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Targeting Viruses to Prevent Obesity

ADENOVIRUS 36 AND HOW IT MIGHT CONTRIBUTE TO OR CAUSE OBESITY

Certainly due to changes in the American lifestyle manifest by overeating and lack of exercise, but could it be also due at least in part to an infection, what is the support for this seemingly outlandish theory and what are the implications for our patients? Welcome to The Clinician's Round Table on ReachMD XM157, The channel for medical professionals. I am Dr. Lee Freedman, your host and with me is Dr. Richard Atkinson, Emeritus Professor of Medicine and Nutritional Sciences at the University of Wisconsin, Editor of the International Journal of Obesity, and the Director and Owner of Obetech Obesity Research Center in Richmond, Virginia.

Dr. FREEDMAN:

Thank you so much for being with us Dr. Atkinson.

Dr. ATKINSON:

Thank you for having me.

Dr. FREEDMAN:

Dr. Atkinson what is the data behind the idea that there are viruses that might cause obesity in humans?

Dr. ATKINSON:

Well, we have been working on this for about 10 years now. There are about 15-20 papers published. It turns out that a human adenovirus called adenovirus 36. There are over 50 human adenoviruses and this was the thirty-sixth one that was discovered. We have inoculated this virus up the nose of chickens, mice, rats, and monkeys and they get fat. The interesting thing is that 100% of the monkeys got fat. So if you got this virus, you get fat. We have done 2 human studies, we have looked at over 500 people in 3 US cities; New York City, Madison Wisconsin, and Naples Florida and we found that 30% of obese people with a BMI of above 30 had been infected and 11% of the non-obese, but anyway we slice it, infected people whether they are obese or non-obese, are heavier than their counterparts than the uninfected and we also look at twin pairs where one had been infected and one had not and the infected twins on average were heavier and fatter than their uninfected. We have also done studies in vitro showing that this virus attacks that fat cell directly and turns on the enzymes that make fat and it also turns on enzymes and differentiation factors that actually make new fat cells

from the fibroblast and adipose tissue.

Dr. FREEDMAN:

So that sounds fairly compelling to me. We have some data where you have actually inoculated animals and they have gotten fat, particularly 100% of all the monkeys, very close to human subject. You have got some observational data from twins as well as the 3-city study and then we actually have a mechanism that has been shown to be in effect causing this.

Dr. ATKINSON:

Right and we have even identified the viral gene that appears to be involved. We can block it and it blocks the effect. We can cut out the gene and stick it in another virus and it causes the effect.

Dr. FREEDMAN:

At this point, are we still talking about it just being a bench concept or are there some possible clinical manifestations?

Dr. ATKINSON:

Well, as I said, from the animal data, 100% of the monkeys got fat, so apparently if you get this virus, you will get fat. So there are a couple of different things that we might think about it, now I have to declare a little bit of conflict of interest because I actually am providing the lab test if someone wants to see if they have been infected. This is a very labor intensity and time-consuming tissue culture test to determine if a person has antibodies. If they have got antibodies, they have been infected.

Dr. FREEDMAN:

But not a simple blood test this is?

Dr. ATKINSON:

No, it is not simple at this point unfortunately. We are trying to make a better blood test. The acknowledges that are used are, for example, a cholesterol test or an HIV test. If the doctor says your cholesterol was elevated, you can say, okay, I will have a heart attack in 10 years by or you can watch your diet, do your exercise, take statin drugs and hopefully put if off, or if the doctor says you have got HIV, you can say, okay I will just die in 2 years or you can take the various AIDS drugs and Magic Johnson is going on 20 years.

Dr. FREEDMAN:

Yeah, yeah.

Dr. ATKINSON:

So, if not so much, if you are already obese, but if you are not obese and you take this test and it is positive, you know two things. One you are almost certainly going to get fat because that is what the data show, but secondly, you can block that. We have got some data that show that individuals who have been infected respond better to weight loss treatment, whether they are monkeys or humans. We have got a couple of different experiments. So it raises some hope that it might be actually easier to prevent those people from gaining weight if they watch their diet, watch their exercise and I like the idea of using obesity drugs; things like Phentermine, sibutramine, orlistat. Those drugs are not very effective, they don not cause a great weight loss if you are trying to treat an already fat person, but there have been a lot of papers that suggest they are pretty good at preventing weight gain and the whole prevention business is what you want, it is a lot easier to prevent the obesity and any, any kind of obesity than it is to treat it once it is already present.

Dr. FREEDMAN:

Were there some people in your studies who had adenovirus 36 and were not obese?

Dr. ATKINSON:

Well, we did. In the study of 500 people from the 3 cities, we found the 30% of obese people, but only 11% of non-obese. Now the question is, does everybody who gets infected get fat or are there people who genetically or otherwise do not get fat or the other possibility for the 11% is they just caught the infection recently and have not had time to get fat and we do not know. We do know that it takes quite a long time, this interestingly in the animals at least; food intake is not different in the infected and the uninfected, but gradually it appears and there is a little bit of evidence that Dr. _____ has found that it alters the metabolic rate and it also probably alters the p.o. mix, so that you are not using fat as well. At any rate, the increase in obesity is slow and actually at least the animals put on fat at the expense of muscle.

If you have just joined us, you are listening to ReachMD XM157, The Channel for Medical Professionals. I am Dr. Lee Freedman and am joined by Dr. Richard Atkinson, Emeritus Professor of Medicine and Nutritional Sciences at the University of Wisconsin and we are discussing adenovirus 36 and how it might contribute to or cause obesity and what we might be able to do about that.

Dr. FREEDMAN:

Dr. Atkinson, did you say those individuals who have been infected do seem to respond a little bit better to interventions?

Dr. ATKINSON:

Yeah. We have got a couple of studies, we actually have not published them yet, but it looks like that individuals who have been infected are sort of hypersensitive to stimuli to lose weight, so they respond a little bit better to obesity drugs and at least monkeys respond a little bit better to diet or actually the humans respond, males at least respond dramatically better in terms of what we are going to do in the future which I think is really important. We are looking and other people are looking to try to find antivirals. There has been one paper published by Dr. _____down at the Pennington Center in Baton Rogue showing that an antiviral that is used against AIDS, they are particularly toxic antiviral compound, but in vitro at least blocks the virus from affecting the fat cells to make them accumulate fat. So the proof of concept is there we are going to need to look at some other things obviously.

Dr. FREEDMAN:

That are tolerated….

Dr. ATKINSON:

That are tolerated. I mean in every case, prevention is better than treatment. So we have at this point a crude vaccine that I do not think I am going to try to do this in humans, but I am working on a better vaccine, and if we can vaccinate obviously children I suppose so that they do not get the virus in the first place, then that would be the best of all possible outcomes.

Dr. FREEDMAN:

In short of that, I could certainly see a program both testing for this like cholesterol and then those who are positive would get more intensive lifestyle interventions and possibly the medications you were talking about.

Dr. ATKINSON:

Yeah, I think it is important

DICTATION ENDS ABRUPTLY