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Escalating COPD Care: From Flares to Long-Term Control

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. Ravi Kalhan.

Dr. Kalhan:
Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Ravi Kalhan, the Louis A. Simpson Professor of Pulmonary Medicine and Director of the Asthma and COPD Program at Northwestern Medicine in Chicago. Today, here with me to discuss our evolving approach to treating exacerbations in COPD is Dr. Meilan Han. She's a Professor of Medicine and Chief of the Division of Pulmonary and Critical Care at the University of Michigan Health in Ann Arbor.

Dr. Han, thanks for being here. It's great to see you.

Dr. Han:
It's good to see you too, Ravi.

Dr. Kalhan:
Well, let's start, Meilan, with the big picture as far as COPD goes and how you're thinking about its impact on patients and how we help patients living with COPD. What are our therapeutic goals when we encounter a COPD patient these days?

Dr. Han:
Well, I think when patients come into our office, the number one thing that they're seeking—and that we would love to be able to deliver—is just helping them feel better. So, that is always the immediate discussion and probably the key focus from a patient's perspective.

But I think, as physicians, we also care about things like exacerbation prevention because we know that's actually tied to longer-term outcomes like lung function decline, higher mortality, and debility. And ultimately, I think the holy grail of therapy would be to alter disease trajectory. Lately, there's been increasing discussions about this concept of disease stability. And while we know that we all lose lung function with age—that's true, and we can't fully prevent that—the literature suggests there are periods where we can, even for our COPD patients, help them be stable in terms of symptoms, lung function decline, and exacerbations.

So, I think to the extent that we can achieve that over a short- to medium-term timeframe, that really should be the goal for us as clinicians.

Dr. Kalhan:
Yeah, I agree. I think that's really important. I've lately been hung up a little bit on this idea of setting the therapeutic expectation with patients—that I'm prescribing a medicine because I actually think it's going to help you feel better, or I actually think it's going to do something about the disease trajectory, or I actually believe that it's going to prevent future flare-ups of COPD. And I've found that it changes the tone of conversations with patients a bit because patients with COPD, I think, sometimes show up like, "I'm short of breath. You can give me an inhaler, but I'm not really sure it's going to do anything." And I don't think I'm in a new wave of optimism in my life; I actually think it's informed by the idea that these medicines do help people

Dr. Han:
Well, I think the challenging thing is that for many years, all we had were short-term symptom relievers, and so patients are also of the mindset that if they don't get immediate symptom relief, then the medication's not working.

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So I think you're right that, particularly with some of the newer medications we have that may or may not immediately improve symptoms but we know are good over the longer term because they prevent exacerbations, you really have to have some solid conversations with patients at the front end to help them to manage expectations. You don't want someone to stop taking something because they don't notice it right away.

Dr. Kalhan:
Well, let's hone in a little bit on exacerbations because they are drivers of a lot of why we end up, as pulmonologists, seeing a patient with COPD. Tell me how you think about exacerbations in terms of the burdens they place on patients in the healthcare system, and then what we can do about them.

Dr. Han:
Well, severity of exacerbations varies. But when we think about the spectrum of exacerbations, even the mild-to-moderate ones can have impacts on quality of life, and losing work. So, the impact is not to be underestimated.

Another thing I also sometimes think about with exacerbations is not just the event itself, but it's living in fear—like, "I just don't feel comfortable going to Europe with my family because what if something happens?" So, it's even that anticipatory anxiety of the event.

So I think the onus is really on us as clinicians to explain to patients why we think these events are important and help them understand the clinical context—what we can do to try to prevent them, and why they're on medications, but then also to actually have a management plan with patients so that they know, "Okay, well, if this happens, I can try this at home. If that fails, I should call in."

But Ravi, what have the conversations with your patients been looking like lately around this topic?

Dr. Kalhan:
Yeah, it's a little tricky because I'm very hung up on preventing exacerbations in COPD. We'll talk more about the guidelines in a minute, but we're told we should prevent exacerbations in people at risk for having them. Yet, for many of my patients, a single exacerbation, in their mind, is often not viewed as that burdensome. They take prednisone or antibiotics as an outpatient. Prednisone actually sometimes comes with some euphoria for them. They're not thinking about the long-term consequences of being on prednisone that you and I worry about.

And they don't, like you were saying, really assign the importance to that single exacerbation as a red flag for how we consider their COPD to be going because an exacerbation isn't just this acute event that happens and goes away; it's a sign of bad things to happen. In the year following an exacerbation, the person's risk of heart attacks is higher. Their risk of repeated COPD exacerbations is higher. It's likely that if they have repeated COPD exacerbations, their lung function will start to drift downward over time or suddenly fall off and never recover to what it was before.

Dr. Han:
Yeah, I completely agree with you. And I think we as clinicians—or maybe even just as pulmonologists as a field—have been accused of not being as aggressive and tolerating too many events, potentially, as being okay before we decide that a more targeted or aggressive intervention is needed.

And I know we're going to move into that question more specifically, but as you know, GOLD just recently made an update. And as opposed to the higher-risk category now being two or more events, it's now one or more, which means we have a new zero-tolerance policy.

Dr. Kalhan:
For those just joining us, this is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Ravi Kalhan, and I'm speaking with Meilan Han about new paradigms in managing COPD exacerbations.

So, Meilan, you just mentioned the Global Initiative for Chronic Obstructive Lung Disease, GOLD, which is our guiding document for how we think about how to treat people with COPD. And you just alluded to it—they have changed to say that exacerbation risk as we think about therapy is defined by having one exacerbation in the prior year that required treatment with either antibiotics or steroids. Can you expand upon that and what we're supposed to do with that information?

Dr. Han:
Well, I think we've been talking for forever about how important these events are. You just mentioned that they can be associated with increased risk for mortality and cardiovascular events, and yet somehow, we have this tolerance for, "Well, you have to have a couple before we'll actually escalate therapy."

And, as you know, I'm one of the deputy editors for one of our respiratory journals, and we've seen tons of papers in the last year come

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in just showing how one event—not just two, but even one—is associated with poor longer-term outcomes.

So if you look at the GOLD document, as you mentioned, one or more really puts you into that higher-risk category, with earlier consideration for addition of inhaled corticosteroids if you're already on, for instance, a dual bronchodilator. And then, as you know, we've also had some additional therapies approved for COPD in the last year, which are additional conversations.

So, I think it moves the whole potential escalation of treatment up, with the whole goal of ultimately hopefully slowing disease progression and preventing some of these bad outcomes we've been talking about.

Dr. Kalhan:

The other thing that's emerged, Meilan, that's really exciting for our field is this idea of finally being able to personalize therapy one way or another. Now, finally, we have a blood biomarker, which is being applied in a lot of contexts. So, can you give us the rundown on blood eosinophil levels and how we should think about measuring them in COPD patients and how we can apply them?

Dr. Han:
Yeah, it's funny. I remember when we first, as a field, started talking about the potential utility of eosinophils, even to guide ICS therapy, I thought, "There is no way this is actually going to be useful." Of course, I was wrong.

But GOLD now recognizes that eosinophils do a lot of things. They can help to signal which patients benefit from inhaled corticosteroids. And the threshold identified by GOLD is there are 100 cells per microliter or more. And then, now, we have two new biologic therapies that were approved for COPD, with strong evidence for benefit in terms of exacerbation reduction, for patients who have eosinophils of 300 or greater. And so that's the GOLD document has now been updated.

So, when I'm thinking about my patients who are still exacerbating despite triple-inhaled therapy, that is honestly one of the first things I'm immediately checking—"We've got these new tools in our toolbox. Is this a patient who I could get on one of these medications, who might benefit from one of these new targeted medications?"

And I will say, it's been super exciting for me as a clinician to have something new to offer, and super exciting just to see how effective these medications are in some patients. What's your clinical experience been so far, Ravi?

Dr. Kalhan:
It's really positive to give a therapy that I know targets a pathway that we think drives disease. I think bronchodilators are really important, and inhaled steroids are really important anti-inflammatory medicines, but they feel like sledgehammers without a precise target in some ways. And it's really nice to be 21st century about it, if you will, and say, "This, we know, is a phenotype that's at risk. The pathway's active in this person, and we're actually targeting it with a precise therapy."

And I think that that's reassuring to the clinician in some ways—that we know what we're doing, and we're not just kind of throwing something at the problem and hoping for the best in someone.

Do you, Meilan, every time you see a COPD patient, measure their eosinophils from the jump? Is it just something you have put in spirometry, objective assessment of symptoms, exacerbation assessment, and blood eosinophils?

Dr. Han:
Well, we don't have it as part of our clinic workflow yet. So, spirometry, yes, but if I'm seeing a patient for the first time, no. I think 60 percent of the time I can find a recent one somebody else has ordered. But if they don't have it, it's usually something, particularly for patients being referred for being persistently exacerbating and having persistent exacerbations, it's the next thing I'm definitely going to get. So if it's not there, it's one of the first things these days that I'm ordering.

And then the interesting thing is, there's actually some recent data on eosinophil variability. And it might be a little bit counterintuitive, but it's actually okay to have variable eosinophil levels. They don't always have to be high as long as they've had one or more high levels, say, in the last year or so. Based on the literature and my own experience, I still have confidence that those are patients who still could benefit. So even if I get a level and it's 200, and then the patient comes back and they're having exacerbations it's still potentially worth rechecking. Sometimes, patients are on oral steroids, and so that can falsely suppress the level.

Dr. Kalhan:
So, Meilan, the other thing that I've come across with my patients, in the context of this topic in specific, is when I talk to them about starting a biologic therapy for their COPD to prevent exacerbations. Some of my patients feel like that's a big deal to do. Do you have any tips about how to discuss this new wave of therapy with our patients and how to apply shared decision-making practices around them?

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Dr. Han:
I think there's a lot of discomfort on the patient side. Inhalers are all they've known, usually. But I think there's also some discomfort on the physician side if you've never prescribed these medications before, and if you've only, say, prescribed something like treatment for alpha-1 antitrypsin deficiency. So, I think what's important to know is that, other than eosinophils, there's no additional testing you really need to do, that patients can even do their first dose at home if they want to. You don't need lab monitoring afterwards.

And fortunately, at least in my office, they've been working through some of the approval processes, and those have actually not been too bad either. So, I think once patients get through that first injection, and once the physicians get through the first script, it gets a lot easier.

Dr. Kalhan:
I think that's true. As the pulmonary community thinks about this, we need to reshape how we're thinking about this in a lot of ways—a therapy that targets a specific pathway and reduces exacerbations actually is probably our long-desired path to disease modification. We should hold on to that and really champion it, rather than sort of come up with the learned helplessness of, "Well, it's pretty complicated." And I'm as guilty of that as anyone. But, really, this is the future of where we are with healthcare, and we should embrace it.

Dr. Han:
This all circles back to the discussion we were having about expectations too. So, it is not just our goal to help the patients feel immediately better in the short term, which they can expect from an inhaler, but to ultimately have better control over the longer term, with some hopes for disease modification and ultimately slowing those exacerbations, with the hope that we can slow disease progression and know at least some of the therapies we have probably also alter mortality as well. So, if I could wrap up our discussion today, it's really about raising the bar for us in terms of having lower thresholds to treat, and it's raising expectations for patients in terms of what's possible.

Dr. Kalhan:
Well, with those very well-stated final thoughts, that'll bring us to the end of today's program. I want to thank my guest and dear friend, Dr. Meilan Han, for joining me to discuss how we can better care for patients with COPD, focusing on exacerbation prevention. Meilan, it was great to have you on the program.

Dr. Han:
It was great to see you as always, Ravi.

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