[music]

Lightfoot So our next speaker is one of the preeminent exercise physiologists, and has been for many years. And so we're very pleased to welcome from the University of California at San Diego, Dr. Peter Wagner. [applause] There you go.

Wagner Howdy.

S3 00:39 Howdy.

S2 00:41 I'm living. January 7th, my birthday. Nothing happened. July 23rd this year, my wife's birthday, 60th, she and I cycled up Haleakala in Hawaii. Those of you that don't know, that's a 10,000 foot vertical gain over 36 miles. We also cycled back down, a lot more terrifying. Why am I even saying this? I'm saying this because what you heard from all of the previous speakers was the importance of physical activity. If I, at the age of 70 plus, and my wife at the age of 60 can do this, so can you. That's not what I came to talk about. I came to talk about some science, actually. And I came to talk about science, not so much for the details of what I'm going to tell you, but much more about what I call the scientific method. And that's because I believe most of you are undergraduates, graduate students, or postdocs, and I just want to encourage you in intelligent thinking about the scientific method. You heard from Miss Yamaguchi exactly the same thing. She talked about failure and then curiosity leading to success. That in a sense is the scientific method.

S2 02:08 And so that's what I'm going to talk about with respect to a very particular element of science relevant to exercise capacity and performance, and that's VO2 max. So I first want anybody in this audience who knows what VO2 max is to raise their hand. I'm not going to ask you any questions, but who knows what VO2 max is? Who's heard of it? Great majority, but not everybody. VO2 max is actually not mysterious. It is what it says it is. It is the maximal amount of oxygen that you or I can grab out of the air by breathing, and through the various transport processes, deliver to our muscles to provide the energy for muscle contraction. One of the longest physiological debates that I know of is on my title slide: what determines maximal VO2? Why can Lance Armstrong win the Tour de France and Peter Wagner would be three days behind? What is the difference? What's the physiologic explanation? And my point is that it's been a debate for so long because of a failure of the scientific method. You know the story, you lose your car keys in a dark part of the street but you look for them where light is because that's where you can see things. You're never going to find them. You have to look for where the problem is.

S2 03:40 That's what this talk is about. The common belief is that it's the finite ability of the heart to pump blood around, and the blood, of course, contains the oxygen. And that's what people have said for so may years because they look at Lance Armstrong and they look at Peter Wagner and they say,"Look at the difference in cardiac function. It's huge." True, it's part of the explanation, but it doesn't explain everything. A particular part of getting oxygen to the cells is the very last step, and I'll talk more about the steps in a minute, but this last step is the step of getting oxygen out of the small blood vessels in the muscle, to the mitochondria in the muscle. That's what's been ignored. So when they look for their car keys where the light post is, that's because they can measure things like cardiac function. But they don't look down here because it's hard to look at. And so I say that the common belief is rubbish. I've been accused of, often wrong, but never in doubt. And this fits the paradigm. But I'm convinced I'm not wrong. I'll show you why.

S2 05:02 There are two guys that sit a street. Now, that should not have come up with their names. This was meant to be a pop quiz for you. Who are these two people? Anybody know [laughter]? Someone did this to me. I'm going to get them after this. But with that said, does anybody know who Peter Habeler and Reinhold Messner are? Anybody got a clue? Well, this next slide should help. Anybody know what this slide is about? Can you read [laughter]? It's about Mt. Everest. It's a beautiful photo. There's a thin red line, which is the path taken by people up past what's called the Khumbu Icefall, which is in Khumbu-- something or other in German-- in blue. And then you see the peak of Everest there on the left. And these two guys, Peter Habeler and Reinhold Messner, made it up to the summit of Everest without bottled oxygen. Now, that's 29,000 feet. That is where I was sitting yesterday, flying here, and I am just glad I had a window that was closed because I would not have been able to sit there, let alone climb the damn thing. And these people, these two guys, got up there. They were the first to do it. It's been done since, but they did it back in the last century before most of you were born. How did they do it? That's my message today, to give you a sense of what it took to answer that question and the failure that happened along the way by some very eminent people.

S2 06:58

The first diagnosis was willpower. They said, "These two guys just have more guts and more willpower than everybody else in this room. That's why they did it." Rubbish. Of course they had a huge willpower. John West-- some of you will know John West. He's a very eminent physiologist. I trained with him. I respect him greatly. Here's what he said in his book, High Life. He said, "Exceptional motivation and incredible obsession probably underlay their ability to do this." And the reason he said that was because he reported that elite, extreme altitude climbers don't have readily identifiable physiological attributes that will explain their accomplishments. So his was a diagnosis by exclusion, which those of you who are physicians like myself know is a last resort approach to life. We don't like to do that. And he made those comments, which are uncharacteristic for him because he is the quintessential physiologist, based upon this paper, the reference to which you can see there, by Oswald Oelz, another Everest summiter and physiologist, who took Peter Habeler, and Reinhold Messner, and a couple of other elite climbers into their labs and measured everything they could measure. And they concluded, and you can read this paper, you can read that they said, "We can't identify anything physiological that explains how they were able to do it and others are not." And my statement is, "You guys looked in the wrong place." There's actually data in their paper that I'll come to you with in just a minute that show how they were able to do this. So I think the problem is solved, and it's based upon very simple logic and strong physiology.

S2 08:57

Because willpower cannot trump, sorry for that word, [laughter] the laws of physics. I put this talk together a long time before the elections. Performance needs oxygen. We all know that the higher you go, the less oxygen there is. If there's less oxygen, then there's less performance. And you can't overcome the laws of physics with motivation. So Peter Habeler and Reinhold Messner must have had better oxygen transport, the ability to get oxygen from the air to their muscle cells. So if we're going to approach this scientifically, and here comes the lecture on scientific method and scientific thought, then you go back and you say, "Well, what does oxygen transport involve?" Just like a car involves an engine, and a transmission, and brakes, and fuel pumps, and everything else. It's a system. You can't just look at one place. You can't just look for the keys under the light because they're probably down the street in the dark. The system for oxygen transport is well-defined. The first step is breathing, obviously. The second step is a step whereby oxygen moves by diffusion from the gas in the lung into the blood that courses through the lung blood vessels. The third step is the circulating of that blood through the pumping action of the heart around the body to the muscles. And the fourth step, the one that I'm focusing on today, the dark part of the street, is the last step of transferring oxygen from the blood to the cells, which again, involves a diffusional process.

S2 10:50 Steps one and three don't suffer with altitude, and there's data for that. I can't give that to you now. But there's lots of data. You can breathe like heck at altitude. The air is thinner, it's easier to breathe. You can breathe all you want. The heart works perfectly well, surprisingly well, at altitude. The normal healthy heart. But steps two and four suffer greatly with altitude because I just mentioned to you they're based upon the process of physical diffusion. And diffusion is a process that depends upon the pressure of the gas, which is much less at altitude for oxygen, and that's the gas we're talking about. So those two steps suffer. So if you want to look for answers to why these two guys could make it up, you look for differences in those two steps. Well, step number two was part of their-- the Oelz paper armamentarium of data that said there wasn't anything particular about that. So that basically says steps one, two, and three were not the explanation. And the paper concluded by saying, "There's nothing going on." But they weren't looking at step four.

S2 12:02 Step four was actually remarkably different in these two guys. And they didn't appreciate it, they being the authors or John West. They found, just like Sue was talking about a minute ago, that the fibers were smaller than in sedentary control subjects, or even in long-distance runners. So smaller fibers mean a shorter distance for oxygen to diffuse. But more importantly, in yellow, gold if you prefer, the number of capillaries supplying oxygen to the muscle was much greater. And not just a little bit greater, but 40% greater. So that's like comparing Lance Armstrong to me, 40% greater. Or actually now, at my age, it's probably more like 100% percent greater, but we'll leave that. This is a huge difference, is my point. And it's been shown, I don't have the data to show you today because of time, that that capillarity is crucial to getting oxygen to the mitochondria. And that is what allowed those two guys to make it up. They could transfer the small amount of oxygen available much more easily. And neither Oelz nor John West, unfortunately, recognized this. And again, the paper's referenced there. So that is the message of that particular story. The body found a way to compensate for the laws of physics. It can't overcome the laws of physics. John West is not right. It's not motivation that gets you up there. You can't get up there without motivation, but it's not sufficient. You got to get the oxygen there. This is how they did it.

S2 14:00 Okay, that's an association. You may say, "Well and good Wagner. You've given us a nice story and a pretty picture of Everest, but where's the proof of what you are saying?" Well, again this would take an hour, and I can't give you that time. I tried to buy that time from my fellow speakers, but they wouldn't sell it to me. So I'm going to tell you in my final couple of minutes just a little bit about-- oh, final minute-- about operation Everest II. Where we measured something called the oxygen pressure in the venous blood, PvO_2, that's the blood coming back from the exercising muscles, as we went up in a chamber, or not we, but subject went up in a chamber from sea level to 29,000 feet over 6 weeks. Hellacious study, but a very good study. And you can see two traces there, a white and blue. One is at sea level and one is at high altitude. And the dots are the measured points and the relationship between the oxygen used by the muscles, VO_2, and the oxygen level in the blood. And you can see there's a big difference at the maximal point, the highest point of exercise, indicated by the arrows. The white point is much higher than the blue.

S2 15:13 And it prompted the question, if the oxygen level can fall to such a low level when you're at altitude, why can't this happen at sea level so you could take more oxygen out of the blood, and therefore exercise more? Why couldn't this happen? Something must be stopping the oxygen from getting out of the blood. What's more, and this is where the scientific curiosity comes in, we noticed that in this study, you could draw a straight line, the green dashed line, through the origin, and the two final data points in white and in blue. That is saying there's a proportionality, and proportionalities in biology don't arise by chance. They imply cause and effect, and 20 years later, of lots of research, the cause and effect relationship is that that proportionality reflects what we call diffusion limitation, the dependence of how much oxygen gets from the blood to the mitochondria on the partial pressure, or pressure of oxygen in the blood as represented by the venous oxygen level. And that straight line relationship, which is very simple, led to a new paradigm of thinking about oxygen transport. So that then becomes the explanation for how Habeler and Messner were able to get there. They just had much better muscle capillarity. Now, why did they? We don't know. That wasn't studied because it wasn't appreciated it was important. So we have these two guys to thank for enlightening us and inventing a new way of thinking about oxygen transport, and what I would like to say is that they taught us that every biological mystery does have a rational explanation is you know where to look for it. And my advice to you is, next time you travel to Everest to climb it, first check your muscle capillaries. Thank you. [applause]

S1 17:22 Nice job, Dr. Wagner. Thank you.

S2 17:24 Thank you.

S1 17:25 Several questions for you. We want to flip one back. We had several about Lance Armstrong. So Lance Armstrong was involved in steroid use. How would that have affected his VO2 max results?

S2 17:36 Good question. I don't know the answer in any truly scientific manner, and as a scientist, I should therefore zip, but how can I, having traveled this far?

S1 17:46 That's right.

S2 17:47 They probably made a really measurable difference because he likely would not have won seven of these things in a row without it. I can't tell you how much. Ed Coil, who is one of our fraternity, measured the guy's VO2, actually, over a period of time. Showed it was extremely high, of course, but never got involved with the drug aspect, so.

S1 18:08 Talked about efficiency quite a bit, and then--

S2 18:10 He talked about efficiency.

S1 18:11 --about his efficiency changed quite a bit.

S2 18:12 Which was very disputed by a lot of people, actually. But that's a whole other story.

S1 18:15 That's a whole other story. And interesting reading, actually, if you're interested. Here's a question, "Do you think the smaller muscle size and increased capillarity of Habeler and Messner is a result of training or genetics, and would you expect to see this adaptation in other elite-type athletes?"

S2 18:31 As somebody said in response to a previous question in a previous talk, the answer's yes [laughter]. Undoubtedly, it's a combination of the two, and it is-- well, let me break up. It's well known that training, endurance training, can and will improve capillarity in the trained muscle, whichever muscle it is. That is well known, and that is definitely part of the basis. And by the way, you see this in patients with disease, heart failure or chronic obstructive pulmonary disease, in particular, are the ones that have been studied. And there you see that if you train them, you can improve their capillarity and you can improve their exercise endurance and tolerance. It's not just the capillarity. As Sue said, there are fiber changes that obviously have to occur in parallel to take advantage of the extra oxygen, but without the extra oxygen, they couldn't do it. So it is definitely training-involved, but I am sure that these two guys had good parents.

S1 19:33 So this question actually hits in your wheelhouse. You haven't told everybody about all your horse work. This is from R. Bowen, from Truitt. He said, "How do observations in racehorses that lose alveoli integrity resulting in blood leeching into the lung tissue affect oxygen transport? Is it possible that other organisms have other limits?"

S2 19:54 This is a planted question [laughter].

S1 19:57 Actually, no. It just came in [laughter].

S2 19:59 Doesn't disprove what I said [laughter]. But anyway, it's a great question. I've studied racehorses. I've studied their oxygen transport. And if you don't know about racehorses, this is a shocking story. Basically, every racehorse will bleed into its lungs, to a smaller or greater extent, during a race, because the lungs have been ignored in the selective breeding over hundreds of years. Racehorses have been bred for cardiac performance, heart performance, and skeletal muscle, metabolic capacity and strength. And nobody has given a rat's you-know-what about the lungs. And the result of that is when a racehorse gets on a treadmill, and you put catheters in and you measure things, then this is what you find. You find the pressure in the pulmonary artery has gone from normal levels similar to mine and yours at rest to the levels that you see in you and me in arterial blood, arterial systemic levels. That's what bursts the blood vessels in the lung and causes then to bleed. They develop a low-oxygen level in the arterial blood. And by low, I don't mean like this from normal, but I mean like this. Their oxygen saturation will drop to 75%, which is--

S1 21:26 If that was in a human, that'd be bad news.

S2 21:27 Yeah. If that was in a human, they'd be in the ICU. This is just remarkable. And they do that because their lungs are too small to allow that diffusive process I mentioned in my talk to deliver enough oxygen across. So they run out of oxygen and the arterial levels are low. Because they can't breathe enough, their carbon dioxide levels build up in the blood because their lungs are small. And so they become very acidotic. And they develop a pH in the blood of 6.9, 6.8. Near-fatal levels. It's remarkable that they can actually do what they do with all this going on.

S1 22:02 Without more problems?

S2 22:04 Well, they do.

S1 22:05 They have problems--

S2 22:05 As I said, they bleed. And sometimes they break down at the end of a race and have to be put down because of these alveolar hemorrhages.

S1 22:13 Excellent talk. Thank you so much for your questions.

S2 22:16 My pleasure. [applause] [music]