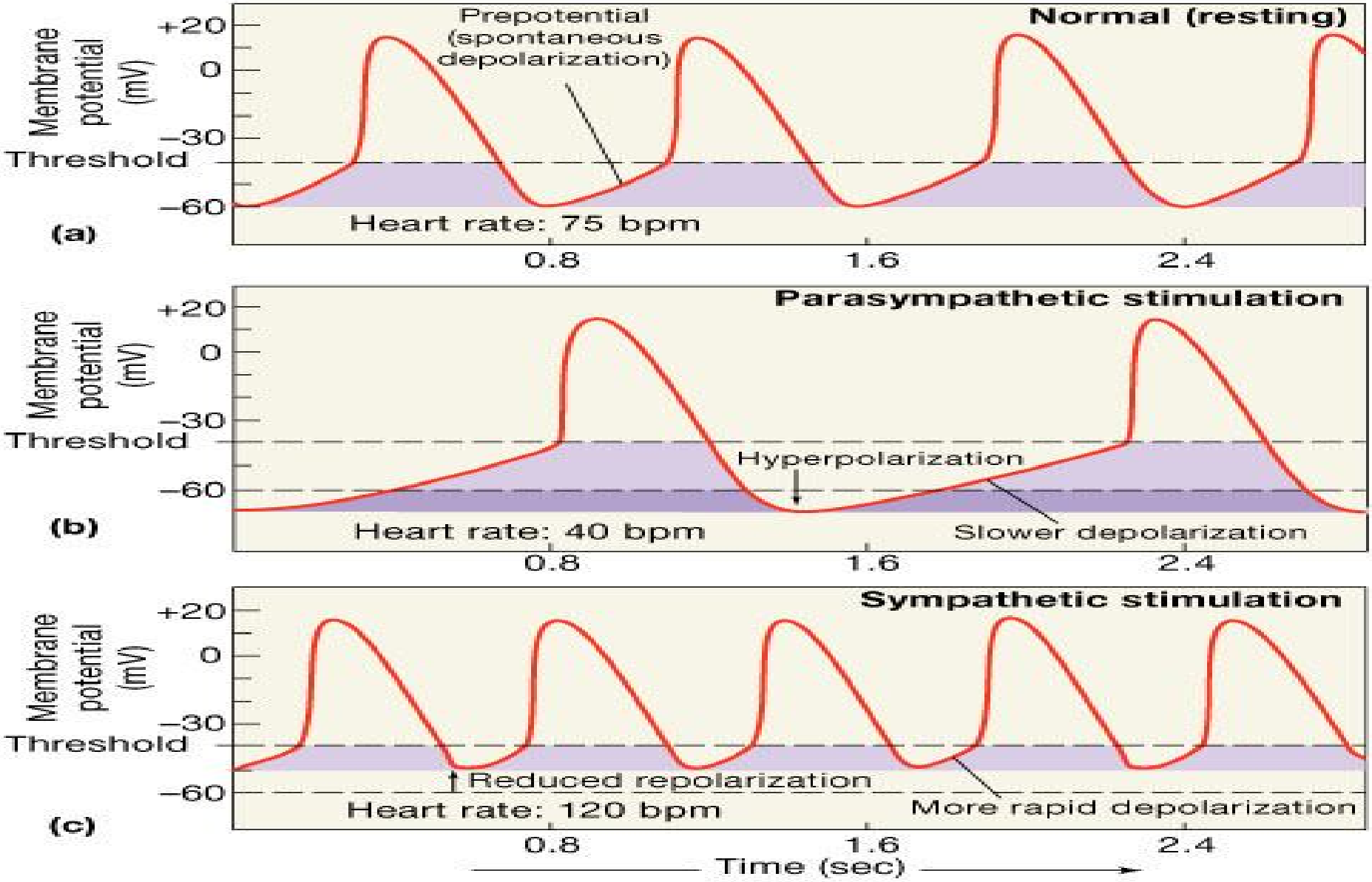
Vascular Baroreceptor Reflex

- Reduced arterial blood pressure decreased baroreceptor activity.
- Increased sympathetic tone to blood vessels.

- Elevated total peripheral resistance and blood pressure.
- (Coronary and cerebral circulation are largely unaffected.)

- Elevated venous tone.
- Reduced venous capacitance, reduced venous volume.
- Increased circulating volume, increased venous return.
- Increased stroke volume, cardiac output and blood pressure.

Pacemaker Function



Acute Autoregulation

Three mechanisms have been suggested to explain acute autoregulation.

1) Myogenic mechanisms

2) Tissue pressure

3) local metabolites

Myogenic Mechanism

- Increased pressure increases arteriolar wall tension.
- Vascular smooth muscle contracts when stretched and relaxed when passively shortened.
- Action is purely myogenic, no mediators required.
- Involves stretch sensitive ion channels on the cell membrane.

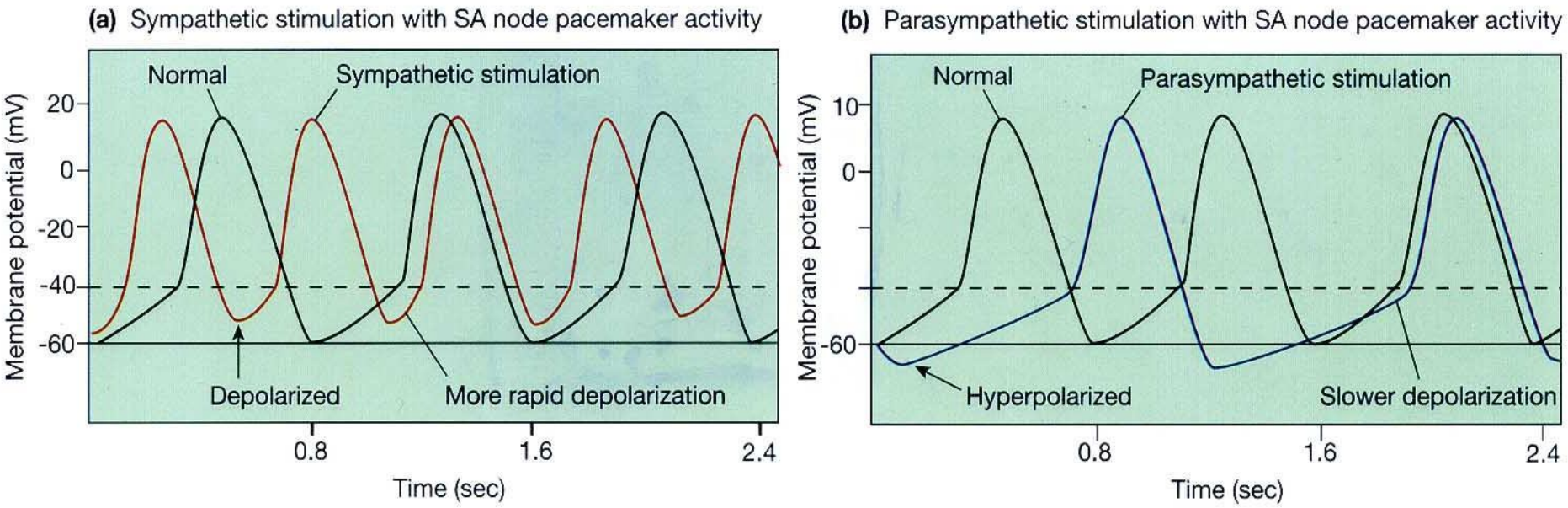
Summary of Metabolic Mediators

♥ O_2	Vasoconstrictor (not pulmonary)(import. brain)
♥ Glucose	vasoconstrictor (at least coronary vessels)
♥ K^+	Vasodilator (skeletal muscle)
♥ CO_2	vasodilator (not pulmonary)(import. brain)
♥ adenosine	vasodilator (coronary)
♥ H^+	vasodilator (import. brain)
♥ PO_4^{3-}	vasodilator
♥ osmolarity	vasodilator

Inputs to blood pressure control includes

- Sympathetic activity
- Parasympathetic activity
- Chemical secretion
- Kidney

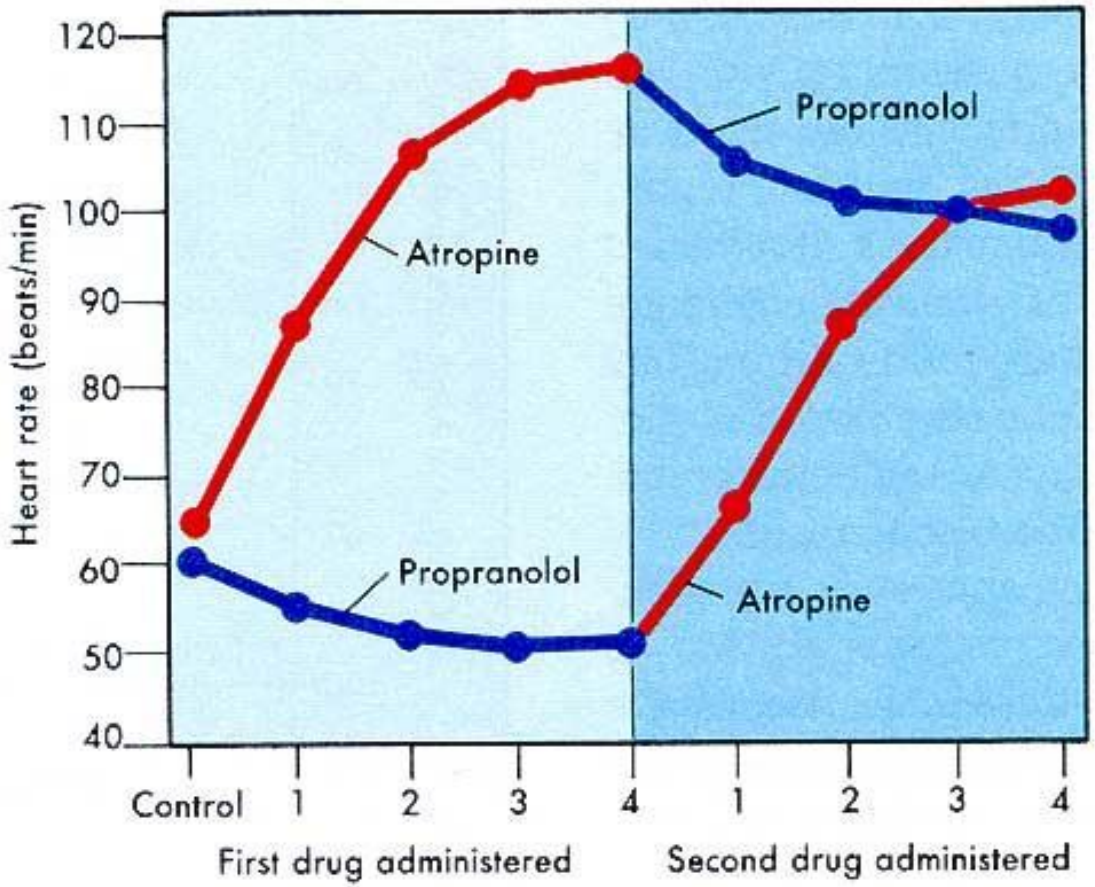
Neural Control of Heart Rate



Noradrenaline (NA) from sympathetic nerves and circulating adrenaline, increase the heart rate and enhances conduction of the AP.

Acetylcholine (ACh) released from parasympathetic nerves reduces the heart rate and conduction across the AV node.

Resting Autonomic Control of Heart Rate



At rest heart rate is under both sympathetic and parasympathetic tone.

Normally the parasympathetic inhibition of rate is larger than the sympathetic stimulation.

Sympathetic activity regulation

- It regulates the action potential frequency of the SA node.
- Regulates vasoconstriction.
- Regulates venomotor tone.
- Stimulate the secretion of epinephrine and renin.

Parasympathetic activity regulation,

- Through the release of Ach, it controls the action potential frequency of the SA node.

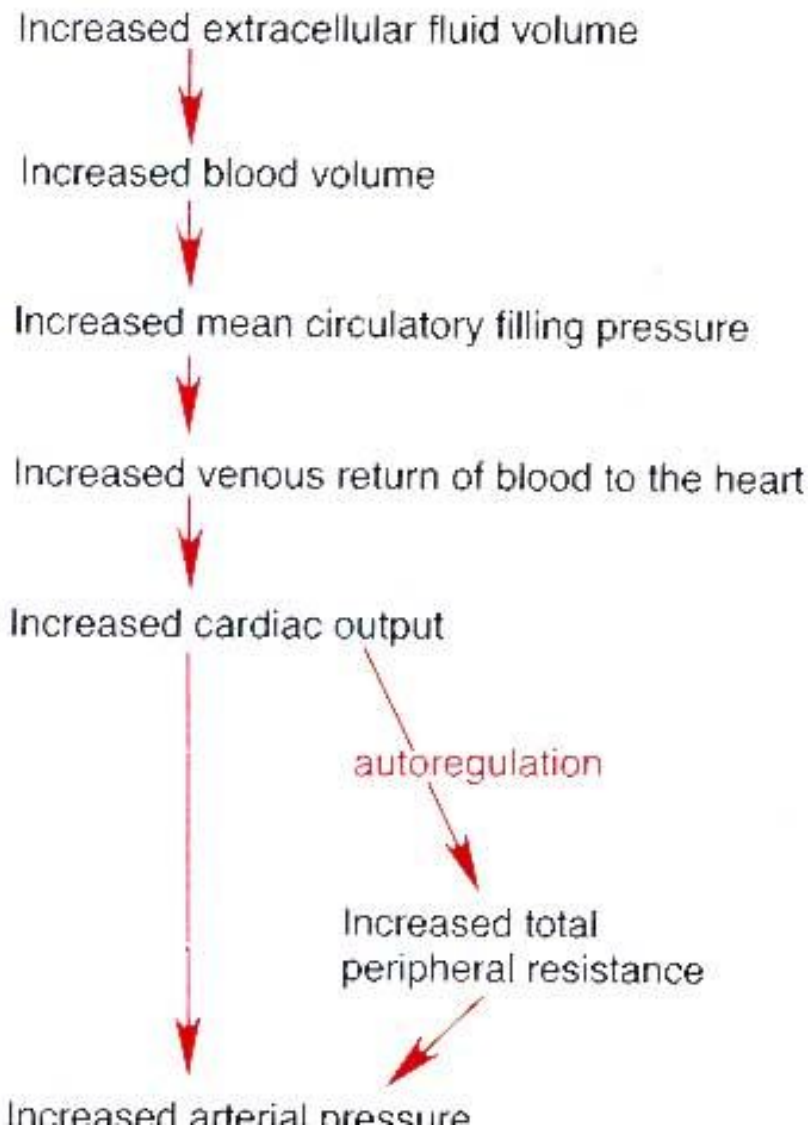
Chemical Regulation

- Epinephrine secretion regulates Venous Pressure, Stroke Volume, and Heart Rate.
- An increase in either venous pressure, stroke volume or heart rate leads to an increase in blood pressure.

Kidney activity regulation

- Kidney regulates the secretion of:
  - Renin
  - Angiotensin II
  - Aldosterone
- Renin and Angiotensin II controls Total Peripheral Resistance.
- Aldosterone controls the urine output.

Extracellular Fluid Volume and Blood Pressure



volume alter blood volume.

Altered blood volume changes the end diastolic volume and filling pressure of the heart.

Changes in cardiac pre-load alter stroke volume and cardiac output.

Altered cardiac output changes blood pressure.

AND by autoregulation changes total peripheral resistance. Further changing blood pressure.

Pressure Diuresis

Urine production is dependent on arterial blood pressure.

A renal output curve (ROC) shows the relationship between pressure and urine volume.

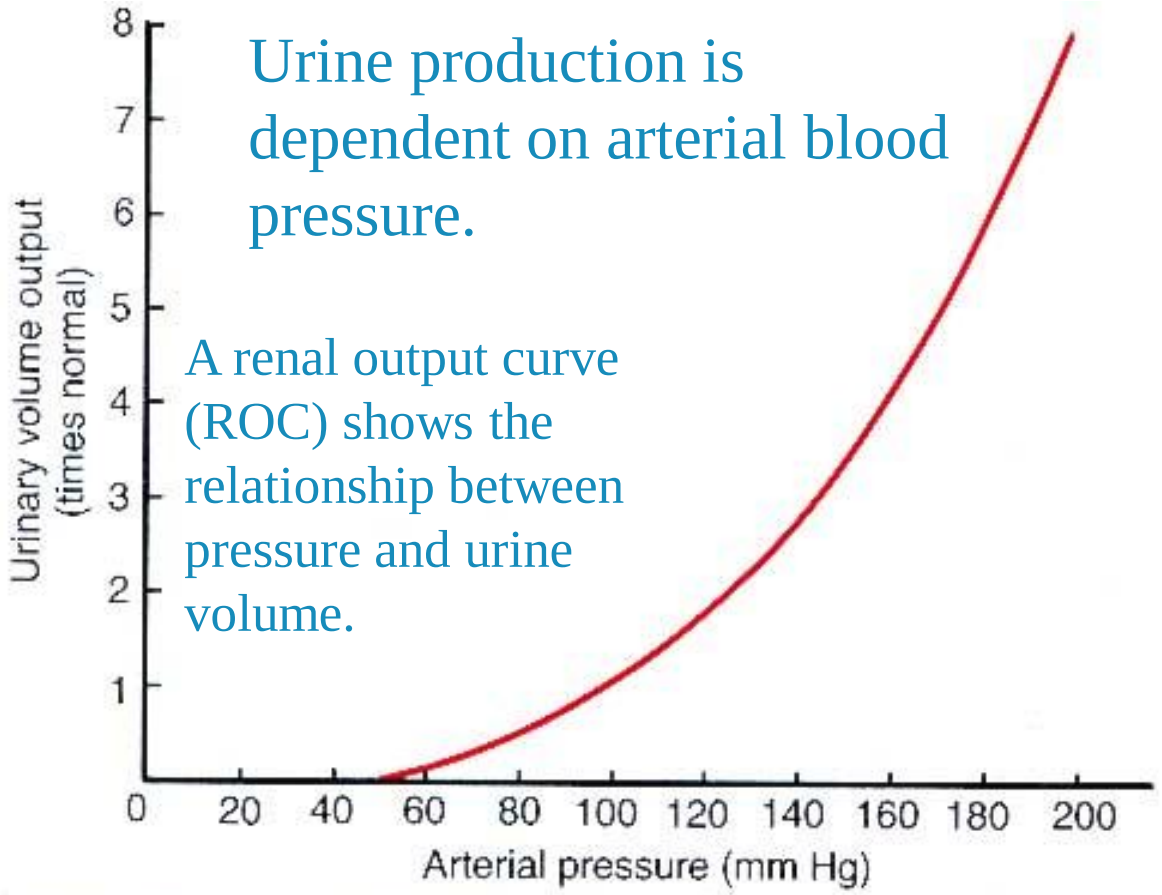


Figure 19–1. A typical renal output curve measured in a perfused isolated kidney, showing pressure diuresis when the arterial pressure rises above normal.

Increased arterial pressure increases filtration and urine production.

Increased urine production reduces extracellular fluid (ECF) and blood volume.

Pressure Diuresis

- ECF volume is maintained only if intake is sufficient to balance loss.
- Loss of ECF volume is dependent on blood pressure.
- Increased blood pressure increases ECF volume loss and blood pressure falls.
- Net loss of ECF stops when blood pressure is sufficient for ECF loss from urine to just balances fluid intake.
- Imbalance in osmolarity is controlled by the osmoreceptor system.
- Salt load is generaly more important than water as the osmoreceptors regulate water to the salt load.

Medicine

- Drugs trying to cure high blood pressure are currently available.
- High blood pressure drugs try to dilate the arteries, so the peripheral resistance would increase and thus the blood pressure would decrease.

Medicine cont…

Other types of drugs are

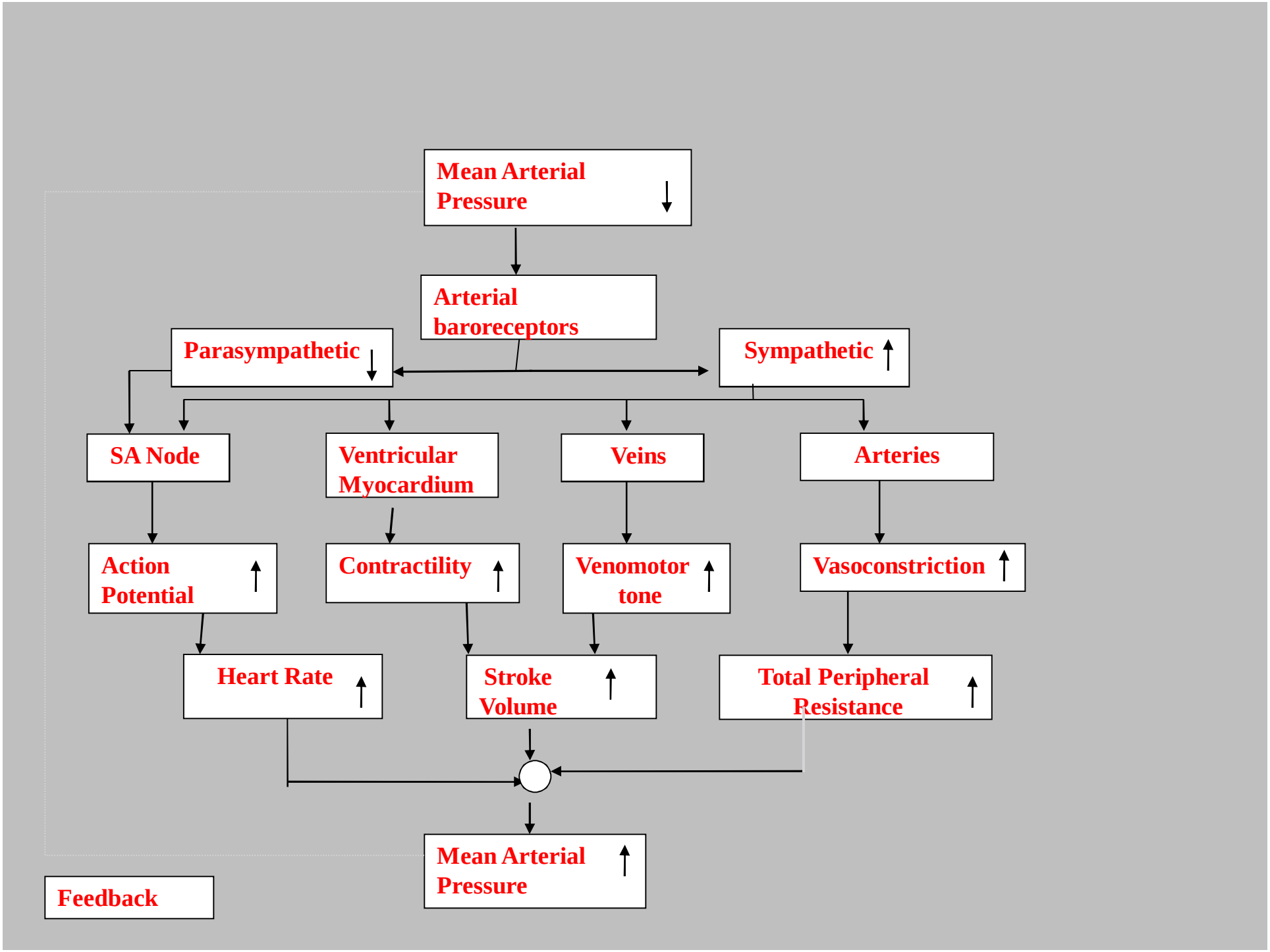
1. Diuretics- which cause the body to excrete water and salt.
2. ACE inhibitors- reduce the production of angiotensin, a chemical that causes arteries to constrict.

Medicine cont…

(3) Beta-Blockers- block the effects of adrenaline, thus easing the heart's pumping action and widening blood vessels.
(4) Vasodilators- expand blood vessels.
(5) Calcium-channel blockers- which help decrease heart contractions.

Conclusion

- Sympathetic, Parasympathetic, chemical activities and kidney control blood pressure.
- Baroreceptors action potential frequency is the input for sympathetic, and parasympathetic activity.
- The output for sympathetic activity involve (1) venomotor tone (2) vasoconstriction (3) ventricular contraction (4) heart rate


Mean Arterial Pressure ↓
Arterial baroreceptors
Parasympathetic ↓
Sympathetic ↑
SA Node
Ventricular Myocardium
Veins
Arteries
Action Potential ↑
Contractility ↑
Venomotor tone ↑
Vasoconstriction ↑
Heart Rate ↑
Stroke Volume ↑
Total Peripheral Resistance ↑
Mean Arterial Pressure ↑
Feedback