Chapter 16 – Cardiac Pumping, Cardiac Output, HR, and Stroke Volume

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To describe the flow of blood through the circulatory system; including the heart, systemic arteries and veins, and pulmonary arteries and veins.
B. To explain the pumping of blood through the heart and the functions of the phases of the cardiac cycle.
C. To explain the organization of the cardiac conduction system and its role in coordinating the pumping actions of the heart.
D. To explain the ionic basis of cardiac pacemaker potentials and action potentials and their role in the control of cardiac contractile cells.
E. To explain the foundation for the measurement of the electrocardiogram.
F. To explain the significance of the P, QRS, and T waves and to calculate heart rate and wave intervals in an ECG print out.
G. To explain the causative relationships between the electrical activity of the ECG and the systolic and diastolic blood flows.
H. To explain the role of heart rate and stroke volume, including end diastolic volume and end systolic volume, in determining cardiac output.
I. To explain the control of cardiac pacemakers and cardiac muscle by the parasympathetic and sympathetic nervous systems, including the adrenal medulla.
J. To explain the control of cardiac function by baroreceptor reflexes.
K. To name representative drugs acting on the heart and to explain their actions.

Cardiovascular Organization

The primary function of the cardiovascular system is to transport oxygen and nutrients to the tissues of the body, and to transport carbon dioxide and other metabolic byproducts away from these tissues. It is of course the responsibility of the respiratory system to obtain oxygen and remove carbon dioxide, the digestive system to initially obtain nutrients and metabolic substrates, and the digestive and urinary systems to remove excess metabolic byproducts.

Circulatory Circuits

The cardiovascular system basically consists of the heart, the pulmonary circuit, and the systemic circuit, as shown in Figure 16.1.

The pulmonary circuit is composed of blood vessels that carry blood to and from the lungs.

- Pulmonary arteries carry blood away from the heart and to the lungs.
- Pulmonary veins carry blood from the lungs and to the heart.

The systemic circuit is composed of blood vessels that carry blood to and from all organs of the body except the lungs.

- Systemic arteries carry blood from heart and to the other organs.
- Systemic veins carry blood from the other organs to the heart.

In addition, lymphatic vessels carry lymph from tissues to systemic veins.

Relationship between the Heart and Blood Vessels

Figure 16.2 illustrates the basic organization of the heart and complements Figure 16.1.

The right side of the heart receives and pumps oxygen poor and carbon dioxide rich blood.

- The **right atrium** receives blood from the systemic circuit via the inferior and superior vena cava.
- The **right ventricle** discharges blood into pulmonary circuit via the pulmonary trunk and arteries.
- The **right atrioventricular valve** (right AV, tricuspid) controls movement of blood between the right atrium and right ventricle.
- The **pulmonary semilunar valve** controls movement of blood between the right ventricle and the pulmonary circuit.

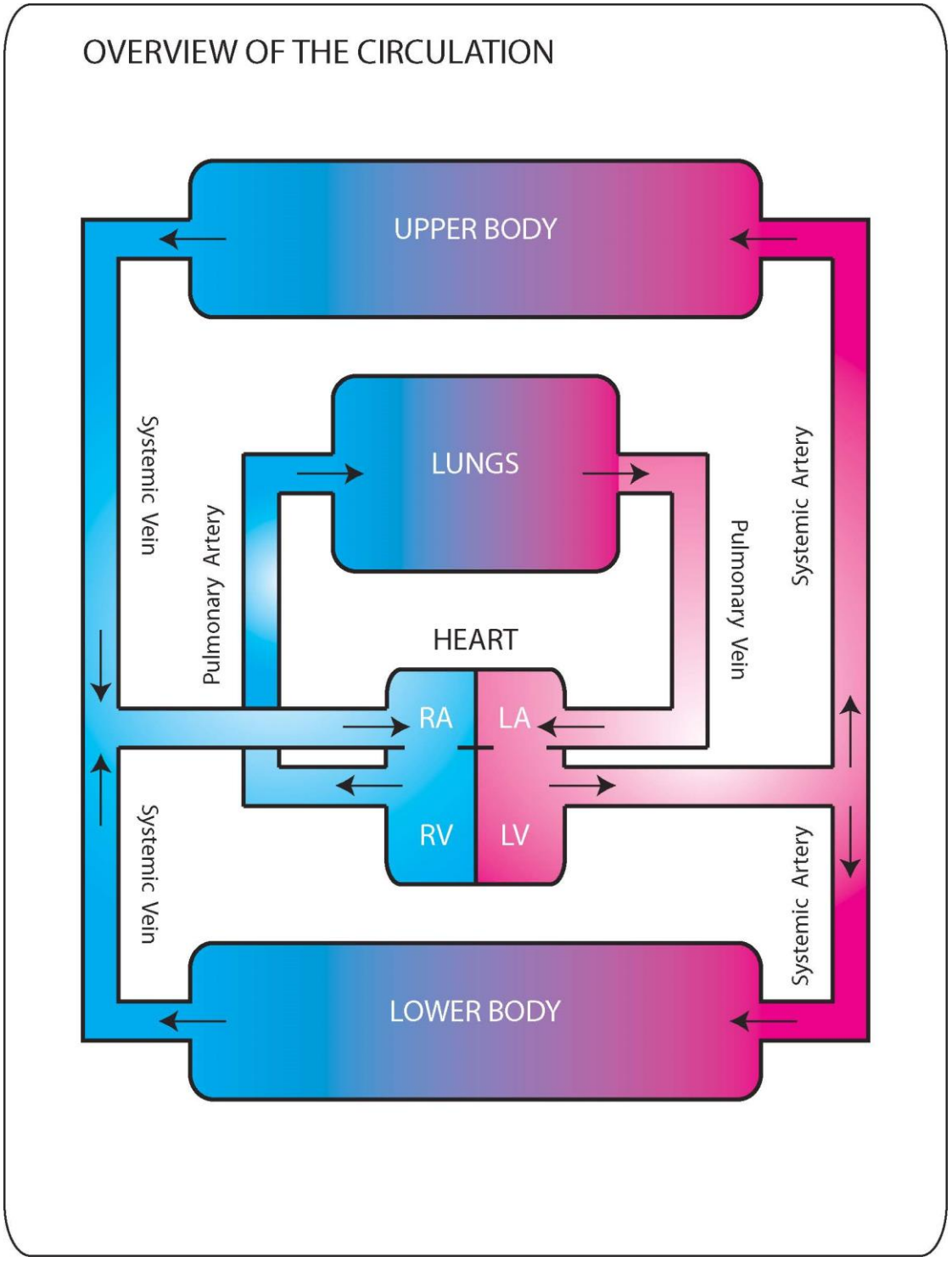


Figure 16.1 © 2007 David G. Ward, Ph.D.

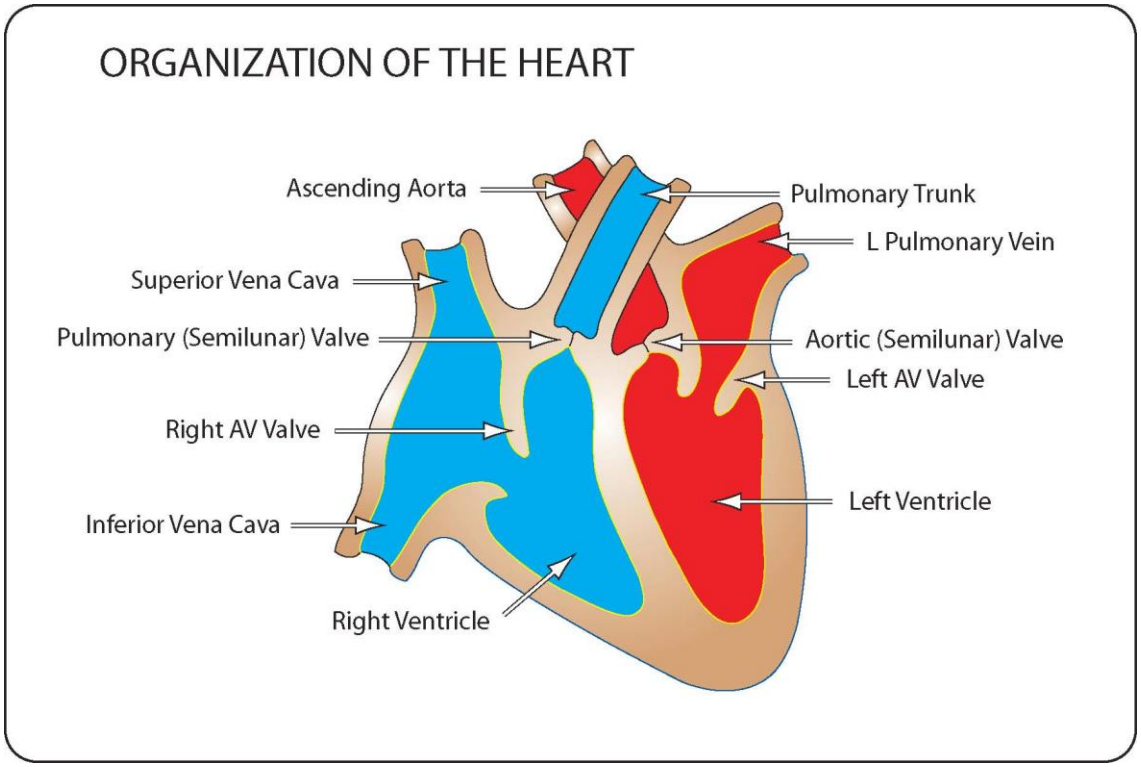


Figure 16.2 © 2007 David G. Ward, Ph.D.

The left side of the heart receives and pumps oxygen rich and carbon dioxide poor blood.

- The **left atrium** receives blood from the pulmonary circuit via the **pulmonary veins.**
- The **left ventricle** discharges blood into systemic circuit via the **aorta.**
- The **left atrioventricular valve** (left AV, bicuspid, mitral) controls movement of blood between the left atrium and the left ventricle.
- The **aortic semilunar valve** controls movement of blood between the left ventricle and the systemic circuit.

Cardiac Pumping

Cardiac cycle

The cardiac cycle corresponds to the period between one heart beat and the next, and is usually viewed starting with atrial contraction, as shown in Figure 16.3.

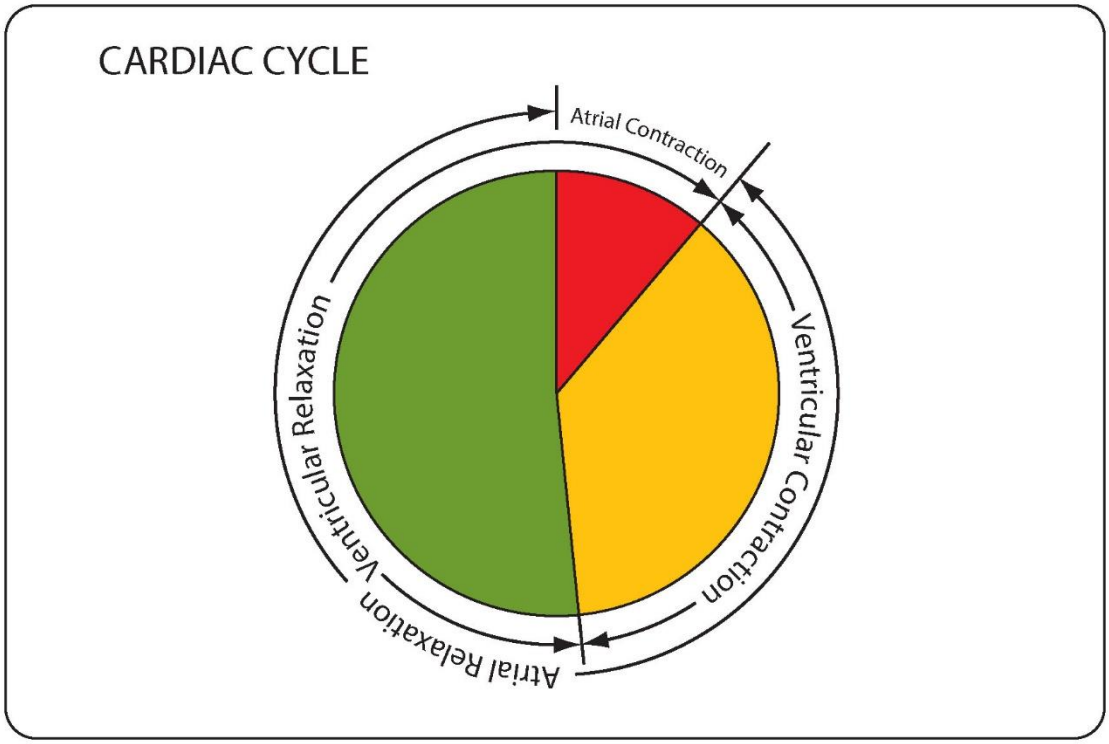


Figure 16.3 © 2018 David G. Ward, Ph.D.

- Atrial contraction is followed by atrial relaxation which continues until the next atrial contraction.
- After the atria contract the ventricles contract.
- Ventricular contraction is followed by ventricular relaxation which continues until the next ventricular contraction.

It is important to recognize that during most of the cardiac cycle the atria and/or the ventricles are relaxing. As the atria relax and the ventricles relax blood is drawn into the heart. Unless there is blood in the heart, contraction of the heart cannot pump out blood. For this reason I am choosing to show the pumping actions of the heart starting with atrial relaxation. The pumping of blood through the heart can be viewed simply as the movement of blood from an area of higher pressure to an area of lower pressure.

- Blood moves from an area of higher pressure to an area of lower pressure

Pumping actions of the heart

The pumping actions of the heart are shown in Figure 16.4.

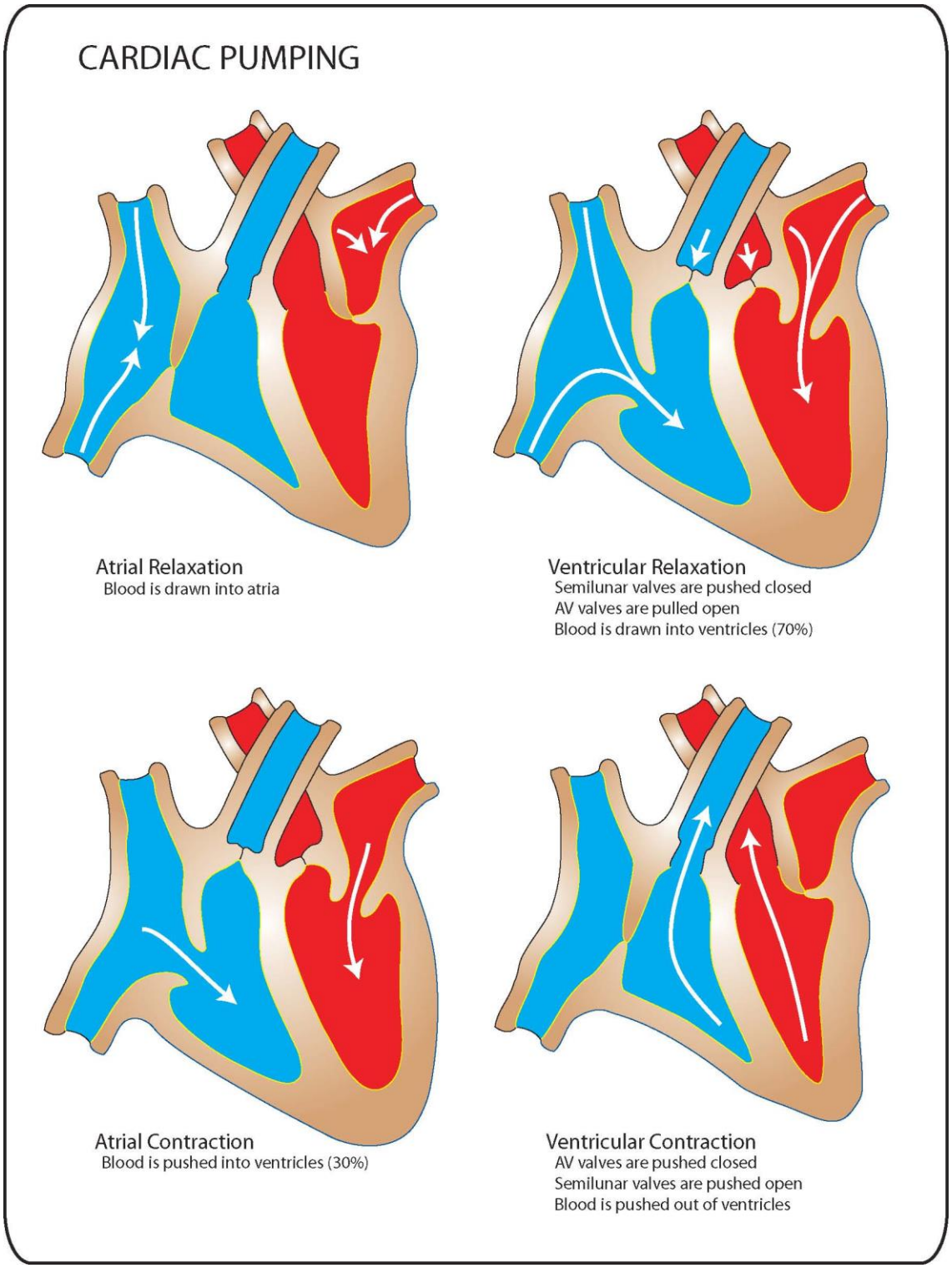


Figure 16.4 © 2007 David G. Ward, Ph.D.

- Atrial Relaxation
    - Leads to a decrease in atrial pressures
    - As the atrial pressures become less than the venous pressures, blood moves from the veins into the atria.
- Ventricular Relaxation (Diastole)
    - Leads to a rapid decrease in ventricular pressure
    - As the ventricular pressures become less than the arterial pressures, the semilunar valves close.
    - As the ventricular pressures become less than the atrial pressures, the atrioventricular valves open and blood moves from the atria into the ventricles.
    - The diastolic pressure differences between the atria and the ventricles leads to about 70% of ventricular filling.
- Atrial Contraction
    - Leads to a rapid increase in atrial pressures.
    - As the atrial pressures increase, more blood moves from the atria into the ventricles.
    - The pressure differences between the atria and the ventricles leads to about 30% of ventricular filling.
- Ventricular Contraction (Systole)
    - Leads to a rapid increase in ventricular pressure
    - As the ventricular pressures exceed the atrial pressures, the atrioventricular valves close.
    - As the ventricular pressures exceed the arterial pressures, the semilunar valves open and blood moves into the arteries.

Coordination of Cardiac Muscle Contraction

We need to remember that there are no valves between the veins and the atria and that the semilunar valves and corresponding arteries are at the top of the heart (base). In order to optimize the movement of blood from the atria into the ventricles during atrial contraction, the atria must contract from the atrial appendages toward the AV valves. In order to optimize the movement of blood from the ventricles into the arteries the ventricles must contract from the bottom of the heart (apex) toward the semilunar valves.

Cardiac conduction system

The coordination of the contraction of the cardiac muscle cells is mediated by the cardiac conduction system, as shown in Figure 16.5.

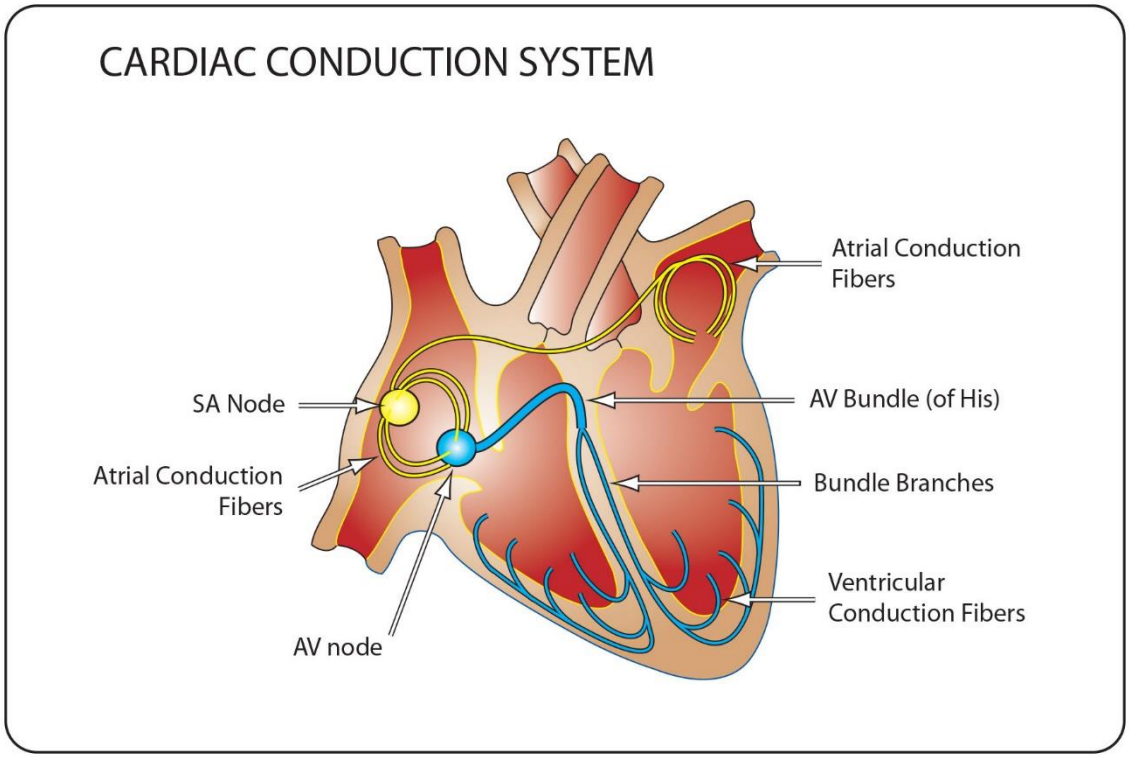


Figure 16.5 © 2014 David G. Ward, Ph.D.

Some cardiac muscle cells are specialized to generate and conduct action potentials. These include cells of the:

- Sinoatrial (SA) node in the posterior wall of the right atrium
- Atrial conduction fibers in the right and left atria
- Atrioventricular (AV) node in the floor of the right atrium near the ventricle
- AV bundle (of His) in the interventricular septum
- Bundle branches in the interventricular septum
- Ventricular conduction fibers (Purkinje fibers) in the right and left ventricles

Pacemaker signals originate in the SA node and travel through atrial conduction fibers into both atria. The atrial conduction fibers are in direct contact with cardiac muscle cells. As signals pass through the conduction fibers, cardiac muscle cells in the atria are stimulated and sequentially contract toward the AV valves. In addition, the pacemaker signals that travel through the right atrial conduction fibers synchronize the activity of the AV node. The AV node in turn generates pacemaker signals that travel through the AV bundle and bundle branches in the interventricular septum to the apex of the heart. Both the AV bundle and the bundle branches are isolated from cardiac muscle

cells. However, at the apex the bundle branches divide into ventricular conduction fibers (Purkinje fibers) that are in direct contact with cardiac muscle cells. As signals pass through the conduction fibers, cardiac muscle cells in the ventricles are stimulated and sequentially contract toward the semilunar valves.

Pacemaker cells

Pacemaker cells are unique in that their cell membranes depolarize spontaneously and cyclically. The cells of the SA node and the AV node are normally the dominant pacemakers. In addition, there are focal pacemaker cells in the atria and in the ventricles. Each of these has different intrinsic rates.

- The sinoatrial (SA) node intrinsically produces about 80-100 action potentials per minute.
- Atrial foci intrinsically produce about 60-80 action potentials per minute.
- The atrioventricular (AV) node intrinsically produces about 40-60 action potentials per minute.
- Ventricular foci intrinsically produce about 20-40 action potentials per minute.

As long as the SA node communicates with the AV node, the atrial foci, the AV node, and the ventricular foci will be synchronized at the same rate as the SA node. However, with damage to the SA node, the AV node will act as an independent pacemaker and generate action potentials at a lower rate. With damage to the SA node and atrial foci, the atria will not contract and "top-off" the filling of the ventricles. When the AV node operates at a lower rate the ventricles will stay relaxed longer and have more time to fill.

into

It is important to point out that the autonomic nervous system has considerable influence on the pacemakers. At rest the parasympathetic nervous system dominates and reduces the rate of the SA node to about 70 action potentials per minute. We will return to this issue toward the end of the chapter.

- Tachycardia refers to a heart rate greater than 100 beats / minute
- Bradycardia refers to a heart rate less than 60 beats / minute

Pacemaker potentials

The cellular mechanisms responsible for the generation of cardiac pacemaker activity are illustrated in Figure 16.6. The cyclic depolarization of the cell membranes of pacemaker cells is due to the opening and closing of several membrane channels. Pacemaker cells are unique in having voltage gated sodium channels that open upon repolarization rather than depolarization.

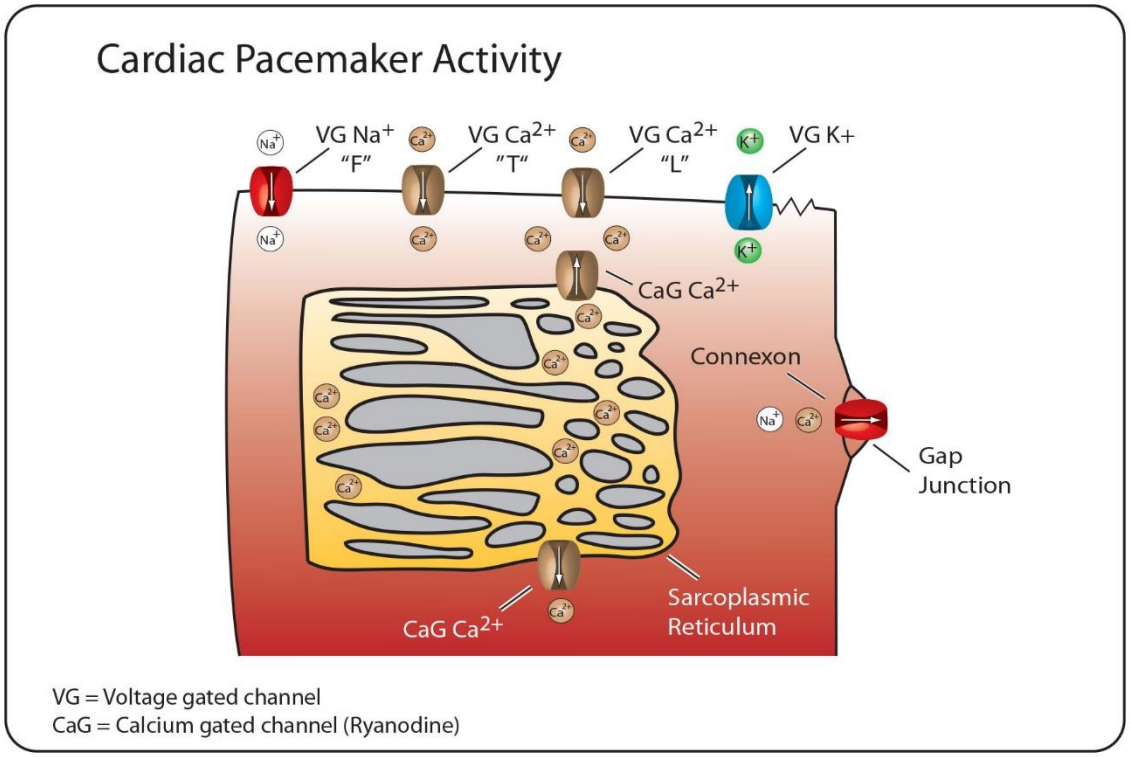


Figure 16.6 © 2014 David G. Ward, Ph.D.

- Voltage gated "F" channels which are Na^+ / K^+ channels that respond to repolarization (not depolarization) by opening briefly and then closing (the movement of Na^+ dominates causing an early depolarization).
- In response to the initial depolarization voltage-gated Ca^{++} T-channels open briefly causing a further depolarization.
- In responses to this further depolarization voltage-gated Ca^{++} L-channels open. (These channels are sensitive to dihydropyridine.)
- The Ca^{++} entry leads to the opening of calcium gated calcium channels in the sarcoplasmic reticulum and further movement of Ca^{++} into the cytosol. (These channels are sensitive to ryanodine.)
- The final depolarization opens voltage-gated K^+ channels.
- The escape of K^+ leads to a repolarization that closes the Ca^{++} channels and subsequently closes the K^+ channels.
- The repolarization causes the cycle to repeat.

The changing membrane potential and the permeability of the "F" Na^+ channels, Ca^{++} T-channels, Ca^{++} L-channels, and K^+ channels of a cardiac pacemaker cell during a cycle are shown in Figure 16.7.

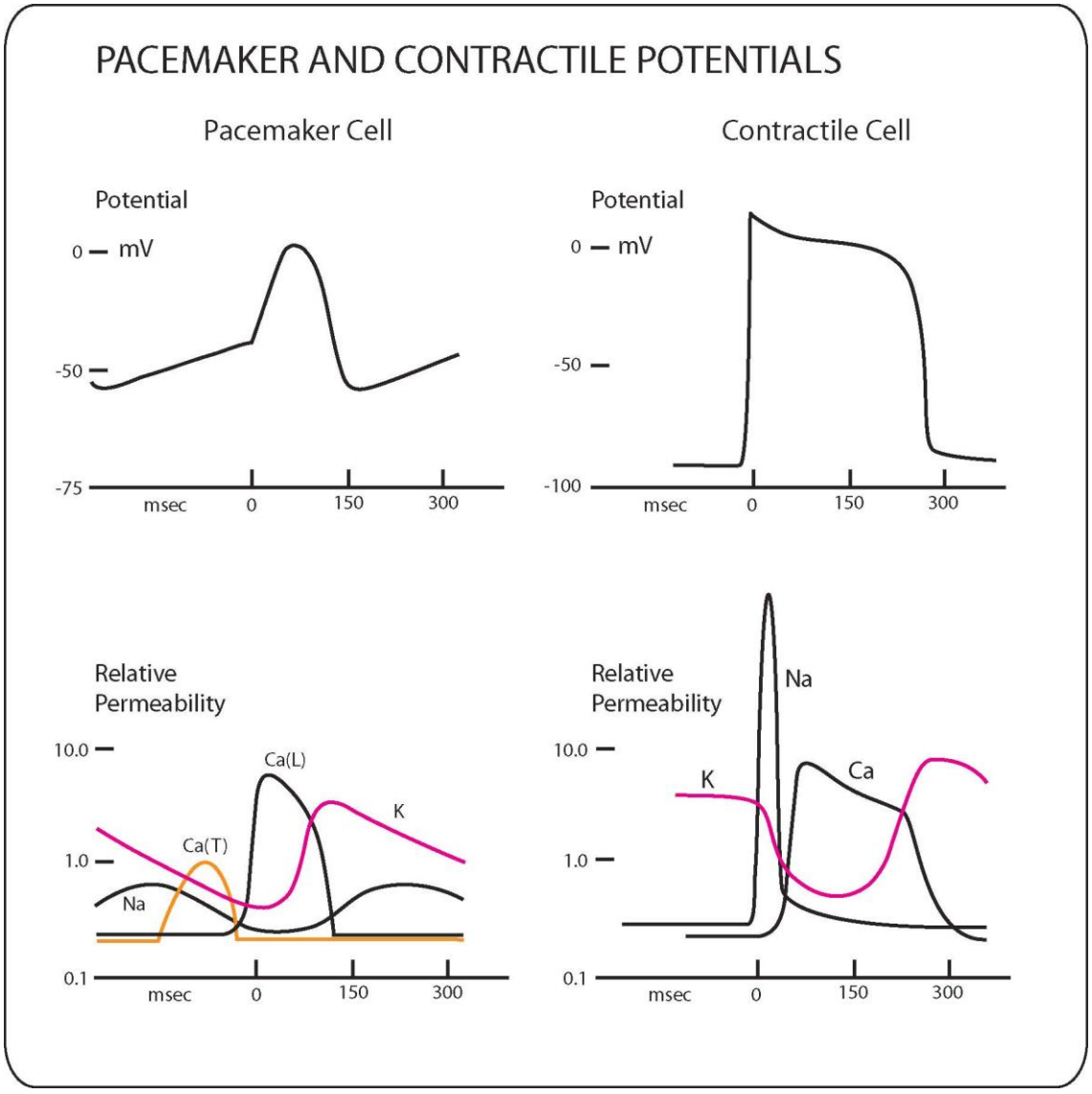


Figure 16.7 © 2007 David G. Ward, Ph.D.

Pacemaker control of cardiac muscle contraction

Cardiac muscle cells are mainly activated by diffusion of cations through gap junctions in the intercalated discs, as shown in chapter 11, Figure 11.11. Control of a cardiac muscle cell by a pacemaker cell through gap junctions is illustrated in Figure 16.8.

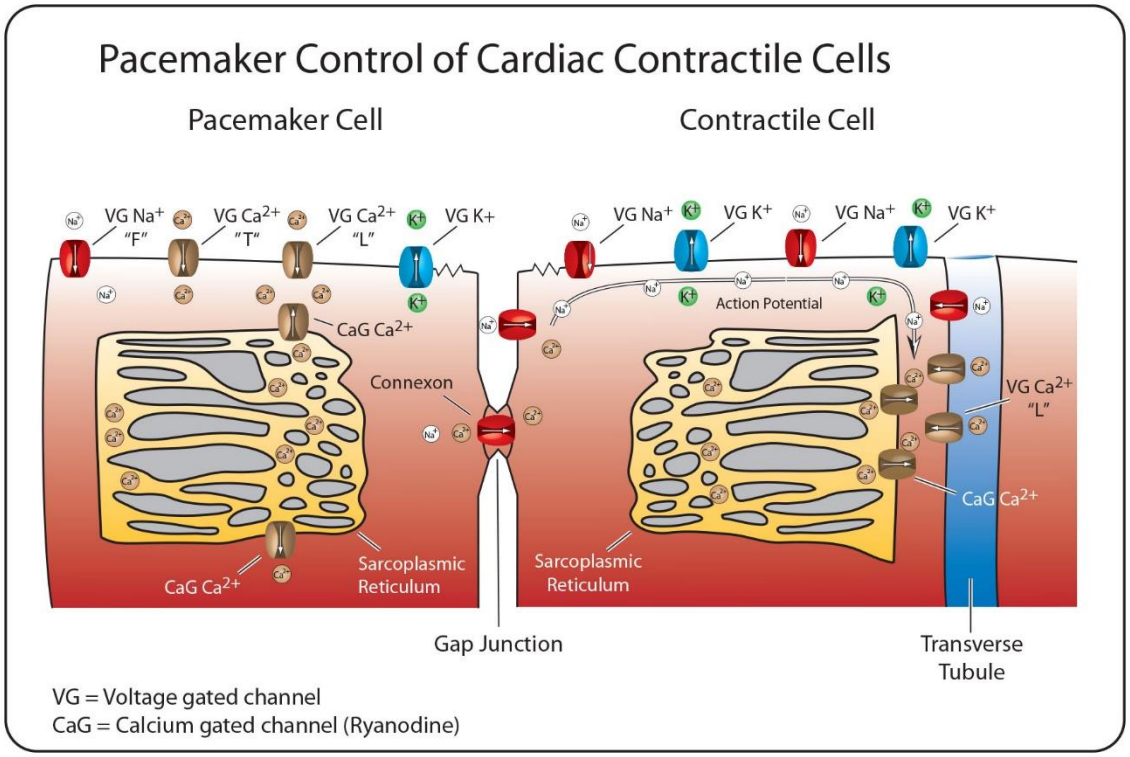


Figure 16.8 © 2014 David G. Ward, Ph.D.

- The influx of sodium and calcium through the **connexon** of the gap junction between the pacemaker and contractile cell leads to the opening of voltage gated Na^+ channels in the sarcolemma of the contractile cell.
- The sequential opening and closing of Na^+ channels and K^+ channels along the membrane produces an action potential like that seen in axons (refer to chapter 8).
- The action potential is conducted across the sarcolemma and down each of the transverse tubules.
- The action potential activates voltage sensitive Ca^{++} L-channels in the transverse tubules and allows calcium to diffuse from the extracellular fluid into the sarcoplasm. (These channels are sensitive to dihydropyridine.)
- The entry of calcium seems to activate some of the calcium gated calcium channels in the sarcoplasmic reticulum and allows calcium to diffuse out of the sarcoplasmic reticulum (SR) and into the cytosol. (These channels are sensitive to ryanodine.)
- Voltage gated K^+ channels open in response to the prolonged depolarization, and subsequently close.
- As shown in chapter 11, Figure 11.6, the Ca^{++} that enters the sarcoplasm binds to troponin and moves tropomyosin away from the binding sites on actin, allows the myosin heads to bind to actin, and causes muscle contraction.

The membrane potentials and the permeability of the Na^+ channels, Ca^{++} L-channels, and K^+ channels of cardiac contractile cells associated with the contraction cycle are shown in Figure 16.7.

Electrocardiogram (EKG)

The electrocardiogram reflects the changes in membrane potential of the cardiac muscle (contractile cell potentials) during the cardiac cycle, as shown in Figure 16.7. The changes in membrane potential of the cardiac muscle cells are measured from the surface of the body.

Standard Limb Leads

Measurement of EKG is based on potential differences between the three combinations of two points around a triangle as worked out by Einthoven.

- Lead I measures the potential difference between the Right Arm and the Left Arm.
- Lead II measures the potential difference between the Right Arm and the Left Leg.
- Lead III measure the potential difference between the Left Arm and the Left Leg.

An example of a normal EKG with lead I, II, and III measurements is shown in Figure 16.9. The significance of Einthoven's triangle is that the sum of the voltages of leads I and III equals that in lead II (Einthoven's law). Hence, if the voltages of two of the standard leads are recorded, that of the third lead can be determined mathematically.

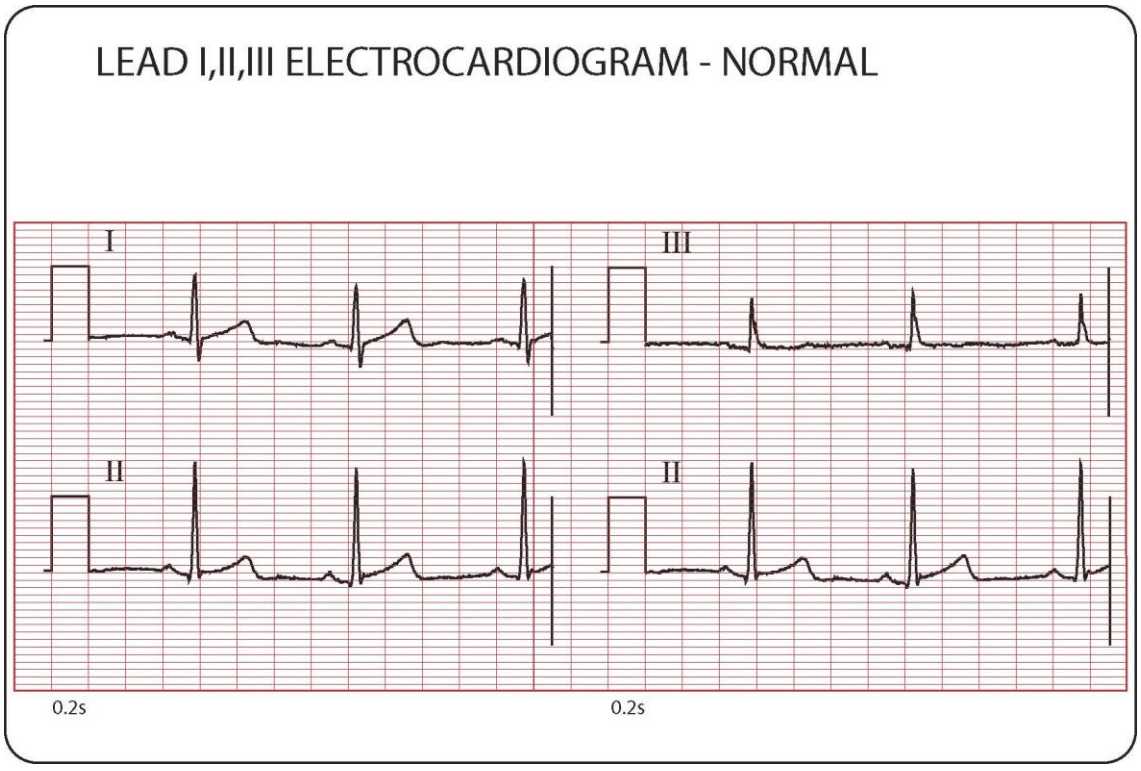


Figure 16.9 © 2007 David G. Ward, Ph.D.

Twelve lead measurements from the skin of the chest are common in the clinical setting. However, the underlying mechanisms remain the same.

EKG waves

In the EKG tracing several waves are prominent, as shown in Figure 16.10.

- The P wave measures depolarization of the atria.
- The QRS waves measures depolarization of the ventricles.
- The T wave measures repolarization of the ventricles.

The timing of the intervals between the waves is of diagnostic importance. The most useful intervals are the RR interval, PR interval, QRS interval, and the QT interval, also shown in Figure 16.10.

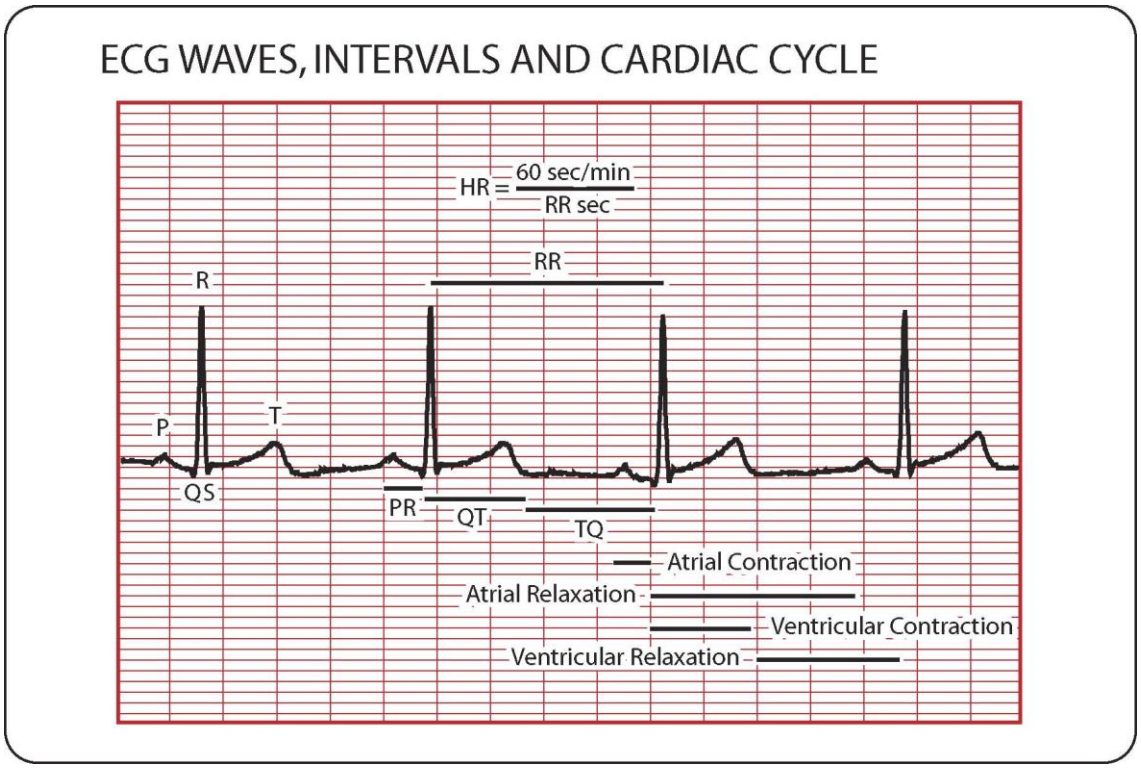


Figure 16.10 © 2007 David G. Ward, Ph.D.

- RR interval
  - The time between the peak of one R wave and the peak of the next R wave
  - The time is inversely related to the heart rate and is 0.857 sec (857 msec) at a heart rate of 70 beats / min

$$\text{Heart Rate} = \frac{60 \text{ sec/min}}{\text{RR interval (sec)}}$$

- PR interval
  - The time between the beginning of the P wave and the beginning of the R wave
  - Represents the time between the beginning of atrial depolarization and ventricular depolarization
  - Corresponds to the time of atrial contraction
  - Usually about 0.17 sec (170 msec)
  - A longer interval may suggest a partial AV heart block caused by damage to the AV node.
  - In total heart block, no impulses are transmitted through the AV node, and the atria and ventricles beat independently of one another.

- QRS interval
  - The time between the Q wave and the S wave
  - Represents the time for the depolarization of the ventricles
  - Usually about 0.08 sec (80 msec)
  - Prolonged by a right or left bundle branch block in which one ventricle is contracting later than the other

- QT interval
  - The time between the Q wave and the end of the T wave
  - The Q-T interval is the period from the beginning of ventricular depolarization through repolarization.
  - The ST segment corresponds to the time of ventricular contraction.
  - Usually about 0.35 sec (350 msec) at a heart rate of 70 beats / min
  - As the rate increases, this interval becomes shorter; conversely, when the heart rate drops, the interval is longer.
  - Prolonged by damage to conduction fibers, ischemia or myocardial damage

- TQ interval
  - The time between the end of the T wave and the Q wave
  - The T-Q interval is the period from the end of ventricular depolarization through the end of atrial depolarization.
  - Corresponds to the time of ventricular relaxation

- QP interval
  - Corresponds to the time of atrial relaxation

Cardiac Pumping and the EKG

Figure 16.11 summarizes the temporal relationships among the pacemaker potentials, the cardiac contractile potentials, and the electrocardiogram, left atrial pressure, left ventricular pressure, and aortic pressure as seen during cardiac pumping.

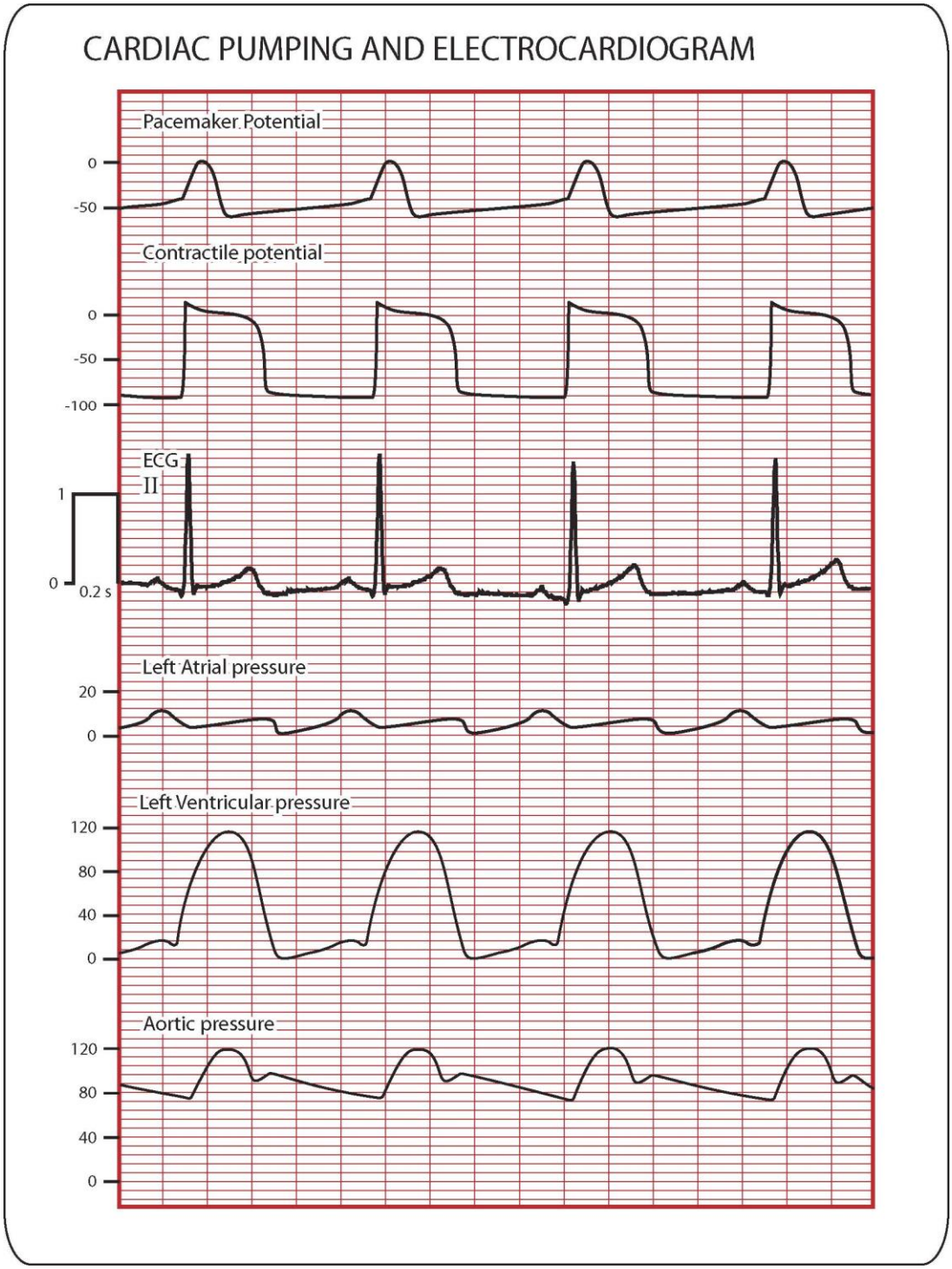


Figure 16.11 © 2007 David G. Ward, Ph.D.

Cardiac Output

The purpose of cardiac pumping is of course to pump blood out of the heart, to the lungs, back to the heart, to the rest of the body, and back to the heart. The amount of blood pumped out of the heart (left ventricle) each minute is called **cardiac output**. A normal cardiac output is about 7% of body weight in kg. For an average person of about 70 kg, their cardiac output would be about 4.9 L / min (or 4900 mL / min).

Cardiac output is influenced by two major factors, the stroke volume and the heart rate.

Cardiac output (CO) = Stroke volume (SV) x Heart rate (HR)

- Stroke volume (SV) is the amount of blood pumped out of the heart (left ventricle) with each contraction.
- Heart rate (HR) is the number of contractions per minute.

With a heart rate of 70 beats / min we can see that the stroke volume would be 70 mL.

4900 mL / min = 70 mL x 70 beats / min

However, stroke volume is influenced by two major factors, the end diastolic volume and the end systolic volume, as shown in Figure 16.12.

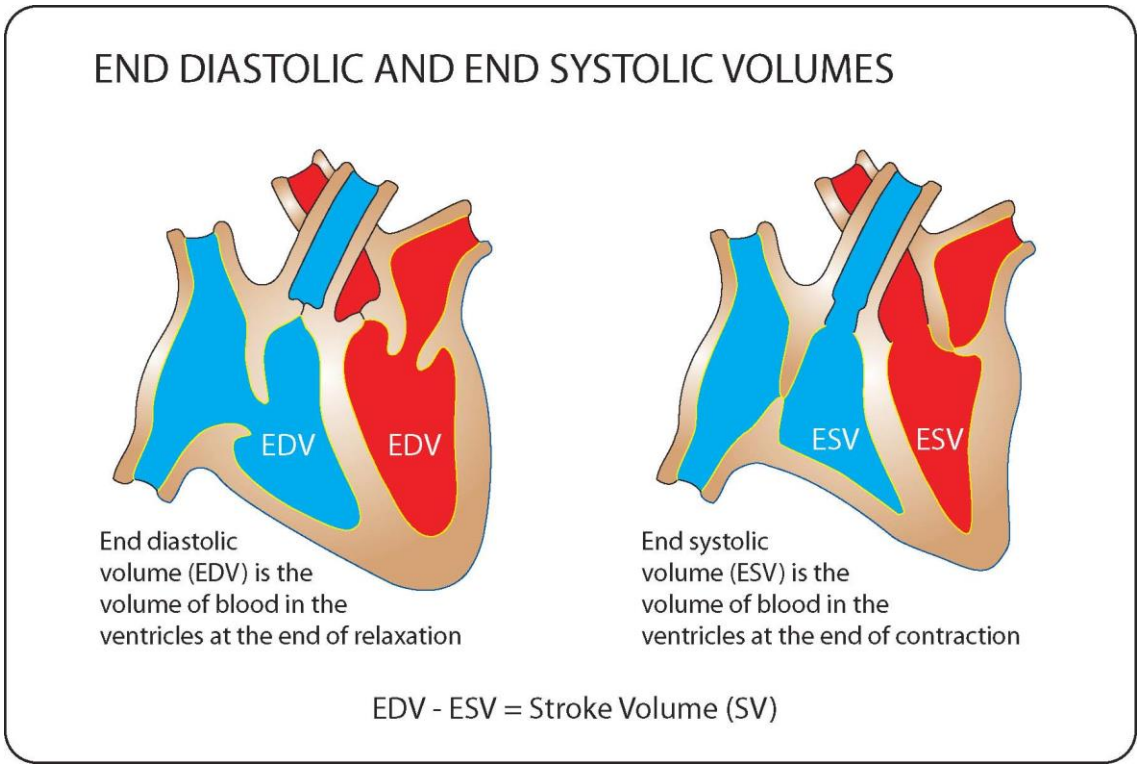


Figure 16.12 © 2007 David G. Ward, Ph.D.

Stroke volume (SV) = End Diastolic Volume (EDV) – End Systolic Volume (ESV)

- End Diastolic Volume (EDV) is the ventricular volume at the end of ventricular relaxation.
- End Systolic Volume (ESV) is the ventricular volume at the end of ventricular contraction.

In turn, the end diastolic volume and the end systolic volume are influenced by vascular factors, as shown in Figure 16.13, as well as by cardiac factors.

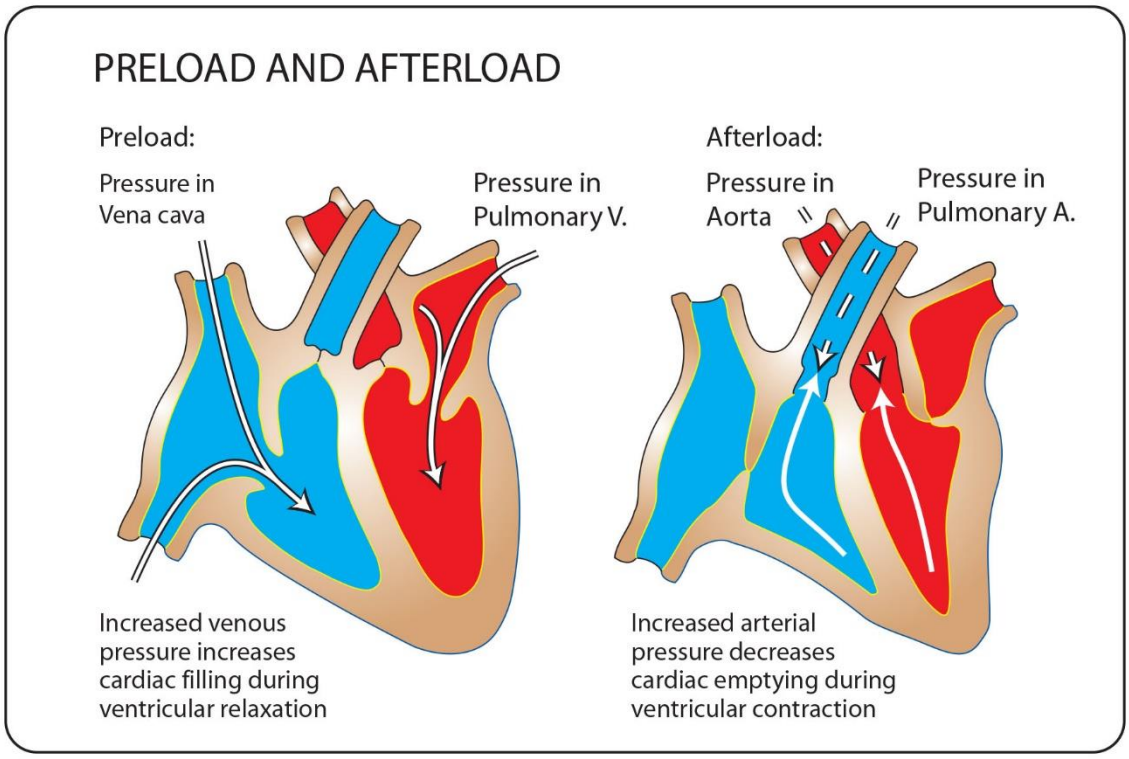


Figure 16.13 © 2014 David G. Ward, Ph.D.

- End Diastolic Volume (EDV) is increased by elevated central venous pressure (preload) and by increased filling time,
- End Systolic Volume (ESV) is increased by elevated arterial pressure (afterload) and is decreased by increased force of ventricular contraction.

Control of stroke volume, heart rate and cardiac output

Together we can see that cardiac output is influenced by end diastolic volume, end systolic volume, and heart rate:

$$CO = (EDV - ESV) \times HR$$

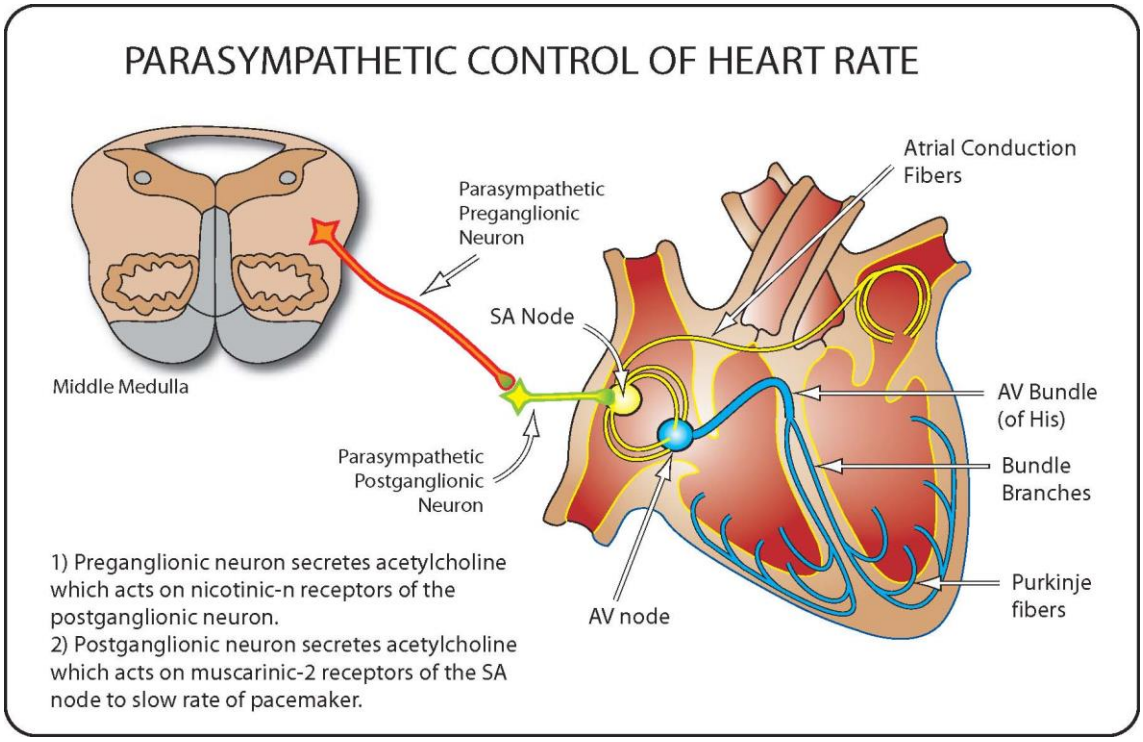
- Increased central venous pressure will increase cardiac filling during ventricular relaxation and increase EDV, and by itself increase CO.
- Increased arterial pressure will decrease cardiac emptying during ventricular contraction and increase ESV, and by itself decrease CO.
- Increased force of ventricular contraction will increase cardiac emptying during ventricular contraction and decrease ESV, and by itself increase CO.
- Increased HR will by itself increase CO.
- Decreased HR will by itself decrease CO.

Neural and Hormonal Control of the Heart

Modulation of Cardiac pacemakers and muscle

Pacemaker cells not only have an intrinsic rhythm generator, their rhythms are modulated by parasympathetic nerves, by sympathetic nerves and by various hormones, such as epinephrine. As we noted earlier, a typical resting heart rate is about 70 beats / minute although the intrinsic rate of the SA node is about 80 – 100 beats / minute. This difference is largely due the activity of the parasympathetic nervous system

Parasympathetic control of heart rate is shown in Figure 16.14. Parasympathetic postganglionic neurons secrete acetylcholine which acts on muscarinic-2 receptors to hyperpolarize the pacemaker cells causing a decrease in heart rate. (The action of acetylcholine on muscarinic -2 receptors is discussed in chapters 6 and 13 and shown in Figure 6.8)



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Sympathetic control of heart rate is shown in Figure 16.15. Sympathetic postganglionic neurons secrete norepinephrine which acts on Beta-1 receptors to further depolarize the pacemaker cells causing an increase in heart rate. (The action of norepinephrine and epinephrine on beta-1 receptors is discussed in chapters 6, 7, 13, and 14 and shown in chapter 11, Figure 11.12).

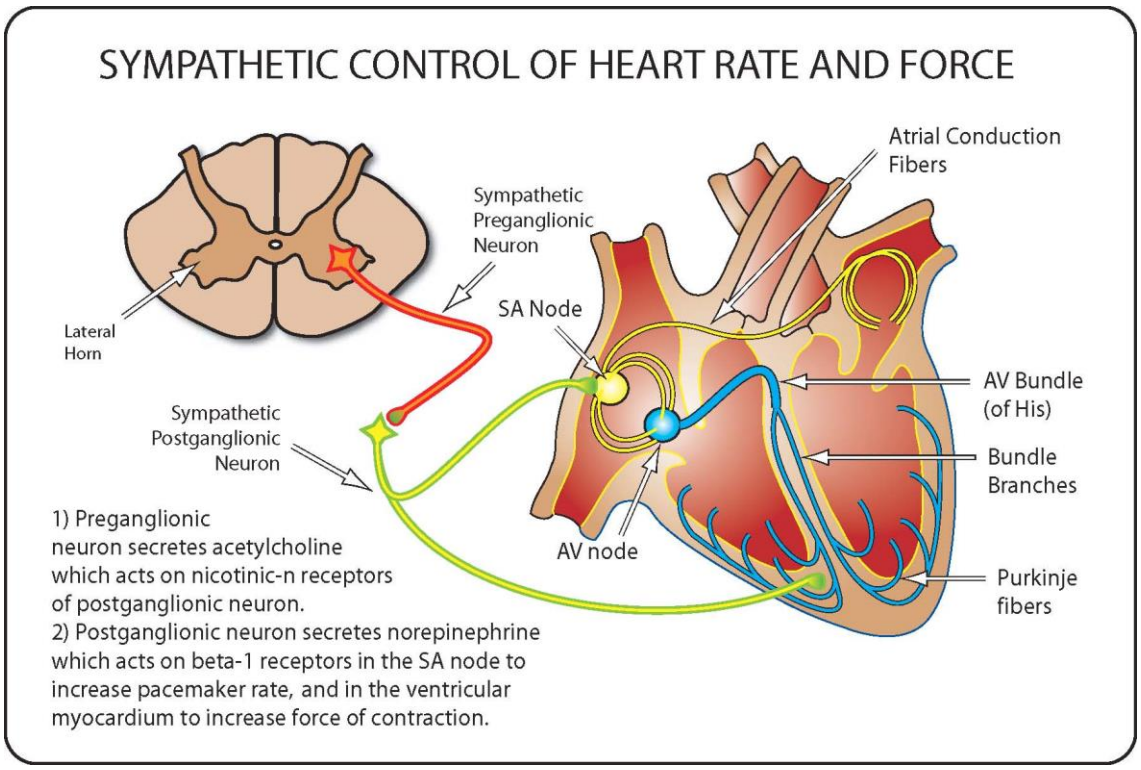


Figure 16.15 © 2007 David G. Ward, Ph.D.

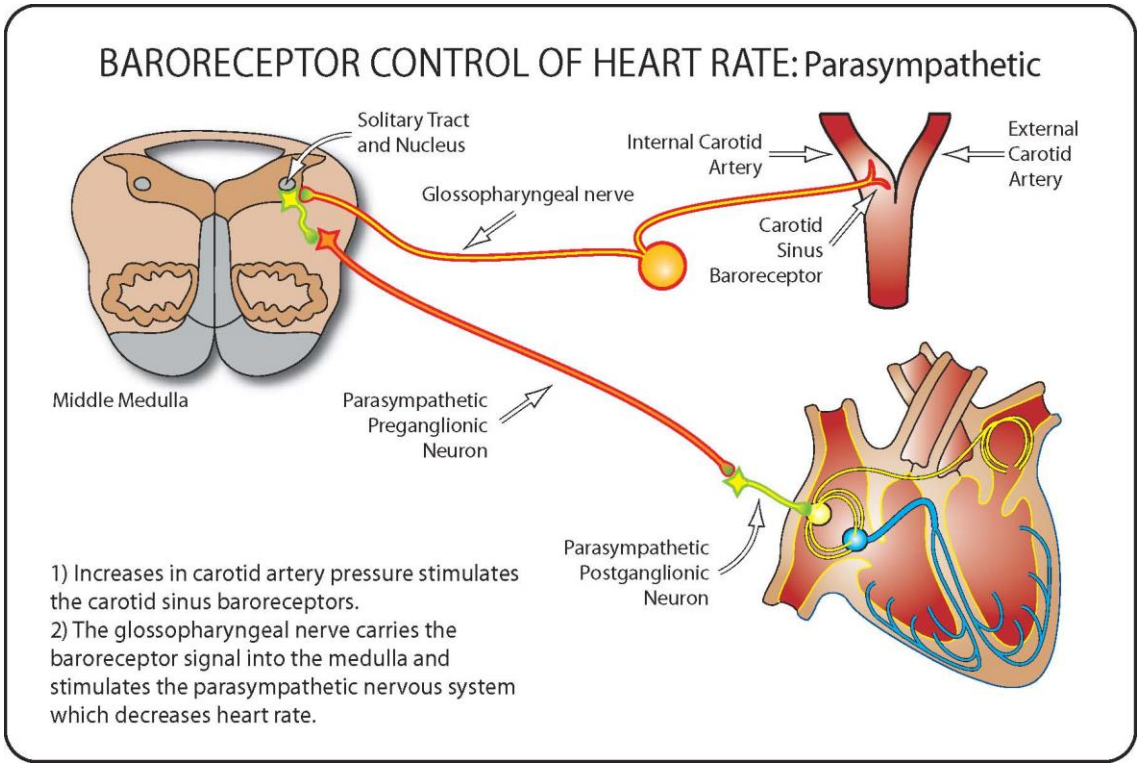
Cardiac muscle cells are not only controlled by the cardiac conduction system, they are modulated by the sympathetic nervous system and various hormones, for example by epinephrine. Sympathetic control of cardiac force is shown in Figure 16.15. Sympathetic postganglionic neurons secrete norepinephrine which acts on Beta-1 receptors to increase movement of calcium into the cytosol and increase the force of cardiac contraction. (The action of norepinephrine and epinephrine on Beta-1 receptors is discussed in chapters 6, 7, 13, and 14 and shown in chapter 11, Figure 11.12).

Baroreceptor Reflexes - cardiac control

The cardiovascular system contains sensory receptors that monitor blood pressures in the neck, trunk, and heart. Signals from these sensory receptors travel to the brainstem where they are compared to reference values. When necessary, cardiovascular responses are generated to normalize the pressures.

- Carotid sinus baroreceptors respond to pressure changes in the carotid arteries going to the head.
- Aortic arch baroreceptors respond to pressure changes in the aorta.
- Cardiac atrial stretch receptors respond to pressure changes in the cardiac atria.

Baroreceptor control of heart rate by the parasympathetic nervous system is shown in Figure 16.16. Increases in carotid artery pressure stimulate the carotid sinus baroreceptors. The glossopharyngeal nerve carries the baroreceptor signal into the medulla of the brainstem and further stimulates the parasympathetic nervous system which decreases heart rate. Although not shown, this same signal inhibits the sympathetic nervous system which also contributes to the decrease in heart rate. The effect of the increase in parasympathetic activity generally dominates the effect of decreases in sympathetic activity.



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In a complementary manner, decreases in carotid artery pressure "de-stimulate" the carotid sinus baroreceptors. This results in inhibition of the parasympathetic nervous system and stimulation of the sympathetic nervous system, causing an increase in heart rate. The increase in heart rate will be dominated by the decrease in parasympathetic activity until the heart rate exceeds 100 beats / minute.

Quiz Yourself

1-5. Matching

A)	QRS waves	represents atrial depolarization	1) _____
B)	PR interval	represents ventricular repolarization	2) _____
C)	QT interval	represents ventricular depolarization	3) _____
D)	P wave	corresponds to time of atrial contraction	4) _____
E)	T wave	corresponds to time of ventricular contraction	5) _____

6-10. Matching

A)	ventricular contraction	blood is pulled into the ventricles	6) _____
B)	ventricular relaxation	blood is pushed out of the ventricles	7) _____
		blood is pulled out of the atria and veins	8) _____
		semilunar valves close and AV valves open	9) _____
		AV valves close and semilunar valves open	10) _____

11-15. Place in order the events responsible for the cycling of pacemaker cells.

A)	Ca^{2+} "T" channels open upon entry of Na^{+} ; "F" channels close	11) _____
B)	Ca^{2+} "L" channels open (for about 150 msec) upon entry of Ca^{2+}	12) _____
C)	K^{+} delayed rectifier channels open after a delay upon entry of Ca^{2+}	13) _____
D)	"F' channels are opened by voltage moving toward hyperpolarization	14) _____
E)	Ca^{2+} "L" channels close and K^{+} delayed rectifier channels close slowly	15) _____

16-20. Matching (stimulus: response)

A)	when carotid sinus pressure decreases	heart rate increases	16) _____
B)	when carotid sinus pressure increases	heart rate decreases	17) _____
		blood vessels constrict	18) _____
		baroreceptor activity increases	19) _____
		baroreceptor activity decreases	20) _____

Fill in

21. The _____ node has an intrinsic rate of about 80-100 action potentials / minute.

22. _____ activates β-1 receptors in the heart and causes rate to _____.

23. _____ activates Muscarinic M_2, G-protein linked receptors in the heart and causes heart rate to _____.

24. Stroke volume (SV) equals _____ - _____.

25. Low arterial pressure will cause a reflex _____ in heart rate.

Study Questions

1. Explain the inter-relationships among cardiac output, heart rate, end diastolic volume (EDV), and end systolic volume (ESV). Include a description of what affects EDV and ESV.
2. Explain the causal relationship between the electrical activity of the ECG and systolic and diastolic blood flow.
3. Explain the significance of ions, especially K^{+} and Ca^{2+}, and various membrane channels, in the production of normal pacemaker rhythms and cardiac pumping.
4. Explain the role of the sympathetic nervous system and various hormones in the control of heart rate and force of contraction. Include the role of baroreceptor reflexes