S1 00:03 [music] Welcome to the Sports Medicine Podcast, brought to you by the Sydney and JL Huffines Institute for Sports Medicine and Human Performance in the Department of Health and Kinesiology at Texas A&M University. At the Huffines Institute, we're always working to facilitate, apply, and bring you the most up-to-date coverage of the wide world that is sports medicine and human performance, all in a language you can understand and share with your friends. And now, here's our host, the director of the Huffines Institute, Dr. Tim Lightfoot.

S2 00:32 Hello, and welcome to weekly edition of the podcast from the Huffines Institute for Sports Medicine Human Performance. I'm your host, Tim Lightfoot, and we're so glad that you took the time to download and you're listening to us today. We have on the other microphone, we have our executive producer, Carlos Rivera. Carlos, say hello.

S3 00:51 Hi, how's it going? Excited to be here today.

S2 00:53 And we have Carlos here actually on the mic, usually you just hear him on the podcast question of the week because we're going to try out a new format for the podcast. We're going to start doing this, you'll probably start hearing these alternated with our regular formats. But we want to give you another look at science in sports medicine and human performance. One of the things, one of the reasons that we do these podcasts is that we want to help people understand what goes into science, number one, but what goes into many of the things that we take for granted? Why do we know that you should drink sports drinks after an hour of exercise? Why do we know how to handle, how to treat cramps and broken legs and so forth? And so there's a real science behind that and my observation, Carlos, has been for years is that every study that we've ever done and we've been fortunate to do quite a few scientific studies, every study we've ever done has a story behind it. And it's a story that we don't put in the article itself because scientific articles are usually very technical, you put an introduction on why you did this study, how you did this study, and what your results were, and what your conclusions were. And we don't yet to give people the behind the scenes. And so we're starting this kind of new podcast approach and we're calling it the stories behind the studies. Are you good with that, Carlos?

S3 02:08 I think it's really informative for so many people because if you've seen our earlier podcast, we kind of start off and we kind of start to dive into maybe an interest of study they have but we kind of get left with the cliffhanger. So I think this is the answer that cliffhanger keeps the episode going. So something to really get more dived into and for the audience to kind of see more the perspective of the person we just interviewed and see more of what went in their head.

S2 02:34 Yeah, and so oftentimes science is presented as, well they had this idea, they tested a bunch of people, and turned out the idea didn't work. Well or did work. And fortunately it's not that cut and dry. There's always challenges with each of these. So we're going to take that approach and we're going to start off today and we're going to, Carlos and I are going to talk about one of our stories, one of the studies that we've done, and you'll hear in future weeks, you'll hear of other folks, you'll hear, we'll have some of our favorites from past podcasts come back on. And so this week, Carlos, I'm going to start with the study that was most memorable to me. So I have been doing studies, I think the first research study I ever did, official one that we wrote up, was in 1983. So whenever you're listening to this podcast, if it's in 2023 or 2037, hopefully we'll be around that long, they'll give you a sense of where we are. But the most memorable study that I ever did was one that we did, I did when I was a post doc at John's Hopkins, it was, we conducted this study about 1989 is when we did it, it was published in 1983 and I'll put the links up to this article on our website.

But if I think of a subtitle for this, it really is, sometimes we really don't know what's going to happen. Now let me explain that a little bit. It was always curious to me as a doctoral student when we started to do studies, many times when you asked for permission to do studies and we have to have approval from human subjects committees or animal committees. They always want to know what you anticipate what will happen. And if you've read enough literature in the area, you know enough about the area, you can kind of guess what is going to happen.

S2 04:10 This one study stands out because we had no clue, we really had no clue as to what was going to happen. And so let me give a little background on this, a little science background. So at one point in my career, I was very interested in why people pass out. Now, you may think, "Well, that's kind of bring," and to some extent it is. Yes, we know that if you pass out, if you lay down, you'll come back usually. Most of the time we know that passing out is due-- you've lost fluid or you've stood upright so fluid has stayed in your legs. We were interested in this at the time because NASA was very interested in this. They were very concerned that the astronauts they were sending up who happened to be in really good shape actually were more prone to passing out than normal people were, and so that set us off on a whole research area where we started to look at whether exercise training would actually influence whether or not a person passed out. And as we looked at that you started thinking about, "Well, what actually makes people pass out?" Yes, we know that when you don't have enough fluid pumped from the heart to the brain you start to pass out, but if you look at humans in particular, in most case humans pass out when they have about 20% reduction in blood volume. You say, "Well, okay. That's--" But the problem is with most mammals, that's nothing. Many mammal species don't actually start to have those kinds of blackout symptoms until they start to lose 60 to 65 to 70 percent of their circulating volume. Why is it that humans are different? What are the actual mechanisms that this blood loss was triggering?

S2 05:36 And so we were faced with a-- we didn't know what was triggering people to pass out. If we knew, maybe we could change this, and especially the astronauts because they were afraid and NASA was afraid when these guys were coming back, and primarily at that time it was guys, if they passed out they couldn't pilot the shuttles and they would crash and it would be ugly and so forth and so on. But there's a real practical aspect to this is that people passing out is the beginning of shock and if we're talking about soldiers on a battlefield or we're talking about patients in a hospital, if we can prevent them from going into shock then there are a lot more positive health outcomes. So it was very interesting for us to try to figure out what this was. So about this time there were three primary hypotheses about what was causing people to pass out and we had looked at a couple and disproven a couple, but there was this one hypothesis that was backed up by animal research and the hypothesis was that as you lost fluid the heart would actually begin to contract upon itself because you didn't have enough fluid in the ventricles so the ventricles are very strong and they were contracting upon themselves, and in the walls of the heart we know there are these receptors that measure stress or stretch, they're stretch receptors, and we also knew that when those receptors were stretched it actually caused the brain to kind of shut down the cardiovascular system. And so again there's been some animal studies and centrifuges and so forth that had suggested that this was the case. That as you lost blood volume, whether it was just pooled in your legs or you were bleeding, that at some point the heart began to contract upon itself, when it contracted upon itself it actually stretched these receptors and you passed out.

S2 07:11 So I was sitting in the lab one day with a cardiologist who used to work with us named Stuart Rowe, a great guy, at Hopkins, and we were talking about this and my point was I don't think we can ever test this on humans because we can't bleed humans out enough, we can't measure the stretch in the walls or whatever. And we sat and chatted about that for a while and he said, "Wait. I've got an idea. Let's do cardiac transplant patients." I said, "What?" He said, "Yeah. Let's test cardiac transplant patients." He said, "Because the heart that goes into a cardiac transplant patient doesn't have that wiring anymore" because when a heart is taken from an individual and put into someone else's chest, none of that cardiovascular neural conduction, none of that is connected anymore. They're just connected to the right atrium. I said, "Do you think we could do this?" and he said, "Sure. Let's try." And so if the hypothesis was correct, then cardiac transplant patients should not pass out, ever. We could take all the fluid out of them and they would never pass out. If this hypothesis was correct. If it was not correct, then they would pass out, like normal. Or they would start to show the signs. And so when we wrote up our permission slips, because we had to get permission, of course, from a lot of different people, to do this. Especially with transplant patients.

S3 08:25 I bet so.

S2 08:26 Yeah. They always ask, "What do you think is going to happen?" Because they want to make sure that you are ready for anything that may happen. I was stumped, because it was like we really don't know what's going to happen. No one has ever done this before. If this hypothesis is really true, and all the evidence at the time suggested it was, these people won't pass out. So there'll be no harm. And so the RB said, "Well, we're not sure about that." They understood our problem but they said, "So let's just, since we don't really know what's going to happen, let's make sure that we do in the safest way possible." So we had to do this in a surgical suit, we had to remove all of our equipment in, we had to have all the emergency docs, the emergency nurses, everybody involved. Now, when we did this type of study, you may be thinking, "How do you take blood out of somebody?" We don't really take blood out, we use a big box called a lower body negative pressure chamber. And you put them in it, and, by the way, this was a technique that was used in the Apollo astronaut days, where they would check to see how well they handle blood loss. And you put them in this chamber and you reduce the air pressure in the chamber and what happens is that blood pools in the lower part of the body. And then you can see all the physiological changes, heart rate goes up, vascular resistance changes, all these things happen until at some point, suddenly, everything turns off. The brain turns everything off, so heart rate goes back down to normal, blood pressure plummets downward, and if you continue on, people will pass out very quickly. Knock on wood, we only had, over the course of 30 years I've done this, we've only had a couple of people pass out. But we can tell very quickly when they're going to go. And so we brought all these patients in. It was a difficult finding, but we found six transplant patients who were willing to participate. They were all about 40 months out-- about 3 and a half years out past their surgery. They were all very successful, they were on immunosuppressant therapy, which all of them are on. We had shown that immunosuppressant therapy doesn't affect any of the cardiovascular responses. And so we found controls that were just exactly like them, except they didn't have a heart transplant. And so we got everything set up. We had to move all of our equipment across the street from one lab in Hopkins. We actually had to take it down, walk it across the street, cross the stop light, and all this other stuff, up into the hospital--

S3 10:32 All the fun stuff.

S2 10:33 Yeah. Into the surgical suit, with everybody going, "What is that? What are you doing?" and so forth. And set this up, and we actually did this over a number of days, so we did this more than once. But I can remember that first morning. It was an October morning and everybody was there. Again, we were all clueless as to what was going to happen. And we had our first patient in, and first patient went through, and he acted just like a healthy individual. We saw the same thing that we would expect. Second one was like that, third one was like that, fourth one was like that, fifth one, sixth one, sixth one. They all acted like healthy patients. We saw the same thing. Matter of fact, they didn't respond as well as the healthies did, which meant that when they had that-- when they lost that denervation around the heart, then there was--they were losing some other kind of toleance, kind of mechanisms. And so, for me, that's a memorable study because we truly didn't know what was going to happen. In one way I was relieved that they showed responses that the normals did. Because that meant that we could treat them like anybody else. And the transplant patients, we didn't have to worry about them not passing out. In another sense it was depressing because we thought we were onto it. We thought we had figured out a way to actually figure this out. And what we found out is that hypothesis was incorrect in humans. And so, since that time I've always kept that study in mind, because when we do any kind of study we think we know that is going to happen, but you never do. And I've been surprised once or twice. Things don't happen like we expect them to happen.

S2 12:04 But it was also a lesson, I think, for our human service committee because it opened up their minds to a possibility about maybe there are times when investigators don't know what's going to happen. And it's not that they haven't tried to figure it out, but they can't just figure that stuff out. So you just take all precautions that you can, and you do the best you can. So this study, Carlos, by the way, we've put up on the on the website. If people want to read it, you can read with that context in mind that we didn't know what was going to happen. We thought we had a way of proving-- and we did disprove this hypothesis. And since this time, since this was published in '93, to my knowledge, no one else has tried this kind of study again, which is also kind of interesting in and of itself.

S3 12:50 Well, I guess you kind of answered my feature question. I was going to ask you a before in your future kind of where this study took afterwards, what was the future of it, and then you kind of talked about that. Was there anything else you want to talk about specifically with the study of maybe how it's impacted some people, or how it's gone on to other people have used it, or modeled maybe towards it?

S2 13:16 Yeah, yeah. Well, it's interesting. One of the interesting thing antidotes that came along with the study was I-- in one sense I'm very pleased people didn't take my bet because a couple months before we actually started the study, before we actually started collecting data, I did a presentation. I was part of a symposium at NASA because NASA, again, was very interested in this. I was very pleased. NASA flew me down to Johnson Space Center, and we had this meeting of all the people in the space program, and I gave a presentation. And I said very clearly, "This is our hypothesis. This is the data that supports it." And I said, "At that point--" and again, this was very early on, very brash in my thinking, in my verbiage sometimes. I said, "I bet my career that this is what's happening." And I said, "We're about to collect the data to actually show." And so to some extent maybe I had a bias going in that this was the hypothesis. I had convinced myself, given the literature, that this was going to be the thing to happen. And so when it didn't happen, I'm really glad no one took me up on that and said, "Okay. You bet you' were wrong, so guess what? You can't do this anymore [laughter]." So we did this kind of work for another 10 years, 10 to 15 years, and then we moved over to genetics stuff. Again, what's interesting is that for people who want to know that mystery in physiology, there are mysteries in physiology, we still don't know what causes people to pass out. I keep an eye on that literature. There's another hypothesis out there that we actually were going to go after. It was very difficult to measure humans that deals with gut blood flow, and it's hard to measure gut blood flow in humans, and how it changes. Again, that mystery is still out there. So if someone wants to go after it, I would encourage them to go after it. I had a friend of mine, it may have been Stuart Rowe, who said to me, "So, Tim, no one's solved this for 60 years, why do you think you can solve it?" And I said, "Because I'm going to work on it." So that mystery is still out there. Again, I keep that in mind because I always figured if you're willing to work on something and be passionate about it, you'll find some answer. The answer we found was it wasn't what we thought it was, and that's how science works, right? We make hypothesis and if they don't work, they don't work. We're going to the next hypothesis. So what do you think?

S3 15:21 Yeah. You kind of answered too what, my question of before the study, kind of the support you got. You kind of going into the study with no one really knowing what the possibilities were. I know you said you were doing your postdoc at the time. So kind of that staff you're under, I guess the person you answer to, what was their opinion on this going-- did they think, "Wow"?

S2 15:42 They had no clue either. My postdoc supervisor was Susan Fortney. And Susan is retired, and she actually retired from the University of New Mexico recently. But we had many conversations about where this was going, and she didn't know. I didn't know. Stuart Rowe, who is our cardiologist on this who had the idea of using the transplant patients. He didn't know. In fact, none of us knew. And again, I think that's one of the few times in my career when we've had an approach and none of us had quite an idea of what was going to happen which was kind of fun. It was kind of scary, but it was kind of fun at the end. So we can't even anticipate sometimes what things are going to happen.

S3 16:26 So now that you can see maybe even being in her position where you are in your career, someone comes up to you with an idea like that, what would your thought be? Maybe not that study, obviously, but something where you're talking about this mystery and it's just something that--

S2 16:42 Well, if they came to me with that idea for that study, I'd say, "We already did it in 1993. We don't need to do it again." But we've had those kind of situations and I encourage all the people that work in our lab, "Hey, if you've got an idea, let's try it. If it doesn't cost us a lot of money and we can do it, and we're not going to hurt anybody or anything, let's give it a shot, see what's going to happen." And because you never know. I've had a couple times where I've had doctoral students come to me with, "Hey, let's do this," and I say, "Fine," and it turns out to be something. And that's what we're supposed to be about. And I'll have my post-documentor, Dr. Courtney, for encouraging me, and Stuart for being there and saying, "Hey, let's do this, let's try it." Because they were as interested as I was. They were as curious as I was. And I think that's what university is supposed to be about and research is supposed to be about. Sometimes we get caught up in the grind of finding money and whether or not the government's going to take our money or whatever, and we forget about-- we're doing this because we're interested in solving mysteries and figuring out what the mysteries are. And there's still a mystery in there, so.

S3 17:41 Sounds good.

S2 17:42 Yeah.

S3 17:43 Well, is there anything you want to leave off with? Kind of to close out this study? Or--?

S2 17:48 What I would say is that, first of all, Carlos, thank you for being on air.

S3 17:52 No problem.

S2 17:53 You're normally a shy person so we're glad to have you on the--

S3 17:55 Usually a little more quiet.

S2 17:56 You're a little more quiet, yeah. Even though the audience doesn't know that you used to have your own radio show [laughter], we'll leave that alone for the time being, right? But really, for the audience, what I want you to understand is that-- and what we want to get through with the story behind the study idea is that people overcome some great obstacles sometimes to do the studies they do. They have great passion for why they're doing-- they often take an inordinate amount of time to figure out how to answer questions, to try to give us a little bit more glimpse of the truth. Because that's what most scientists are about. They're interested in finding out what is real, what is the truth, what can we test, what is provable. And so I would encourage people to come back, stick around, listen for some more stories behind the studies that we do in the future. I think you'll find some interesting stories out there.

S3 18:48 Great.

S2 18:49 And I would encourage people, if you like this, tell us. Send us an email. huffines@tamu.edu. We'll make sure Carlos reads all those. If you didn't like them, send them courtesy to me, but send them to hufflines@tamu.edu and tell us what you think about this new format because again we want to try to do something different, a little bit more fun.

S3 19:09 Yep. I agree. And we might even have to bring you back again because I'm sure you have a lot of studies. We got to shine some spotlight on you as well.

S2 19:17 There's a story behind every study, Carlos.

S3 19:20 Heck yeah [laughter]. Sounds good.

S2 19:22 So I want to-- Carlos, thank you again for your time today.

S3 19:24 No problem.

S2 19:25 And I want to thank all of you for taking the time to download us and listen today. I hope that you're with us next week. We know that we're going to have an interesting, interesting interview next week about the consequences of what happens when NIH funding is cut and a little bit of a story behind a study there as well. So join us next week and until that time, stay active and healthy. Thanks, Carlos.

S1 19:46 Thanks for listening to the Huffines Institute Weekly Sports Medicine Podcast. The executive producer of the sports medicine podcast is Carlos Rivera. The podcast is made possibly by generous support from the Omar-Smith family and the Sydney and JL Huffines family. This podcast is published under an attribution and no derivatives created commons license. That means you can't sell it or change it, but feel free to give it to everyone you know and to talk and blog about us. And in case you were wondering, our openings and closing are provided by johnmilesproductions.com, providing worldwide voiceover services. Music was provided by Dave Zeldner. Find him on the Web at davidzeldner.com. And just so you know, we love hearing from you. If you have questions or comments, please send them to hufflines@tamu.edu. From all of us at the Huffines Institute, we hope you have an active and healthy week. [music]

[silence]