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Deciphering the Link: Proteinuria and CKD Progression in Lupus Nephritis

### Announcer:

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

### Dr. Turck:

Welcome to *Living Rheum* on ReachMD. I'm Dr. Charles Turk, and joining me to help unravel the interplay of proteinuria, inflammation, and fibrosis in lupus nephritis is Dr. Gates Colbert. Not only is Dr. Colbert an Assistant Clinical Professor at Texas A&M College of Medicine, but he's also a practicing nephrologist and hypertension specialist with the Kidney and Hypertension Associates of Dallas, located at Baylor University Medical Center. Dr. Colbert, welcome to the program.

### Dr. Colbert:

Hello, Dr. Turck. Great to be with you today.

### Dr. Turck:

So to get us started, Dr. Colbert, would you define lupus nephritis for us and, in the setting of it, the relationship between proteinuria, inflammation, fibrosis, and chronic kidney disease progression?

### Dr. Colbert:

Sure. So lupus nephritis is an autoimmune disease where a person's own antibodies get activated to attack our end organs, and it can attack the kidney, specifically, but it can also attack other organs around our body, such as our lungs, heart, skin, and joints or it can attack multiple organs at the same time, including a systemic process and a process in the kidneys. Today, we're going to talk about how this affects the kidney specifically, and lupus nephritis is a situation where autoantibodies are deposited into the glomeruli of our kidney filtration. And we can see that this is a problem with a change in our GFR, our creatinine, and our urine sediment, which includes proteinuria, and that might tell us that there's a problem going on and that we would need to consider a kidney biopsy. And once you've done a kidney biopsy, you can then classify the stage of the inflammation, fibrosis, and really destruction of the kidney that's happening through the different classifications that we have from our pathologist. And so we know that we can see on labs, both blood and urine, that there's a problem with the kidney because of a potential lupus infiltration, and the definitive diagnosis is going to come from a kidney biopsy. And unfortunately, we want to try to catch this disease as early as we can because we know that the longer and longer that these antibodies deposit and cause inflammation and fibrosis, the more damage that can occur that maybe could not be turned around.

### Dr. Turck:

I'd love to get some additional details about how inflammation and fibrosis can affect various organs and especially the kidneys.

### Dr. Colbert:

When we have inflammation that's usually caused by antibodies and auto-antibody deposition, this creates a cascade of an inflammatory reaction inside the body, increasing cytokines and really causing systemic problems that we can't even fully diagnose yet. But we know that this inflammatory state can be tracked and is a harbinger of what's to come with death of cell tissue, which eventually leads to fibrosis. And fibrosis is a chronic scar in organs that unfortunately cannot be undone at this time with our healthcare medications and procedures that we have. And it's really important in kidneys because the kidneys unfortunately suck up all the antibodies and an inflammatory reaction occurs inside our glomeruli, which are the filters of the kidneys, and fibrosis sets in—what is called interstitial fibrosis and tubular atrophy, or IF/TA. And this is something that can be quantified on a biopsy and unfortunately cannot be turned around. So we've got to limit the inflammation at the beginning to avoid long-term fibrosis and eventually cell death and

loss of kidney function that could potentially lead to needing a kidney transplant or going on permanent dialysis.

**Dr. Turck:**

Now if we zero in on proteinuria, what's its role in chronic kidney disease and how does lupus nephritis act as a sort of catalyst here?

**Dr. Colbert:**

So I like to describe to patients that protein in the urine should always be zero. We are born with zero protein in our urine, and we're supposed to die in our 80s with zero protein in our urine. So when we see protein starting to occur in our urine, we know that there's a problem, and the protein in the urine is similar to a fire in a house. It's something that we can see. We see that fire burning, and we know there's a problem. But also, the protein in the urine is causing destruction itself. Just like a fire in a home is burning down the structure and the house eventually could be turned to soot and dust, the same thing is happening in the kidney. The protein in the urine coats the nephron tubules and leads to increasing inflammation and eventually fibrosis. So we know when we see protein in the urine, we've got to figure out what's causing it and figure out how to stop it because we know that this is going to be an ongoing and worsening problem if we don't address it correctly.

**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. Gates Colbert about the intricate relationship between proteinuria and chronic kidney disease progression in lupus nephritis.

So Dr. Colbert, now that we know proteinuria plays such an important role, would you share the latest guideline updates from KDIGO on proteinuria and lupus nephritis?

**Dr. Colbert:**

Absolutely. So we're really in an exciting time because KDIGO has become much more current and active in updating their practice guidelines. And we have a new guideline from KDIGO that looks at lupus nephritis specifically. So we have some great guidelines, and there's a lot of enthusiasm and research and discussion going on about how do we track the patients with lupus nephritis and potentially how do we treat them? So we want to make sure that anyone that is seeing a patient with kidney disease or a patient that may be complaining of symptoms that could be lupus, we always want to check for a diagnosis of lupus with our serologies. And then we wanted to make sure we look at our kidney function with our creatinine or our cystatin C and measure our GFR. And then at the same time, we want to look at the protein or albumin in the urine to see if there's what we call active sediment in the urine.

And currently, it's recommended that if you're seeing more than 500 milligrams per gram of urine proteinuria, we need to look at this closer and we need to consider doing a kidney biopsy because it's possible that lupus has started to invade the kidneys. And so it's great to see that we are potentially becoming more conservative in terms of having lower proteinuria be a threshold to do a biopsy for a patient who may have lupus in their kidneys. And I think this is important because we're going to try to catch these patients earlier in their disease state, and we're not waiting until they get to 1,000 milligrams per gram or 1,500 milligrams per gram, which is something that we may have waited for in the past. But now our guidelines are recommending that we do a more thorough workup and we have a lower threshold to act.

**Dr. Turck:**

And what might happen if we don't identify and treat proteinuria early enough in our patients with lupus nephritis?

**Dr. Colbert:**

So as we discussed earlier, we know that proteinuria in the urine is a sign that destruction is occurring, but also the proteinuria causes destruction itself. And so the higher the proteinuria, the higher the destruction and the faster we're going to have GFR loss and fibrosis deposition in the kidneys. And once we have GFR loss because of fibrosis, that unfortunately cannot be undone. So we've got to prevent that fibrosis from occurring in the first place, and doing active surveillance for these patients with our blood work, with our urine tests, looking for proteinuria and active sediment, and then considering a kidney biopsy. This is going to be the best way currently to try and catch this proteinuria and fibrosis from becoming a long-term problem for our patients.

**Dr. Turck:**

With that potential impact on patients in mind, Dr. Colbert, I'd like to ask you one final question before we close. How can we ensure we're proactively monitoring, diagnosing, and treating proteinuria and lupus nephritis?

**Dr. Colbert:**

So I think that we have the responsibility to actively survey these patients as they come into our clinics, either a chronic kidney disease clinic, a GM clinic, a primary care clinic, or our rheumatology colleague clinics. We need to assess patients' complaints, but then look at their signs, their blood work, their urine tests, and any sort of biopsy information that may have been taken from either other organs or a

kidney biopsy. And we need to discuss with our patients and educate them: this is what your disease state looks like, and we have some guideline recommendations for current medications that we can use to control this disease and prevent inflammation and fibrosis from setting into your kidneys. And we really have some great tools that have been approved in the last couple years to really help this specific disease problem of lupus nephritis.

**Dr. Turck:**

Well, given the devastating effects that a delayed diagnosis and treatment course can have, I want to thank my guest, Dr. Gates Colbert, for joining me to discuss the critical importance of identifying and treating proteinuria and lupus nephritis. Dr. Colbert, it was great having you on the program.

**Dr. Colbert:**

Yes. Thank you Dr. Turck.

**Announcer:**

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