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### Vortex Management: Multiprong and Individualized Treatment Approach

#### Announcer:

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#### Dr. Tino:

Hi, everyone. My name is Dr. Greg Tino. I'm a Pulmonary Critical Care Physician at the University of Pennsylvania in Philadelphia. And it's a privilege to be here with my friend and colleague, Dr. PJ McShane, from the University of Texas at Tyler. And we'll be discussing a topic that we've called Vortex Management: A Multipronged and Individualized Treatment Approach to Bronchiectasis.

So Dr. McShane, as you well know, bronchiectasis may have many different causes. So, what's the typical differential diagnosis? And then what's the standard workup for bronchiectasis look like as far as you're concerned?

#### Dr. McShane:

Thanks. Thanks for having me, Dr. Tino. So this is - you're right. This is a very heterogeneous group. And so, there are many broad causes or associations, right, with bronchiectasis. And I think they're - really it falls into two big categories. We try to make sure we're not missing either an immune deficiency or an autoimmune disease.

You know, there are guidelines available, many international guidelines. For example, the Europeans, the British, the Australians have published guidelines on how to work up a patient with bronchiectasis. And there are others. Generally, though, I think if you had to pick the things that they all recommend as a minimum bundle, so to speak, for working at bronchiectasis, there would be - it would be a CBC with respect to the eosinophil count, an immune globulin E to make sure that your patient who may or may not have a history of asthma does not have allergic bronchopulmonary aspergillosis, and an immunoglobulin profile.

I think a lot of the other associations with bronchiectasis can really come out in the history. So especially with regard to the autoimmune history, if your patient has a history of dry eyes or dry mouth, you may want to add on the Sjogren's antibodies. If you think that there's joint disease present, you may want to add on the rheumatoid factor. But generally speaking, I think it's a CBC, immunoglobulins, and the IgE.

#### Dr. Tino:

Yeah, I agree. That's what I do as well. And one of the things that I also find helpful and other things that you factor in when you're looking at what potential causes are is the age of the patient. So younger patients, you would think about some of the genetic causes and immunoglobulin deficiency, etcetera. And older patients, think more of NTM infection, ABPA, that kind of stuff, and, you know, gastric acid aspiration. So it really is I think the point that you've made, which I think is a good one is that it has to be individualized. But there are many clues that can help you in making that differential diagnosis and stand - and starting with an organized devaluation really makes a lot of sense.

#### Dr. McShane:

Yeah, so that's a great point, Greg. I mean, you mentioned the individuality of this disease and how important that is. So you know,

based on that the individual nature of each patient who has bronchiectasis, what constitutes evidence-based supportive care for bronchiectasis?

**Dr. Tino:**

I think the approach is really multipronged for individual patients. And I think there's some common themes. I think airway clearance measures. Almost regardless of what modality you use, the value of airway clearance, I think can't be overstated, especially in symptomatic patients with bronchiectasis and those who experience frequent exacerbations. Obviously, antimicrobial therapy, targeted sputum analysis-based antimicrobial therapy for exacerbations is critically important. And again, targeting specific pathogens, like the hemophilus species and Pseudomonas and staph.

And then beyond that, again, for patients with recurrent exacerbations, you know, we've used a number of inhaled antibiotics and potential antiinflammatory therapy with macrolides, for example.

And then lastly, of course, if you identify a specific etiology, and that specific etiology has therapy that's effective, whether it be steroid therapy for allergic bronchopulmonary aspergillosis, anti-NTM antibiotics for people with mycobacterial - nontuberculous mycobacterial infections, etcetera, those become really important part of what we do.

**Dr. McShane:**

Yeah. Yeah, I think that those are all great points. And I think one of the things that we're always trying to emphasize is the importance of the regular sputum analysis. Really getting that sputum from our patients every few months and looking for AFB surveillance and making sure we know what chronic infection they may be harboring makes a big difference on how we might manage them. And certainly, it makes a difference on whether we might implement chronic macrolide therapy if we know they do not have mycobacterial disease, or if they do have it then we would want to advise them to stay away from monotherapy with macrolides.

**Dr. Tino:**

Yeah, I agree with that, P.J. And one of the things, you know, we always talk about the importance of a partnership with our patients and making informed decisions. But I think it's actually even more critically important for patients with bronchiectasis. And the other thing over the years is the collaboration with physicians and other specialties. Has that been your experience as well?

**Dr. McShane:**

Absolutely. I mean, one of the things that we didn't mention yet that is very prevalent within patients who have bronchiectasis is, for example, gastroesophageal reflux disease, and making sure that they don't have chronic aspiration that's maybe asymptomatic. And so certainly, working with gastroenterologists and having a thoughtful specialist in gastroenterology to really make sure your patient isn't chronically aspirating. You may even partner up with a good infectious disease doctor who may want to help with the nontuberculous mycobacterial infections. A very good rheumatologist is often really necessary to follow these patients. And then, you know, the immune globulin or the immune deficiency, that's a very complex, deep field that is evolving at a rapid pace with genetics. And so I think having a really thoughtful immunologist sometimes is really important with making sure that we're not missing some of these immune glob - or some of these immune deficiency syndromes.

**Dr. Tino:**

Yeah, I couldn't agree more with that. And the other one I would add is probably ENT physicians.

**Dr. McShane:**

Oh yeah.

**Dr. Tino:**

Some of my patients have, you know, concomitant chronic sinus disease, like the patients would see the ID and others where they have really challenging sinus disease that really is - requires more than just antibiotic therapy. And we're fortunate at our place to have to have some really collaborative ENT doctors. But absolutely, and I think the point here is that, that really multidisciplinary care is really important for patients with practices.

**Dr. McShane:**

I couldn't agree more. That's a really great point. I wish I had made it myself but you know, clearing up the sinuses in these patients can reduce their frequency of exacerbations or a good sinus surgery can often do that.

**Dr. Tino:**

Yep.

**Dr. McShane:**

So Greg, this is an exciting time with bronchiectasis. There are new drugs being developed in the pipeline. One potential avenue is

inhibition of neutrophil elastase. These are often called dipeptidyl peptidase inhibitors. Maybe you could share with us, you know, some of the information from the phase 2 clinical trial.

**Dr. Tino:**

Yeah, thanks, PJ. You know, I have been taking care of patients with bronchiectasis for a long time. And had we had this discussion 10 or 15 years ago, it would have been a really short discussion. So, and I'm happy that, you know, that obviously, there's a lot of interest in advancing the treatment of patients with bronchiectasis. So one of those is antiinflammatory therapy, as you mentioned, and there was a published study called the WILLOW trial in *The New England Journal of Medicine* that evaluated the efficacy of a human neutrophil elastase drug, placebo-controlled trial phase 2 trial. And what the primary endpoint from the efficacy standpoint was the impact on exacerbations. And we know that frequent exacerbations really have deleterious effects on patients in the long term. And the study showed that compared to placebo at two different dosing schedules, that there was a favorable impact in terms of decreasing the number of exacerbations during the 24 weeks of the trial, and also decreasing the total number of exacerbations as well as the rate during that same time period.

And based on that trial, there was a recently completed multinational large trial, over 1,500 patients enrolled in a phase 3 placebo-controlled trial, to learn more about and to confirm the results of the phase 2 trial. And like you, I'm anxiously awaiting the results of that trial being available for our review.

**Dr. McShane:**

Yeah, and one of the things that this is contingent upon is that patients who are having exacerbations would be, you know, eligible for this potential therapy. And so I think it really underscores the importance of us educating our patients about what's an exacerbation. I'm always surprised that patients don't always know to let me know about it. I mean, I think they know when they're sick, of course, but they don't necessarily know to label it as such and how important that is with steering their management, if they are having frequent exacerbations.

**Dr. Tino:**

Well, PJ, I appreciate your insight. Always nice to see.

Just to summarize what we talked about and what we've learned. And I think the first is that bronchiectasis has many different causes. And that an organized approach to the identification of specific causes in of bronchiectasis itself is very important, that the care of these patients should be individualized, but there are certain tenets including antimicrobial therapy and airway clearance that are really important across the board, that partnering with our patients as well as other specialists, and we mentioned allergists and immunologists, gastroenterologists, infectious disease specialists, rheumatologists, and ENT are all really important. And that frankly and thankfully, there are some potential new therapies on the horizon that we think will favorably impact or we hope will favorably impact our patients.

So thank you.

**Dr. McShane:**

Thank you.

**Dr. Tino:**

Thank you for listening.

**Announcer:**

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