the DISEASE THEY CALL FAT

SCIENTIST/RESEARCHER
BABAK MEHRARA, MD

Transcript of Scientist/Researcher Video Episode 5

SCIENTIST/RESEARCHER

BABAK MEHRARA, MD

The Relationship Between Lymphedema and Lipedema

I primarily do breast reconstruction and, as you know, breast reconstruction is the most common cause of lymphedema in the Western countries, so I see a lot of patients who have that. I became interested in it in about 2007, 2008 or so. And then during that time, I decided to learn more about it. I was really surprised that there's not a whole lot known about the pathology of lymphedema, so we spent some time reviewing that. And then, because we didn't really have a good idea with the pathologies, and still don't, we did some studies – basic science studies – to figure out what causes lymphedema in patients.

The thing that I couldn't put together was that the sequence of events doesn't fit. So, if you think that lymphatic injury is the cause of lymphedema, which of course starts the problem, then everyone who has lymph surgery would develop lymphedema, but they don't. If you think that lymphatic surgery is the cause of lymphedema, then everyone who develops lymphedema does so immediately after surgery, and they don't. So it usually takes about eight months or a year or so to develop, and those don't really fit with that model, so we tried to come up with a model that explains that.

> **So there's clearly a relationship between fat and the lymphatic system, and I think it's a two-way street. Bad lymphatics can cause fat to deposit, and fat can cause lymphatics to not work very well.**

And the thought that we have is that the lymphatic injury sort of initiates a cascade of events that, in some patients, causes fibrosis, which is scarring of tissues, and in those patients, they end up developing lymphedema. The reason why it takes time to develop is because the fibrosis that's necessary to cause dysfunction, or the lymphatic vessels

to not work anymore, takes time to happen. At some point you reach a threshold where the lymphatic vessels no longer function, and then that's when the lymphedema becomes noticeable.

Lymphedema and Fat

If you look at the pathology of lymphedema, it's actually fat deposition. So lymphedema becomes untreatable because people deposit fat in their arms. So initially, when people have lymphedema, it's really a fluid problem, and that's why it responds to massage and wrapping and things like that. However, over a prolonged period of time, lymphedema is a fat problem because it causes fat to accumulate. For that reason, for example, a very common thing that we do for reconstruction is patients' liposuction. That's a very common method of treatment for lymphedema.

So lymphedema and fat are very intimately related. I think, and we think that – actually it's well known that the lymphatics can regulate fat deposition. So Guillermo Oliver was at this meeting, and has shown that if you have the defects in your lymphatic system, sort of even very minor defects, those animals become obese when they're adults, so it causes fat cells to accumulate.

Of course we know from lymphedema that happens to women, it's sort of a more acute thing. So I think of lymphedema as regional obesity. I think that some women have propensity to put fat in their thighs or hips or whatever. Patients with lymphedema have propensity to put fat in their arm or leg or wherever they have lymphedema, so that's what I think of it.

We've shown in our studies that if you take an animal and give it a high fat diet, that those animals then develop lymphatic problems. They don't clear fluid as well; their immune cells don't traffic as well, so there's definitely a correlation.

I think it would be exquisitely difficult to get rid of the fat surrounding lymphatic vessels. And just normal, regular diet changes, or something other than extraordinary diet changes, probably won't help.

There was a paper a few years ago from the *New England Journal* showing that hyper-obese patients develop primary lymphedema, so lymphedema without another cause. There was another paper from the Scandinavians showing that obese patients have impaired clearance of interstitial fluid. So if you inject fluid into interstitial space, which is where the lymphatics work, they don't clear it as well as lean patients. So there's clearly a relationship between fat and the lymphatic system, and I think it's a two way street.

Bad lymphatics can cause fat to deposit, and fat can cause lymphatics to not work very well. We've shown that very, very shortly after lymphatic injury, if you have accumulation of this fluid, it causes fat cells to grow, and also causes them to deposit more oil in their cells, so they proliferate and they get bigger. There's been recent studies to show that it's certain components of the interstitial fluid that does that, and those things have not been clearly identified yet, but it's a certain subset of proteins within that fluid that does it. So when you're not clearing that fluid out of your system, that's backing up and it's causing the fat cells to proliferate.

When we do surgery, even on the thinnest person you can find, you will always find fat around their lymphatic vessels, around lymph nodes. Fat and lymphatic vessels are intimately associated, so they sort of need each other. We don't know exactly why, and I think maybe it's trophic factors or something the lymphatic vessels are making for the fat to survive baseline. So I think it would be exquisitely difficult to get rid of that fat. And just normal, regular diet changes, or something other than extraordinary diet changes, probably won't help.

It's an interesting topic. It's an evolving area, and I think, the good thing – the good news is that there's a lot more people interested in it. The bad news is that I think we haven't made a whole lot of progress in the last couple years, but hopefully we will.

About Babak Mehrara, MD

Dr. Mehrara is a physician, scientist and plastic surgeon and Director of the Babak Mehrara Lab at Memorial Sloan Kettering Cancer Center in New York City. His research focuses on the regulation of lymphatic regeneration after surgery and development of lymphedema and relationship and regulation of adipogenesis by lymphatic fluid.

AMA citation

Mehrara, B. J. *The Relationship Between Lymphedema and Lipedema.* [video interview] http://DiseaseTheyCallFAT.tv/shop/lipedema/obesity/fat-cells/babak-mehrara The Lipedema Project; 2015.