>> Yes, today is October 16. This is Lecture 16, but you could also call it Lecture 1 in this unit that's described as the cardiovascular, respiratory, and digestive unit. Quite a lot of systems to consider. For the immediate future, we're going to look at the circulatory system, a word which comes from the word circle, of course. And you know, from anatomy, that blood never leaves this circle or circuit. Blood leaves the heart through arteries. It returns to the heart through veins, and at no time is blood ever outside a blood vessel of one kind or another. So, today, we're going to look at your heart, and we'll study cardiac physiology. Three basic agenda items. We want to consider where the contraction comes from, where it originates. We want to consider how it's regulated, because we know it changes from moment to moment. And, finally, we want to get a handle on how we can measure the efficiency of this organ, whether it's doing a good job, or a mediocre job, or a bad job, something called contractile efficiency. So those are the agenda items, and let's begin with the first of those, which deals with where the contraction actually emanates from and what are the events which lead to its excitation? Basically, the heart is somewhat self-contained. I mean, after all, what kind of muscle is it made of?

>> Cardiac muscles.

>> And cardiac muscle is auto-rhythmic, it's self-stimulating. And, so, this automaticity is actually generated from components of the heart itself, so-called non-contractile cardiac muscle fibers. What does that mean, non-contractile? Well, these don't contract, but they generate signals, which serve to pace– that means establish a contractile sequence within the heart. And these non-contractile units are referred to as the pacemakers and the conduction, or conducting, system cells. In terms of anatomy, in terms of words you may recall, these non-contractile elements are referred to as the SA Node, AV Node, the His bundle and branches thereof called the Purkinje fibers. Now, we're not going to dwell much on the anatomy of the heart, because we're going to presume that you recall the basic construction. But, just for review, there are two smaller chambers that receive venous blood. These, above, are called?

>> Atria.

>> Atria. The more powerful, the larger chambers below are called ventricles. So it is common knowledge that the human heart has four chambers. So let's jump right into this. Where does the contraction emanate from? Basically, it emanates from an area in the upper right part of the right atrium, which is called the SA Node, Sinoatrial Node. This is essentially an area which produces and maintains a repetitive pattern of depolarization and repolarization. That means the cells here can't really hold and maintain a resting potential. They're always depolarizing and repolarizing. And, in fact, they do that at a rate about a 100 times a minute, a 100 depolarizations every minute. So the function of the SA Node, which is not something you can see with the naked eye. But the function of it is to essentially set the contractile pace, because it initiates– it starts a wave of excitation, which then spreads from right to left. And how does this voltage move from cell to cell? Remember, these are cardiac muscle cells, and they're

held together or bonded, you could say, by intercalated discs. So this signal moves quickly from cell to cell, traveling through the intercalated discs. So we could visualize, or at least imagine, a wave of depolarization sweeping from right to left, and this wave of depolarization, of course, triggers contraction. Essentially, both atria contract at the same time, and therefore they move the blood down into the ventricles, which are somewhat empty at that moment. Incidentally, the word for contraction, which we're going to use from now on– the word for contraction is called systole, and the word for relaxation is diastole. So this contraction of the atria represents systole of these chambers, and, naturally then, blood moves down into the ventricles. Presumably, the ventricles are waiting for this blood, you could say. That is, they are anxious to receive it, and, next, following the depolarization of the SA Node, will be the depolarization of the AV Node. AV stands for Atrioventricular, and this patch of tissue is located here at the floor of the right atrium. The AV Node is essentially a receiver. That is, it picks up the voltage which arrives from the SA Node, and therefore it receives this depolarization and then acts upon it. That is, it produces and propagates its own wave of depolarization, which spreads through a non-contractile bundle called the bundle of His, capital H-I-S, name for a person. His name was, His. It's also called the AV bundle if you'd like, but this so-called His bundle runs down this wall between the ventricles. And you may recall that wall. It's called the interventricular septum. So in this image, we see the AV Node and the His bundle, which has two branches, left and right, and those branches divide even further into tiny filaments, collectively called the Purkinje fibers, which permeate the outer walls of both the right ventricle and the left ventricle. Now this depolarization, which spreads from the AV Node to the His bundle does not follow SAD polarization immediately. There is something called the SA-AV transmission delay, which doesn't amount to a lot of time, but does have about a tenth of a second pause. And this is easy enough to memorize, but the question is "Why should the signal from the SA Node not immediately cause depolarization of the AV Node?" In other words, why should the ventricle wait– how much? Why should it wait a tenth of a second before beginning its own contraction? There must be a reason, a benefit to this SA-AV transmission delay, and that is what? What do you think?

>> To allow blood [inaudible].

>> To allow blood to fill the ventricle, absolutely, to maximize the output, something we'll call later the so-called stroke volume. So the function of this delay is to allow optimum filling of the ventricles, which therefore optimizes the output from these ventricles. When we say ventricles, we mean both left and right, and they contract simultaneously. The right ventricle putting its blood into the pulmonary artery, the left ventricle putting its blood into the aorta. So after the depolarization of the SA, follows the AV, then the spread through the His bundle, and finally the Purkinje fibers. So textbooks will animate or illustrate that. Step one, depolarization of the SA Node. Step two, spread of this depolarization from right to left. Step three, arrival of this signal at the AV Node. Then a pause. A pause of? [Inaudible] A tenth of a second. Then

those signals will spread through the His bundle and Purkinje fibers, ultimately causing contraction or systole of both the ventricles. This happens over and over again. What's a normal heart rate? Well, actually, 60, 70, 80, it varies. But, interesting, because earlier we said the contractile, or at least the depolarization rate, of the SA Node was what? Did you catch that? The SA Node depolarizes a 100 times a minute. And that's inconsistent with what we just discovered. The heart rate is not a 100 but much less. So that sort of preps us for a topic we're about to consider, and that is "What controls the heart rate?" What keeps it in check? What reduces that intrinsic rate of a 100 down to something like 60 or 70? It turns out the autonomic nervous system does that, but let's put that off for a moment. For now, we want to ask this question "Can these signals, which are generated from within the heart– can those signals be picked up with surface electrodes stuck on your skin?" Of course. And you watch enough TV, and, in fact, you may actually have had this done to you or a member of your family. Patient is lying down, shirt is removed, and these sticky electrodes are placed at strategic sites on the chest and elsewhere. Naturally, we're talking about something called the ECG, an acronym for Electrocardiogram. In some circles, you'll still hear EKG. K is, of course, the German version of cardiac, but we'll call it what? [Inaudible] ECG, and this measures and compares the electrical voltage difference between two points on the body, typically on opposite sides of the heart. These sampling points then are electrodes, which can be placed at the shoulders or on the chest at various sites. It turns out that there are 12 designated locations, standard points, and, therefore, in complete workup, this is called a 12-lead EKG. In lab, next week, we're going to measure the ECG of a volunteer or two, but we're not going to have people disrobing, because, well, it'd be a little bit controversial. And, so, we'll do what are called the primary limb leads, leads I, II, and III. But let's move on. What does the ECG look like? What does it tell us? What is it actually measuring? It's measuring the difference in voltage between two standardized points on the body. These points are usually on opposite sides of the heart. The events that are recorded are obviously reflections of the electrical activity of the heart, and, so, let's break it down. Let's dissect this very iconic squiggle that you see on ambulances and billboards and T-shirts. And most everyone has seen that squiggle and perhaps equates it with heart contraction, but let's be clear upfront. This does not measure the contraction of the heart. This measures the electrical activity of the heart, which can be dissected into these visible events. The first event, which we described, is the depolarization of the atrium, and that essentially comes and goes. That is, it passes across these electrodes and is displayed as the first waveform on a standard ECG. The arrival and the passage of this voltage produces a blip, something like that. And, for no good reason, this has been called the P Wave. The P Wave is the arrival and the passage of atrial depolarization. It's important to understand, then, that this is not a standard neuron action potential, because, if it were, this side of it would be what? This side would be depolarization, and that side would be repolarization. That's not what we're measuring here. We're measuring the arrival and the passage of depolarization. So it's as if we're standing here, and here comes

what? Depolarization, and what? There it goes. The arrival and the passage of just what? [Inaudible] Atrial depolarization. So this event is recorded as the P Wave, and, as we'll see, its voltage is considerably smaller compared to the next one. The next event is actually a three-phase series of changes, a slight downward, a rather radical spike upward, and then a return down, and then back to zero potential difference. So there are three very distinct points in the next event, and, for that reason, this is called the QRS Complex, which is just that. It's a complex measurement of not one thing, but two things. What two things are being recorded at this time? Certainly we've just finished with atria what? [Inaudible] And so what follows atrial depolarization necessarily is atrial repolarization and, at the same time that the atria is R-word. At the same time, the atria is repolarizing, the ventricle is depolarizing. So this complex, which is called the QRS Complex is actually two things happening at once. Atria are what? [Inaudible] Repolarizing. Ventricle is depolarizing. It's, of course, logical to want to dissect this, to want to say "Okay, what part of this is repolarization? What part of this is ventricular or atrial repolarization?" And the truth is, you can't really dissect this, because they're happening together, but, with that said, which of these two events do you think is responsible for this very big voltage change? Which of those two things is mainly being recorded during the QRS Complex? It's not atrial repolarization, its ventricular depolarization, because the ventricle's a much larger muscle, and therefore produces a higher voltage accordingly. So actually, the QRS records two things, atrial repolarization, but it's mostly measuring ventricular depolarization. Once that's over and done, what's the only thing left to do before we repeat the whole process? The only thing left to do is repolarizing the ventricles, and that will follow rather soon and produces a waveform called the T Wave. The T Wave is simply the arrival and the passage of ventricular repolarization. So these are the events of a typical ECG, recorded at two points, and typically recorded from locations that are standardized and, in fact, referred to as leads, L-E-A-D-S. So this might be from Lead II, which we'll measure, indeed, next Tuesday and produces a very normal and recognizable waveform. So to repeat the P Wave is simply the arrival and passage of? [Inaudible] Atrial depolarization. QRS, essentially, measures two things happening together, atrial repolarization along with ventricular depolarization and finally the only thing left, ventricular repolarization, known as the T Wave. In clinical studies, of course, ECGs can be very diagnostic and therefore be used to determine what are called dysrhythmias, also called arrhythmias. In this particular view, you can see the normal pattern, the recognizable P, QRS, and T. Here, you see the events are very crowded, so perhaps you know that's called tachycardia. Here, they're spread out. The name for that? Bradycardia– in short, fast heartrate, slow heartrate. Aside from that, the ECG can be very useful to determine whether there's some dysfunction of conduction within the heart. Let's take this real quick. There's what event, as expected? [Inaudible] P Wave. And let's say here follows the QRS and the T, but is that period of time between the P and the QRS appropriate?

>> No.

>> No. Is that a delay? Yes, and that represents poor conduction, then, between the atria and the ventricles. Something called a– here it is– heart block, a first degree, maybe second, perhaps third-degree heart block, all of which lead to, ultimately, low rhythm or a disconnect between the atria and the ventricles. And, as you may know, the treatment for that, which is not uncommon, is implantation of an electronic stimulator, which most people know is called a pacemaker, basically restoring the rate that is the synchrony between the atria and ventricles. So what have we done? We've knocked out this. The contraction comes from the SA Node. It spreads throughout the atria. It's picked up and received by the AV Node, carried through the His bundle and Purkinje branches, and ultimately leads to contraction of the ventricles after a one tenth of a second delay following the atrial contraction. Again, what's the word for contraction? [Inaudible] Systole. The word for relaxation? Diastole. All right, let's move on to the second topic, and that is "How is contractile rate controlled, or is it fixed?" Of course it's not. Can your heartrate change? Can it drop dramatically? Can it increase dramatically? This number that we threw out there of 60 or 70 is just an average, and, in fact, heartrates can easily double that into 140, 150, even beyond. So something must be in charge. There must be a way of accelerating or decelerating this intrinsic rate. And, so, what are the factors that control or regulate the contractile rate? First and foremost, ANS. What's ANS? Autonomic nervous system. Your heart is the classic example of an organ that receives dual-motor innervation. That means it has sympathetic and parasympathetic innervation. And, here, in this image, we see parasympathetic arrives from the tenth cranial nerve, which is the vagus nerve. Sympathetic come off of the thoracic chain, that is, the paravertebral ganglia. And these are, of course, antagonistic. Sympathetic tends to do what to heart rate? [Inaudible] Parasympathetic slows it down. Remember, the intrinsic rate of the SA Node is what? By itself, without any outside influence, your heart rate would be what? [Inaudible] A 100. So what keeps it in check is the dominance of the parasympathetic acting primarily on the SA and AV Nodes. And this shouldn't be a shock, because we don't have to innervate all the muscle, because the control of the heart is essentially exerted here and here. What I'm saying is if we control the SA or the AV, then we essentially have a handle on the entire heart, overall. So let's jump in. The parasympathetic influence arrives through the tenth cranial nerve, and the neurotransmitter that is released is a familiar one, ACh. Pronounced what?

>> Acetylcholine.

>> Acetylcholine. Now, acetylcholine, at this location, attaches to cholinergic receptors, which, interestingly, are not depolarized, but H-word, what? [Inaudible] so the effect of acetylcholine is to improve, to increase what? To increase potassium permeability, therefore allowing potassium to go which way? Given the opportunity, if we increase the permeability of the potassium channels, more potassium will go? [Inaudible] No, more potassium will go out, and that will not depolarize, but H-word, hyperpolarize. That brings the cardiac resting potential to a more negative position, and does that make it harder or easier to reaching

threshold? And so the net effect is to lower heartrate. Now, acetylcholine also does this. It not only increases potassium permeability, but it decreases calcium permeability. Calcium, as you know, is necessary for the actin and myosin to become engaged. And, normally, in skeletal muscle, where is this calcium found and stored? [Inaudible] In the sarcoplasmic reticulum. Now the heart doesn't have a well-developed sarcoplasmic reticulum. Instead, it relies not on intracellular but.

>> Extracellular.

>> Extracellular calcium. And regardless of that fact, essentially the influx of calcium allows the contraction to be stronger and quicker. So it's important to dissect this information. If we increase potassium permeability, that's going to do what to the resting potential? And if we decrease calcium permeability, that's going to make the contraction not stronger, but weaker. So the bottom line for this effect is that the heartrate and contractility is going to be reduced, and that's consistent with what you know for parasympathetic action. Because parasympathetic is obviously the opposite of sympathetic action. So if I tap this out.

[Taps]

Let's say that's the normal contraction. What would happen if we increase parasympathetic action?

[Taps Slower]

[Inaudible] It would slow down. And it not only would slow down in rate, but it would slow down in contractility, so the contraction is reduced in frequency. It also becomes weaker, which is just a matter of fact. But that also explains this important discrepancy, because what was the inherent rate of the SA Node? The basic rate of the SA Node was.

>> A 100.

>> Hundred times, but yet your ordinary heart rate is much less, 60 or 70, which suggests a dominance, a normal dominance of parasympathetic, which keeps the heartrate in check, in normal circumstances. So what is the antagonistic division of the ANS? What is the opposite of parasympathetic?

>> Sympathetic.

>> Sympathetic. And sympathetic fibers also influence the SA and AV Node. They arrive coming off of the thoracic level of the spinal cord, but, for us, the important thing is that a very different neurotransmitter is used. It's called NE. What's that?

>> Norepinephrine.

>> Norepinephrine, and its effect is to attach to adrenergic receptors, which are located at the sites. Now, it turns out there are at least three kinds of adrenergic receptors. So this one called beta-1. That symbol is not B, it's the

Greek letter beta. So you pronounce this beta-1 adrenergic receptors. And they respond to norepinephrine in this way. That is, norepinephrine depolarizes the cardiac resting potential and it does it by improving permeability to what? [Inaudible] Improving permeability to sodium, which is not unexpected and certainly familiar from our work with neuron resting potentials. And read on. Not only does it improve sodium permeability, it improves calcium permeability. That brings more calcium into the muscle, and therefore the contraction is not just faster, it's also what?

>> Stronger.

>> Stronger. So if we were to tap this out again.

[Taps]

Normal heart rate. What happens when we stimulate the sympathetic? Faster and what?

[Taps Faster]

Stronger. Two things. Sorry. Rate and contractility both improve, and when does this happen? What are circumstances which cause this change, this elevation in sympathetic action?

>> Fight [inaudible].

>> Fight-or-flight, whether it's stress, whether it's exercise, whether it's just panic, it can be certainly familiar to all of us. So sympathetic takes over. Indeed, essentially becomes dominant in a flight-or-fight situation. So the net effect, here, is to increase both heartrate and the force of contraction. But there are other factors aside from the ANS. Never mind the autonomic nervous system, are there chemical influences, natural chemical influences that act on the heart quite apart from the autonomic innervation? The answer is "Yes." And most notably, we're talking about this famous hormone produced and released by the adrenal glands. It's a chemical cousin of norepinephrine. Its name is? [Inaudible] Simply epinephrine. Epinephrine goes by the more familiar name, adrenaline, but the proper chemical name, epinephrine. And it also passes through the circulatory system, as hormones do, and acts on and has a depolarizing effect on beta-1 adrenergic receptors. So never mind the sympathetic nerves, what does epinephrine do as it attaches to or finds these beta-1 adrenergic receptors? What does epinephrine do?

[Taps Faster]

>> [Inaudible] Same thing. It backs up. It reinforces the effect of norepinephrine. And so this is a hormonal influence, which supersedes and, indeed, outlasts the sympathetic effect by itself. This is something you've all experienced, maybe in kind of a fun or unimportant way. But you're walking through your house and somebody decides to pull a little trick and jump out of a closet and it scares you. What happens to your heartrate immediately?

[Taps Chest]

But then after the joke is revealed, what happens to your heartrate, still? The joke is revealed. There's no threat, but notice your heartrate continues for some time. That's not the norepinephrine, that's the lingering effect, the delayed and prolonged effect of epinephrine. So epinephrine supports and further improves the response of the heart to a stressful situation. So acting on the same receptors, epinephrine causes depolarization, which improves the rate and don't forget what, not just the rate, but the?

[Taps]

Force of contraction, overall improving cardiac performance quite a bit. Now, here's another important aspect to epinephrine. Because, think about it, it's one thing to cause the heart to contract faster and harder, but when you ask a muscle to do that, it's important to provide it with what to support that kind of contraction? I mean, if they're going to ask this to contract harder and faster, you've got to give it more what? You got to give it more?

>> Oxygen.

>> Oxygen. You got to improve the blood flow to these muscles, to the myocardium, to the cardiac muscle. And, you know, blood flow to the heart muscle is made possible through coronary vessels. You memorized those, the left, the right, coronary arteries, etc. And those vessels are made of what sort of muscle? What sort of muscle lines and determines the status of a blood vessel.

>> Smooth muscle.

>> Smooth muscle. And smooth muscle is not always contracted and not always relaxed. Usually it's in a semi-contracted form. So here's a rolled up piece of paper, and let's call this normal status of those vessels. Can those vessels be made smaller? That's called vasoconstriction. Can they maybe made wider? That's called vasodilation. What would be appropriate in this situation if we're asking the heart to contract harder and faster? You'd want these coronary vessels to dilate. And, indeed, because they had beta-2 adrenergic receptors, there is a hyperpolarizing effect on that smooth muscle, which causes vasodilation. This, then, provides what to what? If the vessels are dilated, we're getting more oxygen, more nutrients to the myocardium. And, indeed, this is where people get into trouble, because, as you know, what happens to the condition of coronary arteries with age? Do they get more robust, or narrow, or blocked? And would that compromise their ability to dilate in this scenario? And would that put you into trouble if you're on a treadmill or running from a bus or something? Clearly. And, of course, when that happens, you have ischemia. Ischemia means low blood flow, which is otherwise called a myocardial infarction, which is otherwise called a heart attack, which is otherwise called death. And, so, is this a real problem for many people elderly or not? [Inaudible] Yep. So the status of these coronary arterials is important to support– that means provide oxygen and nutrients to the myocardium. And what is the number one killer of people in the US of A? It's not cancer. It's coronary artery disease, which is a function of diet and lifestyle and genetics. Genetics you can't control, but can

you control diet? Yep. Can you change your lifestyle? Yep. So, naturally, these are things that are partially under your control. All right, now, never mind hormones, are there drugs, legitimate drugs or illegitimate– I don't care. Are there drugs that can affect the heart? Of course, there are tons, and we're not going to get into them all, except two categories, which are easy to understand and appreciate from the information we've already given you. First, there are those that are called cholinergic blockers, and that means something that blocks which arm of the autonomic nervous system? What are the two arms? We have parasympathetic and sympathetic. Which of these works through cholinergic receptors? Parasympathetic. So, essentially, a cholinergic blocker is a drug or chemical which blocks cholinergic receptors, and, therefore, cancels or at least reduces the effect of the vagus nerve, that is, the parasympathetic innervation to the heart. So think about it. If you take away parasympathetic, what's left? If you take away parasympathetic what's left is sympathetic. What becomes dominant then? Sympathetic. So what do cholinergic blockers do to the heartrate?

>> Increase.

>> They increase it. Not directly, but indirectly. This is tantamount to doing what in your car? It's not tantamount to increasing the gas. It's equivalent to taking your foot off the brake, and will the car go faster? Yes. So we're not accelerating the heart directly, we're blocking and removing what influence? Blocking and removing the cholinergic or parasympathetic influence, and, therefore, the heartrate will increase. There are a number of compounds that are, in fact, cholinergic blockers, one that you need to know and may already know, especially if you work in a clinical setting is atropine. Even if you watch TV enough, that word will pop up. Atropine is widely used in emergency rooms. What's it used there for? [Inaudible] Not to slow the heart, but to increase the heart, and it does it by blocking the cholinergic receptors, therefore rendering the sympathetic system more dominant. It's a widely used drug. It's a plant extract, and it comes from a leaf called the deadly nightshade, also called belladonna. These are words you may or may not know. Doesn't matter, but that's a word you need to remember. What is it? Atropine. What's it do? It's a cholinergic blocker, taking away what influence? Therefore leaving what in command?

>> Sympathetic.

>> Therefore the heartrate increases. Has useful, clinical value. The other type of agents act on beta-1 adrenergic receptors. And, appropriately, these are called what? [Inaudible] That's not B-blockers, it's.

>> Beta [inaudible].

>> Beta blockers. And the most important one in this category, which I don't have down there is called atenolol, which is a beta blocker. Now, before we move on, what would that do? If we block beta-1 adrenergic receptors, then we're taking away, or at least reducing, what influence? [Inaudible] And what then takes

over? So what does that do the heartrate? Decreases it. You might say, why would somebody want to do that? Well, there are many reasons, but certainly it's a medicine that's used for hypertension. What's that mean, hypertension? [Inaudible] High blood pressure. High blood pressure has many causes, but it certainly can be aggravated by a high and fast what? Heartrate. So atenolol is used to lower heartrate and, thereby, indirectly lower blood pressure. Interestingly, and I learned this not too long ago, that 20% of orchestral musicians. That means musicians that play in symphony orchestra. Twenty percent use atenolol before they perform. Now why would they want to take this drug? Well, what would it do to their heartrate? [Inaudible] And would that perhaps calm them down and ease some of the jitteriness? And is jitteriness something you want to welcome if you're playing professionally? No. So atenolol can be used for stage fright. Ever heard that term? Stage fright, public speaking, performing in front of a public audience? Anyway, atenolol is used– what's called off-label. Maybe you've heard that term. Off-label, meaning, not for what it's supposed to be used for, but for other things, and so it can be prescribed for stage fright or just plain nervousness. Sometimes people can't get to sleep. Would atenolol help? It's not a sleeping pill, but what's it do to your heartrate? [Inaudible] Especially if you're nervous, you're angry, or whatever, it can help calm and therefore bring on sleep perhaps a little more easily. So these are just two sides of the coin. We can either block cholinergic or we can block beta adrenergic receptors. And drugs, in this category, are useful for raising heartrate or reducing heartrate, as we've just said. So, now, we're ready to go to our third topic. We've talked about the origin of contraction. We've discussed how contraction can be regulated. But, now, how do we measure cardiac performance, its efficiency? Actually, this is a pretty simple and straightforward concept, because, fundamentally, what is the heart when you strip away all the fancy fare? It's a pump, and can we rate, can we calibrate, can we calculate the performance of any pump? You go to the hardware store. You say, "I want a pump." They say, "What do you want to pump, and how much do you want to pump?" In other words, that determines what kind of pump and the performance of that pump. So it really is easily reduced to the overall output of this organ. And, so, as a matter of convention, cardiac efficiency is measured as the amount of blood that's pumped from what? The left ventricle every what? [Inaudible] Every minute. Now, you might want wonder, and you should wonder "Why all the attention to the left ventricle?" The left ventricle assumes a lot of importance, because its blood goes into this big, red guy. What's that? [Inaudible] And so that takes blood obviously throughout the entire body. Just to review anatomy, the right ventricle pumps blood only to these organs bilaterally, the lungs. Now, don't get me wrong. We're not saying the right ventricle is not as important as the left ventricle, because if you stop to think about it, where did the blood come from that the left ventricle has to pump? Well, obviously, it came from the left atria, but that came from the lungs. So if you follow this logic, it's easy to see the left ventricle can only pump as much blood as it got from the action of the right ventricle. So it's actually true that the volume that comes from the left ventricle is always equal to the volume that comes from the right ventricle. But,

still, the focus is on the left ventricle, simply because that's putting blood into the aorta, and, therefore, it's providing oxygenated blood to the entire body. So, like it or not, output or efficiency is measured as the volume of blood that comes from the left ventricle every minute. And this reduces to a formula, one of many we'll be dealing with in this unit. It's a mathematical formula. It's pretty easy. Cardiac output– that means the amount of blood that comes out of the left ventricle in a minute's worth of time is simply equal to HR. What's that?

>> Heartrate.

>> Heartrate multiplied by the volume of blood that comes out of the left ventricle with one contraction, and that's a new term for you, something called stroke volume. So if we plug in some numbers here, just for fun, the normal heartrate being 16 or 17, and the normal stroke volume being around 80 milliliters, the astounding fact is that your heart puts out how many liters every 60 seconds? Five, 5 liters. And if you don't have a vision of that, just think of a 2-liter bottle of Pepsi. You got that? And how many is five? Well, that's two and half of that every what? Every minute. In a day, that's 4,000 gallons. And just before class, I thought to myself, how many bathtubs is that? So google that. How many bathtubs come out in a day's worth of time from your heart? It's 60 bathtubs, 60 bathtubs. And even this figure is astounding, because how much blood do you have in your entire body? You're lucky if you have what? Five liters. So that means, every 60 seconds, what percentage of your blood volume finds it way to and from the heart? All of it. Your entire blood volume is pumped every 60 seconds from your heart, and it does that 24/7, 365, until you die. Indeed, the day you die is the day your cardiac output comes down to zero. So I hope we made the case that this is pretty darn, pretty darn impressive. And, so, as we measure the efficiency, we're going to be dealing with heartrate and stroke volume. And before going on, what are the two obvious ways to raise cardiac output? Two obvious ways to raise cardiac output. You can either raise what? [Inaudible] Or raise? Or both, right? So there are two clear methods for raising cardiac output. Do we know how heartrate can be increased? Yeah. What's the primary way the heartrate increases?

[Taps]

Increase what? Sympathetic or decreased parasympathetic. So we know all about this. We don't know anything yet about stroke volume. So let's dissect and analyze and depreciate what stroke volume really is. It's easy to say that it's the volume of blood that comes out of the left ventricle with each contraction, but what does that amount to, and what are the factors that change that value? Stroke volume is the amount of blood that comes out of what? Left ventricle. With how many contractions?

>> One.

>> One. And that's determined by two factors described and abbreviated here, end-diastolic volume subtracting out in systolic volume. What's diastole?

[Inaudible] Relaxation. What's systole? [Inaudible] Contraction. So stroke volume is EDV minus ESV. What is EDV? Now, it's really self-explanatory. End-diastolic volume is the volume of blood that's in the? [Inaudible] Left ventricle at the end of what phase? The end of, D-word, diastole. Should there be a lot of blood in the ventricle at the end of diastole? Yeah, and would you like there to be a lot of blood? Yeah. So end-diastolic volume is just what it says. It's the volume of blood that's in the ventricle at the end of what? At the end of diastole. What then is ESV? That's the amount of blood that's still in the ventricle after the ventricles have done what? [Inaudible] And when I first heard that term, I thought, "Really?" I thought when the ventricle contracted, all that blood went out, but, no. Is there still blood in the heart after it's finished with contraction? Yes. What do you call it? ESV. So if you stop to think about it, if we want a good stroke volume, we want this value to be good. We want that value to be very, very low. We want to maximize EDV. We want to minimize ESV. And this little cartoon here is my attempt to show. This is the heart filled with what? And that's called EDV. This is the heart when it's contracted, and we expect and hope that there's less blood at that time. These are actual images of the heart taken with radiopaque dyes filled up with a catheter. But this is the ventricle at the end of diastole. So this blood is called the what? [Inaudible] And here the heart is contracted. Is there still some blood in the ventricle? Yeah. Not a lot, but it still has to be accounted for, and that amount, which is still there at the end of systole is called end-systolic volume. To say it again, then, we want this value to be what? [Inaudible] And we want that value to be very low. And, obviously, if there's any change in either of these, the stroke volume will be impacted accordingly. So let's get on to it. What are the values? What are the factors which can change or determine EDV? EDV is also called the preload, which means the amount of blood that's in the ventricle at the end of what? [Inaudible] At the end of diastole. Just before S-word?

>> Systole.

>> Just before systole. So if you need some sort of graphic, this is the heart that was full just before it gets ready to do what? [Inaudible] Just before it gets ready to contract. So what determines this preload? First and foremost, venous return. Venous return means what it says. It's the volume of blood that's coming to the ventricle through V-word.

>> Veins.

>> Veins. Now, you might argue. You might say, "Wait a minute, I thought the left ventricle got blood from the left atrium." Well, that's true, but where did the left atrium get it? [Inaudible] From the pulmonary veins, and so this is the essence of this, VR. What's VR? Venous return. So, simply put, if venous return is good, then what will be good in turn? If venous return is good, EDV will be good. If EDV is good, then what? Stroke volume's good. If stroke volume is good, then what will be good? [Inaudible] All right, what's the flip side? If venous return is bad, that'll be bad, that'll be bad, that'll be bad, life

will be bad. And, in fact, maybe it's a bit of a stretch, but what would be a reason that venous return would be bad?

>> Bled [inaudible].

>> You bled out, sure. Princess Diana. She died right there on the asphalt. You know that story, car crash? And the reason she died is that her pulmonary veins were torn from this impact. Therefore, she had zero what? Zero? [Inaudible] Therefore she had zero? [Inaudible] Therefore this was? [Inaudible] And anything multiplied by zero is still what? [Inaudible] So her heart rate might have been a 100, but a 100 times 0 is still 0, and her cardiac output was 0, therefore, she died. So, I know that's sad, but it's an example, an extreme example of poor venous return. So hemorrhage is the number one cause for lowered venous return. The next factor that also influences EDV is ventricular filling time, which means what it says. It's the amount of time you allow the ventricles to do what? Fill. A moment ago we talked about the SA-AV delay. Remember that number? Point one seconds. What was the reason for that delay? Why does the ventricle pause for a tenth of a second before it actually begins to contract? [Inaudible] It maximizes filling and, therefore, improves this process, this measurement called EDV. Sorry about that snafu, so let's go over it again. If the ventricle is allowed to fill, there will be more what? [Inaudible] And if there's more EDV there'll be better? [Inaudible] And therefore there'll be more cardiac output. This is an interesting and somewhat paradoxical influence, because what did we say sympathetic nerves do the heart rate?

[Taps Faster]

And if you increase the heartrate, that would allow less time for what? [Inaudible] So that would do what to EDV? [Inaudible] And that would do what to stroke volume? [Inaudible] Now how then is that compensated for? This is low, but the heart rate is what? [Inaudible] And, therefore cardiac output can still be better even though stroke volume suffers in that case. So that's only good to a degree. We said heartrate's normally 70. What if it goes to 150? What if it goes to 250? Is that even possible? What would be the case if the heartrate is 250 times a minute? Then there'd be almost no time for what? [Inaudible] Therefore, this would be very, very? [Inaudible] And 250 times a very low number still, still produces a very poor cardiac output. So very fast heartrates, although it may sound like it's a good thing, actually reduce EDV, therefore reduce stroke volume, therefore reduce cardiac output. And, by now, you realize what matters in circulation is not heartrate. What matters is cardiac output. So ventricular filling is really, essentially, HR. What's HR? [Inaudible] So if we have a low HR? If we have a low heartrate then we have more filling, therefore, what? More EDV. This makes it sound like a heartrate of 20 would be great. Let's follow that. A heartrate of 20. Are you allowing more filling time? [Inaudible] Would the EDV be good? Would the stroke volume be good? But even though that number's good, you're now multiplying it by 20, and so that's going to subtract from and otherwise lower cardiac output. So the discovery we just made is if the heartrate is very low, that's going to adversely

affect cardiac output, and if the heartrate is very fast, that's going to adversely affect cardiac output too, mainly because the effect upon EDV and, I should say, stroke volume. Now, this is all about the preload. Do we care about the amount that's left over at the end of contraction? Yeah. What's that called? [Inaudible] ESV, and what do we want that to be? Do we want that number to be high or low? Low. And so what factors determine the ESV? First, ANS, plus or minus circulating hormones. So what did we say, earlier on this page, with regard to sympathetic? What does sympathetic do to the heartrate?

>> Increase.

>> And it also does what to contractility?

>> Strengthen it.

>> And if the heart contracts harder, what's that going to do to this number, this value ESV? If the heart's contracting harder, then this is going to be low, and if that's low, then this will be higher. So, obviously, circulating hormones can influence the force of contraction, therefore the volume of this number, the volume of ESV. And to say it again, we want this value to be as low as possible. It'd be great if it was zero, but it never is. We want it to be as close to zero as possible. The other factor that factors into ESV is what's called the intrinsic stretch of the ventricle, which, by itself, doesn't seem to, well, say much. But when the ventricle is inflated with blood, do those walls get stretched? [Inaudible] And what do we know about stretch with respect to tension generated by a muscle? If we stretch the ventricle, it's now going to have ET. What's ET? [Inaudible] And so if we stretch it, it's going to have more ET, therefore, what? [Inaudible] So the stretch of the muscle will improve the force of contraction and therefore do what to that number? Stretch more, contract harder, that number will go? [Inaudible] And therefore that number will go? [Inaudible] So intrinsic stretch is an additional kick, an additional benefit, which is really a function of what? If you think about it, it's a function of EDV. What's EDV? So if EDV is good, not only does that fill the ventricle, it also stretches what? Stretches the? Ventricle. Therefore, introducing ET. What's ET? [Inaudible] Therefore decreasing ESV. If you read your textbook, this is called Starling's law of the heart, a famous physiology scientist discovered this. It determines, or at least influences, ESV. But, finally, and, typically, most importantly, is simply the health of the heart. What happens to the health of the heart as you age? Does it get healthier or not? No, nothing gets better when you age. I'm just being blunt. And so, if the heart is unhealthy as a result of ischemic disease, coronary artery disease, whatever. If the heart is not contracting as well as it should, what does that do to the ESV? If it's not contracting, then the ESV is? [Inaudible] High, and if that's high, the stroke volume will be? [Inaudible] Down. If the stroke volume's down, what's the only way the body can compensate for a lower stroke volume? The only way that the body can compensate for a lower stroke volume is to do what? [Inaudible] And is that prudent when your heart is already not so good? You're asking a poor, sick heart to contract what? Faster. That's a recipe for what? A recipe for disaster,

because the heart will fail, because it is already weak, and you're asking it to do more, and, therefore, ultimately and abruptly, your cardiac output will fall, and that's the day that you go to the emergency room and maybe never come home. So the health of the heart, naturally, is a function of age, diet, exercise, and genetics, and so forth. So, in quick, graphic summary, the amount of blood that is in the ventricle at the end of diastole is called? [Inaudible] EDV. We want that to be as high as possible. The amount that's still there at the end of systole is called? [Inaudible] And we want that to be as?

>> Low.

>> Low as possible, because what we care about is stroke volume. After all, that's going to be multiplied by heartrate, and that's going to determine cardiac output. So some interesting scenarios, here, then. What did we say about hemorrhage? Let's just take that as a categorical what-if. What will hemorrhage do to cardiac output? Well, the truth is it might not affect it all, because it depends upon the amount of what? [Inaudible] Hemorrhage. But let's say significant hemorrhage. Where does the impact first make its impact? [Inaudible] If we have low venous return, then we're going to have low? [Inaudible] EDV. That's going to mean low what? [Inaudible] And what's the only way the body can compensate for low stroke volume is to raise the?

>> Heartrate.

>> But if the hemorrhage continues, if the hemorrhage continues, that'll get low, that will get low, and there will come a point where nothing here will make the difference, and that, of course, spells death. Sometimes you hear people say, "You know, my heartrate is 60, but I have this friend of mine. He's an athlete and his heartrate is only 45. I don't get that. How could a big, buff guy have a heartrate of only 45? That doesn't sound like it would be enough. I mean, after all, he's got a lot of muscle to feed." But, wait a minute, it's not heartrate that matters. It's what? [Inaudible] So is it possible for somebody to have a low heartrate and still have a very adequate cardiac output? [Inaudible] And why do athletes have a low heartrate? Because they have a very good what? [Inaudible] And therefore the heartrate is quite adequate at 50 or less, and is that good? Yeah, because wouldn't you rather have the heartrate lower and have most of the work bore by the contraction of the heart itself? Absolutely. Never mind hemorrhage, what about blood clot? You guys watch enough TV, you know, this is called a PE. What's a PE? A pulmonary embolism. Pulmonary embolism is a clot in the pulmonary system, and if there's a clot in the lungs, then blood's not coming back to the what? [Inaudible] If there's a blood clot in the lungs, then blood can't get back to the left atrium, therefore, what happens is a very low what? [Inaudible] EDV, and, therefore, a very low? [Inaudible] And therefore a very low? [Inaudible] And a pulmonary embolism, of course, can be life-threatening as you'd expect. But never mind that. What is the number-one cause of coronary issues? It's basically narrowed what? Narrowed coronary arterials, and if those are narrowed, then that's going to do what? It's going to do permanent, permanent damage to the heart, and, remember, the

heart's made of what kind of muscle?

>> Cardiac muscle.

>> And if you damage the cardiac muscle, are you going to get new cardiac muscle tomorrow?

>> No.

>> Ever?

>> No.

>> No. So people say, "Oh, he survived a heart attack. He's as good as new." No, not really. Never be as good as new. Is he getting up and around? Yeah, but not because his heart has improved, because his stroke volume is still probably down. What has taken up the slack is an improved heartrate, which can be okay for a period of time. Now, one final thing for today, an important calculation, which is called the EF, or Ejection Fraction, which is just that, a fraction, which is expressed by stroke volume over EDV. So ejection fraction is equal to stroke volume over what? [Inaudible] EDV. Now, think of it. Well, let's put it this way. If end-systolic volume were zero, which it never is. But if it were, then stroke volume would equal EDV, and if these numbers were the same, 1 over 1, what would the ejection fraction be? It would be 1, which would otherwise be a 100%. So what we're asking here is "How efficient is the heart? Does it pump all the blood that it gets?" No. Does it pump a 100% of the blood that it gets? No, because there's always something that doesn't get pumped, and that's the ESV. So if you put in normal numbers for a health person, the ejection fraction is nowhere ever near a 100%. Even in a healthy person, it's 60, maybe 65, which is just a benchmark. So if you read a chart from a patient and it says ejection fraction is 20%, what does that mean? Should be 60%. It means that something's suffering here, and it's probably due to the health of the heart, causing this to be high, causing that to be low, causing the ejection fraction to suffer. So this is a mathematical calculation, which is essentially comparing SV to EDV. The closer these values are, the higher that will be, and, obviously, the further apart they are, the lower that value will be. So ejection fraction, much more than cardiac output, is used in a clinical setting. You'll see that on charts all the time, ejection fraction, and you'd hope it to be what? [Inaudible] Something around 60 or so. So that brings us to the end of this, which was, as promised, three topics, origin, control, and efficiency. Let's put an end to this recording.