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Advancing Care for Refractory Chronic Cough: Diagnostics and Emerging Therapies

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This series is produced in partnership with the American College of Chest Physicians, and this episode is a non-promotional, non-CME educational program brought to you by CHEST in collaboration with GSK. And now, here's your host, Dr. Michael Ghobrial.

Dr. Ghobrial:
Welcome to *Deep Breaths: Updates from Chest* on ReachMD. I'm Dr. Michael Ghobrial, Director of the Chronic Cough Clinic at Cleveland Clinic in Ohio. Joining me today to discuss how we can better manage patients with refractory chronic cough, or RCC for short, are Drs. Anju Peters and Michael Blaiss.

Dr. Peters is part of the Division of Allergy and Immunology at Northwestern Medicine in Chicago, where she is a Professor of Medicine and Associate Chief of Clinical Research and Practice and Operation.

Dr. Peters, thanks so much for being with us.

Dr. Peters:
Thank you very much, Michael.

Dr. Ghobrial:
Also joining us is Dr. Blaiss, who is a Clinical Professor of Pediatrics at the Medical College of Georgia and an allergist at Good Samaritan Health Center of Gwinnett in Georgia.

Dr. Blaiss, it's great to have you with us today.

Dr. Blaiss:
Thanks, Michael. I'm happy to be here.

Dr. Ghobrial:
Thank you. Well, let's dive right in. Starting with you, Dr. Peters, how do we currently define RCC, and how has the language evolved over time?

Dr. Peters:
Sure, Michael. So RCC, or refractory chronic cough, is a subset of chronic cough. Chronic cough is defined as lasting greater than eight weeks, and RCC is the subset where this cough persists despite guideline-directed therapy, treatment of underlying causes, and a thorough investigation and adequate treatment of known cough-related etiologies.

So we know cough hypersensitivity syndrome underlies RCC, and this is where innocuous stimuli—little things like eating, talking, or change in temperature—may provoke the urge to cough. This cough tends to be in the throat area, and we think RCC is characterized by peripheral and central neuronal dysregulation. For example, in RCC, a study has shown that the density of airway peripheral sensory nerves is increased.

And many of us use the terms "unexplained refractory chronic idiopathic cough," and each has a subtle implication for etiology and care. And this use of different terminology very much presents challenges—patients don't recognize RCC as a disease, and there's even some healthcare providers who may not. And this can lead to problems of communicating across different specialties. I think we need to

be more standardized and call it RCC if we mean RCC.

For example, if you call it unexplained chronic cough, that assumes that every test has been done and every medicine has been tried, and that's not always the case. And then, if you call it idiopathic, the patients may think that maybe there is no underlying pathophysiology to this. So I really think we need to get standardized and use the correct terminology. And for now, I think it's RCC.

Dr. Ghobrial:
Great. Now, Dr. Blaiss, what underlying etiologies do you typically explore when patients present with chronic cough?

Dr. Blaiss:
So I think it's very important that when we see these patients who come to our clinic with chronic cough, we do an extensive evaluation—so a very detailed history getting an idea of possible triggers, family history related to allergies, smoking, and what medications they have used for this. Are they on something like an ACE inhibitor, which could be, in fact, triggering their cough?

Also, if we follow the CHEST guidelines, as far as the work-up and management of chronic cough, it talks about looking for red flags. These are conditions where the patient may have some severe underlying condition that is causing their chronic cough—things like hemoptysis or recurrent pneumonia. A patient who has systemic symptoms of, say, weight loss and fever—there may be, in fact, an underlying malignancy.

Now, if all of this particular work-up is negative, and we talked about looking at the most common underlying triggers for chronic cough in the population, doing extensive work-up, and, in many cases, empiric treatment for those conditions—things like upper airway cough syndrome, which would encompass all the chronic sinus problems, rhinitis problems, both allergic and nonallergic. A big factor can be asthma. So, again, doing the particular test there is extremely important. Not as common, but needs to be looked at, is non-asthmatic eosinophilic bronchitis.

And then lastly, but very importantly, is looking for a relationship with gastroesophageal reflux disease. And in fact, is there anything like that going on that may be leading to the patient's problems? And again, if we come up with, nothing as far as one of those other things causing the problem, then as we talked about, this is a diagnosis of exclusion and we can label that patient with refractory chronic cough.

Dr. Ghobrial:
For those just joining us, this is *Deep Breath: Updates from CHEST* on ReachMD. I'm Dr. Michael Ghobrial. I'm speaking with Drs. Anju Peters and Michael Blaiss about the management of refractory chronic cough.

So, Dr. Blaiss, let's zero in on treatment strategies for these patients. What options are currently available and how effective are they in practice?

Dr. Blaiss:
So we have out there many different guidelines that have been published worldwide as far as the management of patients with chronic cough. I think the one that most of us follow in the US comes from the American College of Chest Physicians.

So one thing that we start with is behavioral cough suppression therapy and referring patients who do have refractory chronic cough to speech pathologists who have a working relationship with patients with chronic cough and understand their problems. And behavioral cough suppression therapy is made up of four major components: patient education; laryngeal hygiene, which is extremely important for these patients; hydration, which is extremely important to help control the cough; they teach them different exercises and maneuvers to help with cough control; and psycho education training. So there are studies out there, including randomized control studies, that do show the benefit of behavioral cough suppression therapy for patients with refractory chronic cough.

Now, as far as medical management, at this time, as far as patients with this condition, we do not have any FDA-approved treatments. So everything that we use now is off-label. Probably the most common one that we usually start with are the different neuromodulators. There is some data in the literature that suggests that this can be helpful for some patients with refractory chronic cough, though we do have to worry about tolerability problems. Many patients may have trouble with some of these medications.

Next would be the possibility of low-dose opioids. Again, we have to worry about things like tolerance and, especially with long-term use, the possibility of dependency. And then there is some data in the literature also associated with local anesthetics that in fact have been shown to help some patients, though again, tolerability may be a problem also associated with this.

So, unfortunately, at this time we do not have any approved products, but these are the things that we can do at this time to help our patients that are suffering with refractory chronic cough.

Dr. Ghobrial:

The lack of FDA-approved medications really present a challenge to manage these patients.

Dr. Blaiss:
Absolutely.

Dr. Ghobrial:
Thank you. And if we look ahead, Dr. Peters, can you walk us through some of the emerging mechanisms of action currently in development for a refractory chronic cough?

Dr. Peters:
Sure, Michael. As you mentioned, there is no FDA approved treatment in US. However, there are new treatments in development, which is very exciting. One that is being studied is the P2X3 antagonists that inhibit the P2X3 receptor on the vagal afferent nerves.

Other emerging therapies include drugs that modulate the TRP. There is one opioid agonist antagonist that acts both centrally and peripherally as a kappa agonist and mu antagonist that is being studied. So the good thing is that there are at least some new treatment options that are currently being developed, which hopefully will provide relief to our patients with RCC.

Dr. Ghobrial:
This is exciting. Thank you.

And now, as we approach the end of our program, Dr. Peters and Dr. Blaiss, are there key takeaways you would like to share with our audience about how we can better support patients living with refractory chronic cough? We'll start with Dr. Peters.

Dr. Peters:
Sure. So, Michael, as you know, refractory chronic cough remains a significant clinical challenge. We need better understanding of this disease. We need better treatment options. We know it negatively impacts quality of life and leads to significant physical, social, and psychological impairment.

Hopefully, as we get better understanding of RCC and there's better recognition of RCC as a disease by healthcare providers and the general public, patients with RCC will be diagnosed and treated appropriately, especially as we get newer treatment options.

Dr. Ghobrial:
Dr. Blaiss?

Dr. Blaiss:
I think it's extremely important that we understand that in fact, these patients are really suffering, as Anju mentioned. They have a very poor quality of life associated with this condition. And we have to do everything we can to get them to understand that they do have a particular illness, that we now understand more and more about the mechanisms of refractory chronic cough, and that there's a lot of research going on in the condition, as we've heard. And there are things that in fact, we can do to help to make their life better.

So we need to really understand that these patients are suffering and do our best to help them deal with this devastating condition that they have.

Dr. Ghobrial:
Right. There is hope for these patients and providers as well.

As those key insights bring us to the end of today's program, I want to thank my guests, Dr. Anju Peters and Michael Blaiss, for joining me to discuss our evolving management approach for patients with refractive chronic cough.

Dr. Peters, Dr. Blaiss, it was great having you both on the program.

Dr. Peters:
Thank you very much, Michael.

Dr. Blaiss:
Thank you, Michael. Enjoyed it.

Announcer:
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