



PHYSIOLOGY

FACULTY OF PHARMACEUTICAL SCIENCES

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LECTURE 8, PART (2): ACTION POTENTIAL AND CONTRACTION
OF CARDIAC CONTRACTILE FIBERS

Objectives

1. Discuss histology of cardiac muscle tissue.
2. Discuss action potential and contraction of contractile fibers.
3. Describe electrocardiogram as well as the cardiac cycle.
ECG

(Pages 702-718, 720-726 of the reference).

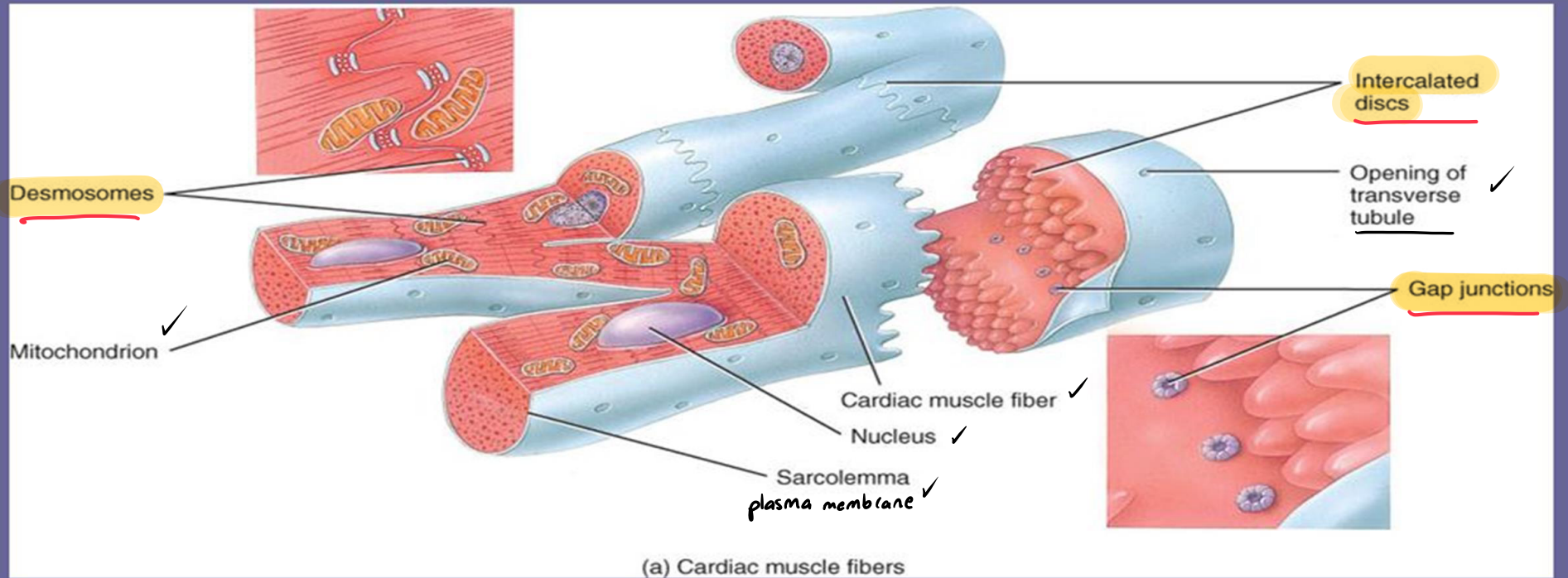
THE CARDIOVASCULAR SYSTEM: THE HEART

- The heart contributes to homeostasis by pumping blood through blood vessels to the tissues of the body to deliver oxygen and nutrients and remove wastes.
- The cardiovascular system consists of the ① blood, ② the heart, and ③ blood vessels.

HISTOLOGY OF CARDIAC MUSCLE TISSUE

- Compared with skeletal muscle fibers, **cardiac muscle fibers are shorter** in length. They also **exhibit branching**, which gives individual cardiac muscle fibers a “stair-step” appearance. تظهر تفرعات
- Cardiac muscle fibers connect to neighboring fibers by intercalated discs, which contain desmosomes, which hold the fibers together, and gap junctions, which allow muscle action potentials to conduct from one muscle fiber to its neighbors. مداخلات
- Gap unit. junctions allow the entire myocardium of the atria or the ventricles to contract as a single, coordinated. عقدة القلب

Cardiac Muscle Histology



lebo

Branching, intercalated discs with gap junctions, involuntary, striated, single central nucleus per cell

2. What feature does cardiac muscle possess that is missing in skeletal muscle?

- A. striations
- B. multiple nuclei
- C. voluntary control
- D. intercalated discs

Answer is D: Intercalated discs join the membrane of one cardiac cell with its neighbour and promote rapid conduction of depolarisation between cells.

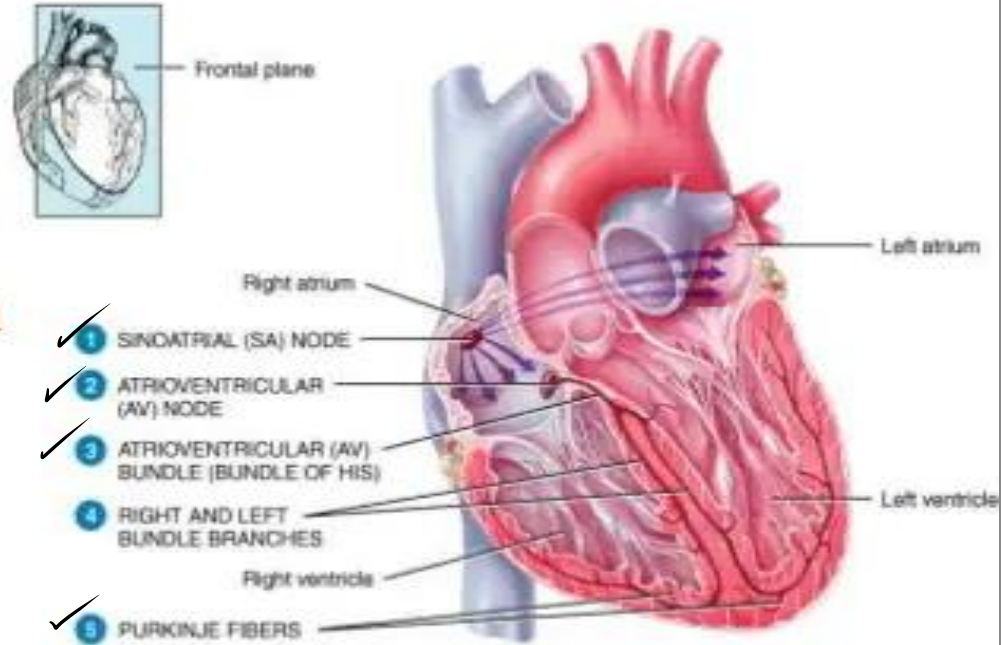
AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

منأصله

- ✓ An inherent and rhythmical electrical activity is the reason for the heart's lifelong beat.
- ✓ The source of this electrical activity is a network of specialized cardiac muscle fibers called autorhythmic fibers because they are self-excitabile.
- ✓ Autorhythmic fibers repeatedly generate action potentials that trigger heart contractions.

Locations of autorhythmic cells

- ❖ **Sinoatrial node (SA node)**
Specialized region in right atrial wall near opening of superior vena cava.
- ❖ **Atrioventricular node (AV node)**
Small bundle of specialized cardiac cells located at base of right atrium near septum → جابر
- ❖ **Bundle of His (atrioventricular bundle)**
Cells originate at AV node and enters interventricular septum Divides to form right and left bundle branches which travel down septum, curve around tip of ventricular chambers, travel back toward atria along outer walls ← تنشأ
- ❖ **Purkinje fibers**
Small, terminal fibers that extend from bundle of His and spread throughout ventricular myocardium



(a) Anterior view of frontal section

20.10a



صورة خارجية للتوضيح -

Autorythmic cells :

superior vena cava

قوس الشرايين الأجر

Arch of aorta

Bachman's bundle

Left atrium

3 Atrioventricular (AV) bundle (bundle of His)

Left ventricle

4 Right and left bundle branches

5 Purkinje fibers

Frontal plane through heart

inferior vena cava

Anterior view of frontal section

1 Sinoatrial (SA) node

Anterior internodal

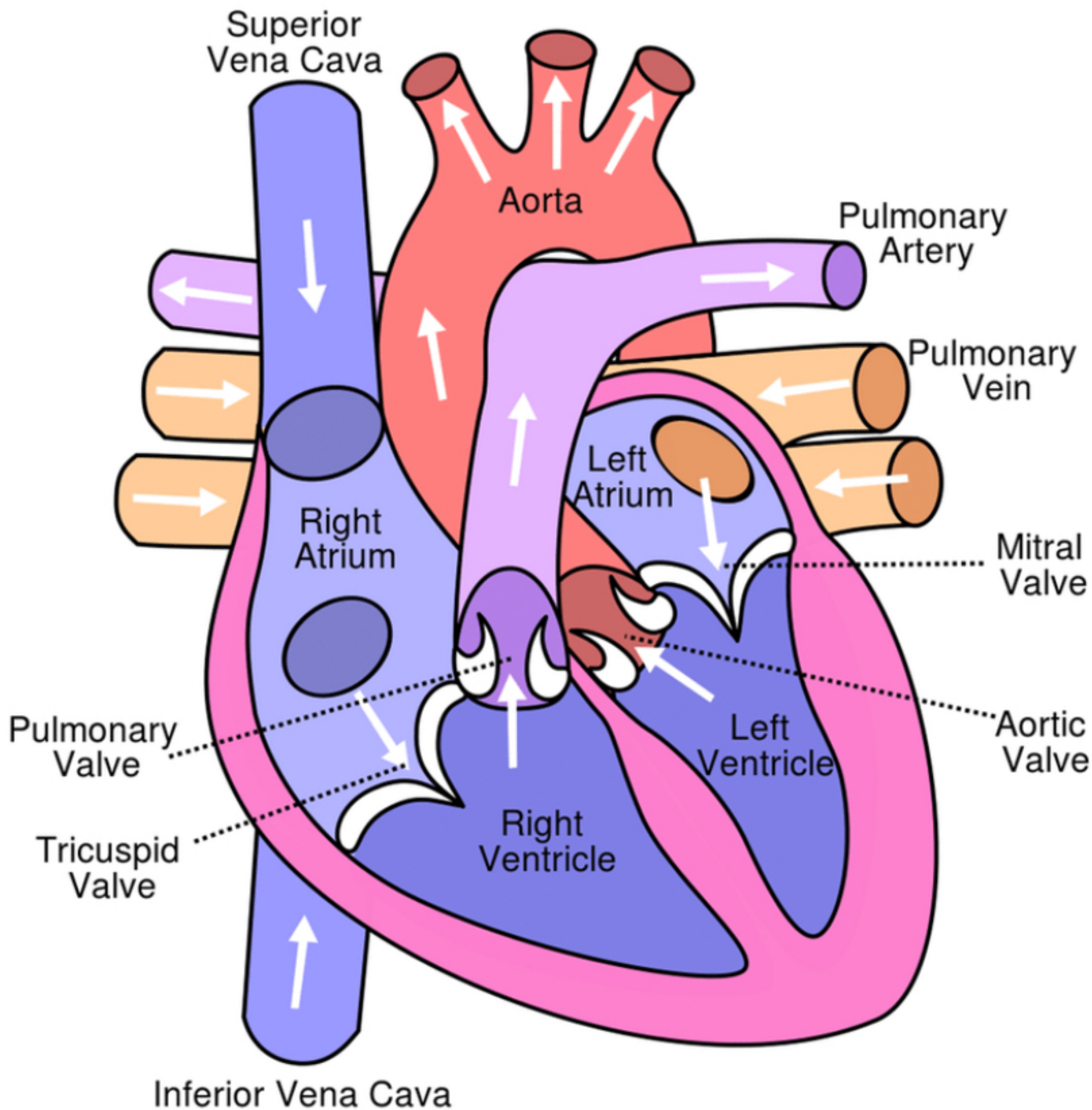
2 Atrioventricular (AV) node

Middle internodal

Posterior internodal

Right atrium

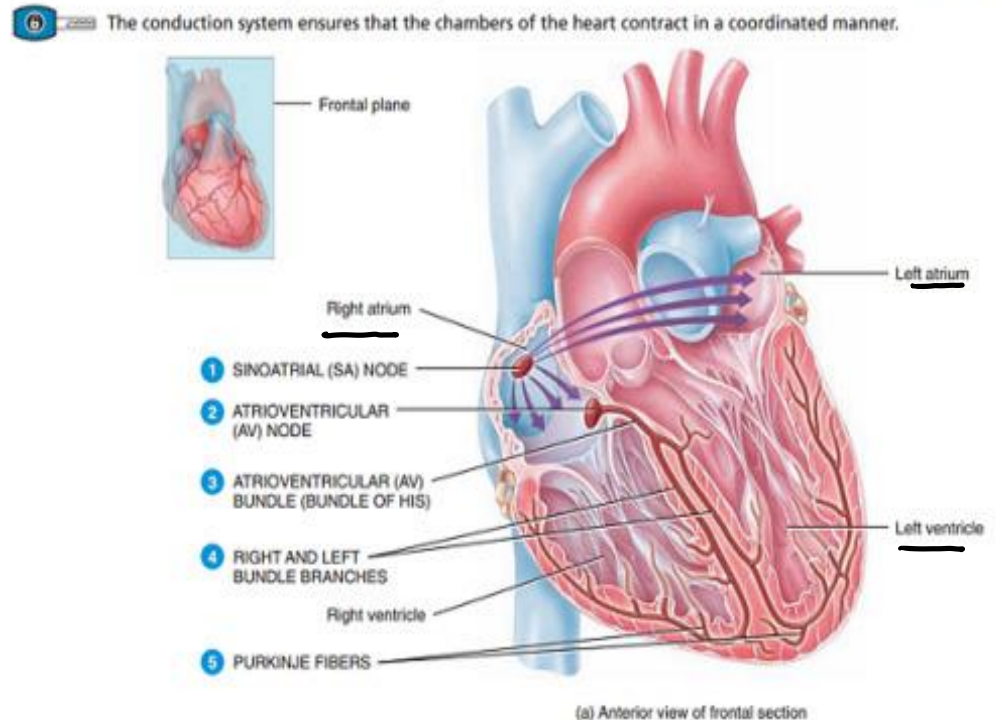
Right ventricle



AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

1. They act as a pacemaker (electrical excitation that causes contraction of the heart).
2. They form the cardiac conduction system.
3. Cardiac action potentials propagate through the conduction system in the following sequence:
 - Cardiac excitation normally begins in the sinoatrial (SA) node.

Figure 20.10 The conduction system of the heart. Autorhythmic fibers in the SA node, located in the right atrial wall (a), act as the heart's pacemaker, initiating cardiac action potentials (b) that cause contraction of the heart's chambers.



AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

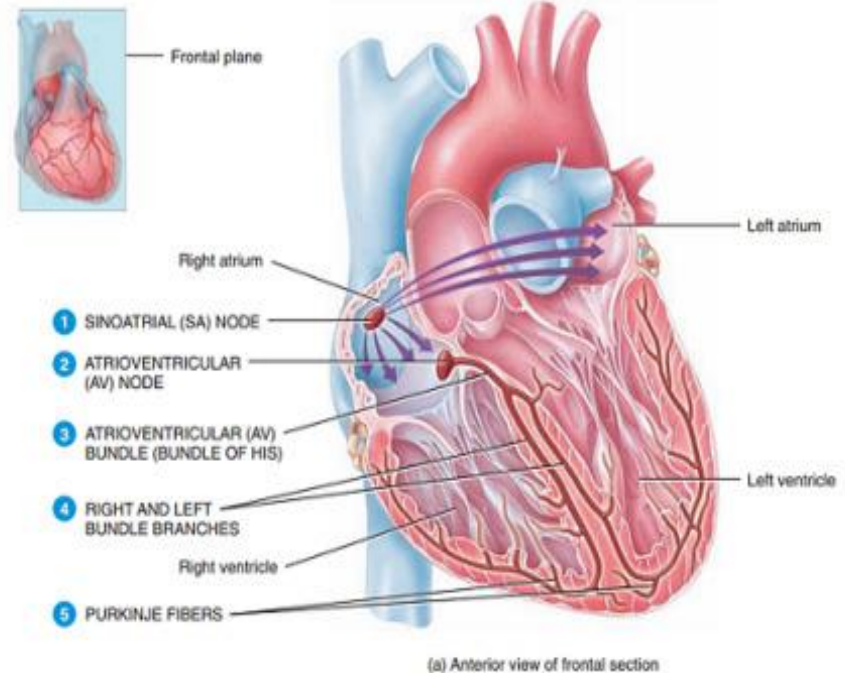
- **SA node cells do not have a stable resting potential.** Rather, they repeatedly depolarize to threshold spontaneously. **The spontaneous depolarization is a pacemaker potential.**
- When **the pacemaker potential reaches threshold**, it triggers an action potential. **Each action potential from the SA node propagates throughout both atria via gap junctions in the intercalated discs of atrial muscle fibers.** Following the action potential, the two atria contract at the same time.

synchronized contraction

Figure 20.10 The conduction system of the heart. Autorhythmic fibers in the SA node, located in the right atrial wall (a), act as the heart's pacemaker, initiating cardiac action potentials (b) that cause contraction of the heart's chambers.



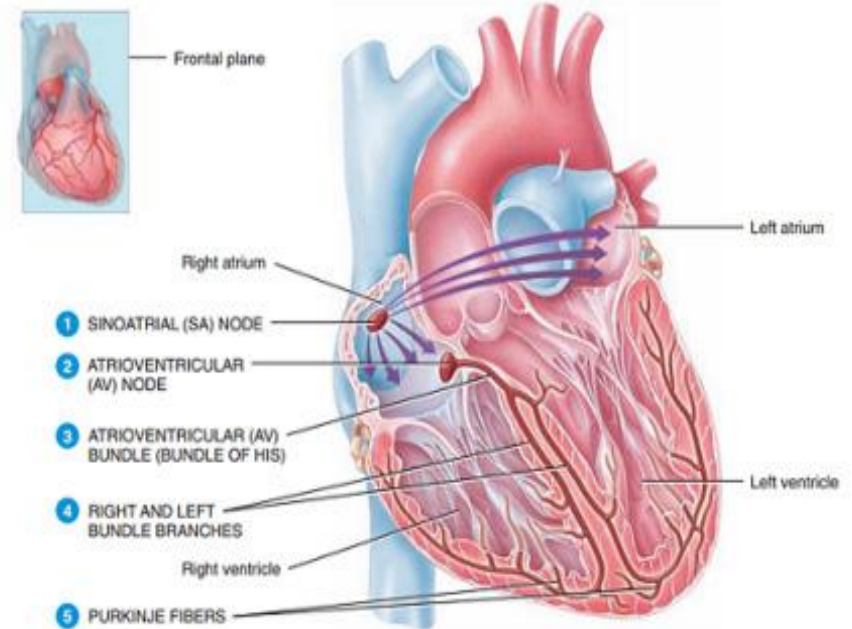
The conduction system ensures that the chambers of the heart contract in a coordinated manner.



AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

Figure 20.10 The conduction system of the heart. Autorhythmic fibers in the SA node, located in the right atrial wall (a), act as the heart's pacemaker, initiating cardiac action potentials (b) that cause contraction of the heart's chambers.

 The conduction system ensures that the chambers of the heart contract in a coordinated manner.



(a) Anterior view of frontal section

- By conducting along atrial muscle fibers, the action potential reaches the atrioventricular (AV) node.

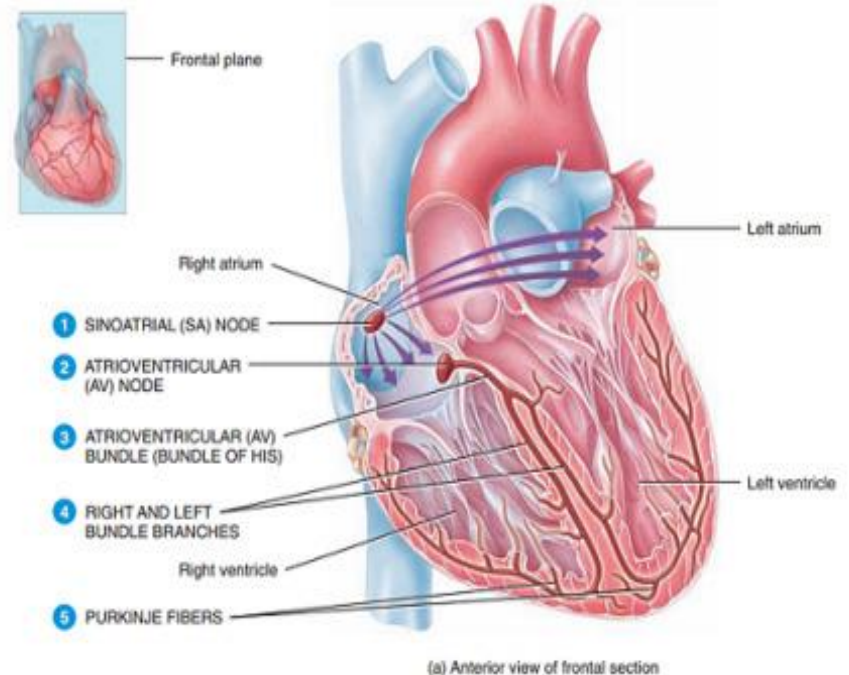
- لأنها تضيّق At the AV node, the action potential slows considerably as a result of various differences in cell structure in the AV node. This delay provides time for the atria to empty their blood into the ventricles.

AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

- From the AV node, the action potential enters the atrioventricular (AV) bundle. This bundle is the only site where action potentials can conduct from the atria to the ventricles.
- After propagating through the AV bundle, the action potential enters both the right and left bundle branches.

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 The conduction system ensures that the chambers of the heart contract in a coordinated manner.

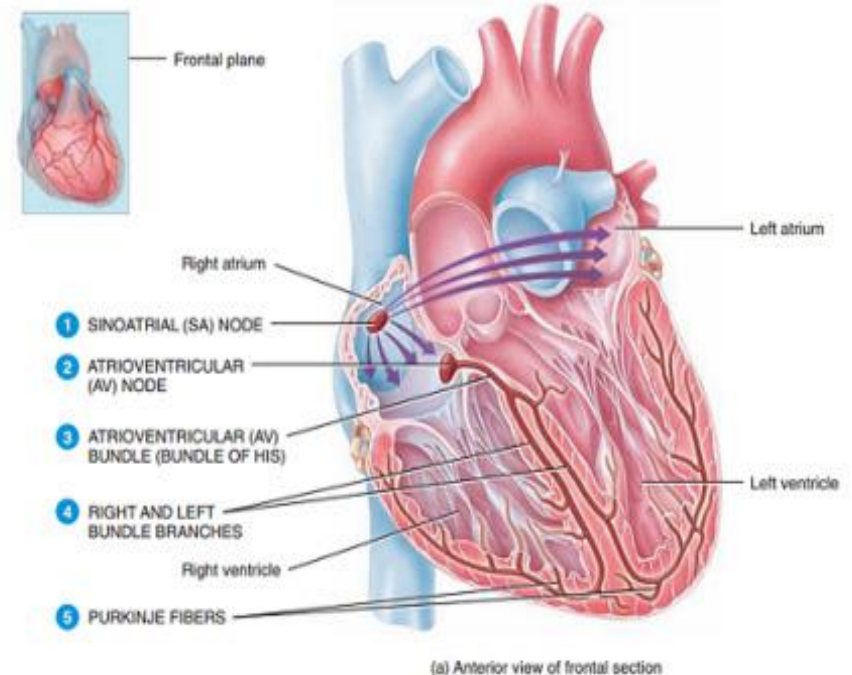


AUTORHYTHMIC FIBERS: THE CONDUCTION SYSTEM

Figure 20.10 The conduction system of the heart. Autorhythmic fibers in the SA node, located in the right atrial wall (a), act as the heart's pacemaker, initiating cardiac action potentials (b) that cause contraction of the heart's chambers.

 The conduction system ensures that the chambers of the heart contract in a coordinated manner.

- Finally, **the large-diameter Purkinje fibers** rapidly conduct the action potential beginning at **the apex of the heart** upward to the remainder of the ventricular myocardium. Then the ventricles contract, pushing the blood upward toward the semilunar valves.
- طرف
هاتفي



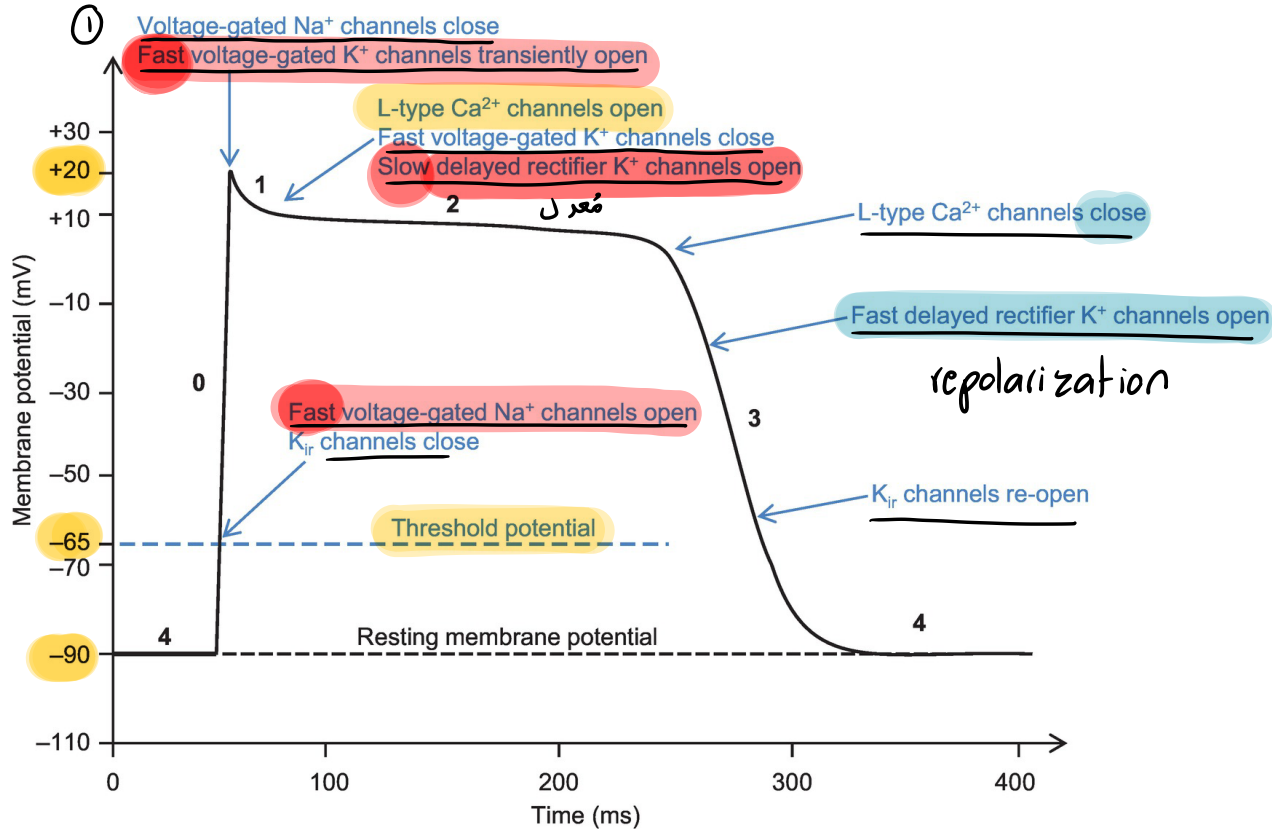
24. Choose the structure known as the pacemaker of the heart from the following.

- A. atrio-ventricular node
- B. sino-atrial node
- C. atrio-ventricular bundle
- D. the bundle of His

Answer is B: The SA node, in the right atrial wall sets the pace of the heart rate.

ACTION POTENTIAL AND CONTRACTION OF CONTRACTILE FIBERS

resting membrane -90
threshold -65
depolarization +20
 $Na^+ \uparrow$

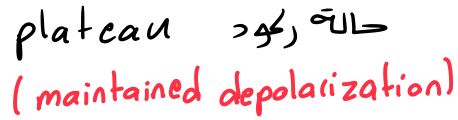


OF CONTRACTILE FIBERS

❖ Depolarization:

autorhythmic fibers, contractile fibers have a stable resting membrane potential that is close to -90 mV .

When a contractile fiber is brought to threshold by an action potential from neighboring fibers, its voltage-gated fast Na ion channels open. Inflow of Na ions down the electrochemical gradient produces a rapid depolarization. Within a few milliseconds, the fast Na ion channels automatically inactivate and Na ions inflow decreases.

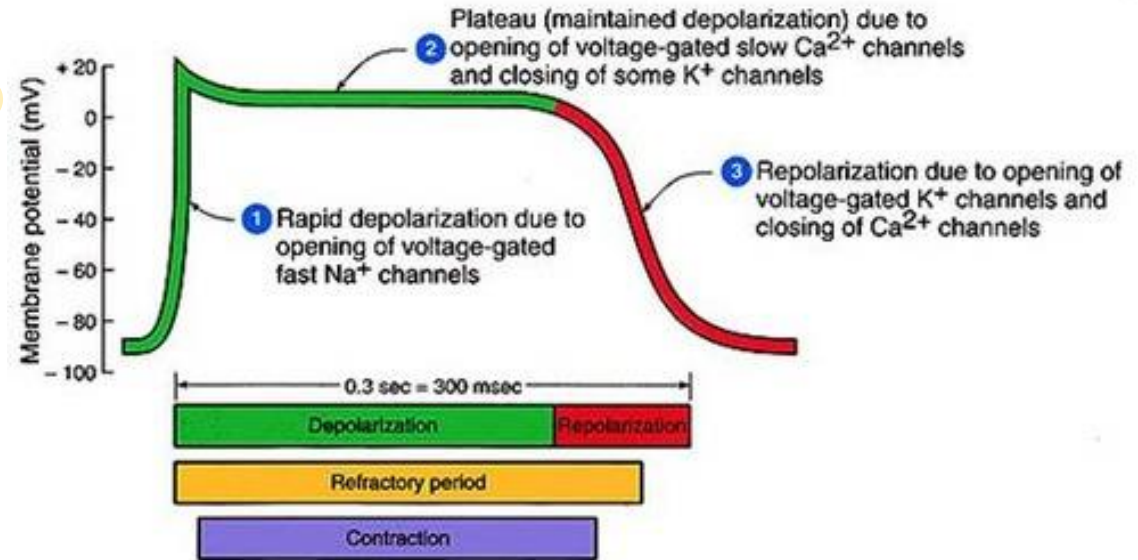


ACTION POTENTIAL AND CONTRACTION OF CONTRACTILE FIBERS

حالة ركبي >

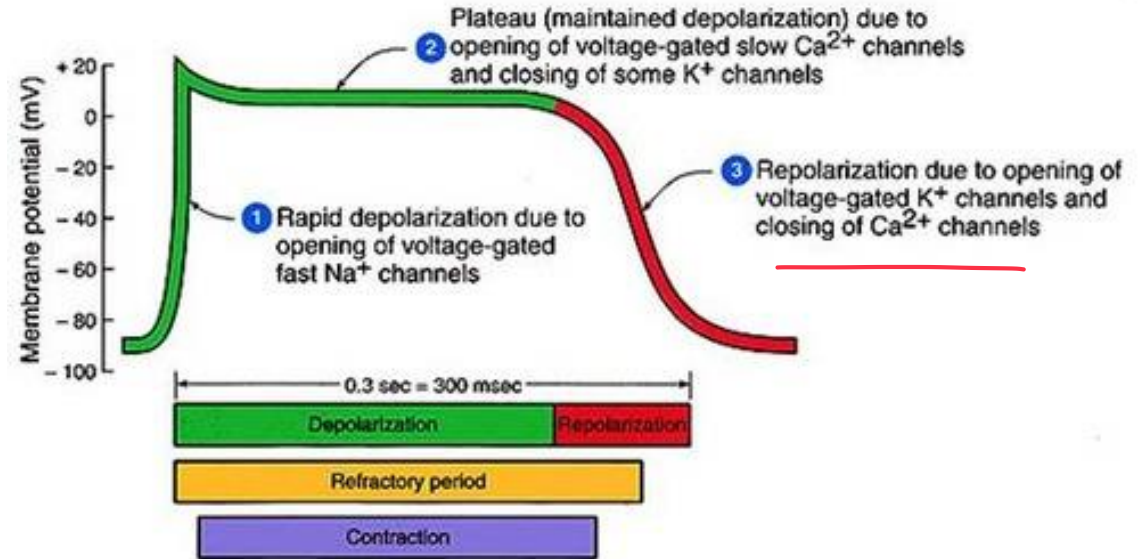
❖ **Plateau:** A period of maintained depolarization. It is due in part to ⁺²⁰opening of voltage-gated slow calcium ions channels in the sarcolemma. The increased calcium ions concentration in the cytosol ultimately triggers contraction. Several different types of voltage-gated potassium ions channels are also found in the sarcolemma of a contractile fiber (calcium ions inflow just balances potassium ions outflow).

$Ca^{2+} \uparrow$ contraction \uparrow



ACTION POTENTIAL AND CONTRACTION OF CONTRACTILE FIBERS

❖ **Repolarization:** After a delay (which is particularly prolonged in cardiac muscle), **additional voltage-gated potassium ions channels open**. Outflow of potassium ions restores the negative resting membrane potential (-90 mV). At the same time, the **calcium channels in the sarcolemma and the sarcoplasmic reticulum are closing**, which also contributes to repolarization.



Following depolarization is always contraction

ACTION POTENTIAL AND CONTRACTION OF CONTRACTILE FIBERS

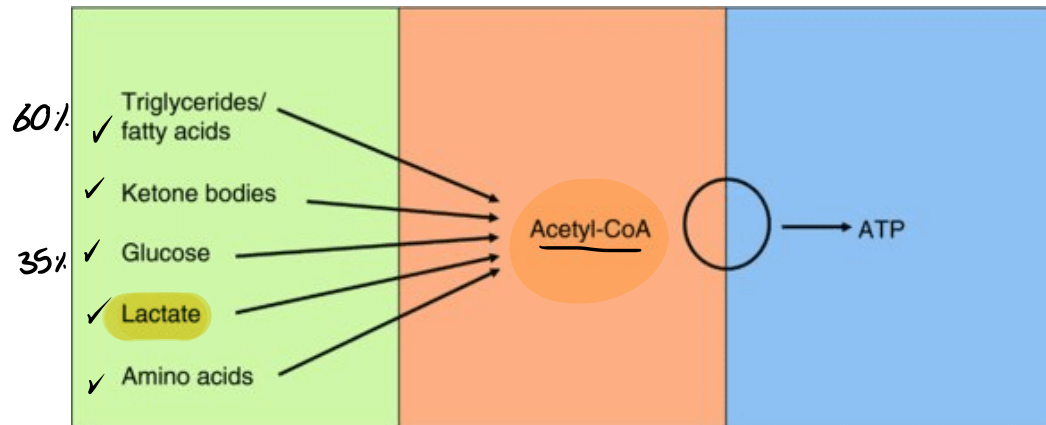
- The **mechanism of contraction** is similar in cardiac and skeletal muscle:
- ❖ The electrical activity (action potential) leads to the **mechanical response** (contraction) after a short delay.
- ❖ As **calcium concentration rises inside a contractile fiber**, calcium ion binds to the regulatory protein troponin, which allows the **actin and myosin filaments to begin sliding past one another**, and tension starts to develop.
- ❖ Substances that alter the movement of calcium ions through slow calcium ions channels influence the **strength of heart contractions**. Epinephrine, for example, increases contraction force by enhancing calcium ions flow into the cytosol. $EP \uparrow \rightarrow Ca^{+2} \uparrow \rightarrow \text{contraction} \uparrow$
- In muscle, **the refractory period** is the time interval during which a second contraction cannot be triggered. The refractory period of a cardiac muscle fiber lasts longer than the contraction itself. As a result, another contraction cannot begin until relaxation is well under way. Their **pumping function depends on alternating contraction** (when they eject blood) and **relaxation** (when they refill).
* **relaxation = filling**

activation = contraction

ATP PRODUCTION IN CARDIAC MUSCLE

- In contrast to skeletal muscle, cardiac muscle produces little of the ATP it needs by anaerobic cellular respiration. → التنفس الخلوي اللاعوائي
- Cardiac muscle fibers use several fuels to power mitochondrial ATP production. In a person at rest, the heart's ATP comes mainly from oxidation of fatty acids (60%) and glucose (35%), with smaller contributions from lactic acid, amino acids, and ketone bodies. During exercise, the heart's use of lactic acid, produced by actively contracting skeletal muscles, rises.

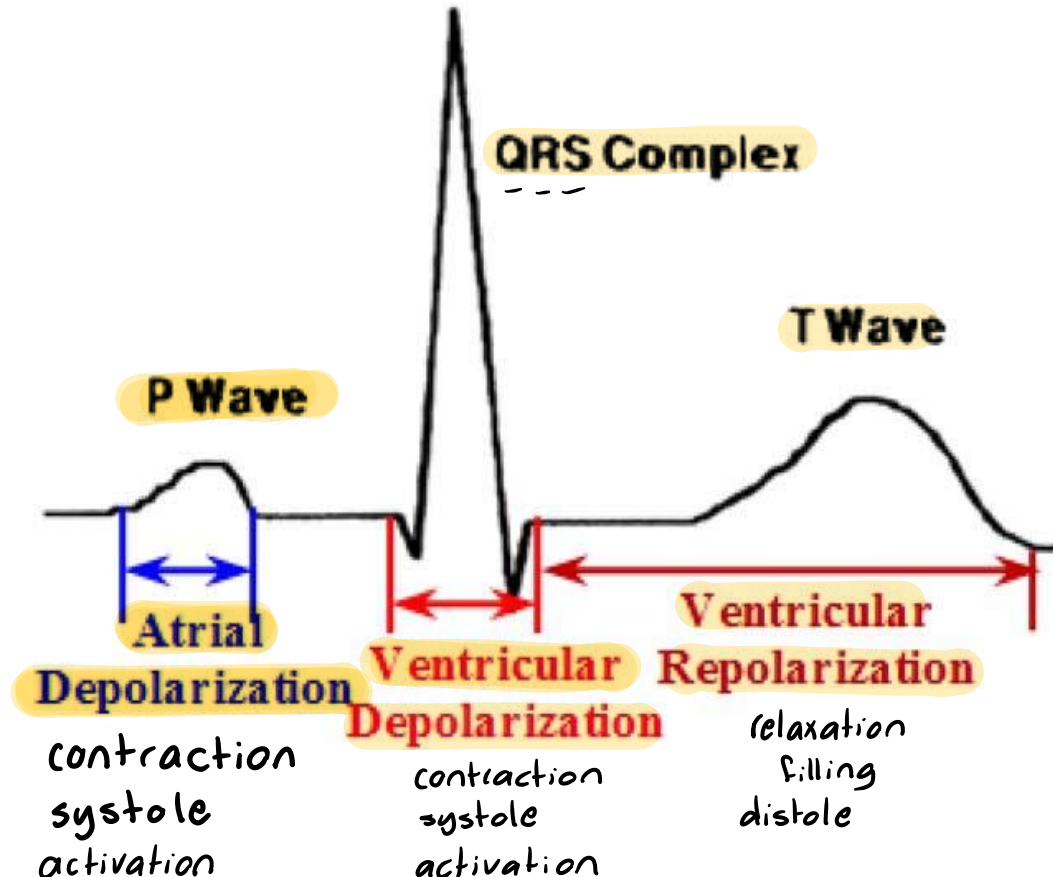
- 1- oxidation of fatty acids 60%
- 2- oxidation of glucous 35%
- 3- lactic acid
amino acid
ketone bodies } 5%



ELECTROCARDIOGRAM




- As action potentials propagate through the heart, they generate electrical currents that can be detected at the surface of the body. An electrocardiogram, abbreviated either ECG or EKG (from the German word Elektrokardiogram), is a recording of these electrical signals. تَحَنُّن
- The instrument used to record the changes is an electrocardiograph.
- By comparing these records with one another and with normal records, it is possible to determine:
 - (1) if the conducting pathway is abnormal.
 - (2) if the heart is enlarged. تَفْخِمْ
 - (3) if certain regions of the heart are damaged.
 - (4) the cause of chest pain.

ELECTROCARDIOGRAM



ELECTROCARDIOGRAM

➤ In reading an ECG, the size of the waves can provide clues to abnormalities.

1. Larger P waves indicate enlargement of an atrium. جلطات 
2. An enlarged Q wave may indicate a myocardial infarction. 
3. An enlarged R wave generally indicates enlarged ventricles.
4. The T wave is flatter than normal when the heart muscle is receiving insufficient oxygen—as, for example, in coronary artery disease. The T wave may be elevated in hyperkalaemia (high blood K ions level). 

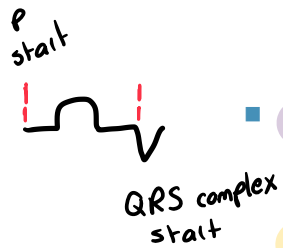
ترتفع

تسريبات ناجي

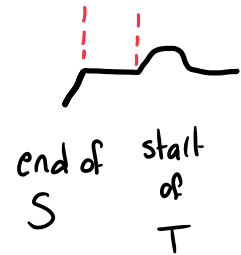
$K^+ \uparrow$ hyperkalaemia

ELECTROCARDIOGRAM

- Analysis of an ECG also involves measuring the time spans between waves, which are called intervals or segments.



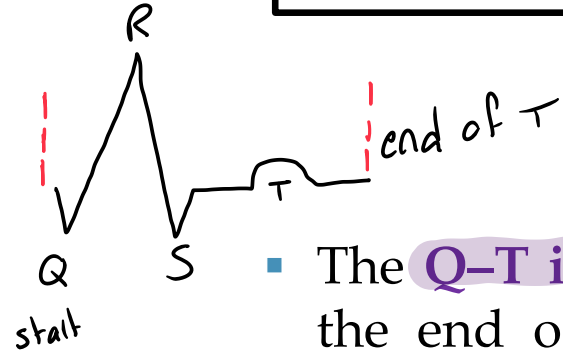
- P-Q interval is the time from the beginning of the P wave to the beginning of the QRS complex. It represents the conduction time from the beginning of atrial excitation to the beginning of ventricular excitation. → depolarisation



- The S-T segment, which begins at the end of the S wave and ends at the beginning of the T wave, represents the time when the ventricular contractile fibers are depolarized during the plateau phase of the action potential.



ELECTROCARDIOGRAM

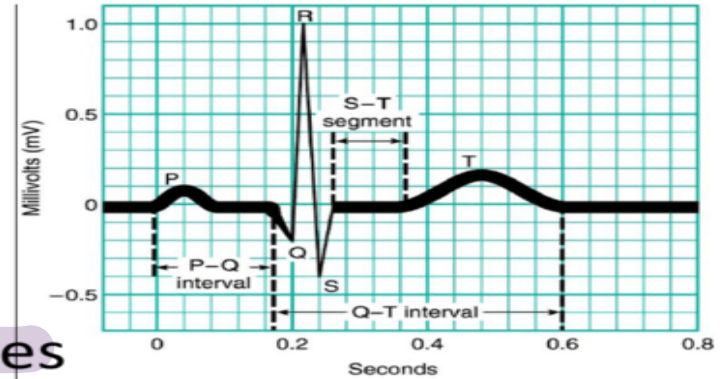


- The **Q-T interval** extends from the start of the QRS complex to the end of the T wave. It is the time from the beginning of ventricular depolarization to the end of ventricular repolarization.

The Electrocardiogram

- The major deflections and intervals in a normal ECG include:

- P wave - atrial depolarization
- P-Q interval - time it takes for the atrial kick to fill the ventricles
- QRS wave - ventricular depolarization and atrial repolarization
- S-T segment - time it takes to empty the ventricles before they repolarize (the T wave)



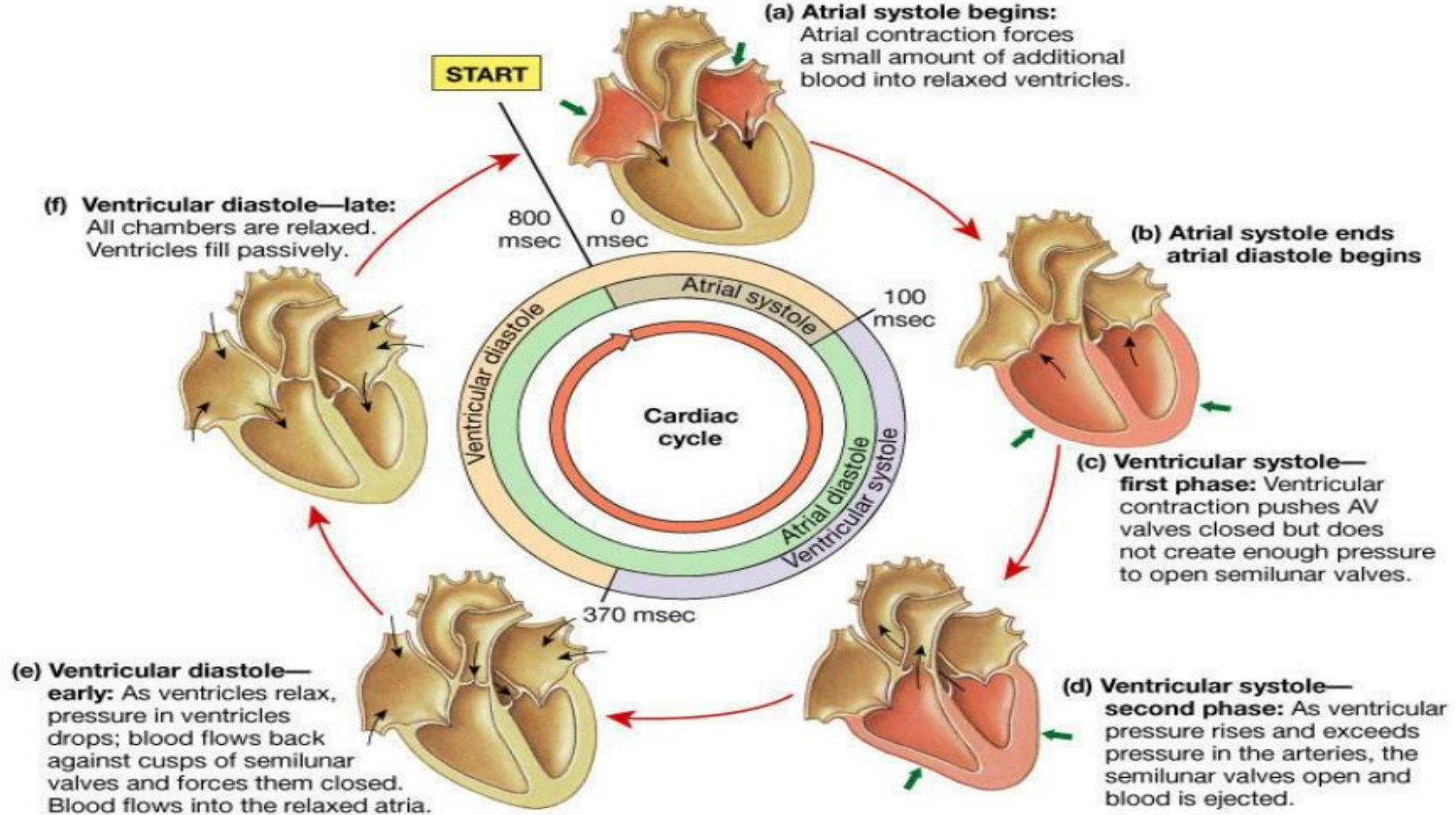
CORRELATION OF ECG WAVES WITH ATRIAL AND VENTRICULAR SYSTOLE *contraction*

- The term **systole** refers to the phase of contraction.
- The phase of relaxation is **diastole**.
- **The ECG waves predict the timing of atrial and ventricular systole and diastole.** *(relaxation)* *contraction*
- ❖ As the atrial contractile fibers depolarize, the P wave appears in the ECG. *following depolarization is contraction.*
- ❖ After the P wave begins, the atria contract (atrial systole).
- ❖ The action potential propagates rapidly again after entering the AV bundle. About 0.2 sec after onset of the P wave, it has propagated through the bundle branches, Purkinje fibers, and the entire ventricular myocardium.
- ❖ Contraction of ventricular contractile fibers (ventricular systole) begins shortly after the QRS complex appears and continues during the S-T segment. *contraction*
depolarization
- ❖ Repolarization of ventricular contractile fibers produces the T wave in the ECG about after the onset of the P wave.
- ❖ Shortly after the T wave begins, the ventricles start to relax (ventricular diastole). *relaxation*
repolarisation
Ventricular repolarization is complete and ventricular contractile fibers are relaxed.

THE CARDIAC CYCLE: PRESSURE AND VOLUME CHANGES DURING THE CARDIAC CYCLE

- **Atrial Systole:** (depolarization) *P wave*
 - Atrial depolarization causes atrial systole.
 - The ventricles are relaxed (The end of atrial systole is also the end of ventricular diastole (relaxation)).
- **Ventricular Systole:** (^{contraction}depolarisation)
 - The ventricles are contracting.
 - At the same time, the atria are relaxed.
- **Relaxation Period:**
 - The atria and the ventricles are both relaxed.
 - Ventricular repolarization causes ventricular diastole. *relaxation*

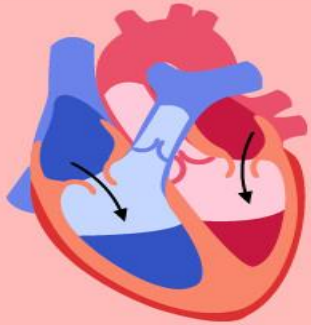
Figure 20.16 Phases of the Cardiac Cycle



PHASES OF THE CARDIAC CYCLE

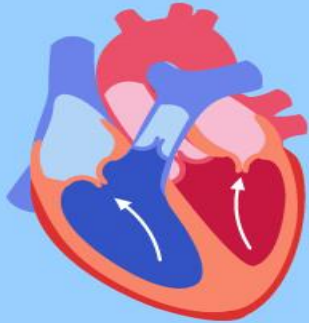
contraction
Atriole systole begins

Atrial contraction forces blood into ventricles



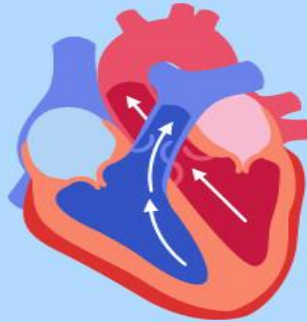
contraction
Ventricular systole (first phase)

Ventricular contraction pushes AV valves closed



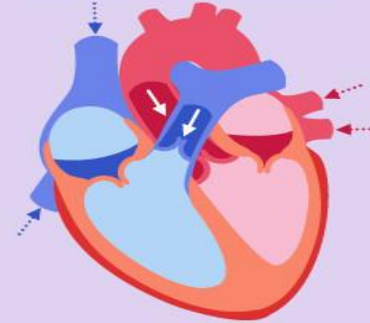
contraction
Ventricular systole (second phase)

Semilunar valves open and blood is ejected



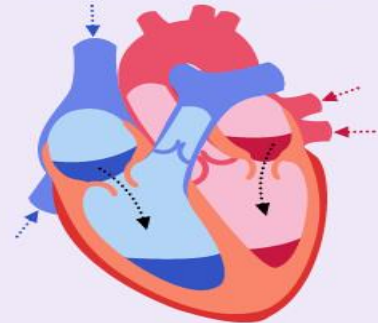
Filling
Ventricular diastole (early)

Semilunar valves close and blood flows into atria



Filling
Ventricular diastole (late)

Chambers relax and blood fills ventricles passively



P
P-Wave
Atria depolarization

AV node

R
Q
S

QRS Complex
Ventricle depolarization

T
T - Wave
Ventricular repolarization

Atrial Diastole relaxation

Atrial Systole

contraction

Atrial Diastole

Ventricular Systole

Ventricular Diastole

17. Which period of the heart cycle is completely occupied by the ventricles contracting?

- A. atrial systole
- B. atrial diastole
- C. ventricular systole
- D. ventricular diastole

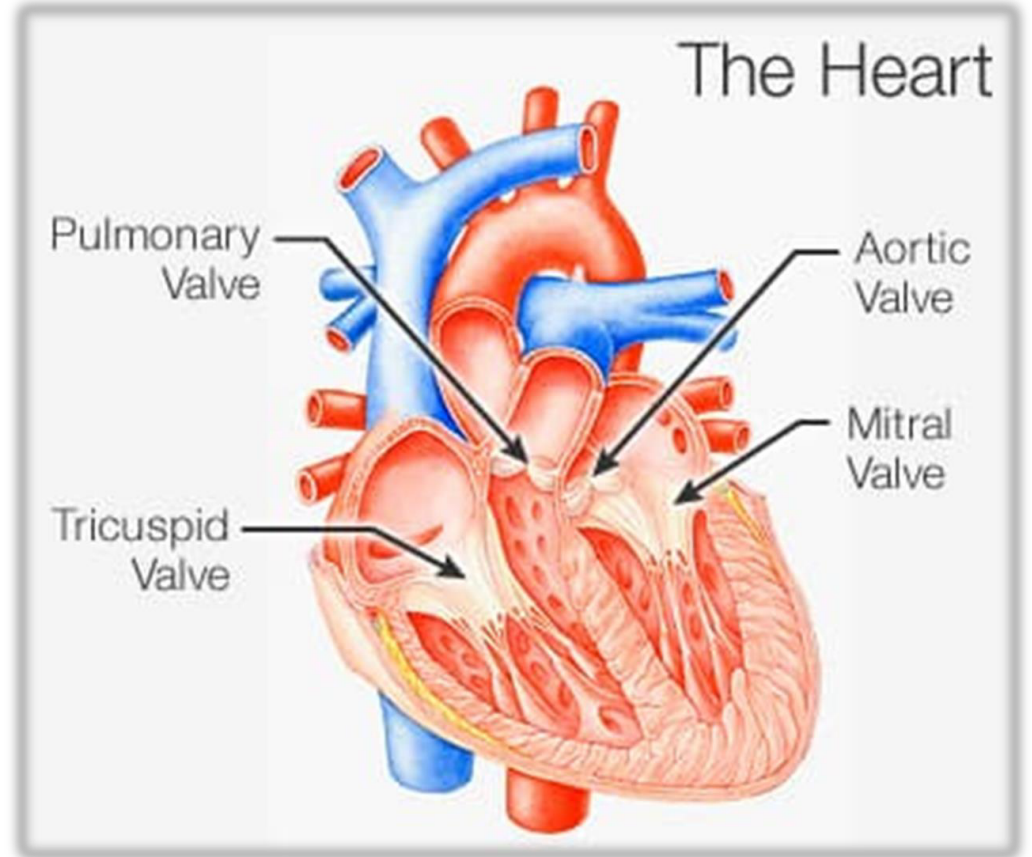
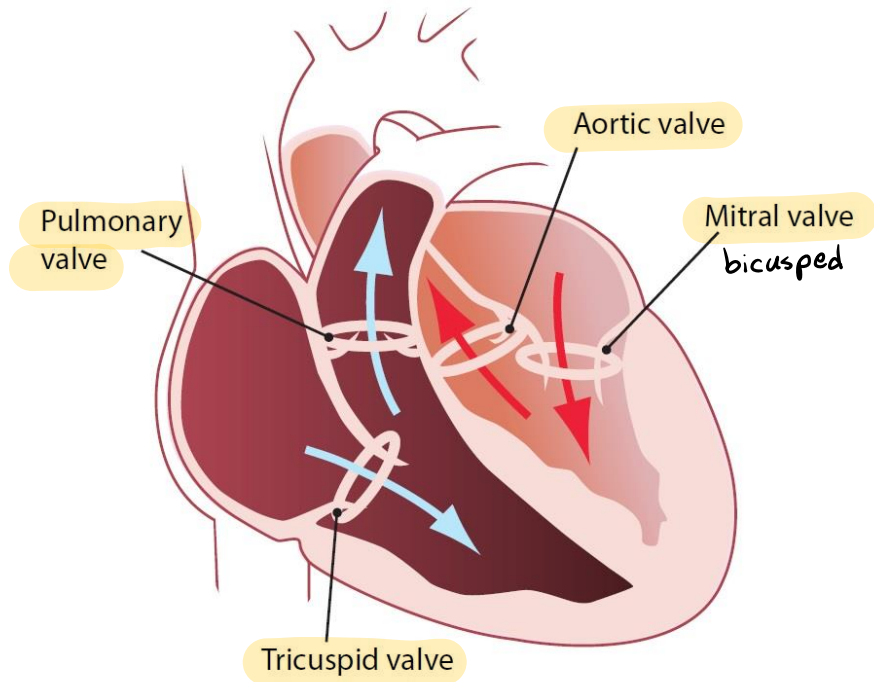
Answer is C: Systole is the term applied to contraction of the cardiac muscle.

11. Which period of the heart cycle is completely occupied by the ventricles relaxing?

- A. atrial systole
- B. atrial diastole
- C. ventricular systole
- D. ventricular diastole

Answer is D: Diastole is the period of cardiac muscle relaxation.

HEART VALVES



3. What is the name of the valve between the left atrium and the left ventricle?

A. mitral valve

B. tricuspid valve

C. semi-lunar valve

D. aortic valve

Answer is A: Also known as the bicuspid valve. The aortic valve is also a semi-lunar valve.

HEART SOUNDS

التسمع

- Auscultation, the act of listening to sounds within the body, is usually done with a stethoscope.
سماعة طبيب
- During each cardiac cycle, there are four heart sounds, but in a normal heart only the first and second heart sounds (S1 and S2) are loud enough to be heard through a stethoscope.
4
- **The first sound (S1)**, which can be described as a lubb sound, is louder and a bit longer than the second sound. S1 is caused by blood turbulence associated with closure of the AV valves soon after ventricular systole begins.
اضطراب
- **The second sound (S2)**, which is shorter and not as loud as the first, can be described as a dupp sound. S2 is caused by blood turbulence associated closure of the semilunar (aortic and pulmonary) valves at the beginning of ventricular diastole. (relaxation)
contraction
- Normally not loud enough to be heard, **S3** is due to blood turbulence during rapid ventricular filling, and **S4** is due to blood turbulence during atrial systole.
relaxation contraction

Heart sounds

- Auscultation – listening to heart sound via stethoscope
- Four heart sounds
 - S₁ – “lubb” caused by the closing of the AV valves
 - S₂ – “dupp” caused by the closing of the semilunar valves
 - S₃ – a faint sound associated with ^{Filling} blood flowing into the ventricles
 - S₄ – another faint sound associated with atrial contraction

CARDIAC OUTPUT

أخرج

- **Cardiac output (CO)** is the volume of blood ejected from the left ventricle (or the right ventricle) into the aorta (or pulmonary trunk) each minute. Cardiac output equals the stroke volume (SV), the volume of blood ejected by the ventricle during each contraction, multiplied by the heart rate (HR), the number of heartbeats per minute:

stroke volume ↑ cardiac output ↑

blood volume ↑

$$\text{CO (mL/min)} = \text{SV (mL/beat)} \times \text{HR (beats/min)}$$

- **Cardiac reserve** is the difference between a person's maximum cardiac output and cardiac output at rest. The average person has a cardiac reserve of four or five times the resting value.

→ maximum - at rest = the difference

REGULATION OF STROKE VOLUME

preload

contractility

afterload

- A healthy heart will pump out the blood that entered its chambers during the previous diastole.
relaxation
- Three factors regulate stroke volume and ensure that the left and right ventricles pump equal volumes of blood: (1) preload, the degree of stretch on the heart before it contracts; (2) contractility, the forcefulness of contraction of individual ventricular muscle fibers; and (3) afterload, the pressure that must be exceeded before ejection of blood from the ventricles can occur.

PRELOAD: EFFECT OF STRETCHING

- Within limits, the more the heart fills with blood during diastole, the greater the force of contraction during systole. This relationship is known as the Frank-Starling law of the heart.
Filling contraction

- The preload is proportional to the end-diastolic volume (EDV), (the volume of blood that fills the ventricles at the end of diastole). Normally, the greater the EDV, the more forceful the next contraction.
preload

- Two key factors determine EDV: (1) the duration of ventricular diastole and (2) venous return, the volume of blood returning to the right ventricle.
Filling

6. The Frank-Starling law of the heart describes the proportional relationship between which of the following pairs?

- A. Stroke volume and cardiac output
- B. Stroke volume and end-diastolic volume
- C. The blood volume in the ventricles and stroke volume
- D. Systemic vascular resistance and stroke volume

CONTRACTILITY

Ca^{+2}

- ❑ **Myocardial contractility**, the strength of contraction at any given preload.
- ❑ Substances that increase contractility are **positive** inotropic agents (promote calcium ions inflow during cardiac action potentials), those that decrease contractility are **negative** inotropic agents (reducing calcium ions inflow).

inotropic agents

+ve	$Ca^{+2} \uparrow$	contraction \uparrow
-ve	$Ca^{+2} \downarrow$	contraction \downarrow

AFTERLOAD

- Ejection of blood from the heart begins when pressure in the right ventricle exceeds the pressure in the pulmonary trunk, and when the pressure in the left ventricle exceeds the pressure in the aorta.
- At that point, **the higher pressure in the ventricles** causes blood to **push the semilunar valves open**. The pressure that must be overcome before a semilunar valve can open is termed the **afterload**.
- Conditions that can increase afterload include **hypertension** (elevated blood pressure) and narrowing of arteries by **atherosclerosis**.

ارتفاع ضغط الدم

تصلب الشرايين

REGULATION OF HEART RATE

■ Autonomic Regulation of Heart Rate:

- ❖ Nervous system regulation of the heart originates in the cardiovascular center in the medulla oblongata. The cardiovascular center then directs appropriate output by increasing or decreasing the frequency of nerve impulses in both the sympathetic and parasympathetic branches of the ANS.
- ❖ Proprioceptors that are monitoring the position of limbs and muscles send nerve impulses at an increased frequency to the cardiovascular center.
- ❖ Proprioceptor input is a major stimulus for the quick rise in heart rate that occurs at the onset of physical activity.
- ❖ Other sensory receptors that provide input to the cardiovascular center include chemoreceptors, which monitor chemical changes in the blood, and baroreceptors, which monitor the stretching of major arteries and veins caused by the pressure of the blood flowing through them. Important baroreceptors located in the arch of the aorta and in the carotid arteries.

H⁺/pH

REGULATION OF HEART RATE

■ Autonomic Regulation of Heart Rate:

HR ↑

- ❖ Through the sympathetic cardiac accelerator nerves: In SA (and AV) node fibers, norepinephrine speeds the rate of spontaneous depolarization so that these pacemakers fire impulses more rapidly and heart rate increases; in contractile fibers throughout the atria and ventricles, norepinephrine enhances calcium ions entry through the voltage-gated slow calcium ions channels, thereby increasing contractility.

$Ca^{+2} \uparrow$ contraction ↑

- ❖ Through Parasympathetic ^{vagus} nerve impulses reach the heart via the right and left vagus (X) nerves: Vagal axons terminate in the SA node, AV node, and atrial myocardium. They release acetylcholine, which decreases heart rate by slowing the rate of spontaneous depolarization in autorhythmic fibers. As only a few vagal fibers innervate ventricular muscle, changes in parasympathetic activity have little effect on contractility of the ventricles.

HR ↓

CHEMICAL REGULATION OF HEART RATE

metabolic
rate

1. **Hormones:** Epinephrine and norepinephrine (from the adrenal medullae) enhance the heart's pumping effectiveness. These hormones affect cardiac muscle fibers in much the same way as does norepinephrine released by cardiac accelerator nerves—they increase both heart rate and contractility. One sign of hyperthyroidism (excessive thyroid hormone) is tachycardia, an elevated resting heart rate.

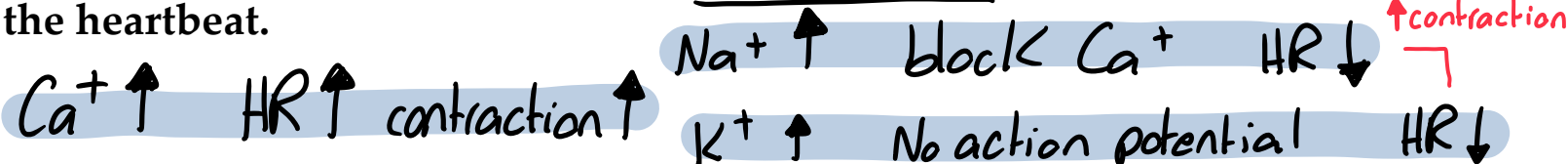
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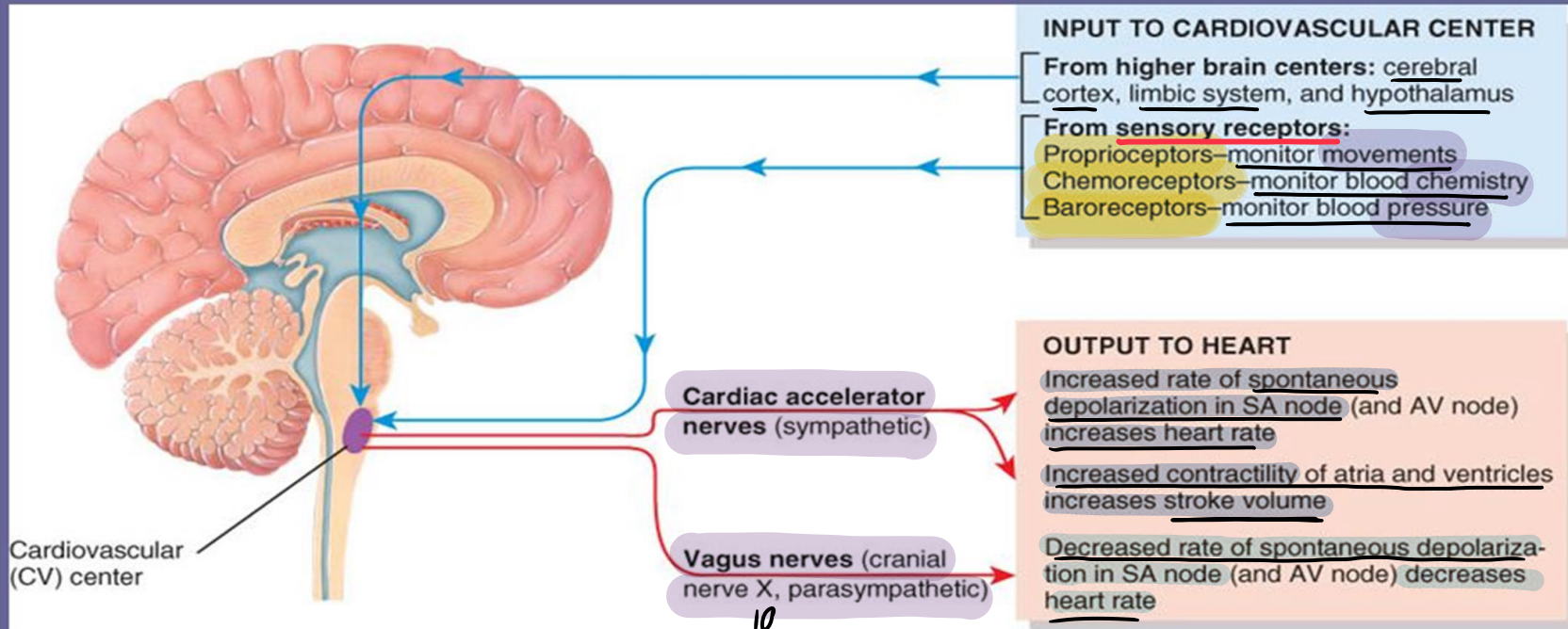
تسارع
القلب

2. **Cations:** Given that differences between intracellular and extracellular concentrations of several cations (for example, sodium and potassium ions) are crucial for the production of action potentials in all nerve and muscle fibers. Elevated blood levels of potassium ions or sodium ions decrease heart rate and contractility. Excess sodium ions blocks calcium inflow during cardiac action potentials, thereby decreasing the force of contraction, whereas excess potassium ions blocks generation of action potentials. A moderate increase in interstitial (and thus intracellular) calcium ions level speeds heart rate and strengthens the heartbeat.

K⁺
inhibition
repolarization



Regulation of Heart Rate



OTHER FACTORS IN HEART RATE REGULATION

- Age, gender, physical fitness, and body temperature also influence resting heart rate.
- A physically fit person may even exhibit bradycardia, a resting heart rate under 50 beats/min.
- During surgical repair of certain heart abnormalities, it is helpful **to slow a patient's heart rate by hypothermia**, in which the person's body is deliberately cooled to a low core temperature.

بطء نبضات القلب

خفض درجة الحرارة

HELP FOR FAILING HEARTS

زراعة

- **Cardiac transplantation** is the replacement of a severely damaged heart with a normal heart from a brain-dead or recently deceased donor.
لـ صوفى
- Cardiac transplants are performed on patients with end-stage heart failure or severe coronary artery disease.