DANNY LENNON: Professor Klaas Westerterp, welcome to the show. Thank you so much for your time today.

KLAAS WESTERTERP: Good morning.

DANNY LENNON: I am really interested to have this discussion because you've published a lot of work in the area related to human energetics, around energy expenditure, human metabolism, weight regulation, all these various important components that relate only to overall health but then to other kind of related fields of say obesity research as well. Just for those listening, can you give us some context of your background academia and what has been the focus of your research up to this point?

KLAAS WESTERTERP: I am a biologist and my first research project was energy metabolism in birds. I continued it as a post-doc in Stirling University in Scotland where I learned the doubly-labeled water technique and there my focus was on flight energetics of swallows, house martins and sand martins – birds that can stay on the wing for 24 hours a day and the question was how could they do energetically. And after this – this was a 3-year period – I went back to the Netherlands again where I come from. There I worked further on starlings for another post-doc piece and then I became lecturer in Maastricht University in the south of the Netherlands where I started in 1982 with measuring

energy metabolism in human subjects, where I was working in the human biology department and that's where I have been since then.

DANNY LENNON: Excellent, and there's been a lot of work that has been very important in this field. So just one of the things that you did mention there was the doubly-labeled water technique that's used to assess energy expenditure. For maybe people listening that aren't that familiar with that technique can you explain basically what it is and its main use within research?

KLAAS WESTERTERP: The doubly-labeled water technique is a technique to measure total energy expenditure of water and water is H2O but you have hydrogen and water you have in your drinking water in two forms. You have normal hydrogen and heavy hydrogen, deuterium. Similarly you have for oxygen, you have in your body O16, oxygen with mass 16 but there's also oxygen with mass 18. In doubly-labeled water these two isotopes are in a higher enrichment than in our drinking water. And what happens when you give subjects a glass of this water? Then the isotopes mix with your body water and then the isotopes are eliminated as a function of your carbon dioxide production, at least, O18. O18 disappears from your body in water, in urine and breath water and things like that and in carbon dioxide by your deuterium, your heavy hydrogen only is eliminated in water. So the difference in disappearance rate between the two isotopes, the heavy oxygen minus that of the heavy hydrogen is a measure for carbon dioxide production.

Basically, what we do and that's what we call the Maastricht protocol is we have a standard protocol where we give subjects a glass of water at night before they go sleeping and in the morning and before they drink the water we collect a urine sample. The baseline urine sample before drinking water gives the concentration of these isotopes in your body water in the urine before you drink the water and next morning it's mixed with the body water and then we get the first sample after the enrichment of the body water. And then you want to measure the disappearance rate of these two isotopes and for this, in the Maastricht protocol, we collect urine samples again after one week or two weeks depending on the

energy expenditure of your subjects. When it's very highly active subjects, one week is the standard observation interval but when people are normally active two weeks and even in very sedentary adult subjects we measured over three weeks. So the example of the high active subjects was one of the first studies we did in Maastricht where we measured the energy expenditure of people participating in the Tour de France, that's a three-week cycling race in France.

DANNY LENNON: Yeah, very interesting. And I think that has a lot of parallels to a previous discussion we had with Dr. Brent Ruby based in the states where they looked at some of the energy expenditures capable of ultra endurance athletes as well as fire fighters that worked particularly long days for multiple days on end and you could see the upper levels of energy expenditure getting extremely high. I think in some cases some of those athletes were capable of getting up to like 17,000 kilocalories per day just purely based on the length and duration of that particular race. And I do want to touch on athlete populations with you later in the show. But just first when we are talking about energy expenditure, there's obviously a number of different components to that, so people will have heard of before about their basal metabolic rate and then obviously you know they will expend energy through say planned activity and exercise sessions. But there's a particularly important component that you've done a lot of work on and you've also talked quite a lot about is the physical activity level and a lot of the different variables that relate to that. Before we get to some of that work, can you perhaps define for people what this physical activity level or this PAL value actually is?

KLAAS WESTERTERP: Yeah, basically when you measure energy expenditure, you want to compare between subjects and the main determinants of your energy expenditure are body size and your physical activity. Now, body size is reflected in the largest component of our daily energy expenditure and that's basal metabolic rate, the energy expenditure for maintaining our body. When you adjust your total for your basal metabolic rate you have a measure of physical activity level of a subject and that's what we do nowadays by measuring total with the doubly-

labeled water technique for instance over one or two weeks. And then you have your daily level of energy expenditure and then you divide by basal metabolic rate, you get a figure and we named it physical activity level or the physical activity index.

This figure of course has a minimum value of 1 for people who don't do anything, they don't eat and then lying down all day. But it goes up to a maximum value and this maximum value is for instance during – it's the highest if we measure it in the Tour de France where these people work at the highest work rate and there the value was between 4 and 5. But for normally active subjects like in the Netherlands for instance, the physical activity level is on average valued like 1.7, 1.75 and maybe in the States it could be even slightly lower, the average level because people maybe are less physically active in general than in a country like the Netherlands where we do a lot of cycling and walking and things like that.

DANNY LENNON: So I think the first thing that will be probably obvious to people is that this PAL value is going to be different among different individuals based on generally how active they are and obviously then there's a cultural component to that like you mentioned the difference say between the Netherlands versus the US. But then also for people who are trying to be healthy and maybe trying to attain a healthy bodyweight, there's a number of different variables are then going to affect or change this PAL value right. So perhaps we can touch on some of them, particularly if we think about two ways people are most likely going to train, change their health or at least to decrease their body fat levels is to eat less food and to engage in more exercise. One of the interesting things that if we take the first component of that is under-eating. I know you have been part of a number of studies that have looked at the effect of under-eating on this PAL value. What are kind of some of the main takeaway points, so the main kind of conclusions that that research has shown us?

KLAAS WESTERTERP: When you don't eat according to what you need, so when you are sick your intake is below maintenance levels, then you are going to be less active. So not eating according to what you need and usually there's a reduction of your physical activity level. And this is

an effect you only see in a negative energy balance. So when you, after weight loss may get to a stable weight you get in a weight maintenance situation again, then this reduction is not visible anymore. So then you get to your –you are able to get to your normal activity level, but during a negative energy balance, you tend to get less active.

DANNY LENNON: Perfect. And that is presumably a – kind of these metabolic adaptations that we get from the body trying to conserve a certain bodyweight or to I suppose maintain energy homeostasis, is the decrease in PAL primarily just a decrease in their non-exercise activity, just purely that the person is less likely to want to move around, is doing less subconscious movement or is there also a number of other things tied into why overall activity level is decreasing?

KLAAS WESTERTERP: I think people just don't have the energy to move around as much as they normally do. So when you try to get these people more active, they tend to compensate the activity during the normal training time. As we have also done studies where we combine an energy restricted diet, it is an exercise program, and usually these exercise programs are maybe for 1 hour a day. And there are 24 hours in a day so what happens then, even when people don't realize they reduce their normal training activity and end up with the same activity level with even better training program.

DANNY LENNON: Perfect. That's one of I suppose the important things from a practical level for people who are in a position where they are trying to say decreased bodyweight over an extended period of time, if they are going to be trying to achieve that via adding in additional exercise, the importance then becomes on at least being conscious of their overall calorie intake and having some sort of accurate gauge of how many calories they are consuming because if not and they just eat based on what they feel, even though they are increasing energy expenditure via exercise, it seems likely that they are going to just balance that out by consuming more calories via the diet. Is that kind of an accurate kind of summation?

KLAAS WESTERTERP: What I would like to say is that first of all, when you try to get weight loss through exercise, you have to realize that when you normally start to do exercise, you also increase your intake. So when you want to lose weight by exercise you have to first of all, to realize that the best exercise for losing weight would be a moderate intensity exercise you can do for longer times, because duration is a very important thing. It's not high intensity that's induced any weight loss when you want to get weight loss through exercise, but more likely through moderate activity you could get some weight loss but then you only get this when you maintain your intake at the same level. And this is something people don't realize, when you start to do exercise, you get more hungry and then they automatically compensate this increase in expenditure by an increase in intake.

So first of all, and you want to lose weight by exercising, what you have to realize that in a negative energy balance you tend to compensate so you have to watch that you maintain the other activities and nowadays there are all sorts of devices maybe they can use accelerometer, you have all sorts of activity monitors nowadays, so they can see what they are doing and whether they compensate yes or not. And this is with regard to activity and this intake, it's something that you see on the scale having when you don't lose weight, when you start to do exercise and you know that your activity level is increased, then apparently you eat more than you did before.

DANNY LENNON: Just when you mention then that – well, when we are talking about exercise I suppose in general, if we are taking the example of someone who is maybe not done any training before or is not involved in a particular type of exercises, relatively new to it, and then takes up exercise as a means to be healthier and then maybe to lose some bodyweight as well, in terms of how that is affecting the physical activity index, as they get better at that particular exercise and their exercise efficiency increases, does that mean that they are going to need to do more of that particular exercise to just keep at the same physical activity index?

KLAAS WESTERTERP: That's one of the things. When you start to exercise initially, your expenditure goes up dramatically more than you would expect from the exercise you are doing because you are doing things very inefficiently. Basically what we saw that the increase in expenditure from a fixed amount of exercise was quite as high as we would expect from theoretical calculations, but after some time, when you continue this exercise, you get to the normal increase we would expect. So you get to a higher efficiency, and that's one of the disappointing things that people understood, they start to exercise, initially you might see a big increase in energy expenditure but to maintain this increase you have to do more and more because your body gets more and more efficient.

DANNY LENNON: Right. So that's why I suppose we see this idea that exercise is extremely important for overall health and can be an extremely important part of bodyweight maintenance, but really for weight loss in the first place, particularly if we are talking about an obese or overweight person that exercise alone is probably not a good strategy to rely on for that weight loss, unless we are consciously doing something on the dietary component?

KLAAS WESTERTERP: Yeah, maybe one of the examples that was one of the studies we did maybe more than 20 years ago was we trained people to run a half marathon, we got maybe 400 people who wanted to join this program but we could only accommodate 32, 16 men, 16 women and we had 9 dropouts out of the 32 subjects we recruited, 5 women and 4 men. They all said they didn't have the time to do the training but in the end they were the people who had the highest weight and they were people with body mass index of 24-25. So we included people in the range of 20 to 25 and the 9 dropouts were all people with a body mass index of 24-25 showing that it's not easy especially for running to do this with a higher weight so people start to complain and they drop out of the program. And probably the best strategy is first of all to get rid of some weight and then you can move around far more easier and it's easier to maintain this activity.

DANNY LENNON: That piece of research is actually a really good example of what we've been talking of this, essentially

the body being really good at regulating its energy needs to kind of match what it's doing and unless there's a conscious way that someone can keep their intake at the same level while doing this extra activity there's going to be – even without them realizing they are probably going to be consuming more to kind of prevent that continued weight loss in the long term. With some of these differences between individuals in their energy expenditure, is most of that coming down to some sort of genetic predisposition or what are the kind of main reasons that we see that different people have different energy expenditures outside of those main variables of say bodyweight? So if we control for their bodyweight what are the kind of main things that are dictating differences between people in energy? Is it down to genetics a lot of the time?

KLAAS WESTERTERP: Yeah, so you have people who have a tendency to get overweight and people who have a tendency to be less active than other subjects, less physically active and all these things boil down to the fact that maybe 50% to 3 quarters of the tendency to get overweight or be less physically active is genetic. So there's a predisposition for people to sit down all day or to move around all day, you have these people who can't sit on a chair for a minute and others you have to bind down on a chair, otherwise they won't sit. So this is really something that we have done twin studies and there you clearly see that there is a very clear resemblance of the physical activity level in monozygotic twins and this similarity is twice as high than in dizygotic twins.

DANNY LENNON: That's an important piece, but just before we move on from that, when it comes down to saying that there's this large genetic predisposition component to determining someone's likely energy expenditure, when we talk about that a lot of that is obviously modifiable by someone's normal habits and behaviors and environment. So it's likely kind of this epigenetic thing, that it's not necessarily their genetics are going to determine that they will of course become obese but there's more – that they are again, if they have that predisposition, they will have to be more mindful of what is environmentally going to be impacting that. Would that be a fair statement?

KLAAS WESTERTERP: Sure. That's similar with this food intake. Some people are very interested in food and they can eat all day and others are not really interested. So the first group is of course very likely to get obese in the current environment and the same with physical activity. You ask these people who tend to sit all day, so they have to put a lot of effort and start to move around than others. It's their genes that make them active all day.

DANNY LENNON: Professor Westerterp, one of the papers that you recently published was with Diana Thomas and it appeared in the American Journal of Clinical Nutrition, and in that you talked about a number of different ideas related to energy turnover, risk of body fat gain. Is there anything that we haven't covered in this discussion so far that was particularly important as part of that paper and some of the ideas that were published there I thought it was a particularly good piece – and maybe for those that haven't read it, could you give a kind of rundown of some of the things you and Dr. Thomas discussed in the recent paper?

KLAAS WESTERTERP: The main problem in all the studies we see so far on bodyweight regulation is that nowadays we can measure energy expenditure and we can monitor physical activity with activity monitors but nobody can measure food intake. So whatever happens to our bodyweight, we can maybe link this to energy expenditure and to physical activity but we cannot link it to intake because we cannot measure it. And the trouble is that intake probably is the main determinant of our bodyweight regulation and this is also maybe understandable when you realize that we spend energy all day. Every minute we spend energy and we can cover our energy expenditure by eating maybe three or more meals a day and when you add up the eating time over to 24 hours it maybe only 30 minutes and that covers our expenditure for 24 hours and it's so easy to eat a little bit more and you don't realize. And this is what we have also clearly discovered when we started with the doubly-labeled water technique, because before we used the doubly-labeled water technique people were thinking that overweight people were overweight because their energy requirement was lower than normal weight people. But since we have the doubly-labeled water

technique we know it's the other way around. Before that, they were basing their ideas about energy requirements on reported intake and when you ask people to report intake, whatever PAL subject, this is always lower than expenditure. And it's specifically much lower than you ask obese people to report intake because they think in general they only eat half of what they really eat. And this is something also that people don't realize that all these eating moments in a day and they just forget about it and when they want to know the intake you always have to rely on self-report and they only report a fraction of what they eat all day. And from these measurements we know first of all that people at higher rate have a higher energy requirement, and we also know that the energy balance mainly determines or the first determinant of energy balance is our energy intake and not our energy expenditure, our physical activity level.

DANNY LENNON: Yeah, for sure. And so with that when we are trying to kind of pull all this stuff together and maybe draw off some take-home points for people or conclusions, based on all the work that you've done and the stuff that you've seen emerge from that research, if we were to try and boil us down to some ideas or practical conclusions for people, I am probably on two sides. So if first we take the example of someone who is already overweight that needs to decrease bodyweight, decrease body fat levels. And then secondly for someone who just wants to maintain a healthy bodyweight over time, what are some of the big things that you think are important to bear in mind with those things or what do we see as a potentially a good strategy with that to try and maintain a healthy bodyweight over a long period of time?

KLAAS WESTERTERP: Yeah, that's of course an important question but the answer is maybe also – it's a bit disappointing, so far very few people are successful in maintaining weight loss. So maybe the first thing to point out is that it's crucial to prevent any weight gain and therefore people should realize that we can very easily eat too much. So first of all try to prevent weight gain because it's necessarily impossible to lose weight. Of course there are examples but when we do weight loss studies maybe there's only 10% in the end that

maintain 50% of the weight loss and the others are all back to normal or even at a higher weight.

Now, when you are more physically active, you do not lose weight from this higher activity level, but when you are more physically active, your energy expenditure is higher and this will allow you to eat a bit more than when you are less active and in the past there have been studies showing that especially at a low energy turnover people have difficulty in maintaining weight especially in the current circumstances where there's food around all day and everywhere. So a higher activity level and a higher expenditure allows you to or gives you a higher chance to maintain your weight because you can eat more than when you are less physically active. But these are all very simple straightforward messages and maybe you would know beforehand anyway. But this is something that can't be stressed enough that tried to prevent weight gain and it's easier to maintain your weight at a higher activity level and at a higher activity level of course there are also many more health benefits like insulin sensitivity, lower risk of cardiovascular disease and so on. These are all well-known things.

DANNY LENNON: Yeah. I think that's a really good kind of summary. It lets us know where people should be placing a lot of their focus. And with that Klaas, when it comes to this area of research that you are involved in, where do you think the future of the field has to go in terms of what would you like to see as the next areas to be explored in research or the next research questions that are examined and that we try and get answers to in this area?

KLAAS WESTERTERP: Yes, one of the things I think it's very important in the current society is that when you think about your health, many things that happen in early life are crucial for what happens in later life and maybe the clearest example is bone mass – bone mass peaks at a young age and then you can only lose. And maybe something similar happens with your muscle mass and so I think it would be very interesting to see how muscle mass develops in early life and my hypothesis will be that that's also short of peak muscle mass at a younger age after you have reached your adult body

size, and then it only goes down. This is something that we also see when we compare for instance elderly subjects, when we compare elderly subjects with different activity level, this doesn't show up in a difference in muscle mass.

So apparently muscle mass is something that also like bone mass peaks at a younger age and then gradually goes down and maybe we can delay the decrease in muscle mass with increasing age little bit, but not so much. I think it's more important to pay attention to how muscle mass builds up in early life. And nowadays the youth is always sitting a lot and maybe not exercising that much anymore, and they are all online all day and sitting behind computers and behind a screen. And this I think could be a very delicate thing because then you are not sufficiently active in life, you might not reach your optimal muscle mass to cover your health in later life.

DANNY LENNON: Yeah, I think that's just a fascinating area and like you say a very important question particularly when we look at the whole area of sarcopenia and sarcopenic obesity and just how much that's affecting the population's health right now and of course which ties largely into decreases in muscle size and muscle strength with age. So yeah, I completely agree, that's a fascinating area. Professor, like I said, this has been a great conversation. I really appreciate you taking the time out of your day to come on and discuss some of your important research which has been very important to the field and has helped a lot with this area, and for taking your expertise and breaking it down and explaining that to us today. So thank you so much for your time.

KLAAS WESTERTERP: Thank you. It was a pleasure.

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