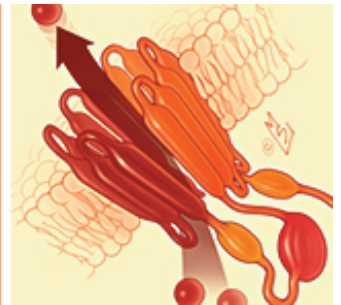




eLITERATURE  
REVIEW

Presented by the Johns Hopkins  
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eCysticFibrosis Review  
Podcast Issue

HOME NEWSLETTER ARCHIVE CME/CE INFORMATION PROGRAM DIRECTORS EDIT PROFILE RECOMMEND TO A COLLEAGUE

## VOLUME 4 – ISSUE 6: TRANSCRIPT

### Featured Cases: *Pseudomonas aeruginosa* Eradication

Our guest author is, Margaret Rosenfeld, MD, MPH, from the Seattle Children’s Hospital and University of Washington School of Medicine.

After participating in this activity, the participant will demonstrate the ability to:

- Discuss the rationale for *early Pseudomonas aeruginosa* eradication
- Identify the inhaled and oral antibiotics that have been compared in clinical trials for early *Pseudomonas* eradication
- Describe the potential adverse effects of early *Pseudomonas* eradication therapy.

This discussion, offered as a downloadable audio file and companion transcript, covers the important issues related to *Pseudomonas aeruginosa* eradication in the format of case-study scenarios for the clinical practice. This program is a follow up to Volume 4, Issue 5 *eCysticFibrosis Review Newsletter – Pseudomonas aeruginosa Eradication*.

The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

#### MEET THE AUTHOR



**Margaret Rosenfeld, MD, MPH**

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#### Unlabeled/Unapproved Uses

The author has indicated that she will discuss unlabeled/unapproved uses of inhaled tobramycin, inhaled colistin, and oral ciprofloxacin.

#### Guest Faculty Disclosure

Dr. Rosenfeld has indicated that she has received grants and or research support from Vertex, and has served as a consultant for Genentech.

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July 29, 2015

#### Next Month’s Topic

eCysticFibrosis Special Edition: Issue 1

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**LAUNCH DATE**

This program launched on February 28, 2013, and is published monthly; activities expire two years from the date of publication.

**STATEMENT OF NEED**

Based on a review of the current literature, including national and regional measures, detailed conversations with expert educators at Johns Hopkins, and a survey of potential program participants, this program will address the following core patient care gaps:

**Disease-Modifying Therapies**

- Clinicians may be unfamiliar with recently introduced disease-modifying therapies and how they are altering the therapeutic landscape for patients with cystic fibrosis.
- Clinicians may be uncertain how to integrate genotyping into therapeutic decisions and how to communicate with patients and families about the relationship between genotype and therapy

**Nutrition**

- Many clinicians lack strategies to persuade patients to adhere to CF nutritional requirements, resulting in low body weight and nutritional failure in patients with cystic fibrosis.
- Many clinicians remain uncertain how to optimize pancreatic function in patients with cystic fibrosis.

**Treating CF Patients with Inhaled Antibiotics**

- Clinicians lack knowledge about the use of existing and emerging inhaled ABX to treat chronic pulmonary infections.
- Clinicians need more information to make informed decisions about the use of inhaled ABX in combination.
- Clinicians lack information about best practices for scheduling ABX therapy to suppress chronic airway infections.
- Common clinician assumptions about treating pulmonary exacerbations lack supporting evidence.
- CF clinicians are not aware of and/or are not actively advocating inhaled ABX patient-adherence strategies.

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**MR. BOB BUSKER:** Welcome to this eCysticFibrosis Review podcast.

eCysticFibrosis Review is presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. This program is supported by educational grants from Aptalis Pharma, Inc; Gilead Sciences Inc.; and Vertex Pharmaceuticals.

Today's program is a companion piece to our eCysticFibrosis Review newsletter: *Pseudomonas aeruginosa* Eradication.

Our guest today is that issue's author, Dr. Margaret Rosenfeld, from the University of Washington School of Medicine.

This activity has been developed for pulmonologists, pediatric pulmonologists, gastroenterologists, pediatricians, infectious disease specialists, respiratory therapists, dietitians, nutritionists, pharmacists, nurses and nurse practitioners, physical therapists, and others involved in the care of patients with cystic fibrosis.

The Accreditation and Credit Designation Statements can be found at the end of this podcast. For additional information about accreditation, Hopkins policies, and expiration dates and to take the post-test to receive credit online, please go to our website newsletter archive, [www.eCysticFibrosisReview.org](http://www.eCysticFibrosisReview.org), and click the Volume 4, Issue 6 podcast link.

Learning objectives for this audio program are that after participating in this activity, participant will demonstrate the ability to:

- Discuss the rationale for early *Pseudomonas aeruginosa* eradication
- Identify the inhaled and oral antibiotics that have been compared in clinical trials for early *Pseudomonas eradication*
- Describe the potential adverse effects of early *Pseudomonas eradication* therapy.

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I'm Bob Busker, managing editor of eCysticFibrosis Review. On the phone we have with us Dr. Margaret Rosenfeld, Associate Director, Center for Clinical and Translational Research at the Seattle Children's Hospital and Professor in the Department of

Pediatrics at the University of Washington School of Medicine.

Dr. Rosenfeld has indicated that she has received grants and or research support from Vertex, and has served as a consultant for Genentech. She has also indicated that she will discuss unlabeled/unapproved uses of inhaled tobramycin, inhaled colistin, and oral ciprofloxacin.

Dr. Rosenfeld, welcome to this eCysticFibrosis Review Podcast.

**DR. MARGARET ROSENFELD:** Thank you very much, I'm very glad to be here.

**MR. BUSKER:** In your newsletter issue, doctor, you reviewed new research that addresses a situation many cystic fibrosis clinicians encounter. A patient presents with a new isolation of *Pseudomonas aeruginosa* from a respiratory culture, and the clinician needs to know what's the safest and most effective action to take. The findings from the clinical trials you reviewed provided a lot of important new information about early eradication therapies, and what I'd like to do today is discuss how some of that new knowledge can be translated into clinical practice. So if you would, Doctor Rosenfeld, start us out by describing a patient scenario.

**DR. ROSENFELD:** A two year old with cystic fibrosis has *Pseudomonas aeruginosa*, isolated from a routine throat swab for the first time. Parents report no change in cough or activity level. You recommend treating with a month of inhaled tobramycin but parents are skeptical and would like to further discuss the benefits and risks of this approach.

**MR. BUSKER:** Okay, a 2-year old patient, first time she shows a *Pseudomonas* infection. What's the rationale for treating new cases like this with antibiotics?

**DR. ROSENFELD:** Well, evidence over the last one to two decades has really lead to consensus pretty much around the world that treatment of early *Pseudomonas aeruginosa* infection with antibiotics to try to delay or prevent chronic *Pseudomonas* infection is really critical to improving the long-term outcomes of our CF patients.

First of all, chronic *Pseudomonas* infection has clearly been associated with poor outcomes in terms of survival, lung function, and other markers of morbidity and that's been seen in quite a few studies around the world. So what we really want to do is to delay or prevent chronic *Pseudomonas* infection, because once the infection is chronic it's virtually impossible to eradicate.

So we really see a window of opportunity to treat the early stages of infection when the *Pseudomonas* is typically very amenable to eradication therapy, and there are several reasons for this. First of all, it's present at a really low density as opposed to the unbelievably high concentrations that are seen later on in chronic infection. And second of all, it tends to be very antibiotic sensitive so easy to eradicate.

So there have been long-term studies, albeit not controlled studies, that have come out of particularly the Copenhagen clinic that have shown much improved outcomes when there has been adoption of a standardized early eradication protocol. So now really all the guidelines from the UKCSF, the Cystic Fibrosis Foundation, a European consensus group, all strongly recommend treatment of early *Pseudomonas* infection with antibiotics. So really the only question that remains is which antibiotic regimen is most effective, and that was discussed in great detail in the newsletter.

**MR. BUSKER:** In the patient that you presented — the parents are probably going to ask you: what's the likelihood that eradication therapy is going to be successful in their child?

**DR. ROSENFELD:** I think you could really reassure these parents that the likelihood of success is quite high in pretty much all the published studies, 80 to 90 percent of patients who had *Pseudomonas* isolated from a throat swab have negative cultures after treatment with a months of inhaled tobramycin.

So in general, if you're judging eradication as negative upper airway culture from a throat swab, then treatment with inhaled tobramycin is quite, quite effective. *Pseudomonas aeruginosa* does tend to recur over a period of time and that may be months or years, depending on the individual patient. In one study the median time to recurrence after initial eradication was 5 months, but that's very much at the lower end of the range in the different studies. For

example, in the ELITE trial discussed in the newsletter, the median time for recurrence after either 28 or 56 days of inhaled tobramycin was 26 months, and in my clinical experience I would say that's probably more what we see as well.

And then it would be important to explain to the parents that this approach would be used when *Pseudomonas aeruginosa* is isolated for a second time, as well. So in general each time *Pseudomonas* is isolated from respiratory culture then there is an attempt to eradicate it with anti-Pseudomonal antibiotics.

**MR. BUSKER:** Now let me get hypothetical here. Let's say that the parents are very resistant to initiating treatment, and together you reach the decision not to treat to eradicate this initial *Pseudomonas* infection. What outcome could be expected?

**DR. ROSENFELD:** So I think it's important to discuss what would happen if the decision is made not to treat and to be very honest about this. You know, it is hard to be sure in the short-term because it's been clearly shown in studies from our group and others that in Europe prior to automatically treating *Pseudomonas aeruginosa* when it's first isolated, that it can clear spontaneously. And in general, early *Pseudomonas* infection tends to be rather intermittent in nature.

However, over time the infection is definitely likely to become chronic and that's really what we're trying to avoid, and it's been shown clearly from quite a number of centers that early eradication regimens delay or even prevent this chronic infection.

**MR. BUSKER:** A hypothetical question now from a different angle. Let's say these parents are information savvy — they've gone on the internet, maybe they've read a blog — and they tell you they're skeptical that a throat swab doesn't really represent the true location of the *Pseudomonas* infection. How would you respond?

**DR. ROSENFELD:** I would respond that the parents have every reason to be skeptical here. A throat swab may not be representative of what's actually going on in the lower airway, and so just because we're looking at *Pseudomonas aeruginosa* isolated from a throat swab or even eradication of that *Pseudomonas aeruginosa* from a throat swab, it's hard to know how effective the treatment has been in the lower airway,

where, of course, the structural airway damage that we're trying to avoid could occur.

We did a study and others have done similar studies that directly compared the results of oropharyngeal cultures or throat swabs to the results of cultures obtained from the lower airway through bronchoalveolar lavage at the same time, and all these studies have shown that throat swabs have a pretty high negative predictive value but a low positive predictive value for the infection that is really going on in the lower airway.

So to put that in plain English, if *Pseudomonas aeruginosa* is not isolated from a throat swab it's unlikely to be present in the lower airway, but if it is isolated from a throat swab, it's a little bit of a crap shoot as to whether it's really in the lower airway.

However, we are concerned whenever we isolate *Pseudomonas aeruginosa*, even from a throat swab, that that is probably something we want to take seriously because lower airway infection probably does come from the upper airway. And so our thought is that if we can isolate it from the upper airway, we may prevent transmission to the lower airway.

**MR. BUSKER:** Bronchoalveolar lavage — would you consider that to confirm *Pseudomonas* in the lower airway?

**DR. ROSENFELD:** Many centers, particularly in Australia and Europe, will really only rely on bronchoalveolar lavage to document *Pseudomonas aeruginosa* infection. And there's a lot of merit to that, one just has to think about the risk/benefit ratio of doing a bronchoalveolar lavage procedure and that could certainly be discussed with these parents.

In general, there seems to be a move towards thinking that isolation of *Pseudomonas aeruginosa* from the upper airway in and of itself is a bad thing as it most likely does lead to increased risk of lower airway infection, so that statement is difficult to prove. So at least in the United States there is more and more of a reliance on upper airway cultures and decision to treat based on those cultures alone.

**MR. BUSKER:** Final question on this patient, and it's one I'm sure the parents are going to ask: what are the risks that might be associated with treatment with a month of inhaled tobramycin?

**DR. ROSENFELD:** So probably the biggest risks in all honesty is the burden of care associated with the treatment. The treatment takes 15 to 30 minutes twice a day, and then there is also the time needed to clean the nebulizer and to get the child settled and so forth.

In addition, as with any inhaled agent, there is a slight risk of a hoarse voice and any inhaled medication can cause cough, though that's not very common. Importantly, there are significant risks associated with long-term or even short-term use of intravenous tobramycin and other aminoglycosides, but when tobramycin is delivered via the inhaled route, the absorption into the system is very low. So the attendant risks of ototoxicity and nephrotoxicity are also very low.

Lastly, there is a risk of emergence of new organisms such as *Stenotrophomonas maltophilia* as was discussed in the newsletter, but the clinical significance of isolation of these new organisms is entirely unclear at this point.

So I think there are many parents that are skeptical about treating with medications in a patient who appears so healthy from the outside, and the key thing I think to convey to this family is that we really are trying to prevent the onset of chronic *Pseudomonas* infection. And that treatment with inhaled tobramycin or other anti-Pseudomonal antibiotics, though to be sure time consuming, is highly effective and with minimal risk.

**MR. BUSKER:** Thank you for first case and discussion, Doctor Rosenfeld. Let me ask you now to bring us another patient.

**DR. ROSENFELD:** A four year old with cystic fibrosis has *Pseudomonas aeruginosa* isolated from a routine throat swab. She previously had *Pseudomonas aeruginosa* isolated from a throat swab one year ago which was successfully treated with a month of inhaled tobramycin.

**MR. BUSKER:** So: a year ago a throat swab revealed *Pseudomonas*, it was eradicated, and now a throat swab indicates she has *Pseudomonas* again. The most appropriate treatment options in this case — what do the published clinical trials tell us?

**DR. ROSENFELD:** Options studied in published studies, and these are all discussed in the newsletter,

have included inhaled tobramycin for 28 or 56 days, adding oral ciprofloxacin to inhaled tobramycin, inhaled Colistin with oral ciprofloxacin for one month or three months, and then lastly, looking at a much more intensive regimen over a prolonged period of time in which tobramycin is administered one out of every 3 months regardless of the status of the culture during that time period, versus administration of tobramycin only at times during which *Pseudomonas* is isolated from a respiratory culture over an 18 month period.

Interestingly, although all these regimens were highly effective, none of the studies showed clear superiority of one regimen over another.

So I would say they're probably all relatively equally effective and in that case it's probably worth thinking about using the simplest regimen with the least potential associated costs, burden of care and toxicity, which would probably in my opinion be inhaled tobramycin therapy alone and just for 28 days.

I should also point out that all of these studies included patients who were having recurrent isolation of *Pseudomonas* as discussed in this case, not only patients who had the very first lifetime occurrence of *Pseudomonas*. And in most of these studies the success rate in terms of eradication were not significantly different between individuals who were having first ever isolation of *Pseudomonas* versus those who are having *Pseudomonas* isolated for the second time or an additional time.

So in summary, I would say that probably the therapy with the most rationale in this individual patient would be one month of inhaled tobramycin, potentially then following up with a throat culture about a week after completing the therapy and if still positive, considering treating with an additional month of inhaled tobramycin.

**MR. BUSKER:** In this four year old patient, would you expect that adding oral ciprofloxacin to the inhaled tobramycin would improve the likelihood of successful eradication?

**DR. ROSENFELD:** So based on the EPIC trial discussed in the newsletter, there is no evidence to suggest that adding oral ciprofloxacin would improve outcomes above and beyond those achieved by inhaled tobramycin alone. In addition, the ELITE

trial, also discussed in the newsletter, had really very high eradications using just inhaled tobramycin therapy without any adjunctive antibiotics. So no, I don't believe so.

**MR. BUSKER:** And treating with inhaled tobramycin for 28 days or 56 days — do you think the longer regimen is likely to improve the chances of successful eradication?

**DR. ROSENFELD:** So this question was specifically addressed by the ELITE trial discussed in the newsletter in which participants were randomized to receive either 28 or 56 days of inhaled tobramycin at early isolation of *Pseudomonas aeruginosa*. And that study showed very high eradication rates with either 28 or 56 days and no superiority of 56 days over 28 days. So I don't think that there is any a priori benefit of treating for 56 days over treating solely for 28 days.

However, our clinical practice is often to treat for 28 days, then repeat the oropharyngeal culture about a week off of antibiotics and if the culture is still positive then treat for an additional 28 days and that seems to work well.

**MR. BUSKER:** Now this patient — she's had two *Pseudomonas* infections within a year — would you consider her to have chronic infection?

**DR. ROSENFELD:** So, no, I would not consider this patient to have chronic infection at this point. There are varying definitions of chronic infection, the one that's most widely used is the Leeds criteria in which the definition of chronic is that more than half of the cultures obtained in a given year are positive for *Pseudomonas*, and she does not meet these criteria. And importantly for her, the likelihood of eradication of *Pseudomonas* at this point is still very high, about the same as the first go 'round. So the prognosis is not any worse for her at this point in time.

**MR. BUSKER:** Would you consider treating this patient with a different agent than what was used to treat her first infection?

**DR. ROSENFELD:** So no study to date has addressed the question as to whether recurrent isolation of *Pseudomonas aeruginosa* should be treated with a different regimen than initial *Pseudomonas* eradication. So we don't have data to suggest whether, for example, if this patient was initially treated with

inhaled tobramycin a different agent should be used. And I don't know that there is a way to really decide.

Perhaps if the time between the initial *Pseudomonas* isolation and the recurrence is short, one might think that the initial eradication was not completely successful and another agent should be chosen. However, if the time between initial isolation and subsequent recurrence is a longer period of time, say over a year, that returning to the initial regimen, say as inhaled tobramycin, would be likely to be effective again.

**MR. BUSKER:** So in this four year old with her second *Pseudomonas* infection, what would be your specific treatment recommendations?

**DR. ROSENFELD:** Well residing in the United States I would most likely recommend treating with one month of inhaled tobramycin, then rechecking an oropharyngeal culture about a week after treatment, and treating for a second month if the culture is still positive. Around the world others might consider using inhaled colistin and oral ciprofloxacin in a similar manner.

**MR. BUSKER:** Thank you, doctor. And we'll return, with Dr. Margaret Rosenfeld from the University of Washington School of Medicine, in a just moment.

**MS. MEGAN RAMSEY:** Hello my name is Meghan Ramsay, nurse practitioner and adult clinical coordinator for the Johns Hopkins Cystic Fibrosis Program at The Johns Hopkins University School of Medicine.

I am one of the program directors of eCysticFibrosis Review. These podcast programs will be provided on a regular basis to enable you to receive additional current, concise, peer-reviewed information through podcasting, a medium that is gaining wide acceptance throughout the medical community. In fact, today there are over 5,000 medical podcasts.

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**MR. BUSKER:** Welcome back to this eCysticFibrosis Review podcast. I'm Bob Busker, managing editor of the program. Our guest is Dr. Margaret Rosenfeld, from the Division of Pulmonary Medicine at Seattle Children's Hospital and the Department of Pediatrics at the University of Washington School of Medicine. And our topic is *Pseudomonas aeruginosa* eradication.

We've been looking at how some of the new information Dr. Rosenfeld reviewed in her newsletter issue can be applied in clinical practice. So to continue: let me ask you to bring us another patient, if you would, please, doctor.

**DR. ROSENFELD:** A five year old has *Stenotrophomonas maltophilia* isolated from a throat swab for the first time. He was treated with a month of inhaled tobramycin four months ago after *Pseudomonas aeruginosa* was isolated from a throat swab for the first time.

**MR. BUSKER:** *Stenotrophomonas* — why do you think this organism is emerging? Could it be a result of the treatment with the inhaled tobramycin?

**DR. ROSENFELD:** That is a very good question. In the trials that were reviewed in the newsletter there is some light shed on this question. First of all, in both the EPIC trial and the trial out of Italy run by Taccetti and colleagues, up to 20 percent of participants had *Stenotrophomonas maltophilia* isolated for the first time from respiratory culture after treatment with inhaled tobramycin or, in fact, other anti-Pseudomonas antibiotics.

Interestingly, this same phenomenon was not seen in the ELITE trial comparing 28 and 56 days of

inhaled tobramycin, also discussed in the newsletter. The Proesmans trial which was the last study discussed in the newsletter, didn't look for treatment emergent pathogens one way or the other, so that particular study doesn't add new insight. So what we're really left with is that there does seem to be a pattern of *Stenotrophomonas maltophilia* being isolated from respiratory cultures after treatment for early *Pseudomonas* infection, but that it's hard to hang your hat a direct cause of that relationship.

**MR. BUSKER:** What do we know about the clinical significance of this organism?

**DR. ROSENFELD:** It's really hard to know what the clinical significance of *Stenotrophomonas maltophilia* is. A number of studies have tried to evaluate this and have not been able to see a clear set of poor outcomes associated with acquisition of *Stenotrophomonas maltophilia*. However, it clearly is more antibiotic resistant than *Pseudomonas aeruginosa* and so may be more difficult to treat.

**MR. BUSKER:** Should we be treating this pathogen with antibiotics?

**DR. ROSENFELD:** Well I would say in the absence of symptoms there is no data to suggest that we should treat just because *Stenotrophomonas maltophilia* is isolated from a respiratory culture. Doing this could lead to emergence of yet another antibiotic resistant organism that is even harder to treat. However, if the patient is experiencing a pulmonary exacerbation, and this is the only organism isolated from a respiratory culture, then I definitely would recommend treating it.

**MR. BUSKER:** Let me ask you about respiratory cultures that show infection with MRSA. Could that be due to *Pseudomonas* eradication?

**DR. ROSENFELD:** That would be very unlikely as none of the published studies has reported a higher rate of MRSA after *Pseudomonas* eradication therapy, in sharp contrast to *Stenotrophomonas maltophilia*. But it may be that this patient has been treated with more antibiotics in general as their disease has progressed after *Pseudomonas* isolation since we know that isolation of *Pseudomonas* is associated with more severe lung disease in general. And so the isolation of MRSA is simply reflective of more intensive antibiotic treatment in general.

**MR. BUSKER:** Thank you for today's cases and discussion, Dr. Rosenfeld. I'd like to change gears now and ask you to look into the future for us, if you would. What do you see as the next steps in expanding clinical knowledge about early *Pseudomonas* eradication regimens?

**DR. ROSENFELD:** Well to be sure, I see that there are quite a few unanswered questions regarding early *Pseudomonas aeruginosa* regimens, and particularly in this era of newborn screening, we have a real opportunity to answer some of these questions.

First of all, I think it's important to have a better understanding of how to treat children in whom the initial eradication regimen is not successful. Should we use a different antibiotic, should we treat for longer, should we treat with intravenous antibiotics, that question has not yet been answered and is very important to get a better handle on.

It's a tough question to answer because the eradication success rates are so high that there aren't very many children at any one center who fail initial eradication regimens, and so this will definitely require multicenter collaboration to answer.

I think another important unanswered question is the role of intravenous antibiotics in early eradication regimens. That's been looked at a little bit by the group at University of North Carolina but still needs much more definitive evaluation and would be an important question to answer, and sort of ties in with the first question, because perhaps we would be most likely to use IV antibiotics in children who have failed initial eradication regimen with inhaled and/or oral antibiotics.

In addition, there are many new inhaled antibiotics that are either available now, such as inhaled aztreonam or coming down the pike and it will be important to study the role of these other inhaled antibiotics in the treatment of early *Pseudomonas* infection. And then lastly but very critically, what are the long-term outcomes associated with these eradication regimens, now that they are becoming much more standard of care are there long-term safety concerns that we're not aware of yet. And similarly, what are the long-term benefits of this treatment in terms of *Pseudomonas*, lung function and other efficacy endpoints.



So I think that all of these questions will be very important to answer in the future, and certainly there will be a lot more important clinical trials that will help us to elucidate some of these answers.

**MR. BUSKER:** Thank you for sharing your thoughts, doctor. To wrap things up, I'd like to summarize what we've discussed today in light of our learning objectives. So to begin: The rationale for early *Pseudomonas* eradication.

**DR. ROSENFELD:** We discussed that the rationale for early *Pseudomonas* eradication regimens is to avoid chronic *Pseudomonas* infection, which has clearly been associated with worse outcomes and worse survival in our cystic fibrosis patients. In early *Pseudomonas* infection, there is a real window of opportunity to treat because the early *Pseudomonas* isolates are typically present at very low density and are highly antibiotic sensitive.

**MR. BUSKER:** And our second learning objective: identifying the inhaled and oral antibiotics that have been compared in clinical trials for early *Pseudomonas* eradication.

**DR. ROSENFELD:** So in the second case we identified the inhaled and oral antibiotics that have been evaluated in published clinical trials that might be used for the treatment of a young child with new isolation of *Pseudomonas aeruginosa*. And we reviewed that those options include inhaled tobramycin, either for 28 days or 56 days, and either with or without oral ciprofloxacin, as well as inhaled Colistin and oral ciprofloxacin for one month or three months.

**MR. BUSKER:** And finally, the potential adverse effects of early *Pseudomonas* eradication therapy.

**DR. ROSENFELD:** In the third case we reviewed the emergence of *Stenotrophomonas maltophilia* as a potential adverse effect of early *Pseudomonas aeruginosa* eradication treatment regimens. And in addition, in the first case, we reviewed the potential risks associated with treatment with a month of inhaled tobramycin, which might include a hoarse voice, cough, and the burden of care associated with the treatment — in addition, of course, to potential emergence of *Stenotrophomonas maltophilia*, though the clinical significance of that organism is not at all clear.

**MR. BUSKER:** Dr. Margaret Rosenfeld — from the Division of Pulmonary Medicine at Seattle Children's Hospital and the Department of Pediatrics at the University of Washington School of Medicine — thank you for participating in this eCystic Fibrosis Review Podcast

**DR. ROSENFELD:** Thank you so much for giving me the opportunity to participate in the podcast, I've greatly enjoyed our conversation.

**MR. BUSKER:** This podcast is presented in conjunction with eCysticFibrosis Review, a peer-reviewed CME and CNE-accredited literature review emailed monthly to clinicians treating patients with cystic fibrosis. This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing.

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