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S1 00:11 Welcome to the Sports Medicine podcast, brought to you by the Sydney & J.L. Huffines Institute for Sports Medicine & Human Performance and the Department of Health & 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. Now, here's our host, the director of the Huffines Institute, Dr. Tim Lightfoot.

S2 00:40 Hello, and welcome to the weekly podcast from the Huffines Institute for Sports Medicine & Human Performance here at Texas A&M. I am your host, Tim Lightfoot. And we are always pleased to bring you another interesting individual from the world of sports medicine and human performance, and this week is no exception. We have Dr. Marielle Engelen with us today. Welcome to the podcast, Marielle.

S3 01:00 Thank you, Tim.

S2 01:00 I'm going to tell everybody a little bit about you, and then we'll just jump right into conversation with you.

S3 01:04 Sure. That's fine.

S2 01:06 Marielle is an associate professor and a co-director of the Center for Translational Research on Aging and Longevity here at Texas A&M. She has multiple degrees. She has a PhD in Physiology from Maastricht University in Maastricht, Netherlands. She did a post-doctoral fellowship in the Department of Respiratory Medicine in Maastricht University. She was awarded the American Society for Nutrition's Vernon Young International Award for amino acid research. And she was also a research associate scientist with Karl Wasserman at UCLA. Many people listening to this podcast will remember Dr. Wasserman, who was always quite an influential member of the exercise science community here in the United States for many years. Again, welcome so much to the podcast, Marielle.

S3 01:52 Thank you, Tim.

S2 01:53 We're so glad to have you. You've been doing a lot of work with respiration and nutrition.

S3 01:58 Yes, that's right.

S2 01:59 And as we looked at your background stuff, you really kind of grouped in this big category. You've researched chronic wasting diseases in the elderly. Can you help us unpack that a little bit as to what that means?

S3 02:12 The loss of body weight and muscle mass that often occurs in patients with diseases like COPD, heart failure, cancer, and then cystic fibrosis.

S2 02:24 I think people don't appreciate the fact that when people have those kind of diseases, that they start to lose muscle mass.

S3 02:31 Exactly. It's very interesting to know that, for example, in the world of COPD, that's already known for a long, long period of time. Whereas, for example, in cystic fibrosis, it's still not clear for a long time. And that's the reason why we switch, also, or switch-- we added an extra research line to it. And to actually implement all the knowledge we

know from other diseases like COPD, also to benefit the cystic fibrosis, in which muscle wasting is a huge problem, too. But it's not really acknowledged so far.

S2 03:02 So, why is it a huge problem? Why does it matter if we lose muscle mass?

S3 03:07 Muscle mass is a problem particularly in these diseases, because it really affects your life. First of all, these patients have lower muscle function, muscle strength, physical activity level, but it also affects them when they are sick. So, when these patients, for example, are admitted to a hospital because of an exacerbation of a lung infection, then they will stay in the hospital for a longer period of time. So, hospitalization stay is longer and they have more complications, the quality of life is lower and they die sooner. And this is applicable not only to COPD, but also to CF, heart failure, cancer, and so on. So, muscle mass is important. I mean, muscle mass, you need to preserve in order to live longer and better.

S2 03:56 And now that's probably coming as somewhat of a surprise to people, because that's not what you hear about when you hear about people that have COPD or cystic fibrosis, you never talk about the muscle wasting side of that. So, your general research area's how to prevent that, I understand. So, is that wasting due to the fact that they're just laying in bed? Is it bed-rest related? Is it disease related? And then I'm, of course, going to ask about how we can fix it. If we can fix it.

S3 04:27 Of course, like you mentioned, physical inactivity is a problem in these patients, and particularly in COPD. When you have a lung obstruction and you are short of breath, you don't want to walk. So, that's definitely a part of it, and multiple factors involved. First of all, you have the negative energy balance, which means that your energy expenditure is higher than your energy intake by default. And the reason why you have a higher energy expenditure in your daily life is because the work of breathing already costs more energy. And besides that, besides the respiratory, is also the muscles. The muscles work more inefficient, so you use more energy during daily life activity. So, just the walking, just being active, already cost a lot of energy. So, that's one part of the equation, so it's and energy disbalance, but also there is an effect on protein mass - and of course, muscle consists of protein. So, there's a negative protein balance too, which indicates there are a lot of factors involved in these patient group, like the inflammation that directly affects your muscle mass. But also hypoxia, which is present in these patients during daily life and during physical activity. And, of course, medication - corticosteroid use plays a role. So, it's multidimensional. There's so many factors involved, all leading to loss of muscle mass.

S2 05:56 So, you talked about the energy output side of things. Do these patients generally eat less as well on the energy input side? Is that another factor? It's the tied dietary factor, they may not eat as much or eat what they should be eating, or--?

S3 06:10 In general, when they are stable, the energy intake is fine, and protein intake is also fine. But the problem is the moment when they are not feeling fine, for example, when they have a respiratory infection. When you don't feel good, you start to eat less. So, at that moment, your energy balance is more affected also by reduce energy intake, in addition to your increase energy expenditure. So, within generally-- right now, we do not know exactly how much they really need when they are stable, but also particularly during exacerbation. Because the energy intake needs to be increased, and also the protein intake needs to be increased in order to preserve the balance. And that's not always the case.

S2 06:50 That's the topic that you have done work, or you're continuing to do work on, is how much protein intake do they need, is there any special supplements that they can

take, et cetera? So, what's the current thinking in your line of work, about how much protein someone needs if they have one of these disease processes?

S3 07:10 Well, right now in the-- as I mentioned, in the CF world, it's not so much already generally accepted protein is a problem. Although we really working hard to change that perception. In COPD, of course, we already know for a longer period of time that there is something wrong. But how much protein you need, it's still not well established. We are developing techniques right now to be able to assess protein requirements, by using stable isotope techniques. Not many groups in the world are actually using stable isotopes to be able to measure that, so I think that's a nice way of getting more information about it. What we think based upon other diseases is, for example, that in the healthy elderly, there is already protein requirement of between 1 and 1.2 grams per kilogram body weight per day. And that for a stable patient, it will be a little bit higher, between 1.2 and 1.5. In case they have an exacerbation - inflammatory exacerbation - this will even increase above 1.5. So, that's what we expect, and of course we still need to do more research on that.

S2 08:15 And that's a little bit higher than the recommended daily intake for just adults, for healthy adults, right?

S3 08:22 Yeah. Now the recommended intake is 0.8, but you talk to the experts in this field and 0.8 is far too low. So, we really are already in healthy elderly in the 1.0, at least.

S2 08:36 So, as you get older, eat more protein.

S3 08:38 Exactly.

S2 08:38 Eat more protein, yeah. So, you talked a little bit about some of the studies that you're doing with the stable isotopes and this really cool technology. And an arm of this - and we were chatting a little bit before we started - was that because you're doing this in humans, and you're often doing this in a disease population of people who have COPD or people who have cystic fibrosis, and oftentimes, in elderly subjects as well. You're doing this all in what we call Bed-Rest Model. Can you tell folks a little bit about the Bed-Rest Model, and when we talk about that kind of research, what are you talking about?

S3 09:11 You mean the studies we are doing in these disease patients?

S2 09:13 Sure, yeah.

S3 09:14 In general, what we do is we ask them to participate in the study, which will last sometimes three hours, but also sometimes five hours. They just lay on the bed and we infuse stable isotopes of amino acid, because we are mainly interested in their protein metabolism. Then when they arrived and they are in a fast state and they lay on the bed, what we actually do is we take some blood samples and then are able to measure how much of the protein is synthesized - build up - as well as how much of the protein is broken down. Actually, the difference will provide you whether you are in catabolic state, whether you are losing muscle mass or not. Of course, you can expect when you are in a fast state, where you didn't get a meal, you lose muscle mass. But it's possible that, for example, basically chronic diseases have already in the fast state and more negative protein balance. So, that's what we do, and then subsequently, we get in certain nutrition, certain protein meal, and then we can see whether respond anabolic to that nutrition, which is-- we expect, of course, a protein build up will be larger than protein break down. But you can actually measure how good they respond to the nutritional supplement, and when you change your protein

intake, whether it'll actually improve it. And so far, we have done that in the COPD, but also in the cystic fibrosis. Of course, you need to put an IV in. So, what we did for example in this the cystic fibrosis kids - because those are pediatric children - that we did the study in the hospital when they were admitted for an exacerbation. Of course, they already had a line in place, so we don't have to--

S2 10:57 Do anything extra, right?

S3 10:58 Yeah. And then it's much easier. You get a nice relation. It's an easygoing study. You take some blood sample, you chat some with them, they take a supplement, and then you measure the response to the supplement, and it gives you a lot of valuable information. Normally when you would provide patients with some proteins and you want to see whether it actually will lead to muscle build-up, it takes a long time before you can actually detect it by water composition techniques, and this is actually a study in which you do in a couple of hours, as I mentioned, and you really get it. The samples will be analyzed by the lab. You get indication, okay, will it actually lead to anabolism, and how much anabolism will it lead to? So, it's a nice, easy-- but still not easy, because, of course, you need some [laughter] expense.

S2 11:47 The thing is that many times that those of us in the research field, we think these things are easy, because we do them every day. We've worked hard to put them together, and we've gotten all the approvals and so forth, but if you step back and you go-- and when we talk to the public, we realize that they really aren't that easy.

S3 12:02 No, and that's also-- that you can also relate it to the fact that there are not many research groups in the world doing this type of studies, because not only-- I think the practical things is not that difficult of thing, but it's more the whole knowledge about the isotopes, but also be able to analyze it, and the enrichment, and the blood, and the [?]. I think just the combination of all these items that makes it--

S2 12:29 Makes the research side difficult.

S3 12:30 Absolutely.

S2 12:31 Yeah. Well, and then you have the recruitment issue, because again, you're recruiting people who are already sick in many cases, or have issues. So, what kind of obstacles do you run into when you start working in these kind of populations?

S3 12:45 Of course, you first have to meet them. You have to build in a relationship with physicians. Of course, when you place an advertisement, I mean, you never get a lot of responses back, so you often have to build up a relationship with a physician, go into the clinic, talk to subjects, and it's very interesting. The moment they get to know you and they participate in one of the studies, they will come back, because they like it, they like attention, but also they like to get more information about how they feel, and why they feel, and what kind of advertise they can get-- advice they can get on their nutritional intake, protein intake. So, that really establish the kind of relationships, so when you have them here, they come back, so that's wonderful. But still, it's difficult. Can you imagine when you're doing a research study in cancer patients undergoing chemotherapy, these people just got a bad diagnosis, they don't feel well and to be able to participate a study, the recruitment is probably the biggest issue in doing your own clinical research.

S2 13:48 I've seen some of your presentations that you've done in the past for some of the breast cancer patients that you've worked with, and it's amazing. I salute you and your research team for actually finding these patients. But these are patients who

have been under anesthesia for eight, nine hours, and to be taking data on them, that's really difficult stuff.

S3 14:08 Yeah, and you need to have very flexible research staff, of course. You have to be there day or night or in the weekend or whatever, because your schedule is dependent upon what's going on with them. You want to be flexible in order to be able to include them in the study. And even, for example, sometimes you have to change your study protocol a little bit to improve your recruitments. At the end, I think it's really worth it, even that it takes time. When you start a human study, first of all, not only get money in, you also have the [IB?] approval it and start setup. You need a certain group of people who will help you with doing the study, and then, reciprocally, you have to-- the patient need to show up, and then you have to-- it's a long process. It's many, many years to finish one study, instead of-- for example, with some of the animal studies, it's shorter, of course, but...

S2 15:06 So, I guess that's one of the messages. These are not studies that you think of in the morning and then do in the afternoon.

S3 15:14 No, absolutely. It requires a lot of preparation, a lot of thinking, and--

S2 15:19 As you mentioned briefly, you have to go through the approval committees here at the university. There's federally mandated human subjects committees that you have to get approval for. The take home message, research is not easy, right [laughter]?

S3 15:32 Yeah, I think research is not easy, but I think translational research, what we are doing, actually provides information that's not only worthwhile for the scientist, but also for the patients. And that's one of the things we always enjoy to do is also, for example, go to the community and talk to elderly, or talk to patients of, or even parents of cystic fibrosis, but also to COPD patients, and just talk about results. And they're very happy to say, "Okay, what can I do for myself to improve my health?" And that's what it's all about. So, it's double worth it to go through that.

S2 16:11 But when they're engaged like that, then they're more passionate about helping you understand, and then you can help them understand, as well.

S3 16:17 Absolutely.

S2 16:19 So, speaking of that passion, one of the things that we talk to our guests about often is why they got into what they're doing. Was there some point in your life that you remember, thinking back, "I'm really interested in respiratory issues"? Or put that another way, how did you wind up where you're at now? From a little girl, did you-- you grew up-- at seven years old, did you, "I want to work on respiratory diseases, look at amino acid balance"?

S3 16:43 No, not really. Actually, I was always interested in disease states. So, I studied the movement sciences, so a lot of exercise physiology, but still I was always interested in the people who are more physically limited. So, that's the reason why I signed up for an internship at the Department of Respiratory Medicine to work with COPD patients and muscle loss, so that's my first introduction, and it was already 1992, but that was the first start. And also, I worked later as a research associate in Dr. Karl Wasserman's lab. Besides just cardiopulmonary exercise testing, there was also one of the investigators. You will know him, Dr. Richard [Casseberry?]. He is doing also studies in COPD, so actually, I did more like lactic threshold, exercise testing with him, and that was a nice follow up of the study I was doing in Maastricht. And when I came back to the Netherlands, I started in my PhD, also in COPD, more looking at protein

[disturbance?] or more in the end the line disturbances of muscle loss. And then went to Little Rock, Arkansas, and then it was a nice possibility to also include the CF and the cancer, because-- what I mentioned, there's so much knowledge available in one disease state, you would like to check whether it's also present in the other one. You can learn so much from the other diseases. Nowadays, unfortunately, that's not often done, and of course you can learn a lot by improving the health, by just looking to what's already found in different diseases. Of course, you have differences among diseases, but you can also learn a lot from them.

S2 18:27 I always respect individuals who make a big leap and move countries to pursue their passion, whether it be research, or on whatever. And certainly that was a big move from the Netherlands to Arkansas, and subsequently to Texas A&M. So, what drove that? Was it just opportunity, or was it interest in what was going on in the United States, or--?

S3 18:52 No, it's already helped that I have stayed for an year. I spent a year in Los Angeles, so I knew how it was to live here in a research community, live in the States and be away from home [crosstalk].

S2 19:03 But that was in Los Angeles, compared to Little Rock, Arkansas [laughter].

S3 19:07 Exactly, but at that moment, my husband and I had three kids, so I think we prefer it more now [laughter].

S2 19:14 More the Little Rock, Arkansas [crosstalk].

S3 19:16 Little Rock, Arkansas than the big city of Los Angeles. Although I had a wonderful time over there, but yeah. So, that opportunity came available to work at the Department of Geriatrics, and I also set up the-- and then the Center for Translational Research, and working there with-- so, we had to start our research again. We're doing human research in COPD, and at that time also the cancer was involved: breast cancer, lung cancer and so on. So yeah, it was a step, but in general, I think it's very positive. And also for the kids, I think it's wonderful for them to have an opportunity to go abroad and see how life is at a different place and a different country and different language and so on. So, I think the more national-- yeah, we like it a lot.

S2 20:02 It's a broadening experience, isn't it?

S3 20:04 Absolutely.

S2 20:06 Well, I'm getting signals that we're starting to run out of time, and regular listeners of the podcast will know that this is the opportunity that we always give our guest to give us their take-home message. If there's one thing you want our audience to remember from what we've talked about today, what would that message be?

S3 20:23 When you have a chronic disease, always be prepared. Which means that when you have a normal body weight, or you feel fine, always take good care of yourself with respect to nutrition, protein, and exercise so that you're prepared in case that something happens-- surgery, or you break something, or in the case of a lung patient, get an exacerbation, that you have your reserves, because you need it. It's very difficult the moment you lose your muscle mass to actually rebuild it again, so you have-- actually a real effect on yourself, by just taking care of your body by good protein and exercise.

S2 21:06 Don't take your muscles for granted, huh?

S3 21:08 Absolutely.

S2 21:09 Fabulous. Well, Marielle, thank you so much for being here today with us. We've enjoyed it.

S3 21:13 Thanks so much. It was really a pleasure.

S2 21:16 And for all those of you that are listening, thank you so much for taking the time to download and listen to us today. If you're a regular listener, you know at this point in the program, we have a podcast question of the week, and here with our podcast question of the week is our producer, Ayland Letsinger.

S4 21:30 What is a general recommendation for protein intake for older populations?

S2 21:34 Great podcast question of the week, Ayland. Thank you. Be the first person to send us an email with the correct answer to that, and you'll win one of our nifty podcast t-shirts. So, once again, thank you, Marielle, for being with us. Thank you all for listening. And one last note here, make sure that you check out the website. We now have the Huffines Institute apps that are both available for Apple products and for Android products, and tablets and phones as well. So, make sure you hit those and download the Huffines Institute app, so you'll know when we have new content up. Until next week. We hope you join us again next week for another interesting person in the world of Sports Medicine and Human Performance. Until next week, we hope you stay active and healthy.

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