Dr. Stukus: Hello. And welcome to conversations from the world of allergy, a podcast produced by the American Academy of Allergy, Asthma and Immunology. I'm your host Dave Stukus. I'm a board-certified allergist and immunologist and serve as the social media editor for the Academy. Our podcast series will use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that are our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The find an allergist search engine on the Academy website is a useful tool to locate a listing of board certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allery, Asthma & Immunology terms of use agreement which you can find at www.aaaai.org. Today's edition of our conversations from the world of allergy podcast series has been accredited for continuing medical education credit. The American Academy of Allergy, Asthma & Immunology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Information about credit claiming for this and other episodes can be found at www.education.aaaai.org/podcasts. Credit claiming will be available for one year from the episodes original release date. For today's episode we are very pleased to welcome Dr. Mark Dykewicz to today's episode. Dr. Dykewicz is the Raymond and Alberta Slavin endowed professor in allergy and immunology at St. Louis University School of Medicine, and the chief of the section of allergy and immunology at St. Louis University. Dr. Dykewicz has a long and distinguished clinical research and academic career including service as a past member of the Board of Directors for both the American Academy and the American Board of Allergy Immunology. He is here today to discuss the 2020 practice parameter update for rhinitis for which he served as the lead author. Neither Dr. Dykewicz nor I have any relevant relationships to disclose. Dr. Dykewicz, thank you much for taking time out of your schedule to join us today. And welcome to the podcast.

Dr. Dykewicz: It's really my pleasure.

Dr. Stukus: I think this is going to be a great conversation and we're going to take a deep dive into what the parameters talk about and some of the advice that they give. But I'd really like to start just by asking you to give us a little background as to how and why this new parameter was developed. Did this originate from a group of allergists just sort of sitting around discussing their personal experiences? Or was there a more formal review of the evidence surrounding various aspects of rhinitis?

Dr. Dykewicz: Certainly, this is a more formal process. The parameter resulted first looking at the outline that had been used for a predecessor document, the 2008 complete joint task force practice parameter on rhinitis. And then with the time interval involved there really was a recognition that we had to very broadly review all literature, update and review the recommendation. A workgroup was convened and among other tasks they developed a list of key clinical questions and topics that should be addressed including some topics that had not been addressed in the predecessor document. There was in the

course of the development, the publication of the 2017 focused document on some key questions for treatment of seasonal allergic rhinitis but then subsequently we turned to development of the more comprehensive 2020 document that we're talking about. And that encompasses all forms of rhinitis from allergic to nonallergic rhinitis.

Dr. Stukus: It is a very comprehensive document. What's the timeframe? How long did this take to develop and write and edit and then finally get published?

Dr. Dykewicz: I could only say years. And I'm sure thousands of hours for myself and my coeditor Dana Wallace. It was a very time intensive process. And one of the things we would develop drafts and circulate them to the workgroup and then also to the joint task force and practice parameter and so many sections went through 10, even 20 revisions until they were completed.

Dr. Stukus: Yeah. Well, we all thank you for all of your hard work and this really is just a great guidance for all of us as practicing clinicians. Who's the target audience for these recommendations? Who is the aimed for?

Dr. Dykewicz: The document was developed to assist physicians and other healthcare practitioners. But also we had and eye to getting enough information so that patients could help make decisions regarding diagnosis and therapy for rhinitis. I would say that we systematically were developing the recommendation to address care of adults and adolescent patients ages 12 to 15. We did include a section on treatment of younger children. But one of the difficulties that we dealt with is that when you look at the data available for younger children you don't have the depth of data and you're ending up extrapolating data from adult studies. Your recommendations by nature have to be more tentative and less certain.

Dr. Stukus: No, absolutely. This is a comprehensive 47-page document. I believe I counted 598 references. So unfortunately I don't think that we'll be able to, nor would anybody want to listen to us go through this line by line. There are also 37 different recommendations that focus on specifics of diagnosis and management. But before we dive into some of these major areas, how do you recommend readers or our listeners use this document? Do they need to go start to finish? Or can they go to certain sections that are more relevant to what they're looking for?

Dr. Dykewicz: What I would suggest is you start out at the beginning of the document where there's a table that's entitled "What is new or newly emphasized in rhinitis 2020". I would start there because that really highlights what are the new targeted areas. For instance, there is mention of four new algorithms which are based on a combination of evidence and expert opinion that can guide the clinician in the treatment of allergic rhinitis and nonallergic rhinitis. The area discusses new tables that can assist in the differential diagnosis of rhinitis and also the diagnosis and treatment of conditions that might mimic rhinitis. And then we really try to highlight those topics that are new or newly emphasized. Going to that, I would then leave review a subsequent table rather-- I would then review a subsequent table that lists all 37 recommendations. And when you run through a recommendation-- when you run through a

recommendation that you find novel or different from your practice I would go to the pertinent section of the document to read the explanation for that recommendation.

Dr. Stukus: I love that you pointed that out because a lot of the information is going to be novel, or it represents a different paradigm shift in how we previously either diagnosed or treated various aspects of rhinitis. So I think that that's really important to keep in mind that, as you stated, this is based upon the body of evidence to date. And this isn't really just the opinion of a couple of allergists out there. So if people read something that seems foreign to them there's a reason for it and there's a deeper dive in the text. Let's get into it. To start off, can you describe the diagnosis of rhinitis and what this term means and some of the cardinal symptoms that go along with it?

Dr. Dykewicz: Sure. Now, although the term rhinitis would connote inflammation, some forms of nonallergic rhinitis such as vasomotor rhinitis or atrophic rhinitis don't really have information at all. So as we started to do in our 2008 parameter we continued to define rhinitis by symptom with the diagnosis of rhinitis suggested by the presence of one or more of the following. And those would be nasal congestion, rhinorrhea anterior and posterior, sneezing and itching. We can then go on to classify rhinitis by pathogenic mechanism. But I would start our discussion there.

Dr. Stukus: So to enter into the equation we just basically have to have one of those either chronic or intermittent symptoms of rhinitis. And then one of the first sections is headlined rhinitis phenotypes. Can you help us better understand what a phenotype is and then give us some examples when it comes to rhinitis?

Dr. Dykewicz: Well, a phenotype can be broadly defined as the observable characteristics of the condition. So if we're talking about rhinitis phenotypes could include allergic rhinitis, different forms of nonallergic rhinitis and that it could include nonallergic rhinitis with eosinophilia syndrome or infectious rhinitis. And then other forms of nonallergic rhinitis such as vasomotor rhinitis or atrophic rhinitis.

Dr. Stukus: And you mentioned before that there are a lot of sort of mimickers that may lead to misdiagnosis or inaccurate classification. What are some of the other conditions that can cause similar symptoms, yet be completely different in regards to their underlying cause or pathophysiology?

Dr. Dykewicz: Right. That's a very important question because you, obviously, have to have a differential in your mind to come up with the right diagnosis. Some common conditions that can mimic rhinitis that include several anatomic causes. And we do note that, for instance, nasal septal deviation is a very common cause of fixed nasal obstruction. Although, it can be a unilateral problem, it also can be bilateral; just because somebody has a stuffy nose on both sides doesn't mean they do not have the septal deviation. Also, we have to be mindful of nasal valve collapse as another anatomic cause or nasal obstruction. The internal nasal valve, of course, is the narrowest portion of the nasal cavity. The anatomical area is bounded immediately by the nasal septum and latterly by the interior edge of the upper lateral cartilage and the anterior aspect of the inferior turbinate. So nasal valve collapse refers to any weakness or further narrowing of the nasal valve and can really result in significant problems with nasal congestion that are not going to respond to medications. And, of course, we have turbinate hypertrophy

which can account for either unilateral or bilateral obstruction. And then chronic rhinosinusitis with or without nasal polyps, pharyngeal nasal reflux and very uncommon conditions of things we have to keep in mind such as cerebral spinal fluid rhinorrhea, ciliary dyskinesia syndrome and, for instance, granulomatous or connective tissue disease.

Dr. Stukus: You're describing a wide range of very different causes of rhinitis. So people can have similar symptoms but yet the underlying cause is just vastly different based upon all of these. So when a clinician has somebody in front of them in the office setting, in the clinical setting and they have concerns about rhinitis, what are some of the questions and answers that they should use to try to elicit the proper diagnosis?

Dr. Dykewicz: I think this is an area that is especially suited to specialist allergists and allergens. And we are very custom to asking the appropriate questions which could include age of onset, duration of symptoms, frequency of symptoms, severity, timing during the year, suspected triggers, the pattern or presentation and the progression of each symptom. History also really would included the success or failure of past therapeutic interventions including both over-the-counter and prescribed medications. You can also really do a full job by looking at family history and a personal history of comorbid and respiratory conditions such as asthma. And then also recognize that speaking of asthma, that a history of symptoms suggestive of asthma might be elicited by a little bit further questioning, so a history specifically a wheezing, shortness of breath, or chest tightness. And be mindful that in terms of allergic rhinitis that can coexist in about 75 percent of all patients with asthma. Of course, you also do want to look at the overall medical, social, and psychiatric history and environmental exposures. And then since you are going to be making some shared decision-making getting a history from the patient as to what their wishes and desires are in terms of selecting diagnostic procedures and treatments.

Dr. Stukus: You're describing really a very comprehensive list of questions. And then with each answer sort of changing the algorithm per se in regards to what the possible diagnosis may be or even next treatment options and things like that. Personally, when you see patients, do you have sort of a standardized approach to it? Or have you just been doing this for so long and you're so good at it that you just sort of can tease out some of these questions? Any advice for our listeners on how they should approach this?

Dr. Dykewicz: Over a period of many years I've developed a template that really elicits these questions. And because I'm also in a teaching setting where I'm rotating residents and students coming in that may not have much background in different types of rhinitis it's really almost a script for them to ask patients these questions. We also have a new patient questionnaire that in a more efficient way, I think, tries to capture responses to these sorts of questions.

Dr. Stukus: We've taken our history. We have some sense of what may be contributing to/causing our patient's symptoms. What are the important elements of the physical exam that we should consider as part of the diagnosis?

Dr. Dykewicz: Well, first of all, we have to recognize that there are no amount of findings that really help distinguish allergic versus nonallergic versus infectious rhinitis. You can see findings such as pale], boggy nasal mucosa, allergic shiners, pharyngeal hyperplasia. I think looking at the nasal septum is important and that's not only to determine, for instance, if there's a nasal septal deviation but to assure that there's no erosion to begin with or a septal perforation. And you want to establish that at baseline prior to prescribing some medication such as nasal steroids that might lead to adverse effects. I also mentioned earlier the importance of nasal valve collapse. So particularly when patients are not responding well to treatment for rhinitis I think the nasal exams should include assessment of the patency of the nasal valve. And the way that's done is by performing the Cottle maneuver where you pull the patient's cheek latterly to open the nasal valve angle. And that could suggest nasal valve pathology and the one explanation for why there's not very good response. And then even though the parameter is on rhinitis we have to be mindful that there are comorbidities. So a physical exam should also look at the lower airway, the eyes, the ears, the skin to identify some findings that could go along with other comorbidities such as allergic conjunctivitis or rhinitis and station two consumption, chronic rhinitis as atopic dermatitis and so forth.

Dr. Stukus: So just to kind of summarize because I think you really touched upon some really important concepts. There's no one finding that says, yes, this is exactly what's causing this patient's rhinitis. But really we're looking for a series of clues of what may be present, or may be absent. Does that sound accurate?

Dr. Dykewicz: Exactly.

Dr. Stukus: Okay. Excellent. I want to go back to something you mentioned because I think it's really important. As I read this document I'm thinking the initial diagnosis but what about follow-ups? Are we still asking the same questions and doing the same exam based upon the response to treatment that was decided upon at the first visit? Or how should we go about that when those patients come back to see us for these concerns?

Dr. Dykewicz: Well, of course, we have to be selective for an established visit as to how much time we can properly devote. But if there's not a good response, of course, asking about compliance with medication which is a major issue. Asking, if there are environmental changes that may be impacting things. And it may well also be has the pattern changed since the initial visit and that would raise questions. I mean sometimes people come back and they develop the intercurrent sinus infection.

Dr. Stukus: Excellent. Why is cough highlighted as a symptom to consider for allergic and nonallergic rhinitis?

Dr. Dykewicz: We felt that cough is a consequence of rhinitis, particularly allergic rhinitis it's often underappreciated. And if we're talking about chronic cough which you formally define in adults as cough persistent for more than eight weeks. This often is not usually due to upper airway cough syndrome, formally referred to as postnasal drip syndrome. You could also have it from asthma or GE reflex disease. But, accordingly, we felt that in a document on parameters it was really important to have some focus on cough. And I would also point out that sometimes there's a sense that cough is considered to be a

comorbidity of allergic rhinitis rather than being viewed as a distinct symptom of allergic rhinitis. And just one statistic that demonstrates how big a deal a cough is there was one large multinational observational study that found essentially, half of patients with allergic rhinitis frequently reported cough as a symptom. Although maybe only 11 percent had cough as the main reason for seeking medical attention.

Dr. Stukus: Yeah, I think that's important to highlight as not to be overlooked. Now, as we move towards testing and things like that, what role does inhalant allergen IGE testing have in the diagnosis of rhinitis? How does that help us identify causes and treatment and things like that?

Dr. Dykewicz: Sure. Well, of course, in the big picture in clinical practice especially in primary care the diagnosis of allergic rhinitis is often made solely by history, for instance, in seasonal allergic rhinitis. We recommend that allergen skin prick testing or specific IGE blood testing be completed to confirm the diagnosis of allergic rhinitis and the compatible history. And that can be really very important to differentiate allergic from nonallergic rhinitis which is very difficult, especially in the case of perennial rhinitis to differentiate that by history alone not very successful. So by performing allergy testing, though, you can provide really informed recommendations about allergen avoidance, choosing appropriate medications. I mean we know that some medications such as oral antihistamines with the leukotriene receptor antagonist would not be appropriate for nonallergic rhinitis. And, of course, conceivably whether the patient would be a candidate for allergen immunotherapy.

Dr. Stukus: Are there instances where you can have incidental findings in somebody who has nonallergic rhinitis and yet they still have elevated IGE testing? And how do you sort that out?

Dr. Dykewicz: That's a very important point because you always want to try to fit together the history with the findings of the allergy testing. If somebody's got some tests that are coming back positive for a couple of seasonal allergens and there's absolutely no uptick in symptoms during those seasons that data is not really relevant. I think, actually, one of the real problems is trying to separate out when you have a patient who may have mixed allergic and nonallergic rhinitis and this is on a perennial basis. You're trying to sort out how much of it might be because of a perennial allergic basis versus a perennial nonallergic. And that's-- well it's problematic and that is why we have to go beyond just looking, slam dunk at the allergy test results and try to fit it all together with a bigger history.

Dr. Stukus: I found something very interesting as I went to the different recommendations. And I saw that there's a very specific recommendation against any type of food allergy, skin or serum testing in the evaluation of rhinitis. I mean this seems like common sense to me, but this was given special attention in these parameters. Why was that?

Dr. Dykewicz: Well, as we sit around for hundreds and thousands of hours compiling these parameters we're really trying to improve patient care. There is a sense that very commonly out there there's a lot of food allergy testing that is going on for patients who are presenting with rhinitis. Outside of the oral allergy syndrome there's really no evidence of IGE mediated food induced nasal symptoms without the presence of anaphylaxis a whole body symptom, things like hives, difficulty breathing, diarrhea. So there's really no indication to test for food allergens when evaluating patients presenting with symptoms of rhinitis. You

also have to be mindful. And this gets back a bit to your question earlier about how you interpret the positive allergy test results. If you're looking at skin testing or specific IGE testing to food those can be less than 50 percent specific for clinical food allergy. And, therefore, it really opens up the possibility of unnecessary food testing leading to unwarranted food avoidance, reducing quality of life, uncalled for financial expenditure and possible nutritional deficiency. So testing with a panel of food without attention to the medical history and the epidemiology of allergic rhinitis in individuals can really results in mismanagement.

Dr. Stukus: I'm glad you stated that. And I'm glad it's in the parameters. I've seen many patients diagnosed with multiple food allergies that they didn't know they had because they went to see somebody due to concerns about seasonal allergic rhinitis. And then they walk out with an egg, and milk, and peanut allergy. So I also agree that it's very important to avoid unnecessary testing when people present with those systems. Now, what do you tell, at the risk getting very controversial here, what do you tell to all those people out there that are convinced that milk makes them have increased mucus production?

Dr. Dykewicz: That is a conundrum. And I face patients like that, too. Typically, I try to defer doing testing with some explanation about it, also stating that avoiding dairy products can have some nutritional problems. Have I, in my career, ever test for milk to try to dissuade somebody from that occasionally. But then you also run into the risk that if it does happen to be positive then you're sort of stuck. It's not an easy answer.

Dr. Stukus: Yeah. It's a very long-standing sort of myth that's out there that we're up against. So we've done a great job-- you've done a great job of really discussing the diagnosis and how we use the history and physical exam to identify different types of rhinitis. Let's transition to treatment options. And I really want to start with the lead on this one. What is the single best first-line treatment for rhinitis across-the-board period?

Dr. Dykewicz: A simple answer an intranasal corticosteroid is the single best most effective treatment for rhinitis.

Dr. Stukus: Okay. So you recommend that's the first line regardless of the symptoms that people are having or even the potential causes, that's the recommendation of the parameter?

Dr. Dykewicz: I would say it's somewhat more of a nuanced answer when you ask the question that way. When we look at the algorithms there's been great deal of thought as to how one might select another option as first-line. For instance, let's we had a patient that did not want to take regular medication. They had allergic rhinitis. They might have short-term symptoms for a day or so. And they were relatively mild to moderate. One might use an inter-nasal antihistamine as an option. Or for very mild symptoms, possibly an oral antihistamine. So that's where you get into the weeds, so to speak, that there could be some consideration of different factors that would make you move towards use of other medications in our repertoire. But, in summary, a nasal corticosteroid is going to be your single best bet.

Dr. Stukus: And when people use intranasal corticosteroids, is it most effective to use them sort of daily and consistently for a period of time to treat symptoms, or can they use them just every once in a while, whenever they start to have symptoms?

Dr. Dykewicz: They are most effective when used on a regular basis, but intranasal corticosteroids can have benefits in PRN use. Now the question is, in terms of evidence, how PRN for PRN use. I actually had been involved in a study years ago, and it showed that if people were using it maybe 50 percent or more of the time as PRN, it certainly could be very effective. But the onset of action of nasal corticosteroids, although the estimate varies, can often be within 12 hours. So it can suit itself to PRN use. I would also say, one other feature of this document is we do have a section in there, looking at the onset of action of different agents in allergic rhinitis. And depending on the patient presentation, the onset of action can be an important factor in shared decision-making as to what medical approach you might go to. And that's in there, if you will.

Dr. Stukus: Oh, that's great. I'm really glad that you pointed that out. And before we sort of move on from different types of intranasal sprays, can we use them concurrently? So can you use your steroid spray at the same time you're using a inter-nasal antihistamine, for instance?

Dr. Dykewicz: Very much so. And we do go through sections of the document to talk about what combination approaches can be useful, and specifically combinations of intranasal corticosteroids with other nasal sprays, such as intranasal antihistamines or intranasal decongestants or intranasal Ipratropium, would certain be an option.

Dr. Stukus: Okay. One of the longest standing and widely available treatment options for allergic rhinitis or other types of rhinitis would be oral antihistamines. These are widely available over the counter, by prescription. But, you know, why should we try to avoid these first generation oral antihistamines such as Diphenhydramine in favor of second generation or newer antihistamines for the treatment of rhinitis?

Dr. Dykewicz: Some information about this has been well-known for some time, but we also reviewed some new information. So information that's been out there includes that the first generation antihistamines can produce sedation, and that may not be subjectively perceived. Performance impairment, lead to poor sleep quality, sleep architecture, and also anticholinergic mediated symptoms such as dry eyes, dry mouth, constipation, or urinary hesitancy. We do have data course that show that first generation antihistamines can lead to performance impairment in school and driving issues. Now, more recently, there've been some concerns raised about whether there's a higher risk of dementia with agents that have anticholinergic properties. And first generation antihistamines, of course, can have anticholinergic properties. Second generation antihistamines don't. And there was one perspective cohort study that we quoted that suggested a link between the higher cumulative use of strong anticholinergics, and that would include first generation antihistamines and tricyclic antidepressants, and the risk of developing dementia. And actually, over 70 percent of those patients with longer-term use being diagnosed with Alzheimer's.

Dr. Stukus: So is the mechanism of action the same if you have a second generation antihistamine? And these would be things like Ceterizine or Fexofenadine or Loratadine or things like that. Does that work the same way as Dyphenhydramine? Or what's the difference there?

Dr. Dykewicz: They work the same way in terms of being an inverse agonist for the H1 histamine receptors. But the first generation antihistamine, if you will, have less activity for the H1 receptor and can affect other receptors, which, in the case of anticholinergic effects, involves the impact that they have on non-histamine receptors in the body.

Dr. Stukus: Okay. So they work similar but more side effects with the first generation oral antihistamines. You mentioned leukotriene receptor antagonists before, and one of the more common forms of that would be the medication Montelukast. Can you explain for us what this does in the mechanism of action and why it's not a first-line treatment for rhinitis? And, in addition to that, are there any precautions that clinicians need to discuss with patients when they prescribe Montelukast?

Dr. Dykewicz: Well, Montelukast, of course, is a leukotriene receptor antagonist. And leukotriene production can be part of the allergic response, and that can vary in terms of the relative importance in different patients. The drug has been approved for use down to age six months for treatment of allergic rhinitis, but we ended up suggesting that the clinician not select Montelukast for initial treatment of allergic rhinitis due to two main reasons. One is, if you look at the relative efficacy compared to other alternative agents, Montelukast is about the same or less effective than oral antihistamines, and certainly less effective than intranasal corticosteroids. And again, as we mentioned earlier, an intranasal corticosteroid would be your preferred therapy for more severe allergic rhinitis. But the second reason that's been emerging is that there are post-marketing reports of rare neuropsychiatric events for Montelukast. And those can include everything from, well, sleep disturbances, depression, anxiety, aggression, psychotic reactions, and suicidal thinking and behavior. We did note, in the document, that we do need some high-quality epidemiological studies to fully evaluate the association and quantify the risk of those neuropsychiatric adverse events. But as a result, in a risk balance-- as a result, in a risk/side effect balance assessment, we really put down on the list the use of Montelukast for allergic rhinitis to limit it to patients who are not treated effectively with or can't tolerate other alternative treatments.

Dr. Stukus: Okay, thanks for explaining that. A lot of people like to use oral or intranasal decongestants whenever they feel stuffy or congested. What's the mechanism of action for these types of medications and what recommendations are made in the rhinitis parameters regarding how these medications should be used?

Dr. Dykewicz: Well, both the oral and the topical intranasal decongestants are alpha-adrenergic agonists. So they can improve nasal airflow by virtue of their effect on causing nasal-based friction and decreased nasal edema. Now, relative to oral decongestants, we did make the point that although Pseudoephedrine has good demonstration of benefits, Phenylephrine does not. And we do not recommend that in our treatment algorithm. Relative to the intranasal decongestants, we don't routinely recommend them for continuous use because of the potential development of so-called rhinitis medicamentosa, where you get alpha receptor Tachyphylaxis. But there is a new recommendation that

we put forth, and that is because we now have some data that shows if you have concomitant administration of an intranasal corticosteroid with an intranasal decongestant, that seems to significantly reduce the risk for development of rhinitis medicamentosa. So we do make a statement that, in patients with consistent nasal congestion who are unresponsive to an intranasal corticosteroid or even an intranasal corticosteroid/intranasal antihistamine combination, you can offer them combination therapy with the addition of an intranasal decongestant for up to four weeks.

Dr. Stukus: Okay. So thoughtful use of it. I mean, I'm hearing this theme from you, over and over again. Thoughtful approaches to diagnosis and management, shared decision-making, and sort of selecting therapies based upon the symptoms you're treating and the diagnosis at hand. There are other intranasal treatments that are discussed in the parameters, including things such as capsaicin, Ipratropium, and cromolyn. Can you briefly discuss that these agents do and how they can best be utilized for treating rhinitis?

Dr. Dykewicz: Sure. Well, to start off with, intranasal Ipratropium is a topical anticholinergic agent. So that does help reduce rhinorrhea, particularly anterior rhinorrhea, and it also works in both allergic and non-allergic rhinitis, in addition to the common cold. So we recommend that, in patients with allergic rhinitis or non-allergic rhinitis who have rhinorrhea as their main nasal symptom, they could be offered intranasal Ipratropium. And also, if the patient is already on, for instance, an intranasal corticosteroid but they're still having persistent rhinorrhea, you could consider the addition of intranasal Ipratropium. Also, Ipratropium could be a well-suited medication for reducing gustatory, food-related, rhinitis rhinorrhea. Now, cromolyn is theoretically an agent that stabilizes mass cells and inhibits mass cell mediated release, although that may not explain all of its benefits. We don't think it has much of a role in treatment of allergic rhinitis generally. Among other things, it's an agent, if you're going to use it on an ongoing basis, requires four to six times a day administration. However, we did look at the use of intranasal-- we did look at the use of intranasal cromolyn as an option that could be used just prior to acute allergen exposure, as there is evidence that that can reduce symptoms of allergic rhinitis from episodic allergen exposure. So, for instance, you have someone who knows they're allergic to pets, they're going over to a home with pets, they anticipate this problem. One option would be to use intranasal cromolyn before they go over there. That said, intranasal cromolyn is not widely available in some drug stores. I think you have to order it online. Lastly, capsaicin, which is a pungent compound found in hot red pepprs, is the selective TRPV1 ion channel agonist that ends up basically reducing parasympathetic hyperactivity in neuropeptide release. So there is evidence that when it's topically applied to the nasal mucosa, it can be helpful for non-allergic or mixed rhinitis, to reduce congestion and rhinorrhea and post-nasal drainage. We didn't come out with a formal recommendation for it, however, in part because, in the US, we don't have, shall we say, consistent products. And when we looked at the literature, different concentrations of capsaicin have been used in studies. So we bring this up as a, if you will, a fallback position that might be considered, but not something that would be mainline treatment.

Dr. Stukus: Have you ever, out of curiosity, put capsaicin inside your nose? Do you know what it feels like?

Dr. Dykewicz: It burns.

Dr. Stukus: I can imagine, yeah. I found that very interesting. And of course, if it's being used and there's evidence to support it, it's important to talk about. But yeah, it's a fascinating treatment. You mentioned this diagnosis, gustatory rhinorrhea or gustatory rhinitis. I love spicy food and my nose tends to run or I sniffle or get a little post-nasal drip when I eat a lot of jalapeños. Is that what that condition is referring to, or does that entail something else?

Dr. Dykewicz: No, that is certainly what we're talking about. And, in some patients, gustatory rhinitis doesn't require particularly hot or spicy food, it can be even some bland food that will elicit problems in some patients. So, in those situations, taking intranasal Ipratropium maybe 15 to 20 minutes before a meal can really prevent some significant drainage that can otherwise be, I would say, in some cases, almost socially debilitating to people, where they don't even want to go out and eat with friends or in public because they're afraid that they're going to have a drippy, runny nose.

Dr. Stukus: Oh boy, sure. We've discussed so many different types of medications and diagnoses thus far, and it seems like all the different medicines work in different ways for different symptoms. You mentioned a couple combinations before, but are there combinations that tend to be more effective than others or can really-- you know, I imagine people with their utility belt and 20 different nose sprays. Can they just sort of squirt anything whenever they want, or is there a method to the madness?

Dr. Dykewicz: We did have several statements that specifically addressed a combination of intranasal corticosteroids and intranasal antihistamines. Now, of course, in practical terms, there's even a product available where both types of agents are combined together. But you could also have uses-- separate bottles with the different component agents. And we did bring up the point that both allergic rhinitis and non-allergic rhinitis, the combination of the nasal corticosteroid and the nasal antihistamine can lead to improved control. In addition, other combo sprays that could be used would be intranasal steroid with an intranasal Ipratropium approach when you have uncontrolled rhinorrhea with the mono therapy of the nasal steroid. We've already discussed use of an intranasal corticosteroid with an intranasal decongestant. In terms of other combinations beyond nose sprays, an oral antihistamine plus an oral decongestant can lead to greater relief, but that has to be given with the consideration of whether the Pseudoephedrine would be tolerated. And of course, there can be adverse effects from that. That does bring up the question about, okay, which combinations only maybe work or don't work at all? And the combination of an oral antihistamine with an oral leukotriene receptor antagonist can have an additive effect, looking at some studies. Although, other studies don't show that. These days, though, because of the problems that have arisen with concerns about the neuropsychiatric side effects, we did not encourage the combo use of an oral antihistamine plus a oral leukotriene receptor antagonist, Montelukast, as a earlier line approach, although that would be an option. And I think one thing that does bear some special discussion, and this was one topic that we had brought up in the 2017 focused parameter document on seasonal allergic rhinitis, and that is the combination use of an oral antihistamine with an intranasal corticosteroid. You know, this is a very commonly-used approach. You have a patient that isn't responding well to an oral antihistamine, you add a nasal corticosteroid. And when you look at the controlled trials where you are comparing the mono therapy of an oral antihistamine versus a nasal steroid versus combined therapy of a oral antihistamine plus a nasal steroid, you actually cannot show superior benefits with the combo therapy as opposed to mono therapy with the nasal steroid. So although

there are some caveats about this recommendation, we are trying to discourage the general combined use of oral antihistamines and nasal steroid with the idea, for many patients, it's really not giving them any incremental benefit over a mono therapy with the nasal steroid.

Dr. Stukus: That is really interesting. You're right, that's sort of been the common practice for a long, long time for a lot of folks who suffer from seasonal allergies. And the bulk of our discussion today and the parameters as well, in regards to treatment, is focused on topical therapy with intranasal sprays. But, you know, you know better than anybody, there's a lot of resistance among our patients in regards to using nose sprays. Sometimes they burn or sting or it just feels funny to put something in your nose. Do you have any practical advice to help patients better utilize these so they're well-tolerated?

Dr. Dykewicz: I mean, I do think the strategy of instructing the patients that there could be runoff, but then having them use, if you will, a nose technique, that you put the spray in the nose first and then they dip down even to the level of the waist, hold 20 seconds, let the-- as I put it, let the spray get into the nooks and crannies inside the nose, and then stand up. That allows some patients to tolerate nose sprays. And, of course, some of the nose sprays among the corticosteroids, for instance, will have different sensory attributes. Some will have smells, some will not. And sometimes a switcheroo can allow a patient to accept things a bit better. Among nasal antihistamines where you can get a bitter taste, I mean, sometimes people tolerate nasal Olopatadine rather than Azelastine. So I work with the patient, sort of warn them upfront there can be some issues, and I think I at least get a lot more people tolerating nose spray approaches than otherwise might be inclined to.

Dr. Stukus: Sure. It's a little different than just throwing a spray at them and saying, good luck. There's a little more education involved. Absolutely. What do these parameters recommend regarding the use of allergen immunotherapy for the treatment of rhinitis?

Dr. Dykewicz: Well, we certainly do think it can play an important role, and we suggest that subcutaneous or sublingual-- we certainly do believe that allergen immunotherapy can play an important role in the treatment of allergic rhinitis, and we do specify that subcutaneous or sublingual tablets can be offered in patients with moderate to severe allergic rhinitis. And considerations would be those patients who aren't controlled well with allergen avoidance or pharmacotherapy, those who might choose immunotherapy as a preferred method of treatment in an effort to avoid the adverse effects of medication or the long-term costs of medications. Or other patients might desire the potential benefit of immunotherapy to prevent or reduce the severity of some comorbid symptoms, such as asthma. So, we certainly do believe there's a clear role for allergen immunotherapy in appropriately selected patients.

Dr. Stukus: Many people prefer the use of natural or alternative remedies as opposed to prescription medications. Is there any evidence that supports treatments such as acupuncture or herbal remedies for the treatment of rhinitis, or any other similar remedies?

Dr. Dykewicz: It's an important question, because some data suggests that up to a third of the population are using complementary health approaches in their health care. So we did a very thorough literature review to look at the evidence for acupuncture and herbal remedies in the treatment of allergic rhinitis,

and we looked at Chinese herbal remedies, mixtures of Indian plants, the plant Butterbur, and overall, the problem was there was a low level of evidence. However, for acupuncture, even though we concluded that we could not make a recommendation for or against the use of acupuncture, we did find results that there could be a modest benefit, although there was mixed data about this. Some of the benefit reported was of uncertain clinical importance. But putting this in perspective, acupuncture was found to be very safe, with no serious adverse effects reported in any study. Now, about the herbal remedies, shall we say the more encouraging data was that about Butterbur, from some randomized controlled trials with ten different products. And it was found that this improved symptoms and quality of life comparably with the nonsedating antihistamine. Now, that said, the National Institutes of Health does warn that Butterbur products can have some Pyrrolizdine alkaloids which can cause liver injury. So they recommend that only products that are certified to be free of these alkaloids should be used. There's also a potential for allergic reactions to Butterbur in patients who are sensitized to ragweed, chrysanthemums, marigolds, daisies, so that has to be kept in mind as well.

Dr. Stukus: Well, thank you, that's so fascinating. Thank you for that wonderful summary on that. Because, as you mentioned, a lot of patients do ask about these types of therapies, so it's always important to know what the evidence supports and at least point them in the right direction. Boy, we've covered a lot of information. And again, we will direct all of our listeners to read the full rhinitis parameters for a detailed discussion and explanation of all these recommendations, including those different algorithms that you mentioned. Did we miss any major areas?

Dr. Dykewicz: I think I would point out that people should read our section on pregnancy. Because there has been some integral information that's become available that raises new safety concerns during pregnancy about the use of intranasal Triamcinolone and intranasal decongestants. And then there's also some additional evidence that supports and extends our pre-use recommendation to avoid oral decongestants. I also would point out that we have written a section on local allergic rhinitis. That, of course, is the entity sometimes referred to as entropy, where there's a clinical history of allergic nose symptoms following allergen exposure but you have negative skin tests or in-vitro tests for IGE and still have a positive nasal allergen provocation challenge. We basically concluded that more research is needed, but that would, reading that section, bring you up to date on our current knowledge about that entity.

Dr. Stukus: Dr. Dykewicz, I can't thank you enough for taking time out of your schedule to be with us today and discuss these very important parameters. And I think this is really helpful, just to walk people through what the evidence shows and highlight some of the recommendations that are put forth there. Before we depart, is there anything else you'd like to add?

Dr. Dykewicz: No, it's been a real pleasure, talking through the parameter. And I guess I would just encourage people to look at the big document. It can be overwhelming because of its length, but there's a lot in there. And especially for allergy immunology specialists, rhinitis is one of our key areas of care, and we want to be fully up to date in what we're doing.

Dr. Stukus: Excellent, well, thank you again.

Dr. Dykewicz: Great pleasure, thanks.

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