**Lecture topic is…**

**(Slide 1) Lecture 7**

**Physiology of blood circulation. Part 2**

**(Slide 2)** Lecture plan:

1. Physical and physiological properties of the heart muscle.
2. Conduction system of the heart.
3. Membrane potentials and ion movement in cardiac conductive cells.
4. Correlation between heart rates and cardiac output.
5. Cardiovascular centers.
6. Other factors influencing heart rate and force of contraction.

**(Slide 3)** Recall that cardiac muscle shares a few characteristics with both skeletal muscle and smooth muscle, but it has some unique properties of its own. Not the least of these exceptional properties is its ability to initiate an electrical potential at a fixed rate that spreads rapidly from cell to cell to trigger the contractile mechanism. This property is known as autorhythmicity. Neither smooth nor skeletal muscle can do this. Even though cardiac muscle has autorhythmicity, heart rate is modulated by the endocrine and nervous systems.

**(Slide 4)** There are two major types of cardiac muscle cells: myocardial contractile cells and myocardial conducting cells. The myocardial contractile cells constitute the bulk (99 percent) of the cells in the atria and ventricles. Contractile cells conduct impulses and are responsible for contractions that pump blood through the body. The myocardial conducting cells (1 percent of the cells) form the conduction system of the heart. Except for Purkinje cells, they are generally much smaller than the contractile cells and have few of the myofibrils or filaments needed for contraction. Their function is similar in many respects to neurons, although they are specialized muscle cells. Myocardial conduction cells initiate and propagate the action potential (the electrical impulse) that travels throughout the heart and triggers the contractions that propel the blood.

**(Slide 5)** Compared to the giant cylinders of skeletal muscle, cardiac muscle cells, or cardiomyocytes, are considerably shorter with much smaller diameters. Cardiac muscle also demonstrates striations, the alternating pattern of dark A bands and light I bands attributed to the precise arrangement of the myofilaments and fibrils that are organized in sarcomeres along the length of the cell. These contractile elements are virtually identical to skeletal muscle. T (transverse) tubules penetrate from the surface plasma membrane, the sarcolemma, to the interior of the cell, allowing the electrical impulse to reach the interior. The T tubules are only found at the Z discs, whereas in skeletal muscle, they are found at the junction of the A and I bands. Therefore, there are one-half as many T tubules in cardiac muscle as in skeletal muscle. In addition, the sarcoplasmic reticulum stores few calcium ions, so most of the calcium ions must come from outside the cells. The result is a slower onset of contraction. Mitochondria are plentiful, providing energy for the contractions of the heart. Typically, cardiomyocytes have a single, central nucleus, but two or more nuclei may be found in some cells.

**(Slide 6)** Cardiac muscle cells branch freely. A junction between two adjoining cells is marked by a critical structure called an intercalated disc, which helps support the synchronized contraction of the muscle. The sarcolemmas from adjacent cells bind together at the intercalated discs. They consist of desmosomes, specialized linking proteoglycans, tight junctions, and large numbers of gap junctions that allow the passage of ions between the cells and help to synchronize the contraction. Intercellular connective tissue also helps to bind the cells together. The importance of strongly binding these cells together is necessitated by the forces exerted by contraction.

**(Slide 7) Human Physiology - Cardiac Cell Types. Video**

**(Slide 8)** Cardiac muscle undergoes aerobic respiration patterns, primarily metabolizing lipids and carbohydrates. Myoglobin, lipids, and glycogen are all stored within the cytoplasm. Cardiac muscle cells undergo twitch-type contractions with long refractory periods followed by brief relaxation periods. The relaxation is essential so the heart can fill with blood for the next cycle. The refractory period is very long to prevent the possibility of tetany, a condition in which muscle remains involuntarily contracted. In the heart, tetany is not compatible with life, since it would prevent the heart from pumping blood.

**(Slide 9)** If embryonic heart cells are separated into a Petri dish and kept alive, each is capable of generating its own electrical impulse followed by contraction. When two independently beating embryonic cardiac muscle cells are placed together, the cell with the higher inherent rate sets the pace, and the impulse spreads from the faster to the slower cell to trigger a contraction. As more cells are joined together, the fastest cell continues to assume control of the rate. A fully developed adult heart maintains the capability of generating its own electrical impulse, triggered by the fastest cells, as part of the cardiac conduction system. The components of the cardiac conduction system include the sinoatrial node, the atrioventricular node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje cells.

**(Slide 10)** Normal cardiac rhythm is established by the sinoatrial (SA) node, a specialized clump of myocardial conducting cells located in the superior and posterior walls of the right atrium in close proximity to the orifice of the superior vena cava. The SA node has the highest inherent rate of depolarization and is known as the pacemaker of the heart. It initiates the sinus rhythm, or normal electrical pattern followed by contraction of the heart.

**(Slide 11)** This impulse spreads from its initiation in the SA node throughout the atria through specialized internodal pathways, to the atrial myocardial contractile cells and the atrioventricular node. The internodal pathways consist of three bands (anterior, middle, and posterior) that lead directly from the SA node to the next node in the conduction system, the atrioventricular node. The impulse takes approximately 50 ms (milliseconds) to travel between these two nodes. The relative importance of this pathway has been debated since the impulse would reach the atrioventricular node simply following the cell-by-cell pathway through the contractile cells of the myocardium in the atria. In addition, there is a specialized pathway called Bachmann’s bundle or the interatrial band that conducts the impulse directly from the right atrium to the left atrium. Regardless of the pathway, as the impulse reaches the atrioventricular septum, the connective tissue of the cardiac skeleton prevents the impulse from spreading into the myocardial cells in the ventricles except at the atrioventricular node. (Figure) illustrates the initiation of the impulse in the SA node that then spreads the impulse throughout the atria to the atrioventricular node.

**(Slide 12)** The electrical event, the wave of depolarization, is the trigger for muscular contraction. The wave of depolarization begins in the right atrium, and the impulse spreads across the superior portions of both atria and then down through the contractile cells. The contractile cells then begin contraction from the superior to the inferior portions of the atria, efficiently pumping blood into the ventricles.

**(Slide 13)** The atrioventricular (AV) node is a second clump of specialized myocardial conductive cells, located in the inferior portion of the right atrium within the atrioventricular septum. The septum prevents the impulse from spreading directly to the ventricles without passing through the AV node. There is a critical pause before the AV node depolarizes and transmits the impulse to the atrioventricular bundle. This delay in transmission is partially attributable to the small diameter of the cells of the node, which slow the impulse. Also, conduction between nodal cells is less efficient than between conducting cells. These factors mean that it takes the impulse approximately 100 ms to pass through the node. This pause is critical to heart function, as it allows the atrial cardiomyocytes to complete their contraction that pumps blood into the ventricles before the impulse is transmitted to the cells of the ventricle itself. With extreme stimulation by the SA node, the AV node can transmit impulses maximally at 220 per minute. This establishes the typical maximum heart rate in a healthy young individual. Damaged hearts or those stimulated by drugs can contract at higher rates, but at these rates, the heart can no longer effectively pump blood.

**(Slide 14)** Arising from the AV node, the atrioventricular bundle, or bundle of His, proceeds through the interventricular septum before dividing into two atrioventricular bundle branches, commonly called the left and right bundle branches. The left bundle branch has two fascicles. The left bundle branch supplies the left ventricle, and the right bundle branch the right ventricle. Since the left ventricle is much larger than the right, the left bundle branch is also considerably larger than the right. Portions of the right bundle branch are found in the moderator band and supply the right papillary muscles. Because of this connection, each papillary muscle receives the impulse at approximately the same time, so they begin to contract simultaneously just prior to the remainder of the myocardial contractile cells of the ventricles. This is believed to allow tension to develop on the chordae tendineae prior to right ventricular contraction. There is no corresponding moderator band on the left. Both bundle branches descend and reach the apex of the heart where they connect with the Purkinje fibers. This passage takes approximately 25 ms.

**(Slide 15)** The Purkinje fibers are additional myocardial conductive fibers that spread the impulse to the myocardial contractile cells in the ventricles. They extend throughout the myocardium from the apex of the heart toward the atrioventricular septum and the base of the heart. The Purkinje fibers have a fast inherent conduction rate, and the electrical impulse reaches all of the ventricular muscle cells in about 75 ms. Since the electrical stimulus begins at the apex, the contraction also begins at the apex and travels toward the base of the heart, similar to squeezing a tube of toothpaste from the bottom. This allows the blood to be pumped out of the ventricles and into the aorta and pulmonary trunk. The total time elapsed from the initiation of the impulse in the SA node until depolarization of the ventricles is approximately 225 ms.

**(Slide 16) Conduction system of the heart - Sinoatrial node, AV Node, Bundle of His, Purkinje fibers Animation. Video**

**(Slide 17)** Action potentials are considerably different between cardiac conductive cells and cardiac contractive cells. While Na+ and K+ play essential roles, Ca2+ is also critical for both types of cells. Unlike skeletal muscles and neurons, cardiac conductive cells do not have a stable resting potential. Conductive cells contain a series of sodium ion channels that allow a normal and slow influx of sodium ions that causes the membrane potential to rise slowly from an initial value of −60 mV up to about –40 mV. The resulting movement of sodium ions creates spontaneous depolarization (or prepotential depolarization). At this point, calcium ion channels open and Ca2+ enters the cell, further depolarizing it at a more rapid rate until it reaches a value of approximately +15 mV. At this point, the calcium ion channels close and K+ channels open, allowing outflux of K+ and resulting in repolarization. When the membrane potential reaches approximately −60 mV, the K+ channels close and Na+ channels open, and the prepotential phase begins again. This phenomenon explains the autorhythmicity properties of cardiac muscle.

**(Slide 18)** The prepotential is due to a slow influx of sodium ions until the threshold is reached followed by a rapid depolarization and repolarization. The prepotential accounts for the membrane reaching threshold and initiates the spontaneous depolarization and contraction of the cell. Note the lack of a resting potential.

**(Slide 19)** The pattern of prepotential or spontaneous depolarization, followed by rapid depolarization and repolarization just described, are seen in the SA node and a few other conductive cells in the heart. Since the SA node is the pacemaker, it reaches threshold faster than any other component of the conduction system. It will initiate the impulses spreading to the other conducting cells. The SA node, without nervous or endocrine control, would initiate a heart impulse approximately 80–100 times per minute. Although each component of the conduction system is capable of generating its own impulse, the rate progressively slows as you proceed from the SA node to the Purkinje fibers. Without the SA node, the AV node would generate a heart rate of 40–60 beats per minute. If the AV node were blocked, the atrioventricular bundle would fire at a rate of approximately 30–40 impulses per minute. The bundle branches would have an inherent rate of 20–30 impulses per minute, and the Purkinje fibers would fire at 15–20 impulses per minute. While a few exceptionally trained aerobic athletes demonstrate resting heart rates in the range of 30–40 beats per minute (the lowest recorded figure is 28 beats per minute for Miguel Indurain, a cyclist), for most individuals, rates lower than 50 beats per minute would indicate a condition called bradycardia. Depending upon the specific individual, as rates fall much below this level, the heart would be unable to maintain adequate flow of blood to vital tissues, initially resulting in decreasing loss of function across the systems, unconsciousness, and ultimately death.

**(Slide 20) What Is A Healthy Heart Rate - What Affects Heart Rate - What Is Maximum Heart Rate. Video**

**(Slide 21)** Heart rates vary considerably, not only with exercise and fitness levels, but also with age. Newborn resting heart rates may be 120 bpm. Heart rate gradually decreases until young adulthood and then gradually increases again with age.

**(Slide 22)** Maximum heart rates are normally in the range of 200–220 bpm, although there are some extreme cases in which they may reach higher levels. As one ages, the ability to generate maximum rates decreases. This may be estimated by taking the maximal value of 220 bpm and subtracting the individual’s age. So a 40-year-old individual would be expected to hit a maximum rate of approximately 180, and a 60-year-old person would achieve a heart rate of 160.

**(Slide 23)** Initially, physiological conditions that cause HR to increase also trigger an increase in stroke volume (SV). During exercise, the rate of blood returning to the heart increases. However as the HR rises, there is less time spent in diastole and consequently less time for the ventricles to fill with blood. Even though there is less filling time, SV will initially remain high. However, as HR continues to increase, SV gradually decreases due to decreased filling time. CO (carbon dioxide) will initially stabilize as the increasing HR compensates for the decreasing SV, but at very high rates, CO will eventually decrease as increasing rates are no longer able to compensate for the decreasing SV. Consider this phenomenon in a healthy young individual. Initially, as HR increases from resting to approximately 120 bpm, CO will rise. As HR increases from 120 to 160 bpm, CO remains stable, since the increase in rate is offset by decreasing ventricular filling time and, consequently, SV. As HR continues to rise above 160 bpm, CO actually decreases as SV falls faster than HR increases. So although aerobic exercises are critical to maintain the health of the heart, individuals are cautioned to monitor their HR to ensure they stay within the target heart rate range of between 120 and 160 bpm, so CO is maintained. It is also important to note that the coronary circulation nourishes the heart during diastole so as the HR increases the ability of the coronary circulation to nourish the myocardium decreases. The target HR is loosely defined as the range in which both the heart and lungs receive the maximum benefit from the aerobic workout and is dependent upon age.

**(Slide 24)** Nervous control over HR is centralized within the two paired cardiovascular centers of the medulla oblongata. The cardioaccelerator regions stimulate activity via sympathetic stimulation of the cardioaccelerator nerves, and the cardioinhibitory centers decrease heart activity via parasympathetic stimulation as one component of the vagus nerve, cranial nerve X. Both sympathetic and parasympathetic stimulations flow through a paired complex network of nerve fibers known as the cardiac plexus near the base of the heart. The cardioaccelerator center also sends additional fibers, forming the cardiac nerves via sympathetic ganglia (the cervical ganglia plus superior thoracic ganglia T1–T4) to both the SA and AV nodes to increase heart rate, plus additional fibers to the atrial and ventricular myocardium to increase force of contraction. The ventricles are more richly innervated by sympathetic fibers than parasympathetic fibers. During rest, both centers provide slight stimulation to the heart, contributing to autonomic tone. This is a similar concept to tone in skeletal muscles. Normally, vagal stimulation predominates as, left unregulated, the SA node would initiate a sinus rhythm of approximately 100 bpm.

**(Slide 25)** At the nodes sympathetic stimulation causes the release of the neurotransmitter norepinephrine (NE) at the neuromuscular junction of the cardiac nerves. NE binds to the beta-1 receptors and opens chemical- or ligand-gated sodium and calcium ion channels, allowing an influx of positively charged ions. NE shortens the repolarization period, thus speeding the rate of depolarization and contraction, which results in an increase in HR. Some cardiac medications (for example, beta blockers) work by blocking these receptors, thereby slowing HR and are one possible treatment for hypertension. Overprescription of these drugs may lead to bradycardia and even stoppage of the heart.

**(Slide 26)** Parasympathetic stimulation originates from the cardioinhibitory region with impulses traveling via the vagus nerve (cranial nerve X). The vagus nerve sends branches to both the SA and AV nodes to decrease HR. Parasympathetic stimulation releases the neurotransmitter acetylcholine (ACh) at the neuromuscular junction. ACh slows HR by opening chemical- or ligand-gated potassium ion channels to slow the rate of spontaneous depolarization and increase the time before the next spontaneous depolarization occurs. Without any nervous stimulation, the SA node would establish a sinus rhythm of approximately 100 bpm. Since resting rates are considerably less than this, it becomes evident that parasympathetic stimulation normally slows HR. This is similar to an individual driving a car with one foot on the brake pedal. To speed up, one need merely remove one’s foot from the break and let the engine increase speed. In the case of the heart, decreasing parasympathetic stimulation decreases the release of ACh, which allows HR to increase up to approximately 100 bpm. Any increases beyond this rate would require sympathetic stimulation.

**(Slide 27)** The cardiovascular center receive input from the limbic system as well as a series of visceral receptors with impulses traveling through visceral sensory fibers within the vagus and sympathetic nerves via the cardiac plexus. Among these receptors are various proprioreceptors, baroreceptors, and chemoreceptors. Collectively, these inputs normally enable the cardiovascular centers to regulate heart function precisely, a process known as cardiac reflexes. Increased physical activity results in increased rates of firing by various proprioreceptors located in muscles, joint capsules, and tendons. Any such increase in physical activity would logically warrant increased blood flow. The cardiac centers monitor these increased rates of firing, and suppress parasympathetic stimulation and increase sympathetic stimulation as needed in order to increase blood flow.

**(Slide 28)** Similarly, baroreceptors are stretch receptors located in the aortic sinus, carotid bodies, the venae cavae, and other locations, including pulmonary vessels and the rightatrium. Rates of firing from the baroreceptors represent blood pressure, level of physical activity, and the relative distribution of blood. The cardiac centers monitor baroreceptor firing to maintain cardiac homeostasis, a mechanism called the baroreceptor reflex. With increased pressure and stretch, the rate of baroreceptor firing increases, and the cardiac centers decrease sympathetic stimulation and increase parasympathetic stimulation. As pressure and stretch decrease, the rate of baroreceptor firing decreases, and the cardiac centers increase sympathetic stimulation and decrease parasympathetic stimulation.

**(Slide 29) Baroreceptors, Cardiovascular and CNS. Video**

**(Slide 30)** There is a similar reflex, called the atrial reflex or Bainbridge reflex, associated with varying rates of blood flow to the atria. Increased venous return stretches the walls of the atria where specialized baroreceptors are located. However, as the atrial baroreceptors increase their rate of firing and as they stretch due to the increased blood pressure, the cardiac center responds by increasing sympathetic stimulation and inhibiting parasympathetic stimulation to increase HR.

**(Slide 31)** Increased metabolic byproducts associated with increased activity, such as carbon dioxide, hydrogen ions, and lactic acid, plus falling oxygen levels, are detected by a suite of chemoreceptors innervated by the glossopharyngeal and vagus nerves. These chemoreceptors provide feedback to the cardiovascular centers about the need for increased or decreased blood flow, based on the relative levels of these substances.

**(Slide 32)** The limbic system can also significantly impact heart rate related to emotional state. During periods of stress, it is not unusual to identify higher than normal HRs, often accompanied by a surge in the stress hormone cortisol. Individuals experiencing extreme anxiety may manifest panic attacks with symptoms that resemble those of heart attacks. These events are typically transient and treatable. Meditation techniques have been developed to ease anxiety and have been shown to lower HR effectively. Doing simple deep and slow breathing exercises with one’s eyes closed can also significantly reduce this anxiety and HR.

**(Slide 33)** Using a combination of autorhythmicity and innervation, the cardiovascular centers are able to provide relatively precise control over HR. However, there are a number of other factors that have an impact on HR as well, including epinephrine, NE, and thyroid hormones; levels of various ions including calcium, potassium, and sodium; body temperature; hypoxia; and pH balance. Many of these factors also influence contractility which refers to the force of contraction of the heart muscle.

Finish for today

The full lecture is at the indicated website.

**Thank you for attention**