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## Uncontrolled Gout: Keys to Managing Its Systemic Consequences

### Announcer:

You're listening to *Living Rheum* on ReachMD, and this episode is sponsored by Amgen. Here's your host, Dr. Charles Turck.

### Dr. Turck:

Welcome to *Living Rheum* on ReachMD. I'm your host Dr. Charles Turck, and joining me to discuss how we can manage the systemic consequences of uncontrolled gout and patients' urate burdens is Dr. Jonathan Greer. Not only is Dr. Greer a rheumatology and internal medicine specialist at Arthritis and Rheumatology Associates of Palm Beach, but he's also an Assistant Clinical Professor of Medicine at both Nova Southeastern University and the University of Miami. Dr. Greer, thanks for being here today.

### Dr. Greer:

Thank you.

### Dr. Turck:

So if we start with some background, Dr. Greer, would you tell us about gout and how it can impact a patient's joints?

### Dr. Greer:

Well, gout is an extremely common form of arthritis. It is in fact the most common inflammatory arthritis in this country. If you add up the incidence of rheumatoid arthritis, lupus, and psoriatic arthritis altogether, it will not equal the incidence of gout, which actively affects about 9 million people in this country currently. About 90 million patients have high uric acid that can predispose to gout. So 10 times that many could potentially develop gout. And this is a real problem for our country as we'll talk about going forward.

### Dr. Turck:

And if we look beyond the joints, what other organs can uncontrolled gout affect?

### Dr. Greer:

There is a high association of gout with the metabolic syndrome. So these patients typically have obesity, high blood pressure, diabetes, and most importantly, kidney damage already. So the consequences are progression of those diseases. There is a direct correlation with uncontrolled gout and risk for cardiovascular events, such as heart attack and stroke. So it's not simply relegated to joints, which people think about, but the systemic manifestations are severe, and this is a public health issue for all of us who are treating patients with gout.

### Dr. Turck:

And so with that in mind, what role does uric acid play in those systemic consequences?

### Dr. Greer:

So uric acid has a lot of different roles that it plays. It is an inflammatory molecule in and of itself. It actually affects blood vessels, and it can affect the endothelial cell function in blood vessels to make blood flow reduced or block blood flow, if you will. That could again lead to heart attack or stroke. It can cause inflammation in other parts of the body. For example, uric acid can deposit in muscle, it can deposit in the eye, and it can deposit in the spine. It can even result in impingement or compression of spinal nerves causing sciatica,

which is kind of weird because we're just thinking about the joints, but this is much more of a widespread disease. They've actually isolated the crystals of uric acid that cause gout in coronary arteries, which itself is also directly inflammatory. So it's not just a joint disease, as I mentioned, but a systemic manifestation. And it turns out that by controlling gout by lowering urate levels, you can actually affect the systemic diseases in a positive way.

**Dr. Turck:**

For those just tuning in, you're listening to *Living Rheum* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Jonathan Greer about the systemic consequences of uncontrolled gout.

So, Dr. Greer, given the far-reaching effects of uncontrolled gout, how can we best be on the lookout for high levels of urate crystals?

**Dr. Greer:**

Well, that's a good question and an important question because uric acid levels are no longer part of the normal chemistry panel. And so if you suspect it in primary care, in orthopedics, and, of course, in rheumatology, you need to order a urate level separately so you can get that information. Now uric acid is soluble at 37 degrees centigrade up to 6.8 milligrams per deciliter. So if you see a uric acid level that's above that range, say 7, 7.58, or above, those patients are at risk for developing deposition of urate crystals, not just in joints but in other parts of the body as I mentioned. It's important to note that laboratory studies or laboratory results that you look at may show a normal range of urate based on a bell curve based on our population, and that could be up to 8, but we know now that above 6.8 milligram per deciliter at 37 degrees centigrade is high. So a high level like that should be considered as a risk factor and patients need to be followed more closely.

Now the majority of patients with high uric acid don't have gout, but they could indeed develop gout over time. They can also develop urate stones, which affect the kidney directly, but there are also other effects where the kidney function declines, leading to high levels of uric acid. And that's because the kidney is the primary organ involved in excreting uric acid. 90 percent of patients who have high urate levels are under excretors, and by definition, those patients have renal insufficiency of some type or another. So by treating that, you can actually preserve renal function. It's a very complicated and widespread phenomenon that people are not aware of in terms of managing hyperuricemia, and therefore, checking the levels is the first step and seeing if patients have disease.

**Dr. Turck:**

And once we do detect high levels of uric acid, when and how should we intervene?

**Dr. Greer:**

That's a good question, and it's a controversial question. The American College of Rheumatology has guidelines, who suggested that after one attack of gout, patients should be considered for treatment. If they have two attacks, they definitely should be considered for treatment with urate-lowering therapy. The same can be said for patients with hyperuricemia and renal insufficiency already or renal stones where you treat hyperuricemia. And hyperuricemia may be playing this role as well in the development of more cardiovascular features. So I tend to use urate-lowering therapies very early on when a patient has their first attack of gout. And the reason for that is that it usually takes years for the urate burden to be high enough to cause gout attacks. And so if a patient has one attack, I know their burden is already high, and I'm going to treat aggressively with therapies to lower uric acid, which are pretty easy to use in most cases. Most patients can respond to the simple, very old medications used in managing uric elevation. Examples are allopurinol and, more recently, febuxostat, which are very effective in most patients to get those levels. And our goal is to get the level of urate below 6.0 milligrams per deciliter. That's if they don't have any obvious, visible tophi. If they do have visible tophi, then we aggressively try to treat it to get the level even lower below 5.0 milligrams per deciliter because there is some evidence that says these urate stones or urate deposits and tophi will reabsorb the lower you get their uric acid level. There are certainly other products that we use in lowering urate, including uricosuric drugs. Probenecid is one, but they're not as effective, and the guidelines actually call for using the xanthin oxidase inhibitors—allopurinol or febuxostat—first to get them under control.

**Dr. Turck:**

And Dr. Greer, what kind of impact can awareness of the risks of uncontrolled gout and proactive management of systemic consequences have on patients?

**Dr. Greer:**

This is probably the crux of the matter. Hyperuricemia is so common; as I mentioned, about 90 million people in this country have hyperuricemia. Most of it is due to our poor dietary choices, our issues with obesity, and the use of high fructose corn syrup, which can be directly metabolized into uric acid, and this needs to be made aware of as a public health issue. Hyperuricemia is so common, and

then leading to other organ damage is a consequence that we should be considering in all of our patients. So we want to be proactive in managing these patients using urate-lowering therapies, but also working with their other organ systems—treating their cholesterol, managing their blood pressure, lowering weight, and, of course, managing diabetes all has a direct role. Now the good news is that by lowering uric acid, you can actually preserve kidney function and reduce the risk for heart disease.

So this is where not just rheumatologists like myself, but primary care doctors should be involved and, of course, nephrologists when it comes to renal insufficiency and cardiologists need to be aware of all this as well. I will add that we've used colchicine for acute attacks of gout, and colchicine is now being used to work with coronary artery disease, and it does have benefits in these patients to reduce their risk of coronary disease, especially in patients with hyperuricemia. So the point is to be become aware of this issue and to manage it. If patients have high disease states, look for comorbidities, including metabolic syndrome, and treat accordingly. Certainly, you can send your patients to rheumatologists to manage hyperuricemia and gout, but I believe the majority of primary care physicians should be able to manage this under their own office shingle.

**Dr. Turck:**

Well, given the impact it can have on our patients, I want to thank my guest, Dr. Jonathan Greer, for joining me to discuss how we can be more aware of and better manage the systemic consequences of uncontrolled gout and a patient's urate burden. Dr. Greer, it was great having you on the program.

**Dr. Greer:**

Thank you so much.

**Announcer:**

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