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### ReachMD

www.reachmd.com  
info@reachmd.com  
(866) 423-7849

### Aspects of Wellness in Rheumatology: The Power of the Mind-Body Connection

#### Announcer Opening Wrap:

This is ReachMD. Welcome to this medical industry feature titled: "Wellness in Rheumatology: The Power of the Mind-Body Connection" sponsored by Lilly.

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#### Dr. Johnson:

This is Dr. Shira Johnson for ReachMD, and we are at the Annual Rheumatology Meeting in Chicago. The word "wellness" in medicine should probably go together with other words or terms like "healthy lifestyle," "quality of life," and so on. But, what does wellness mean, and why should it matter to rheumatologists? Most importantly, what is the documented scientific effective evidence on immunology?

Joining me today is Dr. Andy Laster. Dr. Laster is Co-President of Arthritis and Osteoporosis Consultants of the Carolinas in Charlotte, North Carolina, as well as a member of the Board of Advisors for United Rheumatology.

Dr. Laster, thank you and welcome. I appreciate you being with us today.

#### Dr. Laster:

Great, thank you.

#### Dr. Johnson:

We hear a lot about wellness, but the effects that you describe on the immune system are very specific. What is wellness?

#### Dr. Laster:

It's really hard to come up with a good definition of wellness. There are, I think, some key elements here. One is that it's a conscious choice that people make and requires an ongoing effort to maintain. It really relates to a healthy lifestyle, and importantly, people don't have to be in excellent or perfect health to achieve wellness. I think it incorporates not just physical but also emotional and well-being, and so when we look at wellness and how to achieve wellness, there are 5 basic elements that we think are modifiable that could be a benefit: diet, sleep, mindfulness, social connections and exercise.

#### Dr. Johnson:

So, we know that rheumatologic disease affects the entire body, not just the joints and the muscles. Why should wellness matter to the practicing rheumatologists?

#### Dr. Laster:

Rheumatologists are very data-driven, and we know from measures of disease activity that giving a patient the appropriate drug often can lead to measurable improvement. We see a decrease in swollen joints and markers of inflammation improve, but patients may not feel as well as we think they are doing. When we look at measures of disease activity, there's 1 common element throughout that, and that's the patient assessment, called the Patient Global Assessment. Our goal is treat-to-target, and for treat-to-target we want to achieve disease control.

#### Dr. Johnson:

Same thing surgeons often say, if you have 2 patients to operate with the same diagnosis and one of them believes the surgery is curative and the other one believes he's going to die, he'd rather operate on the one who thinks it's curative, not just because it will be

but because of the mind-body connection.

Dr. Laster:

Right.

Dr. Johnson:

So, what else can you tell us about some of the immunomarkers and rheumatoid disease?

Dr. Laster:

I think I'm kind of a skeptic. And the more I read, the more I believed, and so there's real science behind it, and it really relates to a variety of inflammatory cytokines.

There are studies out there that I think are really fascinating, and if rheumatologists heard about them, they'd want to know more about what's going on. So, one is, if you look at veterans who have been in Iran or Afghanistan who have had PTSD and you follow them out over time—and this was a large study done at the VA—the likelihood of autoimmune disease goes up 2-fold in people who have had PTSD, and that applies to both men and women.

Forest bathing is something that most people have not heard about, but it's very popular in Japan and basically, it's the idea that you go into the woods for a relaxing and recreational experience. They show that forest bathing actually led to an increase in number and activity of natural killer cells, and natural killer cells have an effect on inflammation, and it turns out to be related to the phytoncides, which are the aromatic oils in pine trees. But also, relaxation of being there led to lower levels of urine norepinephrine, which also can lead to increased natural killer cell activity. It's really intriguing.

The other study is a very early one that led to this whole field of psychoneuroimmunology, and that was they took rats and they conditioned them to associate something that was noxious, cyclophosphamide, which can suppress the immune system, with a saccharine solution, and they just did that 1 time, and then a number of rats they continued to give saccharine, and the rats who continued to get saccharine actually had suppression of antibodies to sheep red cells. They had injected sheep red cells later on. And so, the rats not having had any more Cytoxan were conditioned to believe they were getting it, so behavior actually altered the immune system.

Those studies were really intriguing and made me want to look more in terms of what's going on here.

Dr. Johnson:

Can you elaborate a little more on the bidirectional activity between the nervous system and the immune system?

Dr. Laster:

Yes. I think there are 2 things that are intriguing here: the bidirectionality that you pointed out, and then also, sympathetic and parasympathetic nervous system. This bidirectionality applies to the brain and the immune system and the endocrine system, and they are all kind of interacting with each other, and it's called psychoneuroimmunology. Imagine somebody who is stressed that turns out that that triggers the sympathetic nervous system, your fight or flight. If you follow beyond the postsynaptic ganglion, there are active receptors in lymphoid tissue, in the spleen, lymph nodes and other lymphoid organs, and so noradrenaline, norepinephrine diffuse through, and there are receptors on immune cells, on T-cells, B-cells, natural killer cells, and they actually activate them. So here we have a direct contact between the brain, the nervous system and the immune system. What that then does is leads to release of inflammatory cytokines which then feed back to the brain either through neural or non-neural pathways, and that can affect the brain and can affect the brain chemistry. You can see declines in serotonin and dopamine and increased glutamate, and the end result is that can lead to more stress and depression. So, while that whole circle is going on, the endocrine system, this hypothalamic pituitary axis is also involved, and stress can activate that and cause decreased cortisol. So, cortisol, we know, is anti-inflammatory and can be a benefit, but in people who are really stressed, you get this level where you have resistance to the glucocorticoid receptor, and that kind of spins out of control. And inflammatory cytokines at every level, at the hypothalamus and pituitary and the adrenal gland also can lead to inflammatory cytokines. So all of these 3 systems are linked and they are bidirectional.

So, the autonomic nervous system, which we had mentioned earlier, is also interesting and increasingly is really clinically relevant. People may have heard about monitoring for heart rate variability, and it turns out that that is a measure of balance between the sympathetic and the parasympathetic nervous system so that if you have increased parasympathetic tone, you have higher heart rate variability, and it turns out that that is often a good marker for chronic disease.

So, the parasympathetic nervous system is anti-inflammatory, and we'll talk later about meditation, but that actually can increase parasympathetic tone and has anti-inflammatory effect.

Dr. Johnson:

So that leads me to my next question how do you approach wellness with your patients, and what are your target goals for them with that?

Dr. Laster:

So, exercise, to begin with, clearly can have beneficial effects. We know that exercise can affect skeletal muscle, can affect adipose tissue, can affect the vascular endothelium, and has a direct effect on immune cells. Many of the effects of exercise are anti-inflammatory. IL-6 through its Cys binding actually has an anti-inflammatory effect. Exercise will decrease adhesion molecules, which lowers the likelihood of inflammation and can shift macrophages from their M1 to their M2 phenotype, which is also anti-inflammatory. So, there's clear data looking at the immune system that exercise can be a benefit. And, in fact, there have been studies done, small studies, that actually show people who exercise regularly who have changes in the brain, again in the brain volume, that if you exercise regularly, it actually can have an impact on centers in the brain that have an effect on mood and disposition. So, the runner's high or why people feel well may actually be related to physical changes that are going on in the brain related to exercise and the cytokines that are involved.

Dr. Johnson:

So, how do you address this with your patients? Because with rheumatoid disease, sometimes they do become more sedentary and they may be coming to you from a place where they are already not exercising or doing so much, so how do you begin to incorporate the scientific evidence into actual changes in their lifestyle?

Dr. Laster:

Right, great question. I think that clearly, individuals who have significant disease, whether it's rheumatoid or some other type of inflammatory arthritis, may be limited in terms of their activity, and whereas another individual you might recommend, "We want you to do 30 minutes of exercise 5 days a week in moderate exertion," that may be difficult to achieve for people who have inflammatory arthritis, so you just get them to begin, any type of exercise just to start with. It can be broken up during the day. And then incrementally they will see that positive effect, and then that encourages them to do more. Somebody might not be able to get on a treadmill, but they could do water therapy, so it has to be tailored to the individual.

Dr. Johnson:

What about the other areas, the meditation and the diet and the holistic approach?

Dr. Laster:

Yes, so diet I think is now becoming more well-accepted, and there have been studies, actually, in which people who had a Mediterranean-like diet, that inversely correlated with levels of IL-6, which is an inflammatory protein, and also with measures of oxidative stress. There's not one anti-inflammatory food, but it's the Mediterranean diet approach that could clearly have benefit. Sleep also turns out to be important. Many of us don't get enough sleep, and an absence of sleep can have inflammatory effects. And sleep can have a positive effect in terms of increasing blood flow through the brain, allows one to clear toxic metabolites. There's increased ATP that leads to enhanced neurogenesis and neural survival. Interestingly, in rheumatoid arthritis there are sleep studies where if you interrupt sleep compared it to controls and otherwise their sleep patterns were not different, you find that the patients with rheumatoid arthritis who had interruptions of sleep had much higher levels of pain. So, this is really intriguing because, as rheumatologists, we thought, "Well, they're not sleeping well because their joints are hurting."

And it turns out that there may be another component where, because they're not sleeping well, that actually is causing more pain, and that drives the Patient Global, and we have people come in and we think they're doing well but they're not because their Patient Global is so high. So, clearly there we can see the effect that sleep has, and sleep being a beneficial anti-inflammatory.

Mindfulness meditation.

It clearly can cause an increase in parasympathetic tone, and that has a beneficial anti-inflammatory effect. And there have been studies that have been done—actually, one out of Chapel Hill—in which they looked at meditation, and it was tied to social connectedness. Being in contact with people, talking with them, touching them, actually has beneficial effects and can lower interferon alpha and other inflammatory proteins. But in this study they actually showed that this type of meditation, loving kindness meditation, people felt better because they were meditating, and they felt a heightened sense of social connection, which also made them feel better, and that led to increased vagal tone and, through the parasympathetic nervous system, that had a beneficial anti-inflammatory effect. So, all of this turns out to be connected, and you can probably achieve higher levels of wellness if you're working on diet and exercise and sleep and mindfulness and social connections.

And so there are some really neat things out there where it's fairly easy for people to get involved. There are apps for meditation that are easy to use.

Dr. Johnson:

What's the response of your patients? Can you tell us any positive outcomes or people like you who were a skeptic but you kind of changed them with numbers?

Dr. Laster:

I mean, when you begin to talk to patients about it, you can see the light bulb go off. There's this, "finally somebody who listens to me." I think for rheumatologists, it's not just either/or. It's the idea that you can combine traditional medications with these elements that we've talked about. I had a woman who I followed with Behcet's, an inflammatory disorder, and she had severe vasculitis and retinal disease, and then she had osteoarthritis of her hip and she needed to have that replaced, and after she really was not handling it well. She had more pain than we thought. She had tragically lost a son about 10 years earlier. And so, we talked about the role of stress and its effect, and just acknowledging that and making her realize it is clearly a real problem gave her great relief. And so, we've seen that just acknowledging that—and people live busy lifestyles, and they're not sleeping well, they're not eating well—you empower patients. So, it's not just simply taking a pill that the doctor wanted you to take. You become actively involved in your own health care.

Dr. Johnson:

I'd like to thank Dr. Laster for being with us today and for educating us—and we'll pass that on to our patients—on the importance of wellness on the mind-body connection and what it means to them. And it's really a gentle reminder of what it should mean to all of us in our lives.

Announcer Closing Wrap:

The preceding program was sponsored by Lilly. If you have missed any part of this discussion, visit [ReachMD.com/whywellness](https://ReachMD.com/whywellness).

Thank you for listening. This is ReachMD. Be Part of the Knowledge.

PP-BA-US-0634