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Insights Into the Future of Rheumatology

Announcer:
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This episode of *Living Rheum*, titled "Insights Into the Future of Rheumatology" is sponsored by Novartis US Clinical Development and Medical Affairs. The host and speaker have been compensated for their time. This program is intended for health care professionals.

Here's your host, Dr Jason Liebowitz.

Dr. Liebowitz:
Cutting-edge innovations, such as artificial intelligence, machine learning, and wearable technology are evolving care and shaping the future of rheumatology. But what do we need to know about these innovations? This is ReachMD, and I'm Dr. Jason Liebowitz. Joining me to discuss technological innovations in rheumatology is Dr. Michael Putman, an Assistant Professor of Medicine in the Division of Rheumatology at the Medical College of Wisconsin. Dr. Putman is also the Associate Fellowship Program Director and Medical Director of the Vasculitis Program. Dr. Putman, thanks for being here today.

Dr. Putman:
Hey, Jason, thanks so much for having me.

Dr. Liebowitz:
To start us off, Dr. Putman, what are some of the new technologies that you are most excited about in rheumatology for monitoring how patients are doing at home, and helping them engage and connect with their doctors?

Dr. Putman:
That's a great question, and I think there's a lot of interest in this, especially as we've all been spending a lot more time at home and trying to avoid health care settings. You know, this is sort of a basic answer, but something that I'm excited about is patient-reported outcome measures. It's a big passion of mine. I think as rheumatologists, we love to prolong people's life, but I think often, we're really focusing on improving the quality of their life. I think the best way to get to that is just to ask people whether their quality of their life has gone up. And so, I actually really think patient-reported outcome measures from home could be something that would be very valuable. I think there is also a risk of over-monitoring, which we always have to be wary of. Sometimes you get so much information that you don't know what to do with, that it can be actually lead you astray.

Dr. Liebowitz:
That's a great point. We have a wealth of data from wearable technology, and I'm sure more will increase in the future, and we sort of have to separate the noise from the sound. And what are some of the new technologies that you are most excited about, with respect to helping diagnose rheumatologic diseases in patients, and assess disease activity?

Dr. Putman:
That's a great question as well, but, you know, let me start by being a bit of a wet blanket on this one. There's a number of problems with all these new tech for kind of an old profession. You know, the first one – and we've kind of alluded to this – is just that you get so much alerts, and it's unclear how significant that is, and, you know, I think we all are already inundated in our in-baskets with so many things to follow up on, and it could just be one more thing of uncertain clinical value.

And then the other thing that I think is really important is that a lot of these lack validation. You know, there's a lot of interest in tech for sleep monitoring, and counting all of your steps, but none of these things have been validated in rheumatology. And so you really risk

the possibility of chasing things that don't matter very much at the end of the day. But with that caveat, there's a couple of novel twists on some old tech that I am excited about. And one is vascular ultrasound and GCA. I think it's a really interesting modality for facilitating early diagnosis.

Recently there was a publication by Cristina Ponte's group about using it to track disease activity, so I think that there's a lot of potential for that.[1] It's non-invasive, it's available. A lot of us are already using ultrasound for the joints. Very neat publication in *Lancet Rheum* recently, actually showed that the performance characteristics are better than we had expected.[2] So, I think there's a lot of potential there. It's something that I'm doing, and I have a lot of thoughts, but that could be for a different podcast.

And the other one is PET. I think FDG PET is a very interesting modality for rheumatology. You know, there's limitations on affordability and accessibility, that kind of make it hard to get a hold of, but I think that there's a lot of value, in sort of seeing where the inflammation is, that I could imagine that becoming a bigger part of our practice over time.

Dr. Liebowitz:
And I believe that in your practice, you even use PET to help track disease activity in patients with sarcoidosis. Can you speak a little bit more about that?

Dr. Putman:
I certainly have. PET in sarcoidosis is really fascinating. I think some of the most impressive PET scans I've seen have been in sarcoidosis, especially with bony involvement. It's quite astonishing how aggressive that disease can be. I think in patients with sarcoidosis, you always worry about cardiac involvement, and we use a lot of cardiac PET to try to see if there's any involvement of the heart. So that's another great example of – you know, there's some amorphous diseases.

It's hard to know where it is, and it's hard to know when it's active, and there's an enormous amount of value to tagging a little bit of glucose, sending it in there, and finding out what cells are picking it up. And, again, it's hard, cause there's limitations to its use, but if we can get past some of those barriers, I think that we would find a lot of interesting clinical utilities for it.

Dr. Liebowitz:
And can you speak a little bit about handheld ultrasound its current use, limitations right now, and if you foresee it someday being a very valuable tool with enough precision and accuracy to really help us track the things that we need to, in terms of diseases that we treat?

Dr. Putman:
Interesting question. So, you know, a couple thoughts on that. You know, the first one is that, yes, I think it would be great if we all had an ultrasound in our pocket. But, there's a couple problems, and the first one is actually one that I encountered recently. We recently acquired a new ultrasound, which was me begging my office manager for many months to convince the hospital to buy one. And I looked into getting one of these handhelds, and the frequency wasn't sufficient to do what I needed. For temporal artery ultrasound, for instance, you need a 22-megahertz probe with a high quality machine, and the handheld ones were 15-megahertz or so, so not really sufficient to the task.

Then the second thing is what do we do with all of this information? You know, a lot of our clinical trials relied on good, old-fashioned physical exam, and if we start incorporating these ultrasounds into it, we're going to start treating a lot of patients who previously may not have been treated at all, and whether or not that's in their best interest is kind of an open question, in my mind.

Dr. Liebowitz:
Great.

If you're just joining us, I'm Dr. Jason Liebowitz, and this is a special episode of *Living Rheum.* Joining me for this discussion about innovations in rheumatology is Dr. Michael Putman.

I really appreciate your thoughts, and moving on to some even more interesting topics, what are your thoughts on artificial intelligence and machine learning, regarding interpretation of radiology or pathology studies, or just in general clinical use for patients?

Dr. Putman:
So, let me be clear, I am a total sci-fi nerdand I am completely convinced that AI is the future, and moderately concerned that it's going to be completely dystopian. But I do think it's also been the future for many years now, and that future seems to keep not arriving. I wonder if one day, it'll go the way of flying cars, and just be one of these things that we always imagine would happen, but never really came. You know, for me really, the uphill battle in machine learning, and trying to use augmented, artificial intelligence in rheumatology, is that we don't really have a gold standard. To get a good machine learning algorithm, you need to teach it on something, and we don't – our

benchmark is what some rheumatologist really happens to think is the disease.

And so, for clinical rheumatology, I think there's some real limitations to implementation. You know, for pathology and radiology, I can certainly see value there, but I actually think a more interesting way to use it is sort of in the AI augmentation, where, you know, these AI algorithms help humans as more of an assistive device than take over the job entirely, and I could see that being a good role for it, to become more efficient and more accurate.

Dr. Liebowitz:
It's interesting you discussed that. One of my professors in training, Dr. Anthony Rosen, said that, in his mind, computer technology may be able to supplement human abilities, where humans lack. We are not great at working through tedious repetitive tasks, we get bored after a while. But there are areas where humans really exceed – at least right now – a computer or machine capability in terms of creativity, and sometimes, even using intuition to see through a complicated story. So, I appreciate your candor on the subject, and it will be interesting to see how things unfold.

So given all of this, what technologies are currently being used, and what may be used in the future, to identify which patients will respond to a particular treatment?

Dr. Putman:
Yeah, so when you say that it automatically makes me think about precision medicine, which is another, you know, great buzz word. It helps a lot of people get grants and such, even though it may never arrive. I'm guilty of this. You know, it really – this idea of trying to really precisely tailor therapies took off during the genetics revolution, when we sequenced the human genome, and we were confident that we'd unraveled the code, and we could treat everyone with exactly the medicine to fix exactly what was wrong with them. And then, you know, 20 years later you're in clinic and you see a patient. How often do you use genetic information at all, for any decision that you make, and I mean, my experience is almost never. I mean, it doesn't even affect my life. But I'm actually remarkably hopeful for Genomics 2.0. I think that, you know, where DNA failed, I have a lot of hope for RNA sequencing and proteomics. In most of the cells that cause trouble in your body, from a rheumatologic perspective, have the same DNA. It's all you. But they're doing very different things, and I think measuring what they're doing by capturing their RNA, or looking at which proteins they're making, is a much better bet for sort of unraveling the mysteries of rheumatic diseases. I think as we make more progress in that area, I think we'll actually make a lot more progress in, sort of, diagnosing diseases better and treating them better.

The other thing that I'm really excited about now, and I think most of the profession shares this, is somatic mutations. The VEXAS Syndrome, that was published last year, is very exciting.[3] For reminder – for those who don't remember it, it's actually not, it is abnormal DNA in this case that's driving it, but it's not a germline DNA. It's a somatic mutation, so it's like cancer, in the sense that later in life, you pick up this mutation, and that mutation causes the various manifestations of VEXAS via ubiquitination that's impaired and another word I can't say. I think that we're going to see more of those in the future though, and I think that's actually really interesting area for us to make some real progress in some of these diseases.

Dr. Liebowitz:
And since you're in the world of vasculitis, could you also speak a little bit about DADA2, deficiency of adenosine deaminase 2, which has been an interesting discovery – the genetic form of what seemed like a familial sort of polyarteritis nodosa – and how you think discovery of these types of diseases may change the landscape of how we recognize diseases in rheumatology?

Dr. Putman:
Yeah, I actually love DADA2. It's like a huge teaching point for me with fellows. I mean, every fellow has heard me talk about it. And the reason I love it so much is that it speaks to a very deep, deep – not – I don't know if it's problem, but it's a deep bias in rheumatology, which is that our diseases are described phenotypically. You have rheumatoid arthritis because you have polyarthritis, and maybe a lab and maybe an imaging finding. You know, we don't say that you have, you know, rheumatoid arthritis with X aberrant cytokine pathway, or X aberrant mutation – you know, you just have rheumatoid arthritis because it looks like rheumatoid arthritis. So, DADA2 is one of these really brilliant cases, where, you know, we had this phenotype of polyarteritis nodosa, with stroke, and we just called it polyarteritis with stroke. And we didn't have any unique treatments for that, and we didn't have any unique prognostic value to offer patients who had that. So then when DADA2 rolled around, we understood, this adenosine deaminase deficiency is causing this specific presentation, and then that led to us finding treatments that are actually remarkably effective at reducing the rate of stroke.[4,5]

And so, I think that there's a lot of hope in that story, where a lot of our diseases that feel amorphous and ill-defined, it's because they are amorphous and ill-defined. They're phenotypically described. And as we make progress in identifying mutations, or, you know, like I was saying, more cytokine pathways that drive these things, I think we'll start to make real progress, and DADA2, for me, is a remarkably encouraging story. I mean, so much has changed in 5 short years since that was first published. 7 short years, probably.

Dr. Liebowitz:
And looking to the future, what do you think will be the major differences in the practice of clinical rheumatology, 20 or 30 years down the line?

Dr. Putman:
Yeah, well the first thing is more drugs. I think the pace of discovery in rheumatology is really a – it's a thing to behold. There's new trials, new mechanisms coming down the pipeline all the time, and it's really exciting. And you can feel that excitement and passion in trainees. You can also feel the fear. I always tell them that I think we might be the last generation who can actually remember the names of all of them, because it's becoming unwieldy.

In addition to that, though, I think we're going to have more diseases, and I think talking about DADA2, and VEXAS is a great paradigm for where this is headed, where I feel like we have these sort of diseases like polymyositis, which does not exist – for the record, doesn't exist. And over time, we're going to say, you don't have polymyositis, you have SRP myositis. Or, you don't have dermatomyositis, you have TIF1 gamma myositis. And we can give you very specific prognostic information, and a different workup, and a different treatment, based on these sort of slices of old diseases. So, I think there will be more drugs, and more diseases, which is exciting but it's a problem, because I think there's going to be fewer rheumatologists.

On the Workforce Report from 2015, was moderately concerning. There's a huge drop-off in the expected FTEs that rheumatologists will be delivering over the coming decade or two.[6] And I think it's going to be trouble, but I think there's some silver linings to it. We are going to need to adapt, and I think we're going to need to refocus on the areas where rheumatologists can provide unique value. And for me, that's really in treating immune-related diseases. I think we have a lot of value there, and I think that that's going to become a greater part of our practice.

I also think it opens up good opportunities for collaboration. You know, we'll work more with other providers, and other provider types, to kind of deliver more efficient, and better care. But I think a lot will still be the same, and this is me being a crotchety old man. I think we're still going to be doing joint exams, and we're still going to be doing a lot of the things that we do now, treating people with DMARDs and following them over a long period of time, and building relationships. So, I also think that artificial intelligence will still be just around the corner, but I could be wrong.

Dr. Liebowitz:
Well, hopefully, this fascinating conversation, which I have found very stimulating, will inspire many others to enter the field of rheumatology, and will help make up for that shortage. I really want to thank our guest, Dr. Michael Putman for sharing his perspectives on the role of new technologies on the present and future of rheumatology. Thank you so much, Dr. Putman.

Dr. Putman:
It was great. Thanks so much for having me, Jason. It was a lot of fun.

Announcer:
This industry podcast was sponsored by Novartis US Clinical Development and Medical Affairs. If you missed any part of this discussion or to find others in this series, visit reachmd.com/living-rheum. This is ReachMD. Be part of the knowledge.

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