>> Well, it's April 26th. This is lecture 21 in Physiology. We're going to back up just a bit. We introduced the notion of ventilation which is moving air. We said that air moves down a pressure gradient, always from a high pressure to a low pressure. The pressure that's in our environment is called the atmospheric pressure. At sea level, 760 millimeters of mercury. The pressure in your chest is always less than that, and in fact, if fluctuates, as you know now. But, it's called PT the intrathoracic pressure. The pressure in the lungs also fluctuates, bringing air in or pushing it out. And, that's called the interalveolar pressure. So, clearly, there's a cooperative effort here between the chest wall, the diaphragm, the lungs themselves. And so, here's the story. When we contract our diaphragm, the volume of our chest expands. That reduces our PT even further than it normally is. The lungs, then, expand, then their air pressure goes down. And, that draws air in from the outside. That whole process is called inhalation. The opposite is just that. The diaphragm relaxes. That shrinks a bit the chest size, raises the PT, and as a result, the lungs shrink a bit. They never fully collapse, but when they shrink, that raises their pressure inside. And, that forces air out. So, it seems rather straightforward, as long as you understand each of those events. You can understand them, of course, qualitatively or quantitatively. So, we put this on a timeline and we showed you the pressure values that exist. And, we finally talked about some assault to the chest. If you have a hole in your chest wall, will air leak out or air go in? Air will go in. That will raise the intrathoracic pressure, lungs will collapse, and you won't be doing any of the v word anymore. You won't be doing any ventilation. So, that's a medical emergency. It's called a pneumothorax, can happen naturally on the streets around here, as violent as they are. Moving on. Next week, and certainly in clinical settings, there are occasions to measure long volume, just for fun or for diagnostic reasons. They're called PVTs, pulmonary volume tests or pulmonary function tests, and next week in lab, you'll grab one of these things that maybe doesn't look that exciting. It's called a spirometer, and you basically [blowing] blow air through it. And, it will tell you how much air you've moved through it. So, it's a digital device for measuring pulmonary volumes. The kind of breathing you're doing now is kind of laid back and mellow, and that's called v. I should say TV, tidal volume. And, that refers to the amount of air that you're bringing in, also the amount that you're exhaling, which usually match each other. For most events, it's less than a liter. Certainly less than .5 liters in most cases, and so that's the volume that you use without any special exertion. Can you inhale more than that? Can you exhale more than that? Of course. So, you have capacities beyond the tidal volume, and so the tidal volume is simply the amount that you move in or the amount that you exhale with one breath. Now, if you inhale above the tidal volume, then that amount which is beyond the tidal volume is called the IRV, inspiratory reserve volume. And, notice its value. It's quite a bit. At least three times the tidal volume. So, what I'm saying is there's lots of room in there that you normally don't use. The IRV proves that. It's the maximum inhalation above and beyond tidal volume. When you exhale normally, as you just did, can you exhale more if you really try? Certainly, at birthday parties,

you have to blow out those candles. So, you're really bending over and blowing it all out. That amount which is exhaled beyond the tidal volume is called the ERV, and it amounts to less than the IRV but still quite a bit more than the tidal volume, .8 to maybe a full liter. Now, when you exhale fully with all your might, and you might picture your lungs as sort of pancakes in there that are dangling about, flat as a tire. But, no. There's always some air in your lungs no matter how hard you may try. And, that amount which remains there all the time is called the residual volume. Typically, less than a liter, but the point here is that your lungs are never fully empty. And, that's the RV, the residual volume, the air that remains after the ERV. So, that's it. If you add up all those numbers, you have TLC, which in this case stands for total lung capacity. Naturally, this varies depending upon your age, your gender, your height, and so one, one of the reasons for measuring these values is to get a sense of whether you're normal for your age and gender. But, even though TLC is interesting, it's not clinically very relevant. And so, what assumes more importance is VC. VC is vital capacity. Which of these values can you actually move, can you actually change? You can change your tidal volume. You can change your IRV. You can exercise your ERV, but you never touch your RV. So, vital capacity is the total volume of air that you can move with a voluntary effort, and that, then, is a simple formula. That is, it's VC equals TV plus IRV plus ERV. And so, you'll measure your vital capacity in lab next week, and how do you know whether it's normal? You're not going to compare it to me. You're not going to compare it to Donald Trump. You're going to compare it to somebody of your same, what? Your same age, your same height, your same gender. And, we have a formula so that you'll know whether your value is okay or whether you're suffering from some deficiency in that regard. But, basically, pulmonary function tests just show how voluminous your lungs are. Doesn't say how well they work. It just says you have x amount of volume. And, actually, what's more important, certainly on a physiological level, is not the volume but how well you move air. That is their overall efficiency. So, think back for a minute. How did we measure the efficiency of the heart? What was even the name of that factor? Cardiac output. And, cardiac output is multiplying heart rate times stroke volume. In other words, it's rate times the volume. Is there a rate that applies to breathing? Is there a volume that applies to breathing? Sure. So, naturally and somewhat correspondingly, ventilatory efficiency is calculated in the same way as cardiac efficiency. It's not called cardiac output. It's called minute volume which is self-explanatory. Minute volume is the amount of air that you move in a minute. It's an easy calculation. Figure out your breathing rate, multiply it by the volume you're moving, and there you go. So, let's take a breathing rate of 16 just to plug something in. Let's multiply by half a liter which is a normal tidal volume. And, there you go. You're going to move about what? Eight liters a minute. Now, that's pretty impressive if you think about a two-liter bottle of Coke. It's what? It's four of those every what? Every minute. So, once again, pretty impressive as the body is all the time. So, if we think about minute volume, there are two ways to improve it. You're either going to raise the breathing rate, or you're going to raise the tidal volume. And, think

about it. In exercise, does the minute volume go up? And, what's the reason? Well, both the rate and the volume go up. So, both of these approaches, both of these factors come into play, especially with exertion that is during exercise. There are other factors that influence minute volume. Certainly, we have to assume and hope for good diameters of the conducting units. What are the conducting units that represent the most problematic, the narrowest, the highest resistance in the pulmonary tree. It's not the trachea. It's not the bronchi. It's the little guys. Bronchioles. And, is there a pretty familiar condition that many people suffer from where those are narrow or otherwise constricted? Name of that's what? Asthma. Or bronchitis. And so, the diameter of the conducting units sometimes interferes with and creates a crisis for minute volume. And then, we have to assume the performance of the muscular units. And, usually the diaphragm is not a problem, but it can be. And so, that would be a factor. But, usually, what controls minute volume, that is what controls breathing rate and tidal volume is the ultimate control center for the process of breathing, and that's called the inspiratory center, located just next door to the CVC. What's that? Cardio vascular center. Located also in the medulla. So, worth a note. If you knock out your medulla, you knock out the CVC, you knock out the inspiratory center. You're dead. So, clearly, we're going to focus now on the activity, the importance of the IC, the inspiratory center. Because basically, it controls, it regulates the process of ventilation. Something we take for granted. Do you worry at night when you go to sleep, "I might not wake up because I'll stop breathing,"? no. You take it for granted. Breathing is just automatic. You don't think about it. You don't have to think about it, and you can thank the medulla and the inspiratory center because actually, it's in charge. I mean, think about it. What's the muscle that does all the work? Diaphragm. Is that autorhythmic? Is that a cardiac muscle? Is that a smooth muscle? No. It's a skeletal muscle. So, really, in this case, the brain is the responsible party here. And, again, the inspiratory center is where this signal, where this control emanates. So, we can think of the inspiratory center, I like to think of it as a kind of metronome. You know, that thing on a piano that goes tick, toc, tick, toc to the music? It sets the pace. Basically, the inspiratory center is made up of a bunch of neurons that are self-depolarizing. That means they can't hold the resting potential. They're constantly d-word. And then r-word. All the time. They depolarize and repolarize, depolarize and repolarize. And, in that sense, then, they're like a metronome in that they set the pace for normal breathing. A pace that can be changed, but nevertheless a basic rhythm. So, these self-depolarizing neurons essentially maintain a cycle of inflation followed by deflation. And, we don't think about it because, remember, the medulla is not part of your conscious, central nervous system. It's all done, thankfully, in the background. So, let's investigate the inspiratory center. We show it here just as a yellow circle. It's located in the medulla. During its depolarizing phase, it sends signals along motor nerves to the inspiratory muscles, and it causes them to contract. And, of course, what's the most important of the inspiratory muscles? Diaphragm. So, essentially, the signals are sent through the phrenic nerve, and the diaphragm contracts. That is, it lowers, and the chest volume

increases. Intrathoracic pressure decreases. Lungs expand. Their pressure goes down. Air is drawn in. So, depolarization of these neurons essentially causes the inspiratory muscles to contract. And, that bring about inhalation. Now, what follows depolarization? Obviously, r-word. Repolarization. But, it's important to emphasize that repolarization doesn't cause relaxation of these muscles. That would happen anyway. So, notice the substitution here. We don't have the word cause. Repolarization allows the inspiratory muscles to relax. And, that brings about the opposite of inhalation, namely exhalation. So, this diagram attempts to show that. During the active phase, during the depolarization phase, the inspiratory muscles are stimulated. That causes them to contract, and that brings about inhalation or inspiratory efforts. Then, when these neurons repolarize, that allows for these muscles to relax, and that enables deflation. More of less, these are two second intervals. Although, usually, expiration take a little bit long. That is a little bit longer than inspiration. So, so far, this is the basic template. This is the basic pattern. This is the basic way it works. Depolarization causes the muscles to contract. That bring about inhalation. And then, repolarization doesn't cause the muscles to do anything, but it does allow the inspiratory muscles to relax. And, that brings about the deflation of the lungs. Okay. Great. Now, of course, we all wish it was that simple, that is, there's more to the story because although this is the basic mechanism that promotes and cases these events, there are influences that regulate even this and allow for changes beyond the normal rhythm. So, one of those influences that resides outside the medulla is the so-called pneumotaxic center or pneumotaxic area which is located nearby in the pons. Now, the word "pneumotaxic" is a bit foreboding, but what does that mean? "Pneumo" means air, and "taxic" means to move. So, it's named because it helps to move air more efficiently, and you'll see why. Because its influence is basically to send inhibitory impulses to the inspiratory center. Now, that seems odd. In fact, it doesn't even seem good, but here's the deal. The function of the pneumotaxic center is to limit, to cut short the period of inspiration. Therefore, bringing about and facilitating what? Expiration. The importance of that sentence is not obviously, but let's think about it. When it comes to ventilation, is inhalation important? Yes. Is exhalation important? The point is we don't want to have air stagnant. What's that means stagnant? Not moving. Is it important to keep air moving all the time? Yes. And so, the function of the pons, the pneumotaxic center is to do just that. To limit and cut short the period of inspiration so that we don't dwell on inspiration and, therefore, bring about immediate what? Exhalation. We all put too much emphasis on inhalation, getting oxygen, but it is getting rid of carbon dioxide equally important? So, getting air moving, keeping air moving, is certainly what it's all about. And so, the pneumotaxic center limits the period of inhalation. Let's just graph that real quick. In fact, you'll do this in the lab when you measure your own respiration, and it will look like this on the computer. So, this is inhalation, and that is exhalation. Inhalation and exhalation. Without the pneumotaxic center, things would be different. We'd still have the basic template, the basic imprint of the inspiratory center. But, it might be more like this. And, therefore, we're dwelling on what stage?

We're dwelling on the inspiratory stage, and during that time, air's not m-word. Moving. And, that's inefficient. So, in simple terms, the pneumotaxic center makes breathing more efficient. It prevents that hesitation or dwelling on the inspiratory stage. Now, what are the other factors, some of them known to you and some of them perhaps new to you, that can and do intervene from time to time to influence minute volume or just your breathing pattern? One of them is the forebrain itself. That is the cerebrum. What does that mean? Can you voluntarily get involved in breathing? If you think about it, can you control your breathing? Could you stop it momentarily? Can you accelerate it? Can you slow it down? Do you have voluntary override of the inspiratory center? Sure. And, you utilize that override all the time because when you swallow, do you have to stop breathing for that period of time? You do. And, when you're talking. Actually, think about it. The only way you can make sound is not moving air in. It's always moving out. And, that's amazing because some people talk so often, that is so quickly without interruption that you wonder how they're taking a breath. So, my point is as you talk, you necessarily have to intervene, and therefore alter this normal breathing pattern. Swallowing, talking, crying, all those things cause an upset to the normal breathing pattern. Even sneezing. What is a sneeze? Think about it. Never mind what it does or what causes it, but obviously, that's a very forceful, rather propulsive expiration. And, that naturally sometimes is prompted by the forebrain. So, in summary, can the cerebral cortex get involved in the actions of the inspiratory center? Sure. But, here's a question. Is it possible for you to voluntarily decide that you don't want to live anymore, and so you're going to hold your breath until you die? Is that possible? You might have tried it, and you find that you cannot commit suicide by just holding your breath. So, there must be some limit to this forebrain intervention. And, we'll get to that in a moment. It's obviously a self-protective, you don't really want to do that, kind of mechanism. And so, the forebrain has limits in terms of how influential it can be on the inspiratory center. Another factor that controls breathing is a reflex. It's called the inflation reflex. It was first worked out by two physiologists. Their name was Hering and Breur. So, guess what? It's called the Hering-Breur reflex in their honor. You can read more about it in your book. But, it's also known as the inflation reflex. And, it is, well, a reflex. And, what sort of things, what are the components of a reflex? What are the things that have to be involved to make a reflex work? R-word, you got to have a receptor, got to have a sensory nerve, got to have an intact spinal cord or brain. So, yeah, all those things are involved. And, this reflex, essentially, is made possible by what are called stretch receptors that are located, not in the airways, not in the big ones anyway. Located in the bronchioles of the lungs. And, as the name implies, they respond to stretch. Now, what would be the status of the lungs, that is to say, are the lungs stretched when they're inflated or when they're deflated? Inflated. Hence, they are stretch receptors. And, think about it. If the lungs are inflated, if they're stretched, what would you want that to do? Would you want the signal to cause the lungs to inflate more, or to stop inflating as a result of that stretch? Stop. So, this is a protective mechanism that basically prevents overstretch or over inflation of the lungs

which could be damaging because if the lungs are inflated too far, it's just like a balloon. They have the possibility of tearing. And so, this guards against that. The stretch reflex, basically, inhibits, then, the inspiratory center. And, it works or feeds back through the vagus nerve to the inspiratory center. Its function is right there. It prevents excessive inflation which could be damaging to the tissue that is damaging to the lung tissue itself. As important as that sounds, and indeed it is, it's not operating right now. None of you are really huffing and puffing. That is, you're breathing rather subdued. That is the tidal volume. After all, this only responds to lungs when they're really fully, fully, fully stretched. So, the only time that this mechanism really protects or comes into play is when you're exerting your respiratory system. In other words, during exercise. Otherwise, it's kind of just there not doing anything. But it does prevent injury to the lungs during exercise. So, now, we can superimpose a few more things that we've talked about on this basic template. Recall the inspiratory center's the center of the story. They issue out signals that bring about contraction of the inspiratory muscles, bringing about lung inflation and so forth. Then, we have the pons. The so-called pneumotaxic center. Remember, that was designed to limit the period of inspiration to keep air moving. Then, we talked about the cerebral cortex, and notice we've got a plus sign and a negative sign. Which means simply this, can you accelerate your breathing if you want? Can you stop it if you want? Okay. So, that's the influence, then, of the forebrain or the cerebral cortex. And, finally, this little diagram here shows what looks like a spring. It's not really a spring, but this is a receptor. What do you think? It's probably the stretch receptors. And, they react to a deflated lung or an inflated lung? A really inflated lung. And, they report back, and notice the negative sign. Negative sign, meaning that they tend to inhibit or stop the further activity of the inspiratory center. So, these are some of the sort of peripheral or at least related influences to and on the inspiratory center. But, we're not done. Because obviously, well, maybe not obviously, but certainly you're not surprised that here are chemical factors that are worth monitoring in the blood and relate to the responsibilities of the respiratory system. In other words, this is what I'm talking about. Are there chemical factors in the blood that the respiratory system would want to know about in order to act accordingly? What are the two chemical constituents in the blood which basically are the responsibility or at least the concern of the respiratory system? Oxygen and carbon dioxide. So, shouldn't there be receptors for those gasses, and shouldn't they, somehow, report to or have an effect on the inspiratory center? Of course. So, chemical control is essentially monitoring blood gasses, and you'd guess, and certainly it's sort of true, that one of the most important gasses to monitor is the concentration of oxygen. So, are there chemoreceptors for oxygen? And, the answer is yes. In fact, if you've been keeping up with the lectures, you already know this because these are the same chemoreceptors located in the same area which had a positive influence on the CVC. They're located in the carotid and the aortic bodies. Think about it. Would these receptors be sensitive to low oxygen or high oxygen, you think? They respond to low oxygen, and so they are an early warning of low oxygen levels. Which naturally would be concerning.

What effect would you hope they'd have on the inspiratory center? What effect would you have they'd have on minute volume? Should minute volume go up or down in the face of low blood oxygen? It should go up because that would move more air, and hopefully acquire more oxygen. And, therefore, solve or correct the problem. And indeed, that's true. They have excitatory connections. These receptors excite, not only in the inspiratory center, but they excite at the same time the CVC. And, this shouldn't be shocking because think about it. Is it good enough to improve the efficiency of the lungs to move more air if you're not also moving more blood? There'd be nothing accomplished. We've got to move more air, and we've got to move more what? Blood. In order to really get the job done. So, it's not shocking to find that these receptors don't just stimulate the inspiratory center. They stimulate the cardiovascular center. And so, does cardiac output improve? Yes. Does minute volume improve? Yes. Is that a cooperative, logical response to low oxygen? So, it makes perfect sense. Let's put it on a graphic, quantitative scale here. And, we'll look at minute volume which is the way we measure ventilation efficiency. And five, five marks the normal minute volume. So, even though we haven't put it up there yet, what if we were to artificially lower oxygen levels in the blood? Lower oxygen levels. What would happen to minute volume, you think? It would increase. And so, let me say it again, if we artificially or experimentally or whatever lower oxygen, you'd sort of expect that minute volume would go up accordingly, right? And, it does, but kind of shocking because it doesn't go up linearly. It's kind of sluggish at the first part, and then it really starts escalating as oxygen levels get really, really low. So, I remember when I first learned about that, I though, whoa. You'd expect the body to be very sensitive to low oxygen and really jump on it if there's any slight depression of oxygen. But, what this graph is saying, what it basically shows is that the body doesn't react very quickly to lowered oxygen levels. And, that's a bit of a shock because we put so much importance on maintaining oxygen levels. So, in summary, do we have receptors that are monitoring blood levels of oxygen? Yes. Where are they found? They're not found in veins. They're not found in capillaries. They're found in the carotid and aortic bodies which are in the arterial system. They react, not to high oxygen, but low oxygen. And, they not only cause minute volume to go up, they also cause cardiac output to go up because they promote or stimulate the CVC, too. So, okay. That much is pretty easy, that is it's logical. It makes sense, and we're happy to see it. But, remember, is oxygen the only concern? Is that the only gas that really is important in this system? You see, it's not just getting oxygen. We have to get rid of what? CO2. And, would high levels of CO2 represent a concern or be dangerous? You bet. And so, certainly, when this was being investigated years ago, it was presumed that now that we've found the oxygen chemoreceptors, let's go look for carbon dioxide chemoreceptors. And so, a lot of effort, lot of research to find receptors that respond to what? CO2. High CO2. Because certainly, their existence was suggested. When you raise the carbon dioxide levels in the blood, an amazing thing happens. That is, minute volume increases really fast and very steeply. And, in fact, if you had to say, is the body apparently more sensitive to declines in oxygen or is it more sensitive

to rising levels of CO2? And so, the extension of that observation is that apparently the body cares more about what? Seems to care more about a build up of CO2 than it does to a decline in oxygen. In short, it responds earlier and quicker to rising levels of CO2 than it does oxygen. And, that's a bit surprising, but we'll explain and justify why that is in a moment. With this observation, and that's all it was. This is an observation. Physiologists said, "Okay, there must be receptors for this gas," because, you know, the inspiratory center's not just guessing. It must be getting some information. So, there's got to be what? There's got to be oxygen. I should say carbon dioxide chemoreceptors. So, the hunt was on. And, for the longest time, they really couldn't find any receptors that were specifically responding to CO2. And then, it became clear that there really aren't many, if any, and that what we're seeing here is not really a response to CO2 at all but something else. It was discovered that in the brain, there are chemoreceptors that respond to rising levels of what? Hydrogen ions. Rising levels of hydrogen ions in the fluid that bathes the brain. What is that fluid that circulates in and around the central nervous system? CSF. And, there is a connection. There's a connection between that and carbon dioxide because, think about it. Carbon dioxide is a biproduct of metabolism. Yes? And what's formed with it all the time? And so, CO2 and water are produced all the time naturally and unavoidably as a result of metabolism. Here's the thing. CO2 and water will react and form H2CO3 which is what? Carbonic acid. It's a weak acid, but it's an acid anyway, and it will ionize into bicarbonate. That's what this is. And, hydrogen ions. Okay. So, is there a correlation, then, between hydrogen ion buildup and the buildup of CO2? I mean, after all, remember that idea of law of mass action? This is a reversible chain of events. What would cause it to go from left to right would be any buildup of? And, when there's a buildup of CO2, then, will there be a buildup of hydrogen ions? Yes. And, will those hydrogen ions leak into or otherwise effect the pH of the CSF? What's the CSF? And, would that jeopardize the health, the welfare, the normalcy of the neurons in the brain? Yes. So, it turns out that this purple curve here that we're attributing to a response to what, to high? CO2. Is really not, really not the direct result of CO2, but rather the buildup of? Hydrogen ions. Which are directly related to and caused by a buildup of CO2. And, in fact, that answers the question. What question? How come you can't kill yourself by holding your breath? As you hold your breath, are you still manufacturing CO2 and water? Sure. And, is that converted to carbonic acid? And, is that going to raise the concentration of hydrogen ions? And, will that, at some point, stimulate the inspiratory center, like it or not? Yep. And, therefore, override, override your voluntary desire to hold your breath indefinitely. And so, as a kind of stunt, and as a demonstration of this, in lab next week, we're going to ask you to hold your breath, just for fun. See how long you can do it. And, some of you will do it for longer than others. But, what limits your breath holding, and this is surprising to many, because the average person, if you walk up. And, let's find an average person. I don't know. But, the average person you ask, "What's happening when you hold your breath?" They'll say, "Well, you're losing oxygen, and finally, your body, you know, has to breathe because it needs oxygen." It's not

true at all. What's happening is the buildup of what? And the acidification of the cerebral spinal fluid which forces and overrides that voluntary decision to hold your breath. So, what's the world record for breath holding? I happen to know, at least unless, unless it's been broken in the last few days. And, you can google this because maybe it has been broken. But, many of you know David Blaine. What a great guy. He's crazy. Yeah, he's the guy that, you know, eats wine glasses for lunch. I'm not joking. Anyway, he's the world record holder for breath holding. I'm going to show you the video because it's no joke. It's not smoke or mirrors or trickery. He actually did it, and not easily. But, what do you think the world record. Some of you may know, so don't spoil it for the rest of you. But, what do you think? Throw out some answers. Eight what? Hours or minutes or seconds? Not eight hours. Okay. Let's be realistic here. Okay. I guess you guys are, it was 17 minutes 4.4 seconds. That's pretty impressive. I'm impressed. Didn't come close. But, if any of you think you can break that, we'll definitely get the media out here. Now, how can he do that? Didn't he run out of oxygen? Well, again, it's not the oxygen, but the buildup of what? So, anyone who needs, that is engaging in activity where breath holding is important. And, what is a legitimate activity where breath holding is important? Diving underwater, right? For whatever. Pearls or gold nuggets or whatever. You'll find that before they dive, they don't just say, "Well, let's go for it." And, they don't just say, "[gulp] I'm going." They'll do what? They'll hyperventilate. [heavy breathing] And, the average person, again, thinks what? Oh, I understand that. You're getting more what? Oxygen. You're moving more air, but actually you're not getting anymore oxygen. What you are getting rid of is CO2. And, therefore, you're starting with a very, very low level of CO2. Therefore, buying time until it builds up to this critical level. And so, CO2 turns out to be the most important influence, and anything that can restrict or delay the buildup of CO2 allows for better breath holding. And, we'll demonstrate that because we're going to ask you to do what, you think? Not just hold your breath, but then do a little bit of hyperventilation. You'll easily double your breath holding time. If you try. Now, just to prove that this is not CO2 but hydrogen ions, let's look at a graph that actually compares minute volume to CSF hydrogen ions. That is the buildup of hydrogen ions. And, if you look into the basis for this data, it's quite appalling actually. They must have had some paid volunteers. But, they had human volunteers, and we put a catheter into their spinal cavity and put acid in there. Yeah. They got paid for it. And so, they dripped acid into the cerebral spinal fluid with the subject just laying there. Guess what happened to their breathing? Well, that happened to it. In other words, the breathing accelerated. The minute volume increased from the get go. Demonstrating and confirming what? What we thought was the result of a buildup of CO2 actually is a buildup of? Hydrogen ions. Affecting the pH of the cerebral spinal fluid. And, you might wonder, okay, I get that. But, why is that a big deal? Well, it's a very big deal because is acidification of the cerebral spinal fluid going to jeopardize the performance of the central nervous system, you'd think. So, it turns out that oxygen is kind of second in terms of priority, rather protecting the pH of the cerebral spinal fluid assumes

the greatest importance. So, now, for the rest of our time, a question which up front sounds simple enough, and that is what happens to minute volume when we exercise? We know the answer to that. It's really common knowledge. But, let's say. You're on a treadmill. You're walking. Now, you're running. What happens to minute volume? What is minute volume, just to be clear? It's breathing rate, we'll call it breaths per minute, breaths per minute, multiplied by tidal volume or whatever the volume is, right? So, I'm sure you know from your own experience that when you exercise, does your breathing rate go up? Sure. Do you breathe deeper at the same time? Yeah. You do, and we'll prove that in lab. There's no mystery. There's nothing to prove there. Everybody knows it. The question is what causes that. Now, here's where we want to be very, very clear on what the question is really asking. What causes it? We're in search of an explanation not a justification. So, once again, your average person is going to say, "Well, your body needs more oxygen, so you're going to breathe harder. But, that's not physiology. That's the t-word. Teleology. To say something happens because it needs to happen is not an explanation. It's a justification. So, that's not what we're after because of course your body needs oxygen. But, does that answer the question? What's the question? What caused it to happen? What are the possibilities? Is it possible that during exercise the oxygen levels have gone down, and that triggers the chemoreceptors? That's possible. Is it possible that when you exercise, the carbon dioxide levels go up, and that translates to hydrogen ions? And, that stimulates the inspiratory [inaudible]? Those are possible, but just because they're possible, are they really operational in this case? How could we do that? What experiment could we form? Put somebody on a treadmill. Is it possible to put a catheter in their arterial supply and actually monitor in real time the oxygen and CO2 and pH of the blood? Is it possible? Sure, it's possible. So, let's do it. We know up front that when you exercise, the minute volume will increase steadily and rapidly. So, that much you could prove yourself on a treadmill. You know it. In other words, the harder you work, the more extensive the exercise. Minute volume improves and steadily so. In fact, notice there's no delay here. Even mild exercise will accelerate minute volume, and it gets greater and greater the harder you work. This is something you all have confirmed, so there's no doubt about it. So, we're not out to prove that this happens because we know it happens. What we're out to prove, what we're out to answer is why does it happen? Not a justification, but an explanation. What are the possibilities that we thought or at least discussed so far? Maybe it's due to a buildup of carbon dioxide. Maybe it's due to a decline in oxygen. Maybe it's due to some buildup of hydrogen ions. Let's see. Let's not just assume. Let's see. What happens to oxygen levels, oxygen concentration in the blood as you exercise? Surprisingly, they don't change in a healthy individual. Now, I know when I first heard that, I said,"Whoa, whoa, whoa. Wait a minute." When you exercise, your cells are, well, your muscles are contracting. They're using more oxygen. Certainly, then, oxygen must fall during exercise. But, what's increasing, even with early and mild exercise is minute volume. So, of course, your muscles are using more oxygen. Why, then, isn't oxygen in the blood suffering? Because

even though you're using more, you're acquiring more. And, you're acquiring more because breathing is increased from the get-go. After I heard that, I said, "Well, whoa, whoa, whoa. I still don't buy that." Because we've talked about exercise producing this scenario, this possible condition. I mean, isn't it true that when you exercise, there may be lactic acid formed? And, lactic acid is only formed when? Lack of oxygen. So, how can lactic acid be formed if the blood levels of oxygen are never declining in a healthy individual? Well, the deal is lactic acid is formed inside the muscle, right? And, can there be low levels of oxygen in the muscle even though there's plenty of oxygen in the blood? Sure. So, those seemingly incongruous facts are indeed true. In other words, there can be high and normal levels of oxygen and there can be local deficiencies in oxygen in the muscle. But, the important part is this. Do you consume and use more oxygen in exercise? Yes. But, is there a decline in oxygen with exercise? No. Why not? Because breathing increases from the very beginning. Therefore, even though you're using more oxygen, you're also replacing it. Again, this applies only to healthy individuals. If you're not healthy, if you have lung issues or whatever, then it's a whole different story because even though you might be breathing more, you may not be exchanging gasses properly. And so, this could suffer. But, in healthy individuals, it does not. So, with that said, can we attribute this green line to a decline in oxygen? No. Because there isn't any decline in oxygen. So, maybe it's due to a buildup of CO2. But not. Because when you exercise, CO2 does not build up. In fact, notice that as exercise gets very strenuous, CO2 does not build up. It actually goes what? Down. How's that? Aren't you producing more carbon dioxide when you exercise? Yeah, but at this point, you're really moving air, right? You're moving so much air that even though you're producing more carbon dioxide, you're getting rid of more than you're producing. So, quite surprisingly, there is no buildup of CO2, not in the healthy individual anyway. And, therefore, can we say that this green line is due to a buildup of CO2? And, if it's not due to a buildup of CO2, we're already probably doubting that it could be a buildup of hydrogen ions. Because is there a connection between hydrogen ions and CO2? So, if there is no buildup of CO2, you might say, "Well, there probably won't be any buildup of hydrogen ions." But, wait, can hydrogen ions be formed from other than carbonic acid? Are there other acids that might raise the levels of hydrogen ions? Yes, that's the LA. What the? But, lactic acid is only going to occur if there's anaerobic conditions, and that might be certainly not in the beginning of exercise. But, only with prolonged and extensive exercise. So, finally, then, if we graph the hydrogen ion concentration, we see there's no change in hydrogen ion concentration except that it does raise a bit. But, not in the beginning. Only as we get really, really intense here. And, what's intensity have to do with this little rise in hydrogen ions that we see here? Intense exercise might make it more likely for areas to be suffering from local, anaerobic situations. Therefore, producing what? Lactic acid. So, this little rise here which comes only with extreme exercise is probably due to the circulation or production and introduction of lactic acid into the blood. And, that's not really going to satisfy or otherwise explain why exercise promotes breathing. Because this effect,

even though it's true, this effect is occurring pretty late. So, could this have anything to do with this? No. So, even though it might contribute, it's not an early contributor, and probably not a contributor to any great extent. So, what were out theories? We thought maybe this was due to a decline in oxygen. No. We thought maybe it was due to a buildup of CO2. No. We thought maybe it would be due to a buildup of hydrogen ions. No. So, if it's none of those, what explains this immediate rise in minute volume which apparently has nothing to do with blood gasses or pH? Turns out, again, that the O2 levels don't change. The CO2 levels don't change, and the pH, although it may rise, I should say, become acidic, it does so only with intense exercise. So, none of these are good candidates for this rather immediate rise in minute volume. So, okay. I'll cut to the chase. What is it? Actually, it's a number of factors, the first kind of unexpected. The motor cortex of the brain. In other words, the cerebrum. When you decide to run, do you issue motor action potentials to the muscles involved? I mean, of course you do. You decided to run. And so, that decision to run not only stimulated muscles, but it also sends APs, action potentials, not just to the muscles, but also to the? Inspiratory center. And, if you think about it, well, that's beautiful. Because if you're going to ask the muscles to work, let's also ramp up the action of the inspiratory center at the same time. And, indeed, that's what happens. And then, also, when you exercise, are there receptors in your joints that detect the movement of those joints? Those receptors are called? Mechanoreceptors. They're located in diarthrotic joints and in the tendons of skeletal muscles that move those joints. And, what's a mechanoreceptor respond to, you think? Movement, exercise. And, would these receptors, that is, would the information from these receptors be useful for the inspiratory center to know? In simple terms, would the respiratory center like to know that you're exercising? And, would it respond appropriately, you suppose? Yeah. So, essentially, this is corroborative information telling the inspiratory center, yes, there's exercise going on, and not only excite the inspiratory center but also the CVC. This is very easy to demonstrate. You can do it at home. Just have somebody laying on their back on the carpet at home, and then lift their leg, grab them by the shoe or something. And, just flex and extend, flex and extend their thigh like this. And then, do it faster. They're not doing anything, what? You're doing the work. What's going to happen to their blood pressure and their breathing even though they're not moving a muscle? It's going to go up. And, that's not this, but it is that. So, the mechanoreceptors reinforce, and therefore, help to raise minute volume as you'd expect. In fact, a and b are the primary reason for this green line. And, it's great that that's the case. Because just think about this. What if we didn't have a and didn't have b? Then, breathing would not increase as it does in the early phases of exercise. Allowing what to deteriorate? If this didn't kick in and breathing didn't increase, what would happen to these blood gasses if we didn't really engage the inspiratory center from the get-go? Oxygen levels would what? CO2 would go? And then, the body would be in this panic, catch up mode where it would never really catch up. So, this prevents changes, serious, degratory [phonetic] changes to oxygen and CO2. And, there's even more, although these are lesser in terms of

importance. Thermal excitation, which means simply the effect of heat. When you exercise, do you generate heat? And, most of the time, the body has ways of eliminating that heat. Vasodilation, sweating, even this. When you exercise, do you breathe more? Of course, yes. And, do you exhale CO2? Yes. Do you exhale water? Yes. Do you exhale heat? So, exercise gets rid of heat simply, by many means, but by exhaling. Anyway, certainly, when you get very, very intense, it's harder and harder to get rid of that heat. And so, in those conditions, the inspiratory center may actually warm up a bit. Remember, this is kind of in defiance of this homeothermic principle that we spoke of. Isn't the body normally 98.6? but, in very, very intense exercise, might that temperature rise to spite the best efforts of the body? And, would that heat warm up the inspiratory center at some point even a little bit? And, would that stimulate these neurons? I mean, we saw it in the turtle heart, right? You put warm ringers on the turtle heart, and it's faster. So, this is possibly an effect, but it's not going to be an early effect. It's going to be a late effect. And so, that's a minor effect. In other words, certainly third place at least. And then, I suppose last, you'd expect hormones to be involved, maybe epinephrine. Is epinephrine released during exercise? That much we know because epinephrine comes from what gland? And, is the adrenal gland innervated by, stimulated by the sympathetic nervous system? And does the sympathetic nervous system respond to exercise, fight or flight, etc., etc.? So, is epinephrine expected during exercise even if there's no threat or fear involved? Epinephrine is. But, wait a minute. Does epinephrine have anything to do with breathing? The answer is yes and no. Epinephrine doesn't affect breathing rate because that's under the influence of the inspiratory center. After all, the muscle that's responsible for the rate is a diaphragm. But, does it effect volume, and if so, how? Remember the lungs are fed by these airways called trachea? Bronchi, bronchioles. Are the bronchioles surrounded by and defined by smooth muscle? Is smooth muscle susceptible to epinephrine? And, what does epinephrine do to the tone, the tension, the contraction of the smooth muscle? It dilates them. Is that appropriate? Is that expected? Does that make sense, and is it good? Yeah. Because that would help move more air, and therefore improve the volume. So, epinephrine is a factor because epinephrine works on beta what? Two adrenergic receptors located on the smooth muscle of these bronchioles. And, of course, I can't help but think and refer back to asthma, as long as we're on this topic of bronchioles. What's the problem with an asthmatic attack? What's happened to the bronchioles? For whatever reason, they're what? Vaso. They're constricted. Bronchiole constriction. Does that interfere with volume? And so, what's the remedy? That is, what is the first aid measure for folks that have that crisis? Epinephrine vapor. Acting on beta two adrenergic receptors. Opening up the airways, and therefore, improving MV. What's MV? Minute volume. So, as we leave you, if someone were to say to you, "What causes breathing to go up during exercise?" Are you going to say, "Well, it's the body's attempt to get more oxygen,"? No. That's not physiology at all. Is it the body's attempt to get rid of carbon dioxide? No. What is it due to? It's due to a, b, c, and d. It's due to this activation of the muscles that are involved and the simultaneous

stimulation of the inspiratory center. It also is promoted by mechanoreceptors. Why are these good? Because they both act, what's the word? Immediately. Do these act immediately? Yep. Are we happy they act immediately? Because chemoreceptors don't act immediately. They have to wait for there to be a what? A decline is oxygen. So, these two really protect these blood gasses, that is protect from the rise in CO2 or the decline in oxygen. And so, a and b are most important. C and d are less important. C sometimes doesn't even apply. Why not? You've got to really exercise to heat up the inspiratory center. I don't think I've ever been there.

[Laughter]

And then, epinephrine. Yeah, that's a, you know, again, you have to exercise pretty intensely. And, it's not my game. So, basically, that's it. And, in lab next week, are we going to ask you to exercise. Heaven forbid, yes. Now, don't panic. Don't stay home because of it. It's going to be 30 seconds of running in place. You can handle it. And, will the minute volume increase? Will it increase from the get-go? Is it because of a decline in oxygen? Build up of CO2? Nope. Those two right there. So, it'll be fun to confirm that. I can't wait to see how long you can hold your breath, too.

[Background Conversations]