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A Practical Guide to Chronic Spontaneous Urticaria

Announcer:

You're listening to *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. Now, here's your host, Ryan Quigley.

Ryan Quigley:

This is *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. I'm Ryan Quigley, and joining me to talk about the pathophysiology, diagnosis, and treatment of chronic spontaneous urticaria, or CSU for short, is Dr. Jonathan Bernstein. Not only is he a board-certified allergist and immunologist, but he's also a Professor of Medicine at the University of Cincinnati.

Dr. Bernstein, welcome to the program.

Dr. Bernstein:

Thank you.

Ryan:

So let's dive right in, Dr. Bernstein. Where does CSU fit within the broader chronic urticaria landscape, and what makes it distinct?

Dr. Bernstein:

Chronic urticaria is a term that could include people who have inducible hives, which is triggered by physical or mechanical factors or temperature. It could be by scratching. People get dermatographism. And we call that inducible hives, chronic inducible urticaria.

But people with CSU typically have hives that are going on longer than six weeks, and they're not caused by any obvious known trigger like a food or an allergen. They occur spontaneously. The lesions last less than 24 hours. They travel in different parts of the body. They're very itchy.

25 percent of patients with chronic spontaneous urticaria have an inducible component. About 40 percent of patients with chronic spontaneous urticaria have swelling called angioedema, which is soft tissue swelling. So this is the nature of the condition that we're talking about.

Ryan:

And when we think about what's driving CSU symptoms, what role do mast cells and related inflammatory pathways play in the disease?

Dr. Bernstein:

Mast cells are a primary cell in chronic spontaneous urticaria. When they're activated through different pathways, they can release mediators like histamine and other bioactive mediators. They can also release certain cytokines that can perpetuate inflammation. We know that mast cells directly interact with sensory neuronal cells; they have direct interactions with mast cells.

Mast cells play a central role, and there are other effector cells or neuronal cells in close proximity that interact that make this a very complex disease to treat in some cases.

Ryan:

Now, if we look at this from a clinical standpoint, how do you evaluate a patient with suspected CSU?

Dr. Bernstein:

Well, you take a very good history when you evaluate a patient. You have to get a history: when it started, what's the frequency, what percentage of the body is covered with lesions, and if there's associated soft tissue swelling. Do they have an inducible component?

What kinds of treatments have they tried? Over the counter? Prescription? And then you think about quality of life and what impact it's had on their work activity, personal leisure activities, and overall wellbeing. So all of these factors are necessary.

Externally, we try to get a good history of their other concomitant medical problems, but we don't spend a lot of time talking about inciting agents, because, as I've mentioned, chronic hives is not commonly associated with a specific food or a specific medication. Those typically are associated with acute urticaria, where they occur suddenly and, when you avoid the stimulus, that goes away. In these patients, it persists. And that's a big problem, which resolves in a lot of frustration, because they end up avoiding every food, and they can't figure out how to stop the hives because it's not related to that. So this is how we initially collect information about urticaria.

Ryan:
For those just tuning in, you're listening to *On the Frontlines of Chronic Spontaneous Urticaria* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. Jonathan Bernstein about how we understand, diagnose, and treat CSU.

So once you diagnose a patient with CSU, Dr. Bernstein, what's your approach to treatment based on current guideline recommendations?

Dr. Bernstein:
Well, again, we try to understand. Do they have just chronic spontaneous urticaria? Do they have chronic spontaneous urticaria with angioedema? Do they have an inducible component?

But generally speaking, all patients with hives are started on second-generation H1 antihistamines. And these are typically non- to low-sedating medications. And many times, they've already been on one a day. The recommendations are, to up dose, up to four times the recommended dose. So if someone's on one pill a day, we'll go up to two pills twice a day.

And there are H2—histamine type two—receptor blockers, but those have low evidence for being very effective, and they're not highly recommended. There are other agents, such as leukotriene-modifying agents like montelukast that block leukotriene receptors. And again, the evidence is also low and conditional, but there have been some reports that it may be marginally effective in some patients, so those might be used as well.

But once you get to that point and patients are still having hives, then you have to start thinking about next steps, which would be biologics or small molecules. We do have, now, a number of these agents available. We have omalizumab and we have dupilumab. These are both biologics that have been approved for the treatment of urticaria. And we also have remibrutinib, which is a BTK inhibitor that's now approved for the treatment of chronic spontaneous urticaria.

Of course, before we had these other two agents—or even remibrutinib—we would use drugs like cyclosporine, which is an immunosuppressant that works to reduce lymphocytes, C cells, that might be relevant in the pathogenesis of hives. And it does work, obviously, in some patients, but it has some side effects and toxicity associated with it. So that's why we're happy that there's some other alternatives.

But in addition, while I'm evaluating these patients, I will get some additional blood tests to look at certain markers. I might get something called a total IgE. I might get a thyroid peroxidase antibody to see if they make autoantibodies. I'll get complete blood count with differential. A c-reactive protein. These are tests that will help us to know what we can expect in terms of response, not only to antihistamines, but response to some of these other agents.

But that's how we would initially start the evaluation. And we follow an algorithm, going from the antihistamines to the next step, which would be either omalizumab, dupilumab, or remibrutinib. The latter two—remibrutinib and dupilumab—are listed as conditional, only because we don't have as much data on these drugs as we do with omalizumab, which has been out since 2014.

Ryan:
Now, CSU can place a substantial burden on patients. So can you tell us how it impacts their quality of life and how patient-reported outcome measures can help us better assess and manage that burden?

Dr. Bernstein:
So we use patient-reported outcome measures to assess patients. We use something called the urticaria control test. We use something called the Urticaria Activity Score 7, which is recorded over seven days. And we use quality of life questionnaires that are disease specific. So we have chronic urticaria quality-of-life scores.

So all of these should be done at baseline before treatment, and then one can follow them to see how they're responding. But ideally, what we would expect to see is significant improvement in all of these validated questionnaire responses. Patients who have chronic hives are miserable. It interferes with their sleep; it interferes with work; it interferes with leisure activities and daily activities. They're not

comfortable. They're always itching. They've got unseemly welts all over their body. People look at them like there's something wrong with them.

So it is significantly impactful on their life. I agree that patient-reported outcome measures are really essential in quantifying as well as qualifying how these hives are affecting their lives.

Ryan:

Well, we've certainly covered a lot today, Dr. Bernstein, but before we close, let's look to the future. How do you see biomarkers and emerging therapies shaping the future of CSU care?

Dr. Bernstein:

I think we have a significant number of patients who don't respond to H1 antihistamines who have persistent, difficult-to-treat chronic spontaneous urticaria, as well as chronic inducible urticaria. So I think some of these newer agents that have been approved for use for the treatment of these conditions will make a significant impact on patients' wellbeing.

It'll help reduce hives—hopefully completely prevent hives—and improve their quality of life significantly. So I look at there being a big impact in the future. It's important, though, that given the cost of these drugs, that we use these drugs appropriately and to always try to step down over time to see if patients are in remission. Because normally, patients with chronic hives can go under remission spontaneously over a three-to-five-year period of time. So we should always, once patients are well controlled, try to step down and see, are they controlled or do they still need to be continued on treatment?

Ryan:

That's a great way to round out our discussion on this topic. And I want to thank my guest, Dr. Jonathan Bernstein, for joining me to discuss our approach to diagnosing and managing chronic spontaneous urticaria. Dr. Bernstein, it was great speaking with you today.

Bernstein:

Thank you.

Announcer:

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