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Key Diagnostic Barriers & Guideline Updates for Pneumonia

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You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This is a non-promotional, non-CME disease state educational podcast produced in partnership with the American College of Chest Physicians and is supported by bioMèrieux.

Here's your host, Dr. Randy Young. Dr. Young is physician who specializes in pulmonary and critical care medicine in Hummelstown Pennsylvania.

Dr. Young:
What are the current diagnostic challenges in treating pneumonia? And how can we best manage our patients with pneumonia? Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm your host, Dr. Randy Young, and joining me to answer these questions is Dr. Daniel Feinstein, a Physician Executive at Novant Health who specializes in Critical Care Medicine.

Dr. Feinstein, welcome to the program.

Dr. Feinstein:
Thank you so much, Dr. Young. Nice to be here.

Dr. Young:
Dr. Feinstein, let's begin if we can with an overview of current diagnostic challenges in pneumonia. Can you tell us t about the effect of using antibiotics?

Dr. Feinstein:
Sure, absolutely. I think anyone who works in this space recognizes that it's a difficult diagnosis to make and work through. We run into pulmonary edema and CHF and atelectasis, and mucus plugging and pleural effusions and all that put together. Sometimes there's pneumonia hiding in there, and sometimes there's not. I think that medicine is difficult. This kind of echoes that for sure.

I think we need to recognize that viral pneumonia is quite common, and probably about 80 percent of community-acquired pneumonia is viral. So we need to identify the cause, the etiology of the pneumonia, and determine if this is bacterial, or is this a viral pneumonia. Because obviously, the treatment modalities can be quite different in terms of, for example, treating a pneumonitis from a virus potentially with steroids as opposed to antibiotics.

I think another difficult area with diagnosis and challenges in pneumonia, is identifying those patients who have a viral pneumonia but also have a bacterial superinfection on top. I think that we need additional tools in our toolbox, and additional labs and history and imaging and all the traditional things we try to utilize.

So currently, the standards that we have for diagnostics are imaging sputum culture, maybe the associated blood culture for someone who's septic from pneumonia. We obviously need to pay close attention to where the patients come from. Is it nosocomial or community-acquired exposure? But a lot of these diagnostics are slow to result. And a lot of times as you know, Dr. Young, we end up with nondiagnostic testing. I think a good example of how this is so difficult is blood culture. So blood cultures for sepsis, for example, are patients we know have septic shock - everything about them is septic shock- 50 percent of the time, we actually have cultures that are positive. And maybe 20 percent of the time, do we even know the source? So that puts us in a predicament, as clinicians, where we end up providing empiric antibiotic use, prolonged courses, really without a clear end in sight and without clear endpoints and decision tools.

Dr. Young:

Thank you for that great overview, Dr. Feinstein. Can you elaborate a bit now on the CAP Guidelines, commenting especially on the use of procalcitonin testing in the setting of pneumonia?

Dr. Feinstein:
ATS and IDSA published the 2019 CAP Guidelines. And they sought out to basically answer 16 questions. And two of those questions pertain to procalcitonin and appropriate duration of antibiotics. They stated that they recommended empiric antibiotics for clinically and radiographically confirmed community-acquired pneumonia, and that antibiotics therapy should be considered to be provided regardless of the procalcitonin result and if the patient is unstable. This was one of the initial points. I don't think that anyone as a clinician is going to alter or should alter their providing of antibiotics in a patient who is unstable or that you have pretty high clinical and radiographic confirmation that this patient, in fact, has pneumonia.

Now, having said that, you can compare COPD, acute bronchitis, and community-acquired pneumonia, which I think, is a little bit more difficult. And if we look at the use of procalcitonin, that's the group that certainly still has a benefit in the use of procalcitonin for antibiotic stewardship, but it's lower than acute bronchitis and COPD.

The percentage of patients, in my mind, and you can comment on your practice, that actually have a clear-cut imaging confirmation I think is low. So I think the large majority of these patients, whether it's 80 or 90 percent, we don't have that clear-cut confirmation.

The next part that I want to comment in terms of CAP Guidelines, is the comment they made that the duration of antibiotic therapy can be reduced in patients with CAP with the use of procalcitonin-guided pathways. And so, I think that this speaks to the power of using PCT that are negative with a good clinical progress to discontinue and shorten durations of antibiotics. This speaks to the overexposure that we've seen over the last 20 years. We started out at 14 days of antibiotics, and then we say 10, and then it goes down to 7 or 8. And then it goes down to 5 in terms of guidelines. And this just shows you that we have an opportunity right in front of us to shorten durations without harm. And that, in my experience, is where PCT comes in. The trending adds a significant amount of confidence to discontinuation of antibiotics with a good clinical status.

We will always, of course, are going to combine our laboratory data with the patient's clinical status. And it increases the area under the curve in terms of accuracy and makes it safe. And that's what we've basically seen, I think in a lot of the data with PCT algorithms.

Dr. Young:
Thank you for those very insightful comments. For those of you who are just tuning in, you're listening to *Deep Breaths: Updates from CHEST* on ReachMD. My name is Dr. Randy Young, and I'm speaking with Dr. Daniel Feinstein about the management of patients with pneumonia.

Dr. Feinstein, could you discuss some of the current ways in which you utilize procalcitonin for the management of pneumonia?

Dr. Feinstein:
Yeah, absolutely, Dr. Young. So, I've been using PCT for direction with how to manage patients with CAP since 2010. And I like to utilize it to help us with a differential diagnosis between a bacterial pneumonia and a viral pneumonia, and also trying to detect those patients who have a viral pneumonia on respiratory panel testing, but have a superinfection of a bacterial pneumonia.

I have to keep in mind, of course, that a virus produces interferon gamma, which does block the production of procalcitonin. The studies looking at using this as a differential diagnostic tool are quite good, and some of them are as large as about 275 to 300 patients with very low false positives. I think that the level of the PCT matters. So if we have a concern that there is a potential false positive or a slight increase in procalcitonin, of one or two or three, I think that we can potentially have a discussion about that patient being falsely elevated. But those PCT values that are six and seven and eight and nine, I don't think there should be much of a concern that those would indicate a bacterial process.

Where it's always been at for me is antibiotic stewardship. Of course, antibiotic stewardship is so important nowadays to make sure we're responsible for antibiotic administration to reduce the duration of antibiotics that are not indicated. I like to use procalcitonin, of course, and combine it with the patient's clinical progress or lack of to help us make some good decisions in terms of antibiotic administration. It's a very difficult medicine sometimes, and we all get that. But if we're out there utilizing antibiotics and not correctly, this leads to increasing resistance patterns, of course antibiotic reactions and C. diff and other things that we have touched upon. I like to use procalcitonin for its negative predictive value

Dr. Young:
Dr. Feinstein, based on those remarks so far, could you provide a few personal examples of the success you've had using procalcitonin testing in your pneumonia management?

Dr. Feinstein:

Yeah, absolutely, Dr. Young. As I stated, I've been using this since 2010. Have become very confident and comfortable with the use of the negative predictive value of cases in the intensive care unit. We take care of patients commonly who have mono-viral infections, such as influenza, or other viruses either with or without mechanical ventilation. And the key in my practice has been, of course, to provide empiric antibiotics up front in the patient who is sick but to use procalcitonin in the ER as a baseline and to follow that trend for over up to 96 hours to see an 80 percent reduction or negative values with a good reasonable clinical status. And those are the opportunities that I've had with tremendous amount of success of discontinuation of antibiotics.

I think we'd be remiss if we didn't comment about COVID patients. Very difficult group of sick patients to take care of, in particular in the first two surges. These patients, up front, all got antibiotics because of how sick they were, which was the right thing to do. However, we really need to continue to try to find means such as the use of procalcitonin and trending patient's clinical status to discontinue antibiotics over time. And so, in my practice these patients would commonly get additional superinfection, antibacterial antibiotics, and then would trend PCT over time with even just a stable clinical status to discontinue antibiotics. I do my best to utilize CT findings and other imaging to try to support the discontinuation. But I think that we rightfully so, we're very aggressive with antibiotics in this patient group. We have to find a means to shorten the duration of these antibiotics in these patients. This is a patient group that can be very sick, but this is the importance of trending procalcitonin over time.

From my review of the literature of recent, the negative predictive value of procalcitonin in COVID patients is good and remains to be as good as those with other viral pneumonitis. It's the positive predictive value that has some concerns and therefore, I would be a little bit cautious with some elevations in PCTs, even those patient groups.

Then there's the kind of patients who have a positive predictive value use of procalcitonin. Those are the patients who are culture negative. They have lack of progress potentially, and so we're thinking about escalation of therapy. We're thinking about are we missing an organism? Are we missing a resistant organism? Is this a patient who has pneumonia and also a source control problem? And so in my practice, I've certainly utilized procalcitonin in those patient groups to nudge me along to escalate therapy potentially with more aggressive antibiotics for resistant patterns, or even push me to get that additional CAT scan to look for that pleural effusion, or loculation, based on lack of progress, and the potential of an elevated and arising procalcitonin, despite what we're doing for these patients.

Dr. Young:
Continuing along those lines, could you please continue to review some of the data associated with PCT and how we use it in our approach to pneumonia?

Dr. Feinstein:
The ProHOSP trial by Philipp Schuetz, I think was very impactful. That was published in *JAMA* in 2009. That is a trial that looked at procalcitonin utilization for lower respiratory tract infection, including community-acquired pneumonia. And that showed a robust 39 percent reduction in antibiotic exposure without harm.

There was a very interesting trial called the ProREAL trial by Albrich in *Archives of Internal Medicine*. They basically tried to mimic what real life looked like with using procalcitonin in clinics in Europe, where they also could send the bloodwork into the hospital, where they were connected to the hospital, and in emergency rooms and in the hospital. And it also showed a statistically significant reduction overall with the use of procalcitonin to the tune of about 1.5 days' reduction in antibiotic exposure.

One of the studies I want to bring up was the ProACT trial, which was from Huang. I think most of us probably reviewed that in the *New England Journal of Medicine* in 2018. And that was a trial that looked at about 14 hospitals in the United States, in the emergency rooms of using PCT to try to guide therapy one way or the other with antibiotics in the LRTI group, so community-acquired pneumonia, COPD, and bronchitis. And in that trial, it didn't show any difference in days of antibiotics. But if you look very closely at that trial, the clinicians in those 14 hospitals had minimal to no exposure or experience in the use of procalcitonin, and minimal education. And so, because of that, there was minimal compliance for the use of PCT on their patients. Sometimes about half the time. So from that, I think we learned that if we're going to be using algorithms for procalcitonin use, which we know does not cause harm, we need to have some experience associated with those institutions, and then education to push forward with compliance.

Dr. Young:
Those were very helpful. Do you have any thoughts on future directions in the use of PCT testing and where we might be in the next few years?

Dr. Feinstein:
Yeah, Dr. Young, as I mentioned briefly, I really think that it's time to take all the tools in our toolbox and try to come up with algorithms

to utilize many of the diagnostics that we have. So, in my mind, combining procalcitonin with clinical progress or lack of with a rapid multiplex PCR respiratory panel is basically where the future is.

One of my favorite patient groups, I smile when a patient is getting better, and they're doing reasonably well, their procalcitonin is negative, and I have a rapid multiplex PCR respiratory panel that is positive, let's say for a rhinovirus. That, to me, is a patient that gives us an opportunity for sure to discontinue antibiotics and shorten the duration of antibiotics that potentially is just not necessary.

Dr. Young:
Thank you. As our program comes to a close, Dr. Feinstein, do you have any final takeaway thoughts you might like to leave with our audience?

Dr. Feinstein:
I appreciate the time today, Dr. Young, and for having me. I think that we just continue to have challenges in the diagnosis of pneumonia, which in turn affects therapies and decisions, of course, with antibiotics and the concerns of harm from there. It just seems to me that we have more tools in our toolbox to guide more responsible behaviors with antibiotics. I think we need more data. But we have improvements and diagnostics that are going to continue to help us guide therapy in the right direction over the years to come.

Dr. Young:
With those key takeaways in mind, I want to thank my guest, Dr. Daniel Feinstein, for joining us today. Dr. Feinstein, it was great having you on the program. Thank you very much.

Dr. Feinstein:
Thank you, Dr. Young. It was a pleasure.

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