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Closing the Gaps in Care: A Look at Diagnostic Challenges for Severe Asthma

Announcer Intro:
You're listening to ReachMD, and this is *Deep Breaths: Updates from CHEST*. This is a non-promotional, non-CME disease state educational podcast brought to you by American College of CHEST physicians in collaboration with and paid for by GSK. Your host today is Dr. Tom Corbridge - pulmonologist at Northwestern University and a senior medical lead at GSK.

Dr. Corbridge:
Severe asthma is often an uncontrolled disease that places a large physical, emotional, social and economic burden on patients. Depending on the criteria used, up to 74 to 84 percent of patients with severe asthma have an eosinophilic phenotype, which can be driven by allergic or non-allergic triggers.

Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I am your host, Dr. Tom Corbridge, and joining me today is international expert, Dr. Michael Wechsler, Professor of Medicine in the Division of Pulmonary Critical Care and Sleep Medicine at National Jewish Health in Denver, Colorado. Mike, welcome to the program.

Dr. Wechsler:
Thanks so much for having me. Great to be here.

Dr. Corbridge:
It's a pleasure. So, let's start out with some definitions pertinent to today's discussion. Tell us about severe asthma and controlled/uncontrolled asthma.

Dr. Wechsler:
Well, severe asthma is a type of asthma that doesn't respond well to standard asthma treatments, whether it's standard controllers, such as inhaled corticosteroids or long-acting bronchodilators. It's really patients who continue to have symptoms, continue to remain poorly controlled, or require those kinds of therapies in order to maintain control. Asthma control, in and of itself, is distinguished from severe asthma in that it is asthma that continues to cause symptoms, continues to cause the symptoms of asthma such as shortness of breath, cough, wheeze, chest tightness, all of which might be occurring in these patients and may be associated with rescue medication use, interference with daily activities, waking up from nights. So, any asthma that continues to be symptomatic despite use of standard care therapies, is considered to be poorly controlled.

Dr. Corbridge:
And so that group of patients with severe asthma requiring significant medication, such as high-dose ICS-LABAs or the use of OCS in the prior year to a significant degree, and then what you're describing as the frequency in that patient group of having active symptoms suggesting that poor control. So, in your busy clinic, how are you making these assessments?

Dr. Wechsler:
So I think it's really important to take a good history. You want to evaluate for the signs and symptoms of asthma in your patients. You want to see whether or not there's evidence of bronchial hyperactivity, airway hyperresponsiveness, at least by history. And then you want to evaluate the degree to which they have airflow obstruction, so using spirometry is one way. We also utilize in our clinic the Asthma Control Test to evaluate control. Simple five-question questionnaire which asks questions about frequency of rescue medication use, frequency of symptoms during the day, interference with daily activities, and things like that. And then, we also want to ask about exacerbation, so how frequently is the person having exacerbations? Is it once a year? Is it twice a year? How often are they requiring

oral corticosteroids for management of their asthma? So, that's the basic workup we do to evaluate whether or not someone is well-controlled or not well-controlled, and also to evaluate how severe they are.

Dr. Corbridge:
So you're seeing patients with severe asthma. They're on significant amounts of inhaled medication, and many of those are not in control, and for the assessment that you have just nicely outlined. I'm interested now in your thoughts regarding looking at these patients and phenotyping them, maybe some of the challenges that you face in trying to phenotype, and how we establish where a patient sits along that T2-high, T2-low spectrum.

Dr. Wechsler:
It's important to evaluate what type of asthma an individual has, and you could do that by phenotyping and/or endotyping, and I think it's important to define those two terms. So, the phenotype is the set of observable characteristics of an individual that result from the interaction of genotype with the environment, and the endotype is really the specific biologic mechanism that explains the observable properties of that individual. So, phenotypes can be categorized into triggers. Does the person have allergic or non-allergic asthma? Does the patient have aspirin-exacerbated asthma, infection-associated asthma? But you can also phenotype patients based on characteristics. Are they smoking? Are they obese? Are they old or young? Are they black or white? Those are all phenotypic characteristics. And then you can also evaluate phenotype based on the clinical presentation of asthma. Does the patient have exacerbation-prone asthma? Does the patient have childhood-onset asthma? Does the patient have a history of allergic asthma? Those characterizations of phenotype have not been too helpful in terms of identifying strategies for treatment, and so what we've evolved into, in the last several years, is now we endotype people. We want to figure out what type of asthma the individual has, in terms of the mechanism of disease. And the way we do that is through different biomarkers. We want to evaluate whether the patient is eosinophilic. Do they have high blood eosinophils or high sputum eosinophils? Do they have more of an allergic endotype, that's more IgE mediated and do they have a propensity for allergies to make their asthma worse? Or do they have more of an IL-13-mediated type of disease, that's characterized more by airway hyperresponsiveness or elevated nitric oxide? And so, when we think about the types of asthma, those are the kinds of things we're thinking about.

Dr. Corbridge:
So when you boil that down to seeing the patient in clinic, what would be the key biomarkers then, that you would assess in any given asthma evaluation?

Dr. Wechsler:
So, in addition to performing spirometry, I get allergy skin testing and a measurement of IgE. I do exhaled nitric oxide measurement in every visit. And I also measure eosinophil counts in the blood, and sometimes in the sputum as well if the blood eosinophils are on the lower side, and if I want to try to figure out what's going on in that person's asthma.

Dr. Corbridge:
For those just joining us, this is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Tom Corbridge and I'm speaking with Dr. Michael Wechsler about challenges of diagnosing and managing patients with severe asthma.

Well, Mike, as we mentioned, patients with severe asthma are often uncontrolled, placing them at risk for exacerbations and use of oral corticosteroids, either by way of bursts or by way of maintenance therapy. I'm interested in your thoughts about your approach to patients who are requiring OCS.

Dr. Wechsler:
Yeah, the patients who are on chronic oral corticosteroid therapy are certainly the most challenging. We know that chronic use of oral corticosteroids is associated with significant adverse effects including risks of cataracts, glaucoma, osteoporosis, increased risk of an infection, adrenal insufficiency, and growth suppression in children, amongst others. And so, I think it's incumbent upon all of us to try to avoid use of oral corticosteroids chronically, in all of our patients, and even short courses can be deleterious to our patients. So, my general approach is to identify if there is some mitigating cause that could be affecting those patients.

I want to evaluate if they have comorbidities that could be contributing to the underlying asthma, whether it's reflux disease, whether it's sinus disease, whether it's vocal cord dysfunction or sleep apnea, and address those specific comorbidities. Second of all, I try to get my patients down to as low a dose of corticosteroid as possible, and sometimes there are patients who come in on 10 mg of an oral corticosteroid, and I will step them down, quite slowly, one milligram per week even sometimes more slowly than that to try to get them down to avoid some of the adrenal insufficiency that could be causing them to require such higher doses. And then, I'll evaluate biomarkers in these patients, because so many of them, even if they're on oral corticosteroids, may continue to have elevations of biomarkers, and for those patients, I want to consider utilizing biologic therapies for some of those patients, to address their unmet needs. I also want to evaluate for adherence to their inhaled therapies as well. Make sure that they are adherent to their current standard

of care medications.

Dr. Corbridge:
And you mentioned that biomarker determination on patients with OCS. How does being on an OCS affect your biomarker evaluation?

Dr. Wechsler:
So, for the most part, when you're on an oral corticosteroid it suppresses most of the Type 2 biomarkers. It suppresses eosinophils. It suppresses exhaled nitric oxide, it suppresses even IgE levels in many of our patients. And so, what the GINA guidelines say is that in those patients who are on oral corticosteroids, presume that they have got Type 2 inflammation, and treat them accordingly with biologic therapy, because it's likely that the biomarkers that you'd utilize to determine that they have underlying Type 2 inflammation may be abrogated by these systemic corticosteroids. So, for those patients, I presume that they have got Type 2 inflammation and I treat them accordingly, with any of the biologics that may be indicated for corticosteroid reduction and/or have been shown to reduce corticosteroids.

Dr. Corbridge:
Great, thank you. Well, before we wrap up, Mike, are there any other thoughts or take-aways that you'd like to share with our audience before we wrap up today's session?

Dr. Wechsler:
I think that we're at a really exciting place in asthma management, particularly for patients with severe asthma. I think back twenty years ago, when I first started seeing patients with severe asthma, and we really didn't have any biomarkers. We treated all asthma patients the same way, and I think what we've come to realize is that asthma is a very heterogenous disease, and we're gaining more and more insight into the pathophysiology of the disease. Just our recognition that we have different endotypes, different biomarkers that we have, and so I'm excited because we've developed several new biologic therapies over the last couple of decades that have really transformed the way we manage our patients with asthma. And I'm looking forward to the future because I think that there's so much more to learn. I think that we're going to develop newer biomarkers, newer therapies, better biologics than what we currently have. But I'm excited that we at least have the biologics that we currently have to help address the unmet needs of many of our patients.

Dr. Corbridge:
Thank you, Mike. Well, with those take-aways in mind, I'd like to thank Dr. Michael Wechsler for joining us to discuss the challenges of diagnosing and managing patients with severe asthma. It was great to hear your insights on this important condition. Thank you very much.

Dr. Wechsler:
Thanks so much.

Announcer Close:
This episode of *Deep Breaths: Updates from CHEST* was brought to you by the American College of CHEST Physicians in collaboration with and paid for by GSK. To access other episodes of this series, visit ReachMD.com/CHEST, where you can Be Part of the Knowledge. Thanks for listening!