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## Managing Primary Immunodeficiency: Why Steady-State IgG Levels Matter

### Announcer:

You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by CSL Behring. Here's your host, Dr. Brian McDonough.

### Dr. McDonough:

This is *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and joining me to explore the management of primary immunodeficiency, or PI, and the clinical benefits of maintaining steady-state immunoglobulin G levels, or IgG for short, is Dr. Niraj Patel. Not only is he an Associate Professor of Pediatrics at Duke University, but he's also a pediatric allergy and immunology specialist at Duke's Children's Health Center, Allergy and Immunology Clinic in Durham, North Carolina.

Dr. Patel, welcome to the program.

### Dr. Patel:

Thanks, Brian. It's good to be here.

### Dr. McDonough:

To get us started, Dr. Patel, can you talk about maintaining steady-state IgG levels and why consistency is so important?

### Dr. Patel:

So maintaining IgG levels is important because immunoglobulin, or IgG, helps protect your body from infections. The IgG level that is maintained in your body needs to be at a full level in order to prevent illnesses and infection. When that IgG level is not steady or it tends to fluctuate, then the protection level also tends to drop off. And if that happens, then a person may be at increased risk for susceptibility to infections.

### Dr. McDonough:

With that in mind, you talk about the fluctuations. What factors could influence IgG levels, and what are the potential consequences of those fluctuations?

### Dr. Patel:

So there's lots of things that can influence your IgG levels. It starts with whether you are able to produce enough immunoglobulin and also whether you're losing it. Losing it may not necessarily mean that you have an immune problem. People who have chronic diarrhea called protein-losing enteropathy or folks with nephrotic syndrome can actually pee and poop out immunoglobulin, causing their IgG levels to go below the normal range.

With problems with production, that can be things like a primary immunodeficiency disease, things that somebody is born with, or after your birth, you can have things that are done to you to drop your levels of immunoglobulins, such as medications like biologics. Other things would be chemotherapy or a bone marrow transplant.

Even when you are not producing enough immunoglobulin or let's say you are being replaced with immunoglobulin, you can still have problems trying to keep that level of immunoglobulin. So particularly in patients that have primary immunodeficiency disease or those who have chronic infection, like chronic intestinal diarrhea, not only do they have problems producing immunoglobulin, but they also have problems holding on to that immunoglobulin, and that can play a big role in trying to maintain steady-state levels. Comorbid medical conditions associated with immunodeficiency, like bronchiectasis, can cause problems in maintaining higher levels or even normal

levels of immunoglobulin because they tend to speed up the metabolism of IgG, causing drops in immunoglobulin levels.

**Dr. McDonough:**

So those levels are obviously very important. How then can we monitor these levels to really ensure optimal patient outcomes?

**Dr. Patel:**

Yeah. So there's a couple of ways to monitor IgG levels both from a laboratory standpoint, but also from a clinical standpoint. It's very intuitive that you could measure IgG levels by blood work and that can give you a good idea on where the patient is at in terms of their IgG steady-state level. If the IgG level is low, obviously then, they would be at increased risk for infections.

Another way to clinically monitor a patient would be to see how they're doing. Say somebody who has low immunoglobulin levels is put on immunoglobulin replacement; then you could get an idea of how their levels are doing just simply by seeing how they're clinically doing. Are they well? Or are they having continued frequent infections?

**Dr. McDonough:**

For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Niraj Patel about the clinical benefits of maintaining steady-state IgG levels in PI care

Let's turn our attention now to subcutaneous immunoglobulin, or SCIG therapy, and achieving and sustaining consistent IgG levels compared to intravenous immunoglobulin, or IVIG administration. Dr. Patel, what are the advantages here?

**Dr. Patel:**

So there's obviously differences in subcutaneous IG, or SCIG, and IVIG. When subcutaneous immunoglobulin is used, it generally involves more frequent dosing, which also is in smaller doses compared to IVIG. For example, with subcutaneous IG, the most common is once-a-week dosing of immunoglobulin, so maybe 25 percent of a monthly dose, versus IVIG, which is once-a-month dosing. That can have impacts on steady-state levels. If you're dosing with IVIG once a month, then you can have very large high-peaks initially after the infusion of IgG followed by a natural decay over a period of 28-days, and you could even go below what's considered your healthy IgG level, or biological level, or a low serum trough. Where that is avoided is with subcutaneous IgG, where you're getting small and more frequent dosing to maintain a steady-state level. And steady-state level immunoglobulin obviously has advantages in terms of being less likely to have breakthrough infections or frequent infections.

**Dr. McDonough:**

I know as a family doctor that trying to get patients to be compliant and to work with things is always a struggle. This is really complex. So how can we work with our patients to ensure optimal treatment adherence and outcomes?

**Dr. Patel:**

I think bottom line is first of all, communication. If the provider and the patient are communicating in terms of how the experience is going, that I think is probably one of the biggest parts that affect patient compliance, when patients feel like the medication is too overwhelming or they're having certain issues with administering the medication or with side effects of the medication. Oftentimes, these are not relayed on to the provider, and many types of providers are not seeking those types of problems with medications. So I know in my clinical practice when I have somebody who's on immunoglobulin replacement, the first thing I want to know is how are the infusions going, whether they are going well or whether they're not. And if they're not going well, how can we troubleshoot to help that patient? I think also just helping patients understand what the experience is supposed to be like. One of the most common side effects of subcutaneous immunoglobulin might be a local swelling or redness at the site of the injection, and to a patient, they may mistake that for an allergic reaction and they may want to stop the medication. So I think educating patients and telling them what to expect, such that these infusions are not allergic reactions, they're actually normal parts of the process.

And I think to go back to subcutaneous IG and in terms of differences of subcutaneous IG and IVIG, giving the patient an idea of what to expect. With subcutaneous IG, generally those smaller, more frequent doses usually potentially results in a better quality of life because of fewer systemic side effects. So we know that with subcutaneous IG, the rate of systemic side effects are much lower than with IVIG, and that can improve compliance, and it can also improve adherence to the regimen and just create a more effective and meaningful experience and adherence for the patient.

**Dr. McDonough:**

So that communication obviously is really important to bring the patient into the decision-making process and the care. Before we end today, Dr. Patel, would you share any final thoughts about the importance of the consistency of PI care?

**Dr. Patel:**

Yeah. I think consistency, obviously, is important with any chronic disease. The fact that patients are identified and then placed on

therapy—in this case, immunoglobulin therapy—I think maintaining that consistency with patients and patient adherence. With subcutaneous IG, I think the advantages are you don't need IV access; that's a huge advantage for folks who have lack of venous access. I think the quality of life is very important, too. And again, with any chronic diseases, I think you're more likely to be adherent to a medication and to a process if your quality of life is good. With subcutaneous IG, typically you could administer at home, which is huge. You don't have to wait for an infusion center to be open Monday through Friday if you want to infuse on a weekend. I think also for patients who have to travel to an IVIG center, that can be very daunting. It may be very far. You know, a couple of hours there, a couple hours back. And so, you know, you start to add up all of those items, and I think it results in a better chance for an improved quality of life, which again, goes back to patient adherence, patient outcomes, and making that treatment work for the patient.

**Dr. McDonough:**

They're great key points to think about. And as we close today's program, I want to thank my guest, Dr. Niraj Patel, for joining me to discuss the importance of maintaining steady-state IgG levels in the management of primary immunodeficiency. Dr. Patel, it was really great having you on the program.

**Dr. Patel:**

Thank you, Brian.

**Announcer:**

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