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Diagnostic Challenges in Refractory Chronic Cough: From Burden to Solutions

Announcer:
You're listening to CME on ReachMD, and this is *Deep Breaths: Updates from CHEST.* This activity, titled "Diagnostic Challenges in Refractory Chronic Cough: From Burden to Solutions" is provided by The American College of Chest Physicians and is supported by an independent medical education grant from GSK.

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And now, here's your host, Dr. Sandy Khurana.

Dr. Khurana:
Welcome to CME on ReachMD. This is *Deep Breaths: Updates from CHEST*, and I'm Sandhya Khurana, Professor of Pulmonary and Critical Care Medicine at the University of Rochester and Director of the Mary Parkes Asthma Center. Today, I'm joined by Dr. Shahzad Mustafa and Dr. Ashley Wilk to talk about the diagnostic challenges in refractory chronic cough, or RCC for short. Dr. Mustafa is Division Head of Allergy, Immunology, & Rheumatology at Rochester Regional Health and Clinical Associate Professor of Medicine at the University of Rochester School of Medicine and Dentistry.

Dr. Mustafa, welcome to the program.

Dr. Mustafa:
Thanks so much for having me, and I look forward to the discussion.

Dr. Khurana:
Also joining us is Dr. Wilk, who is Associate Professor in the Department of Medicine and Primary Care and Section Chief of Family Medicine at Illinois College of Osteopathic Medicine at the Chicago School.

Dr. Wilk, thank you for being here.

Dr. Wilk:
Thank you.

Dr. Khurana:
That's great. We're looking forward to this program. So let's start with a patient you've probably seen, I think we've all probably seen, a 52-year-old woman, no significant past medical history, who presents for evaluation of a nonresolving cough. Her cough begins after what feels like a routine cold at first. It didn't seem like a big deal. She expects it to resolve on its own. She tries several over-the-counter remedies, but nothing provides lasting relief. A few weeks later when the cough hasn't gone away, she visits urgent care. She's reassured, often treated empirically, commonly with an antibiotic, sometimes a short course of oral steroids, but the cough persists. At the next visit, an inhaler is tried. When that doesn't work, reflux is considered, and she starts another medication. Months pass by. She follows up with another clinician, still without clear answers. And eventually, six months or so later, after that first cough started, she's referred to a specialist for further evaluation. This is really the diagnostic journey, the odyssey we're talking about: multiple visits,

multiple empiric treatments, a lot of time lost before a structured plan is in place. So, what we want to focus on in this episode is how to disrupt the cycle and move earlier to a consistent guideline-directed pathway that brings clarity both for clinicians and patients.

Just as background, in 2025, *CHEST* completed a needs assessment of 423 pulmonologists in the U.S. and found that most patients with chronic cough had already seen two or more clinicians before specialty referral. Also, U.S. administrative claims data study suggests that approximately 17% of adults with chronic cough meet criteria for potential RCC. These data really highlight the burden of this condition and the frequent delay in RCC diagnosis, and together, these findings underscore the importance of an earlier implementation of a guideline-directed diagnostic pathway to reduce delays and avoid redundancy.

CHEST has put forth cough evaluation guidelines. So with all this being said, let's review the *CHEST* guidelines for a diagnostic pathway for chronic cough in clinical practice. Chronic cough is cough that lasts more than eight weeks. A structured, sequential approach helps minimize trial and error. RCC is cough that persists despite guideline-directed evaluation and treatment of an identified cause. When a cough remains unexplained after a comprehensive guideline-directed evaluation, we call it unexplained chronic cough. So, when evaluating a cough that has been persistent, it's important to confirm the duration, that it's been ongoing for more than eight weeks. We characterize the cough in terms of its quality, triggers, review any exposures and medications, particularly ACE inhibitors that are classic unrecognized triggers for cough, and then assess for any red flags to guide the urgency and to initiate testing.

So the key red flags that we think of, that I think of when I'm evaluating a patient with chronic cough is associated fever or weight loss, dysphonia, hemoptysis; are they having significant associated dyspnea; any other features that would suggest serious cardiopulmonary condition; and then ensure that baseline testing is completed; for example, chest imaging or spirometry, PFTs as appropriate before moving to more targeted pathways.

So I'm going to turn now to you, Dr. Mustafa. What other important considerations are there when it comes to approaching refractory cough or cough that's been persistent?

Dr. Mustafa:
So yes, when we are evaluating chronic cough, I think it's important to consider the most common etiologies, cough-variant asthma, upper airway cough syndrome, reflux, and focusing on this differential diagnosis helps us pursue more directed therapy rather than multiple empiric therapies. One way to do this is to use objective measures when indicated to support or confirm key diagnoses, such as spirometry, which has been mentioned before, lung function testing, even bronchial hyperresponsiveness testing, before concluding the workup and labeling it RCC. I want to caution clinicians. Patients often ask if they can use cough suppressants, but in mucus-producing diseases like COPD, inappropriate cough suppression may actually impair mucus clearance and contribute to sputum retention and increase the risk of infection, so we don't want to focus on cough suppression rather than preferably to find a diagnosis and treat that more in a directed fashion. When treatable conditions have been appropriately evaluated and treated without meaningful improvement, *CHEST* guidance supports transitioning to RCC, cough hypersensitivity framing, and next-step management planning.

Dr. Wilk, I'd love to hear your thoughts on this as well.

Dr. Wilk:
Documentation of previous treatments, including specific details on duration, adherence, and patient response, helps prevent duplicate trials and supports efficient progression through a *CHEST* guideline-directed diagnostic sequence. Include baseline test results, medication exposure and history, as well as what has already been evaluated or ruled out so that specialists can pick up at the correct step rather than restarting the workup. Features such as cough triggered by phonation or talking, frequent throat clearing or voice change can signal upper airway or laryngeal contributors that warrant targeted evaluation. ENT assessment can clarify upper airway contributors and reduce recycling through empiric trials when laryngeal drivers are suspected.

Dr. Mustafa:
I'd like to add that persistent cough is associated with significant impairment of quality of life. It can be associated with embarrassment, social withdrawal, anxiety, fear of perceived contagion; people think you're sick; they're asking if you're sick; contributing to psychological distress, reduced quality of life—that's been mentioned—it affects work productivity in adults and school absenteeism in children. So I think it's important to be aware of the impact of quality of life that chronic cough can have and how important it is to address.

Dr. Khurana:
Thank you both. I mean, this is, you know, these are things that we think of on a daily basis, a really helpful discussion so far. For those just tuning in, you're listening to CME on ReachMD, and this is *Deep Breaths: Updates from CHEST.* I'm Dr. Sandhya Khurana, and I'm speaking with Drs. Shahzad Mustafa and Ashley Wilk about the diagnosis and management of refractory chronic cough.

So let's talk about why are we even addressing this? Why should this be a priority for clinicians and patients? Refractory cough really is a burden for the patients. You know, it disrupts sleep, drives fatigue, impairs work productivity, limits social functioning. And in cough hypersensitivity phenotypes, symptoms can be really triggered by even low-level exposures like exposure to certain odors or cold air, talking, eating, just things that we do on a daily basis.

Is there anything else you'd like to add in terms of the burden of cough?

Dr. Wilk:
I'd like to add that, in primary care, refractory chronic cough often leads to repeated office visits, empiric treatments and fragmented care, which results in increased patient frustration as well as increased healthcare utilization. Without early *CHEST* guidance-directed evaluation, delays can compound burden and prolong the diagnostic odyssey, as we were saying before.

Dr. Khurana:
Yeah, it seems like this is something that is impacting patient, but also clinicians at primary and specialist level. So let's shift gears and talk about referral. Pulmonologists like myself are often the first specialists that are seen after primary care for evaluation and management of refractory cough, and it's really important to perform a systematic guideline-based evaluation. I think these patients have been through a lot of empiric treatment, so it's important to document which treatable conditions have been identified and addressed and what additional testing, if any, is still needed before a diagnosis of refractory chronic cough becomes a working diagnosis.

Dr. Mustafa, at what point should a specialist referral be considered for coordinated, multidisciplinary care so evaluation and management can move forward? And what should clinicians know about behavioral cough suppression therapy and when to refer?

Dr. Mustafa:
A multidisciplinary approach is very important, and referral to ENT should be considered for laryngeal symptoms—throat-clearing, dysphonia, cough consistently triggered by talking or voice changes, or suspected inducible laryngeal obstruction—prompting ENT evaluation for upper airway laryngeal contributors as part of the *CHEST* guideline-directed pathway. When referring to ENT or any colleagues, a referral summary is certainly helpful to avoid repeated empiric trials and should include how long the cough has been going on, trigger profile, key laryngeal symptoms and prior history of therapeutics that have been tried, for how long, were they adhered to, were their side effects, and were they effective, plus any objective testing that has already been done. We've mentioned things like spirometry and lung function testing. Behavioral cough suppression therapy should be positioned as an active management step. This includes education, cough suppression techniques, vocal hygiene, psychoeducational counseling, and considered early when cough hypersensitivity features are present or symptoms persist after common cause trials.

Now, Dr. Wilk, what role does primary care play in this process, and how can we address an important consideration of disparities in management and referral?

Dr. Wilk:
So, in primary care, we coordinate across the different specialties by first setting expectations with the patients. We more or less will set out a stepwise plan and discuss each visit has a purpose and explain to the best of our abilities what each visit with each specialist's purpose is so the patients are less frustrated. We work to document what has been evaluated and treated along with the responses that were received with each trial of the treatments, and including the patient goals, such as improvement in sleep, their daily function and activities, social impact and quality of life, so that subsequent visits can stay patient-centered and efficient. Disparities are another big factor, as you mentioned. So these can be reduced by anticipating geography and insurance coverage barriers, including access to care, such as speech-language pathologists, and planning referrals early and proactively to address socioeconomic barriers, such as time off work for the patients, transportation, out-of-pocket costs, etc., as these can really delay the completion of the treatment pathway.

Dr. Mustafa:
And to build off of that, laryngeal symptoms and cough triggered by talking or voice use are common in RCC and may signal upper airway, airway laryngeal contributors. Timely ENT assessment, including laryngoscopy when indicated, can clarify laryngeal pathology, such as inducible laryngeal obstruction or laryngopharyngeal reflux disease, and reduce repeated empiric trials that do not address underlying driver of the chronic cough.

It's, I think, very important to consider geographic and coverage barriers that can delay appropriate referrals to our ENT colleagues or speech and language, language pathologist services. When laryngeal features are present, early coordination with speech and language pathologists and behavioral techniques and clear documentation of triggers and functional impact can improve access and reduce delays to care.

Dr. Khurana:

Thank you both. I think you bring up an important point about disparities, and I'd like to dig a little bit more into this. And I'm going to send this back to you, Dr. Wilk. What disparities more, most commonly delay a guideline-directed evaluation? What can clinicians do to reduce those delays?

Dr. Wilk:
That's an excellent question and something that we most certainly need to address with each and every patient we see. So first of all, geographic barriers can delay care. Patients in rural or underserved areas may face long travel distances, limited specialist availability and difficulty completing the sequential testing, so doing our best to consolidate evaluation locally and leveraging telehealth services when appropriate can help to maintain a *CHEST* guideline-directed pathway.

Next, insurance and coverage constraints interrupt care and continuity. Prior authorizations, unfortunately, delay and result in limited coverage for speech-language pathology services and behavioral cough suppression therapy. These can stall evaluation even when clinically indicated. Early authorization and documentation of the functional and quality of life impact may reduce our delays.

Socioeconomic disparities in respiratory symptoms have persisted for decades and in some cases widened. Repeated National Health Examination Surveys from 1960 to 2018 demonstrate that disparities in cough prevalence have increased over time across income and education strata. These data suggest that structural socioeconomic factors influence both symptom burden and access to timely specialty care, reinforces the need for proactive identification of barriers and deliberate referral coordination within a *CHEST* guideline-directed framework.

Dr. Khurana:
Thank you, Dr. Wilk. You know, it's given us a lot to think about, and clearly, there's a lot of work to be done ahead. And those final comments bring us to the end of today's program, and I want to thank my guests, Dr. Mustafa and Dr. Wilk, for joining me to discuss how we can optimize care for patients with refractory chronic cough. Thank you both for being here. We really appreciate it.

Dr. Mustafa:
Thank you so much for having me.

Dr. Wilk:
Thank you so much.

Dr. Khurana:
And I'm Dr. Sandhya Khurana, and I hope you'll join us for Episode 2, where we connect today's *CHEST* guideline-directed diagnostic pathway to the neurobiology of cough hypersensitivity, including the ATP P2X3 signaling and what's emerging in mechanism-informed therapies. In the meantime, please visit the Bridging Specialties landing page for the full curriculum, including the interactive diagnostic pathway infographics, adaptive AI case simulations, the patient journey video, and a 3D MOA animation. Thanks so much for listening.

Announcer:
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