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Insulin-Like Effects on Exercising Muscles

### INSULIN-LIKE EFFECTS ON EXERCISING MUSCLES

Is working out too tough for you so why not just skip the exercise and pop a pill. Welcome to the Clinician's Roundtable. I am your host Dr. Larry Kaskel, joining me today is Dr. Laurie Goodyear Core Director and Research Investigator of the Joslin Diabetes Center and she is here to discuss the importance and effects of insulin-like effects on exercising muscles.

#### DR. LARRY KASKEL:

Dr. Goodyear welcome to the show.

#### DR. LAURIE GOODYEAR:

Thanks for having me.

#### DR. LARRY KASKEL:

Well you know I think we all know that exercise is good for you, but tell me a little bit about why regular exercise is so good at reducing the risk of getting type 2 diabetes.

#### DR. LAURIE GOODYEAR:

Okay well exercise as you said has so many different health benefits, but particular for people with type 2 diabetes, we know that exercise can actually promote glucose uptake into the muscle and that results in lowering of blood glucose concentrations. So during exercise when your muscles contract, the blood sugar goes right into the muscles. We also know that exercise can make the muscles more sensitive to the actions of insulin. So when you eat a meal and your insulin levels go up, the insulin works to promote the glucose the blood sugar going into the muscles and if you eat after exercise, then the insulin works a lot better and that results in lowering of insulin levels so both of those things are really primary to the ability of regular exercise to decrease risk of diabetes.

**DR. LARRY KASKEL:**

Now is there any reason for someone to not exercise, can you think of any? Someone who has got high sugars, prediabetic, diabetic any reason they should not exercise assuming they have normal knees and they normal heart.

**DR. LAURIE GOODYEAR:**

The only patient group that really may not be able to exercise or exercise in a more limited manner is people with type 1 diabetes if their blood sugars are not under control. If their blood sugars are very high, then it can have detrimental effects to exercise, but for everyone else for almost under all conditions and physical state, people can exercise at least to some extent.

**DR. LARRY KASKEL:**

Dr. Goodyear can you take me down to the cellular level and help me understand what insulin is doing with the cell membranes on skeletal muscle cell.

**DR. LAURIE GOODYEAR:**

Well what happens is again once the food is eaten and the insulin is secreted from the pancreas, it goes to the different tissues including the muscle and the insulin binds to special receptors, special insulin receptors that sit on the muscle cell and this elicits a whole host of signals within the cell that then result in the movement of these transporter proteins, we call them glucose transporter proteins they go from inside the cell to the surface of the cell and then they promote the sugar, the blood sugar, the blood glucose to come into the cell and that results in the lowering of blood glucose.

**DR. LARRY KASKEL:**

Is there anything out there that kind of disrupts the normal function of insulin receptors. I mean are cellular membranes affected by their fatty acid composition, for example if you have too many omega 6 versus omega 3, is there anything to that?

**DR. LAURIE GOODYEAR:**

Well there is some evidence that the lipid content of the muscle can affect the signaling within the membranes, but the main problem in people with type 2 diabetes are people that have insulin resistance such as people with various prediabetes what happens is not so much what happens on the membrane, but inside the cell it seems that the signaling molecules that signal the movement of these glucose transporter proteins becomes defective and it does not work and so the muscle is insulin resistant and cannot take up the glucose.

**DR. LARRY KASKEL:**

Can you tell me what your research is really focusing on these days and what you are doing day to day.

**DR. LAURIE GOODYEAR:**

Well the primary work in my laboratory is to understand not so much how insulin works, but how exercise works and how muscle contraction works to promote the uptake of glucose into the muscle. As I just mentioned, insulin works through a particular mechanism and we know that exercise does the same type of thing it also promotes glucose going into the muscle, but we also know that exercise works through a very different mechanism. So in people with diabetes while their muscle is insulin resistant their ability for exercise to promote glucose uptake into the muscle is preserved and so we are really trying to understand on the molecular level what's happening inside the muscle what are the signaling proteins that mediate in these important effects of exercise to increase glucose uptake into the muscle.

**DR. LARRY KASKEL:**

So what have you learnt recently let's say in the last year that kind of takes conventional wisdom and throws it out the window that if you were to publish the community would say that makes no sense, I do not believe you.

**DR. LAURIE GOODYEAR:**

I do not know if they doesn't make sense, I think that what we started to learn is that the signals by which exercise works are very different than how insulin works and that makes sense because we know that exercise can increase glucose uptake into the muscle in people with diabetes where as insulin doesn't. What has been sort of the consensus or the hypophysis of the last 10 years or so is that this molecule called AMPK is the key to this exercise effect and lot of pharmaceutical companies are making drugs to mimic the effects of exercise working through AMPK, but what we have found with exercise is that AMPK isn't the only story that there must be other molecules that are also being activated and are also regulating the effects of exercise. So I think this is something that some people are going to raise some eyebrows about because it's almost become dogma that this AMPK molecule that's the target, that's the molecule, but I think that we are generating more and more data to suggest that there are other molecules that are also important in the muscle.

**DR. LARRY KASKEL:**

**If you have just tuned in you are listening to The Clinician's Roundtable on ReachMD XM160, The Channel for Medical Professionals. I am Dr. Larry Kaskel your host and I am talking with Dr. Laurie Goodyear a Core Director and Research Investigator at the Joslin Diabetes Center and we are talking about the importance and effects of insulin like effects on exercising muscles.**

Dr. Goodyear you mentioned that some pharmaceutical companies are working on a pill that would mimic exercise I think it is called AICAR, I have no idea what it stands for, can you tell me what that is?

**DR. LAURIE GOODYEAR:**

Okay well AICAR is compound called ACAR or ICAR. It has actually been around for a long time and what this compound does is it can be taken up into cells and it can activate this AMPK molecule and as I said before. We now know if you activate AMPK, you can increase glucose uptake. That's not the only mechanism by which exercise works, but we know if you can activate that you can increase glucose uptake. So this was really the basis for identifying AMPK as a drug target. Now AICAR has actually been around for a long time. We know that it has many other effects in the body and in skeletal muscles. So it can increase glycogen levels in the muscle, which is very important for performance, it can have effects on the liver. So it can have many positive effects some of which are similar to exercise, but it is not really a viable drug that can be used in patients. If you treat patient or give the patient AICAR, you would need to

give it in very high doses and it can result in very high levels of lactate and there is some other problems with using the drug.

**DR. LARRY KASKEL:**

I have read lot about resveratrol and that high doses of that may actually also help increase endurance by actually enhancing mitochondrial function, any thoughts on that?

**DR. LAURIE GOODYEAR:**

Yes there has been some very interesting data that is emerging on resveratrol and it may actually work through AMPK, a similar mechanism. So it will be very interesting going forward to see whether you know optimal doses can be obtained and that this will turn out to be a viable drug and will potentially again mimic some of the effects of exercise.

**DR. LARRY KASKEL:**

Lets go back to the exercise in a pill concept, that may sound great to couch potatoes, but to me it sounds very brave new worldish, and it does not sound like anything good can from it. Do you see any downsides to exercise in a pill?

**DR. LAURIE GOODYEAR:**

Well I think there are lots of potential downsides to exercise in a pill. There are so many benefits, health benefits of exercise that I think everyone in the diabetes community or the exercise scientists would tell you that it will be virtually impossible to make a pill that will mimic all the effects of exercise. Now having said that, it is possible that you can make a pill that mimics the effects of exercise say on glucose uptake, that could have glucose-lowering effects and in fact as I was talking before about AMPK we know now that metformin or Glucophage actually works on AMPK. So it is not totally out of the question that a pill that mimics some of the effects of exercise can have some potentially good effects for people say, who have diabetes, but I just think it is impossible given this tremendous number of benefits of physical exercise on heart disease, stroke, high blood pressure, lipid profiles, breast cancer, colon cancer, depression it just seems impossible that you are going to take 1 pill and it is going to mimic all these effects of exercise.

**DR. LARRY KASKEL:**

But there are people and patients out there that have an aversion to exercise just like my children have an aversion to eating healthy foods. How do you take that patient and take the knowledge and translate it from their brain to their muscles and create action.

**DR. LAURIE GOODYEAR:**

There is couple of approaches, I am not certainly not a psychologist in terms of motivating people to exercise, but I think that the American public in general does not understand the importance of exercise. I do not think we have done a good job communicating the tremendous benefits of exercising. So many aspects of ones life in terms of health. So I think that is #1. The second thing is that I think most people almost everyone would enjoy exercise and would participate in exercise if they found some type of exercise that they liked to do. No one wants to go out and do a type of exercise that they don't like to do. So if people can find a type of exercise that they like, then they will stick with it and they will continue to exercise. I think the trick is finding an exercise that is appropriate, that fits in. There

are many types of exercise that are social, so you know walking with a group of friends or playing tennis, playing doubles tennis. So there is lots of ways to exercise that can be very enjoyable and once someone finds that type of exercise, I think the benefits are real and they are able to continue and stay motivated to maintain the exercise.

**DR. LARRY KASKEL:**

Dr. Goodyear I know that last month the US Department of Health and Human Services came out with some physical activity guidelines. Have you had a chance to look at them and do you think they are of high quality?

**DR. LAURIE GOODYEAR:**

I think they are very high quality, the people on the panel that developed this really absolute experts in the exercise science and physical activity field, they spent tremendous amount of time poring over all the literature and I think they have come out with excellent and reasonable guidelines. The bottom line is that for healthy adults, they should exercise 2-1/2 hours a week of moderate intensity more of course is better, but that is the minimum and that basically breaks down to 30 minutes of moderate intensity exercise 5 days a week and I think that for just about everyone there is a way that you can find to do that much exercise.

**DR. LARRY KASKEL:**

What do you feel is a worse molecule for endothelium in terms of contributing to or even initiating atherosclerosis, is insulin toxic, is it sugar that is toxic, what are your theories?

**DR. LAURIE GOODYEAR:**

I think it's really a combination. I don't think that there is one specific molecule one specific problem it's a culmination of events. Inflammation is now we know is important in some of these effects, so I believe it is a combination of many different factors.

**DR. LARRY KASKEL:**

All right on that note, Dr. Laurie Goodyear of Joslin Diabetes Center, thank you very much for coming on this show.

**DR. LAURIE GOODYEAR:**

Thank you very much.

**DR. LARRY KASKEL:**

I am Dr. Larry Kaskel and you have been listening to the Clinician's Roundtable on ReachMD XM160. If you would like to comment on any shows that we have done, please visit our website at [reachmd.com](http://reachmd.com), which features our entire library through on-demand podcasts or you can call us toll free at (888 MD-XM160) and thanks for listening.

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