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### TB Testing in Turmoil: A Look at Care Gaps During the COVID-19 Pandemic

Dr. Doghramji:

The fight against the COVID-19 pandemic diverted many healthcare worker's attention away from other diseases in an attempt to combat this devastating disease. But did this shift provide gaps in care for some of our other airborne diseases, such as tuberculosis? This is *Tackling TB* on ReachMD, sponsored by QIAGEN. I'm Dr. Paul Doghramji. Joining me to review the impact COVID-19 has had on TB testing is Dr. Jeffrey Starke, an Infection Control Officer at Texas Children's Hospital and a Professor of Pediatric Infectious Disease Medicine at Baylor College of Medicine. Dr. Starke, thanks for being here, today.

Dr. Starke:

My pleasure. Thank you for asking me.

Dr. Doghramji:

So, Dr. Starke, zeroing in on tuberculosis testing across our healthcare facilities, can you tell us what changes you observed amid the COVID-19 pandemic?

Dr. Starke:

Well, there've been a lot of changes in a couple different ways and most of them not good, to be perfectly honestly. The number of reported cases of tuberculosis in the United States dropped precipitously in the last year. None of us believe, and the models tell us, that that's not a real decrease, that the real problem is that people with tuberculosis were not coming in to be appropriately diagnosed. And we're really afraid that we're gonna see a surge of cases in the next year or two. I'm a pediatrician and we're particularly worried about this for children because so many of our children with tuberculosis are picked up through contact tracings, which have really been delayed or in some cases, not occurring at all.

The other thing that's happened is that in many health departments in particular, the resources that were previously devoted to tuberculosis have been diverted to go into efforts to control COVID. Remember that one of the main activities of tuberculosis control is contact tracing. And of course, now everybody is used to the phrase 'contact tracing' in regards to COVID. Well for most health departments the expertise in contract tracing was within the tuberculosis program. And so in virtually every jurisdiction I know of the tuberculosis people have been poached, if you will, into the COVID area and the tuberculosis has gone relatively neglected; it just wasn't seen as important.

There was an incident, I remember in my clinic, we were seeing a child with tuberculosis and there was a mother who was coughing, and the staff was very, very concerned about the mother having COVID and when they were told, 'Oh, don't worry, the mom only has tuberculosis,' everybody sort of relaxed. And I think that just kind of typifies what our attitudes have been about COVID and about tuberculosis.

So we know that contact tracing for TB has suffered. We know that there's been some misdiagnoses; we also know that COVID and TB can coexist, and they seem to make each other worse actually. And we also know that some adults with tuberculosis have been misdiagnosed as having COVID or they had acute COVID but what was missed was their underlying tuberculosis. So there's a lot of different ways that the COVID pandemic has affected TB. And unfortunately, most of them in a negative fashion.

Dr. Doghramji:

Wow, very interesting. Now what is the ideal TB testing protocol for both employees and in patients in healthcare facilities?

Dr. Starke:

Well I don't think there is just one ideal testing protocol. And and for one reason, it depends on what's going on in your community and/or

the population that you serve. If you're in a referral hospital, for instance, that serves a lot of patients who come from other areas of the world where there's more tuberculosis, well then the issues may be a little bit different than if you have mostly a local or colloquial hospital that's in a low prevalence area.

OSHA still wants us to be testing and protecting healthcare workers and we should be doing that. In some high-prevalence areas, testing is still going on every year. But in many other areas, it's going on every two years or every three years. It is still recommended that there be periodic testing of some periodicity and that hospitals, clinics, other facilities look very strongly at their results to determine what they should do going forward.

Dr. Doghramji:

Very interesting and very helpful. Can you speak about the importance of investing in TB testing for both employees and patients? Is it safe to say that turning resources away from tuberculosis to fight against COVID-19 will not work?

Dr. Starke:

Well it was inevitable that resources were gonna be turned away from TB for COVID, so that's already happened. What's gonna be critical is that those resources are returned. And one of the things we're concerned about is, boy there's a lot of burnout among healthcare workers, including in public health departments. And that's what determines what goes on in the community. And you can't divorce what goes on in the healthcare facilities from what's actually going on in the community, as well. So it'll be really important to pay attention to tuberculosis-related resources.

We are still seeing tuberculosis. I have some fear actually that we've had tuberculosis in healthcare facilities that has gone undiagnosed, which means there may have been some exposures that weren't known about. And when we do some, it will be very interesting when we look at the next round of routine infection control-related testing for employees to look at the numbers and see whether we are seeing any increased rates of infection among hospital employees. It'll be very important to do that locally in one's own facility and community. But it will be very important for the states and CDC to look at that information as well to see if we have created a little bit more danger related to TB in hospitals inadvertently because of COVID.

Dr. Doghramji:

For those just tuning in, you're listening to *Tackling TB* on ReachMD. I'm Dr. Paul Doghramji and today I'm speaking with Dr. Jeffrey Starke about the impact of the COVID-19 pandemic on TB testing.

So Dr. Starke, why is it so vital for healthcare systems to get back to on-board testing for TB and has a decreased amount of TB testing during the pandemic led to an increase in TB cases and deaths?

Dr. Starke:

Well I'll answer the second part first. As we said just a little while ago, the number of cases that have been reported has actually gone down but nobody believes that that's true. And the reason it's gone down is because we've taken away the resources in the community in particular that are designed to find TB cases. And particularly find them when they're less severe before they're even sick enough to come into the hospital, frankly. I also think that the sort of attention of people has been diverted away from TB toward COVID, so when a patient comes in with signs and symptoms that could be either COVID or TB, because they can overlap, everybody's just focused on COVID. So a lot of us are very concerned. Certainly, there have been misdiagnoses in the community and probably also some misdiagnoses that have occurred within healthcare facilities as well.

It's gonna be critical that we get back on-board, and I would argue if anything, we need to be even better than we were before COVID because we probably have a backlog of people who need to be identified and appropriately tested and then appropriately treated. I think the next year in tuberculosis is gonna be really, really interesting.

And by the way, I have to say this as well, these problems are incredibly magnified throughout the world and particularly in places that have really high burdens of tuberculosis. I mean, we have 9,000 cases a year in the United States, which is hardly trivial, but many, many countries, of course, have hundreds of thousands and even millions of cases, if you consider places like China. And they are being ravaged by COVID right now, which means that their tuberculosis control programs are also being ravaged in terms of personnel and time and resources. So, again, I think when people come to use from other countries, tuberculosis is gonna be if anything a more important issue than it's been even in the past and we're gonna have to pay attention to that.

Dr. Doghramji:

And could you comment on using the interferon gamma release assay, or IGRA, as a baseline test if the healthcare system is not testing annually?

Dr. Starke:

Well, our thinking about testing for tuberculosis infection has really, really changed over the last decade. One of my colleagues wrote a commentary piece recently in the pediatric literature, in essence stating it's time to retire the tuberculin skin test. And I have to admit that I'm in that camp, as well. The TB skin test has been a wonderful test that's really been important for tuberculosis control in the United States.

And when tuberculosis was more prevalent than it was now, test sensitivity was the major driving issue. And the tuberculin skin test is pretty good for that. But the problem now is, especially as we're expanding some testing, test specificity also becomes important and there are so many false positive results with the tuberculin skin test due either to previous BCG vaccination or to exposure to non-tuberculosis microbacteria in the environment. And that's where the IGRAs really have a huge advantage because they do not cross-react with BCG vaccines and they do not cross-react with most of the non-tuberculosis microbacteria in the environment, including the microbacterium avium complex, which is the major one throughout the United States.

To be sure there are some false-positive results with the IGRAs, there tend to be very low-level positives that are transient and when the test is repeated normally those go away. Within healthcare settings, there has been the concepts of what's called conversion and reversion. If you're testing many, many, many healthcare workers in a facilities, you'll have a small number that will suddenly test positive and you don't know why, but they test positive with very low numbers. And that's called conversion. But if you do nothing with those folks, don't treat them or anything else, and then you retest them, the vast majority tend to revert, in other words, they turn back to having a negative test. That little bump in the positive IGRA could be due to lots of things, maybe allergies, non-specific immunologic reactivity and so forth. But the truth is that especially for large populations of healthcare workers in a low prevalence area like the United States, the performance characteristics of the two IGRAs really are better than the performance characteristics of the tuberculin skin test.

The major criticism has been cost. But I don't think people look at cost the right way. Tuberculin skin testing is fairly inexpensive if you count only the actual tuberculin that needs to be used, the syringes and so forth. But the real cost of tuberculin skin testing, there's two. Number one is time, because people have to go back and have the test read and it's a lot of time from employees to be off work or away from their duties. The other thing is false-positives are expensive because those workers have to be worked up and evaluated and then there may be concern about whether they potentially have disease or not and could be contagious and so forth. We don't want false-positive results in healthcare workers. The IGRAs are more expensive in terms of the purchasing price, the actual cost of the test, but when you take into effect time, any you take into effect the rates of false-positive tests, then they become actually quite cost-beneficial. I think what most places are doing now is an amalgam of having availability of both IGRAs and tuberculin skin testing. It's particularly important to be doing the IGRAs when you have healthcare workers who've received a BCG vaccination. And as we know, we have many, many folks who work in health facilities in the United States who were born in other countries and received a BCG vaccine and they are many of them are really at risk for having false-positive TB skin tests. And that creates all kinds of anxiety and so forth. So really in that population in particular, we're better off using IGRAs than tuberculin skin test.

So the bottom line is, both tests, skin tests and IGRAs, are potentially useful, but I think for the vast majority of people, probably the IGRAs, have many, many advantages and are being used increasingly within healthcare facilities all throughout the United States.

Dr. Doghramji:

Lastly, Dr. Starke, I want to open up the floor to you. Do you have any take-aways that you'd like to leave with our listeners?

Dr. Starke:

Yeah, I do have a few takeaways. I mean, number one is TB continues to be a major public health problem in the United States. Again, right around 9,000 cases pre-COVID. If it were 9,000 cases of some other important infection, people would be all up in arms about it. But because it's tuberculosis and it's been around for so long, people tend to not pay as much attention to it as they did.

We're also starting to see tuberculosis under very different circumstances. We have probably somewhere between 13 and 15 million people in the United States who have tuberculosis infection or what's also called 'latent tuberculosis infection,' many of whom have gone untreated. And they are at risk of developing tuberculosis in the future.

We have tens of millions of patients now in the country that are immuno-compromised and many of them are immuno-compromised, not only by underlying conditions, but also by medications, whether it's steroids or biological response modifiers, immunomodulators, and so forth. And as we use those drugs more and more, if we're not extremely careful about screening those patients for tuberculosis infection and frankly, we are gonna run into a fair number of tuberculosis cases completely preventable cases in that population.

So tuberculosis is not gonna go away. And until we do a better job of controlling it throughout the world, we are gonna continue to see tuberculosis in the United States. And we've been diverted a little bit by COVID here, the world has been tremendously diverted by COVID in terms of tuberculosis, and we've gotta get back on the beam or we're gonna have a little, mini explosion of tuberculosis in

many areas of the United States.

Dr. Doghramji:

Well thank you, Dr. Starke for providing us with an in-depth understanding of TB testing amid this pandemic. As we slowly open up and return to normal, this information will definitely be helpful for our listeners.

I want to thank my guest, Dr. Jeffrey Starke, for speaking with me about the impact that the COVID-19 pandemic has had on TB testing in our healthcare facilities. Dr. Starke, it was great having you on the program.

Dr. Starke:

Thank you very much for having me.

Dr. Doghramji:

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