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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Latent TB Screening Strategies for High-Risk Patient Populations

Announcer:
This is ReachMD, and you're listening to *Tackling TB*, sponsored by Qiagen.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Approximately 1.7 billion individuals are latently infected with TB. Let's consider that figure, which represents about a quarter of the world's population. It is nothing short of staggering but knowing this alone doesn't address how we can advance efforts towards ending this global epidemic, one patient encounter at a time. So, let's get right to it.

This is Tackling TB, and I'm your host, Dr. Jennifer Caudle. Joining me to share the keys to recognizing and addressing at-risk patient populations with latent TB is Dr. Lee Reichman, former Professor of Medicine and Epidemiology at Rutgers University, and founding Executive Director of the Rutgers Global Tuberculosis Institute. Dr. Reichman, welcome to the program.

Dr. Reichman:
Thank you, Dr. Caudle. Thanks for having me.

Dr. Caudle:
So, Dr. Reichman, let's start with some level-setting for our audience. We know TB is both curable and preventable. And yet, it continues to be a major public health issue across the world. Why is there such a glaring discrepancy here?

Dr. Reichman:
Well, probably the main reason, at least looking at it from the point of view of the United States, who some would call a very developed country, is it's not sexy, and even though it's prevalent, people forget about it. It doesn't call attention to itself. So it's sort of there, infecting ten to fifteen million American people, who are all at some variable risk of getting active, infectious TB. But the usual family physician, or internist, doesn't think of it a lot, and thus actually, probably misses some cases.

Dr. Caudle:
Help us understand who the highest risk populations are for this infectious disease.

Dr. Reichman:
Well, the people who are at risk of TB are people who have been in contact with someone who has active, infectious TB, because as you said, TB is a communicable disease, and being communicable is based on the amount of time you spend with someone who has active TB. Now, getting infected with the tubercle bacilli just means you are added to the pool of ten to fifteen million Americans, or a quarter of the world's population, who are infected. Some of them are at high risk of becoming active and infectious, and those are the people we should be concerned about. People who are immunosuppressed, people who are taking immunosuppressive drugs, such as Infliximab, or something for psoriasis or rheumatoid arthritis. And people who have had TB in the past, don't know about it, but still harbor organisms so that they can break down with active TB.

Dr. Caudle:
Are there any clinical signs or symptoms that clinicians need to look out for? Or is the patient history our main guide to recognizing latent TB before it manifests into active disease?

Dr. Reichman:
I think the answer to that would be yes, yes, and yes. Sure there are clinical signs, but they're the clinical signs of respiratory illness,

even the same clinical signs that we now see with COVID-19 – fever, shortness of breath, cough. And, historical points are, "Do you know, or have you ever been close with someone who has had active tuberculosis in the past? Is there active tuberculosis in your family that you've forgotten about?" So, both of those things should rise the index of suspicion, so the practitioner does think, we have to do investigations, to see if this person is indeed infected with the tubercle bacillus.

Dr. Caudle:
And how does the entrance of COVID-19 factor into the equation? Does it complicate TB recognition efforts further, or is it sensitizing clinicians to screen high-risk patients faster?

Dr. Reichman:
I think both. It does complicate the diagnosis, because especially now, when it's so prevalent, it's the first thing that a primary care physician will think about. Someone comes in with fever, cough – he says, "Oh my God, this is probably COVID-19." Hopefully, he'd be able to get a test to see if this is indeed COVID-19. But before COVID-19, he would have thought of pneumonia, or even tuberculosis, and the presence of COVID-19 being prevalent in our society now doesn't mean he automatically should not think of other causes of fever, chills, shortness of breath, and he should do a test for tuberculosis infection. And the other thing, I think, that's very, very important is with the prevalence of COVID-19, so many health care workers are at risk of getting infected, and actually putting themselves in the line of getting infected, some might even be afraid to deal with people who have respiratory symptoms. But with PPE or personal protective equipment, this should not be a problem, and they should be able to examine the patient, spend time with the patient, and make the diagnosis. And I think the final issue there is in the past there was always a great stigma with tuberculosis, which is paradoxical, because tuberculosis is preventable and curable. Now, there probably is a stigma with COVID-19, and both of these factors make it difficult for the practitioner to deal with a patient.

Dr. Caudle:
For those of you who are just tuning in, this is Tackling TB on ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Lee Reichman, from the Rutgers Global Tuberculosis Institute, to bring us up to speed on risk-based screening strategies for tuberculosis.

So, Dr. Reichman, let's turn our attention to testing strategies. First, which diagnostic tools do we need to have at the ready? And are any approaches currently in use more or less helpful to the cause?

Dr. Reichman:
Well, as we mentioned before, tuberculosis is a two-stage disease. You have active, transmissible tuberculosis and that is largely diagnosed with first symptom screen, and then a physical examination, and then a chest X-ray. 'Cause a chest X-ray will show if there are enough organisms to be visible and suggest that this individual with the symptoms, such as cough and fever, is indeed infectious. But it's preventable and curable. And the best tool for screening to see if a person's infected is the Interferon-Gamma Release Assay. In the past, the test used for TB infection was the tuberculin skin test, which was injecting some antigen from tubercle bacillus under the skin, waiting 48 to 72 hours, and seeing if there was a bump on the skin. And that was effective, but sort of counterintuitive in a period of time when we're doing high-tech to make the diagnosis of TB infection depend on feeling a bump on the skin. So Interferon-Gamma Release Assays have been developed, and these are biochemical tests, which are done in the laboratory with a little bit of blood to do a venipuncture; you get the blood, you send it to the laboratory, and the laboratory is able to tell you if the individual is infected with the tubercle bacillis. So this is the most effective way of diagnosing TB infection.

Dr. Caudle:
What are some gaps or barriers we need to address when it comes to testing patients for TB, especially in high-risk populations?

Dr. Reichman:
Well, the first, of course, is index of suspicion. You're not gonna test for TB unless you think of it, and if you're thinking of other things, or forgetting that TB is prevalent in high-risk populations, and sometimes actually in low-risk populations, you're not gonna do the test. And if you don't think about it, you don't do it, and if you don't do it, you don't find the answer. So I think that's one of the most important gaps. And the other gap is lack of familiarity. The tuberculin test is a very familiar test. When we were medical students, we did it on all of our patients, and we learned to do it, hopefully pretty well, although research has shown it's usually not done very accurately. Then comes along the Interferon-Gamma Release Assay, which is much more sensitive, much more specific, and it's a one-visit test, and physicians don't think about doing this test or some of them don't know that it's available and therefore lose this opportunity to make the diagnosis of TB infection.

Dr. Caudle:
Now, even though our focus today is on improving recognition and detection, I'd also like to spend a moment on therapeutic considerations for latent TB, because clearly, getting faster and better at detection only gets us somewhere when we have something to

do next. So, what are those next steps, with a positive test?

Dr. Reichman:
Well, I'm really glad you asked that question, because there's no reason to do these tests for tuberculosis infection unless you're gonna do something about it. Now in the past, and I think some of your listeners might remember, if someone had a positive tuberculin test, they give 'em a year of Isoniazid. Now remember, these are individuals who feel well. They don't have any complaints, and they have to take a pill once a day for a year. And, we know that people don't take medicines well, and they certainly don't take medicines when they are feeling completely well. So we need better treatments for TB infection. And there's a lot of research that's been done, and we now have several new regimens which are highly effective, very short, and very well tolerated. And the one that the Centers for Disease Control highly recommends is the 3HP regimen, three months of rifapentine, which is like rifampin, but a long-acting rifampin, and Isoniazid, given once weekly, twelve doses. So with twelve doses of a highly effective, well tolerated regimen, the individual is no longer at risk of getting active tuberculosis. Now, we like to give our medicines with TB directly observed, to make sure the individual remembers to take them. But studies have shown that the three-month regimen taken once weekly, self-administered therapy, is almost as good as directly observed therapy. Now there are other regimens for people who can't tolerate Isoniazid, like four months of rifampin, taken daily, or one month of Isoniazid and rifapentine, taken daily. But the three months of once weekly Isoniazid/rifapentine is preferred by CDC, and is highly effective and well tolerated, and after your patient takes that regimen, you can kiss 'em goodbye – no follow-up is required, and they're not gonna get TB.

Dr. Caudle:
And before we wrap up, Dr. Reichman, are there any take-home messages you'd like to leave with our audience today regarding latent TB?

Dr. Reichman:
Latent TB is very prevalent. It's often forgotten, and when you're treating a patient who comes in with active tuberculosis, you think, gee, you had this symptom, that symptom, or an abnormal X-ray, or your contact to your grandfather, who had TB. Why didn't we treat you with the simple regimen to prevent this, and now we have to treat you with six months of four drugs, some of which are less well tolerated. That's totally unnecessary. So, prevention of tuberculosis goes a very long way in giving our patients the best care. And the second take-home message, I would think, is in this era of COVID-19 that everybody's thinking about, don't forget that there are other causes of those symptoms, and think TB.

Dr. Caudle:
Well, Dr. Reichman, with that thought in mind, I'd really like to thank you for joining me to update how we can better recognize and address latent TB in practice. It was great having you on the program.

Dr. Reichman:
Thank you very much for having me.

Announcer:
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