Advanced Concepts in Pediatric TB: Infection Control

Welcome. Today we present Advanced Concepts in Pediatric TB: Infection Control, Source Case and Contact Investigation.

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Dr. Alvarez, I turn it over to you now.

Thank you, Karen.

Let's go ahead and start. First, I want to review the objectives. My hope is that at the end of this session, the participants will be able to compare contagiousness of children of different ages with pulmonary TB, and apply this to planning investigations; discuss the importance and indications of source case investigations; plan evaluation for contacts of patients with various forms of TB disease; and discuss infection control guidelines for a child hospitalized with TB disease.

I usually try to incorporate cases, so we will start with this. I want to give you this from the beginning. All of the cases that we're going to discuss today are real cases; these things really happened. Before the case, I want to review some key terms that we're going to be talking about in this session.

Case is a particular patient with TB disease, and all TB cases are reportable.

Contact is someone who has been exposed to tuberculosis by sharing air space with a person that has infectious TB. This is also known as an exposed person.

Index case is the first case or the first patient who comes to the attention of the medical community as an indicator of a potential public health problem.

And a source case is the case or person who was the original source of the infection for secondary cases or contacts. This person, the source case, can be the index case; but it's not always the index case.

So let's jump to a review of the case.

The index case is a two-year-old African American male, who presented to the emergency room with an eight-day history of fever and cough. He was evaluated there and diagnosed with pneumonia; and he was prescribed amoxicillin, as usual. After five days, his fever was not getting better; so he was brought back to the emergency room, and it was decided to admit him to the hospital for IV antibiotics. He was started on ceftriaxone, and he continued to have fever; so vancomycin was added, and he continued to have fever. His past medical history was not significant for really anything.

His family and social history was significant; he was living with the mother and two older siblings. He had attended a daycare center since he was seven months. He had no history of travel or contact with adults with HIV, IV drug users, homeless, or incarcerated individuals.

On physical exam, they couldn't find anything except for a fever of 41 degrees Celsius. And this is his initial chest x-ray that was taken in that year. So you can see that this x-ray is not normal. This is what caught the attention of the physicians and the radiologists, and this was read as a possible opacification in the right middle lobe. It was described by the radiologist as a round pneumonia, which is typically seen

with pneumococcal pneumonia. So that's why he was started on IV antibiotics, thinking that this was a bacterial pneumonia.

However, after seven days of pretty broad-spectrum IV antibiotics, he continued to have fevers; and that's when they called an infectious disease consult. When we evaluated him, we recommended to do a CAT scan to figure out what exactly what was going on. The concern at that point was if there was maybe a congenital anomaly there or a foreign body or something different than the suspicion for bacterial pneumonia.

The CT scan was performed, and I'm just showing you one part here that shows there were significant highlighting polyneuropathies on the right side, and one of the lymph nodes was so big that it was compressing the right main bronchus. So based on this, we decided to evaluate him and expand the differential diagnosis.

So a TST was placed, and it was read as 10 millimeters of induration. We also recommended gastric aspirates. They were sent times three. He was started on INH, rifampin, and pyrazinamide; and the fever resolved after three days of starting therapy. He was discharged home to continue medications under a DOT. His gastric aspirates finally were negative, all of them.

This is a case – a two-year-old African American male with a clinical case of pulmonary TB. The question is: What would you do next?

I would like for you to answer this question before we proceed. The options are: obtain a biopsy of hilar lymph nodes to confirm TB; since the patient is responding to anti-TB medications, you need to complete the six months of therapy; plan and conduct a contact investigation; or plan and conduct a source-case investigation.

I will give you a few seconds if you will enter your answers.

[Pause for responses]

I can see that most of the people are agreeing with the fourth option, which is plan and conduct a source-case investigation.

Emily, you can close this and we'll continue.

And I agree with you; that would be the next thing to do.

Let's talk about source-case investigations. These kinds of investigations are different from contact investigations. In the source-case investigation, we are looking for the person who transmitted the TB to the child or the patient. We know that TB in children less than five years of age indicates a recent transmission. And young children usually do not transmit TB to others. So the source-case is usually an adult or an adolescent caregiver.

A source-case investigation should be considered for all children less than five years, but especially if they're less than two years of age, that have TB because we know that usually kids under two years of age, when they develop TB disease, usually occur within the first six months of exposure – six months to a year. So we have a pretty good indication that they were exposed to somebody with contagious TB during that period of time.

Source-case investigations are important for public health and also as a diagnostic measure. For public health, we try to identify the individual who infected the child but that, understandably, is also transmitting TB to others. So it's an infectious person that doesn't know the diagnosis and is spreading it. But the diagnostic value of a source-case investigation is that when we identify a person, and he's a pretty good link to the index case or to the child, then obtaining sputum from that source case usually has a better yield than obtaining gastric aspirates from the children. So if we can isolate the organism from the source

case, we can assume that the child has the same organism; and we will have susceptibilities of the organism.

I usually get asked questions about source-case investigations for children with latent tuberculosis infection. We know from experience that it's not very productive and it's not very cost-efficient. So when deciding to do source-case investigations for LTBI, you need to consider if really it's worth doing it. And it's only recommended for children less than two years of age who have LTBI, and if the data is monitored to determine the value of the investigation.

The procedures for the source-case investigation are pretty similar to the standard contact investigation, and I will go through that in a few minutes. But the source-case investigation needs to especially focus on patients or associates who have symptoms of TB disease, and should begin with the closest associates and expand only if you can't find the source case in the closest contacts of that patient.

Going back to our case, a source-case investigation was conducted. All in the household were tested, and they were negative; so the investigation was expanded to the daycare. I told you that he had been in daycare since he was seven months old. At the daycare, we identified three of the staff that had a positive TST but negative chest x-ray.

However, a month later, one of the workers from the daycare, who had been tested initially and had a negative TST, had a history of chronic cough. And then she was eventually diagnosed with pulmonary TB that was cavitary and smear positive. So this was the source case.

So the question is: What do we do next?

The next step really is a contact investigation. It's important to notice the difference between source-case investigation and contact investigation. And notice that for the two-year-old who was diagnosed with pulmonary TB, we conducted a source-case investigation; we did not conduct a contact investigation. However, now that we have an adult with infectious TB, we decided to conduct a contact investigation; so the strategy is a little different.

Contact investigations are important because it's a prevention strategy. On average, 10 contacts are identified for each person with infectious TB in the U.S. Of the contacts, usually 20% to 30% have LTBI. So if you think about 10 contacts, you'd think two or three people would have LTBI; and one person will have TB disease. And of the patients that develop disease, approximately half of them develop it in the first year after the exposure.

Contact investigations are useful because they help us find and treat additional TB cases, potentially interrupting future transmission of TB. It also allows us to find persons that have actually developed latent tuberculosis infection and treat them so that we avert future cases of TB.

Contact investigations are particularly important in pediatrics. In the United States, we divide up how we discover the cases in pediatrics; and they are discovered either actively or passively. Actively means via contact investigation or screening of high-risk groups, and passive means that the patients who develop symptoms are evaluated for symptoms. Depending on the literature that you review and the articles that you review -- there are several publications on this – up to 25% to 80% of the children with TB are identified in contact investigations. So this highlights the importance, especially for pediatrics.

The contact investigations are conducted by the Health Department, but it's important to realize that these are very difficult and complicated activities. It requires many independent decisions and time-consuming interventions. So in deciding when to conduct a contact investigation, a lot of factors ought to be taken into account. The Public Health officials should decide if the contact investigation is necessary based on the case, and the contacts should be assigned priorities. And they should be evaluated according to their priorities.

The factors that predict the transmission or likely transmission of TB -- which is what the Health Department takes into account when deciding when to conduct a contact investigation -- the factors are the anatomical site of the disease; the positivity of the sputum; radiographic findings, such as cavitation; behaviors or procedures that increase aerosolization of respiratory secretions; age; HIV status; and administration of effective treatment.

The characteristics of the index case that are associated with an increased risk of transmission include pulmonary, laryngeal, or pleural TB. I want to stop here and say that pleural TB, even though sometimes we don't see infiltrates in the lung, the recommendation is to include it in the same category as pulmonary TB when deciding to do contact investigations or not. The other factors are: sputums are positive on AFB smear; cavitation on chest x-ray; adolescent and adult patients; and if no treatment or ineffective treatment is in place.

Once the decision is made to conduct a contact investigation, the Health Department goes into this process of determining what the infectious period is so that they can identify which contacts they need to test. In determining this, they take into consideration the approximate dates of the symptoms, the result esophagus the smears, and the extent of the disease. In general, it is recommended to start the infectious period three months before the diagnosis of TB. Sometimes the infectious period is started a lot earlier, and this is in cases where the patient clearly has a history of having symptoms, especially cough, for longer periods of time.

Once the infectious period is decided, then there is a list of contacts that are prioritized according to certain characteristics. The priority of the contact is decided based on the characteristic of the index or the source patient; the characteristics of the contacts that have been exposed, including especially the age, the immune status, and other medical conditions that predispose them to develop TB disease; and also according to the type of exposure they have.

I'm not going to go into detail on this, but in this table you see an example of how our contacts are classified according to priorities. And so the high priorities and the medium priorities are the contacts that should be evaluated first. I want to bring to your attention that patients who are less than five years of age, just because they are at high risk of developing TB disease, are considered high-risk and high priority; also patients that have medical conditions, like HIV; and contacts in a congregate setting.

So we'll go back to our case. As I said, after the worker was identified, a contact investigation was conducted. Fifty-two children were identified as being exposed within the previous three months. They were identified, and all of them were tested – had a review of systems, physical exam, TST, and a chest x-ray.

Twenty-four children had a positive TST; and of these, five additional children were diagnosed with pulmonary TB, and one patient had pulmonary and meningitis. Eighteen children had latent tuberculosis infection. Twenty-eight children had negative TST and x-rays, and they were started on window prophylaxis if they were less than five years of age. All of them were retested after 10 weeks of the exposure; and in the re-test, two more children were detected as positive.

This case really highlights the importance of daycare settings, and they are definitely a high priority for contact investigation. This is because the children who attend daycare are usually less than five years of age, which means that they are at higher risk of developing TB disease and more severe disease. They have prolonged exposure, since most of them spend the whole day in the daycare center. And because they are infants and toddlers, they are usually in close contact. Depending on the size of the daycare center, there could be crowding and poor ventilation. And all of these create the perfect environment for the perfect storm.

If you compare the slide that I showed you before – the averages for the general population contact investigation – as I said, usually 10 contacts are identified; we identified 52 exposed children. Usually 2 to 3 out of 10, or 20% to 30% of the contacts, have LTBI; we had almost 40% of the children had LTBI. But more importantly, in general, usually you find 1% of the contacts have TB disease; and half of them

develop it during the first year after the exposure. We actually had 12% of the children that were exposed developed TB disease, and all of them developed it within the first six months after exposure. So I just want to make sure to highlight the importance of doing a contact investigation when there is TB in a daycare setting.

Once we decide who needs to be evaluated, the next thing to discuss is what evaluations we do on the contacts. So unless they have a history of having a previous positive TST or IGRA or have had TB and been treated, then you should do this: a TST or an IGRA. If a TST is used, the induration that is used to call a positive is 5 millimeters or more in any contact. If the TST or the IGRA is negative, then we should repeat the test in 8 to 10 weeks; this is what we call the "window period." And this is 8 to 10 weeks after the last exposure -- not after the last test, but after the last exposure. If the second test is positive after the initial negative, then the contact is classified as recently infected; and this means that this person is at higher risk for developing TB disease.

All of the contacts that have positive TST or IGRA, or if they report any symptoms consistent with TB even if they don't have a positive IGRA, need to have a complete history and physical; a chest x-ray; and other tests as indicated, depending on what symptoms they have.

I do want to give an explanation about the window period prophylaxis. This is not done routinely on all of the contacts; but it is decided taking into consideration the frequency, duration, and intensity of the exposure and the risk factors for TB disease among the contacts, especially the age and the medical conditions that predispose them to develop TB disease if they get infected.

Based on this, the way we manage contacts that are younger than five years of age is the following. It's a little bit different than contacts that are older or have no risk factors. When children less than five years are identified as contacts, they should all have an evaluation that should include a TST, a chest x-ray, and review of symptoms and physical exam – all of them – all of that evaluation.

If all of that is negative, then we start them on window prophylaxis, which is really a primary prophylaxis. They are started on INH, and then they have a repeat TST placed 8 to 10 weeks after their last exposure. If the repeat TST is negative, you can stop the INH. And I have to say also, if they didn't develop any symptoms. If the repeat TST is positive and they have not developed any symptoms, then they continue the INH to complete nine months of treatment for latent tuberculosis infection. If at any time during the window period the patient develops symptoms – fever, cough, or anything that is suspicious for TB – they should be reevaluated and investigated again for possibility of active disease.

Prophylactic treatment is a little bit different, and this is obviously prophylactic because you have to exclude that TB disease. But this is recommended for persons that have a high risk and in which you cannot really exclude LTBI because it's hard to interpret the IGRA or the TST. That includes persons with HIV, persons taking immunosuppressive therapy for organ transplant, and persons taking anti-tumor necrosis factor alpha agents. Because in these patients, the interpretation of the TST or the IGRA is questionable because they may be allergic and unable to respond, and they have a very high risk of developing TB disease, then these contacts should actually receive nine months of INH, assuming that they did get the infection.

So in these patients, we do the TST and the Interferon-Gamma Release Assays; and if they are positive, then we know for sure. But even if their TST and IGRA and their chest x-rays are negative, they are started on INH and treated for nine months, so they don't have a repeat TST done.

I call this the story that never ends. So going back to our case, seven months later – you can imagine how active we were during those seven months – but when we were thinking that we were out of the woods, a high school student with no risk factors was diagnosed with pulmonary TB. He had cavitary and smear-positive pulmonary TB.

So the question is: Where did he get it from, and how is this related to the daycare center?

Well, he was the grandson of a friend of the worker, and he had had occasional contact with her, with the source case, before his diagnosis. However, he had not been identified as a contact in the previous investigation. And we know that he got it from her because we were able to isolate MTB, and he was genotypically identical to the source case. So this is an example of what happens when we miss somebody during the contact investigation, especially persons that are at high risk, like adolescents are.

So because he had cavitary and smear-positive TB and he was a teenager, a contact investigation was conducted at the high school. Initially, there were 197 contacts identified; this is based on students that shared the same classroom or teammates and bus riders with this teenager.

In the first round of testing, 8% of the students were positive by TST; and when they had the repeat test done 8 to 10 weeks later, we found another 18 students with LTBI. So that's 17%. And because this is a large number of conversions on the second round of TST, we expanded the contact investigation; and an additional 206 contacts were investigated. And the ratio of TST at that point was 4%; so we identified another eight patients. And we stopped there. All of the contacts that were identified as converters, TST, had negative x-rays; and basically none of them had TB disease.

So when do we determine to expand a contact investigation? We basically need to take into consideration the extent of the recent transmission. So if there is an unexpectedly large rate of infection or TB disease in the high-priority contacts, if there is evidence of a second-generation transmission, if there is TB disease in any of the contacts who are not a high-risk or medium priority, if there is infection in any contacts that are less than five years of age, and if there is a high degree of conversion in the repeat TST or IGRA testing.

And the story never ends; it keeps going and going and going. So one month later, a seven-month old male, cousin of the high school student, was diagnosed with pulmonary TB. This is true. All of the stories are true; I'm not making these up. This patient, this seven-month old baby had been identified as a contact and had been evaluated by his primary care provider. He had a TST that was negative, and he was asymptomatic; so no further intervention was done. No chest x-ray was done; and basically, they said he was negative and that's it.

A month later, he presented with fever, wheezing, and a productive cough. And his chest x-ray showed a right hilar adenopathy and right upper lobe infiltrate. We did gastric aspirates on him, and they were positive by smear and by culture.

And the story keeps going and going and going and going. This baby had attended a small child care center. I'm truly not making this up. Because the baby had extensive disease, had significant cough, and his smear was positive on the gastric aspirate, and frankly because by this time there was lot of anxiety among the public and the community because of the previous daycare and then the teenager and the high school, we decided to conduct a contact investigation in the child care center. We identified four workers and eight infants, and all of their evaluations were negative. So there was no transmission of TB in the second day care center.

So why not do contact investigations in young children? And this is why I put that up as an example. We just need to go back to remember the transmission, how the transmission occurred. We need to remember that it's an airborne infection. So in order to acquire the infection, the contact would have to inhale the droplet nuclei produced by an adult or an adolescent that had pulmonary or laryngeal TB. And the infectiousness correlates with the number of organisms expelled.

So we don't usually conduct contact investigations usually in young children because they have very low yield. Most children with TB are not contagious -- I'm talking about young children – because compared to adults, they are less likely to have a productive cough; they are less likely to generate force to aerosolize an organism; and they usually do not have large numbers of organisms.

The other thing to remember is that children that have extrapulmonary TB are not infectious unless the disease is in the larynx or they have open abscesses or lesions.

So when do you consider a contact investigation in children? Even though the transmission from children is rare, it can occur in certain circumstances. And that includes when the children have what we call "adult-type disease." That means that they have extensive upper lobe disease and cavitation. Also, when there are procedures that create aerosolization of the bacilli. So children that have to undergo bronchoscopy or induced sputums without the necessary precautions should undergo contact investigation.

So let's say a child is admitted and gets a bronchoscopy, and there is no suspicion for TB; so no precautions are taken at the time of the bronchoscopy. Then a contact investigation should occur there to see if there was any transmission because there were not enough isolation precautions.

And I want to clarify here that gastric aspirates are not associated with transmission. So they're not considered high risk procedures for aerosolization on the bacilli.

Let's talk a little bit about infection control. I am not going to discuss all of the recommendations because there are too many, and there could be a whole lecture on this. The guidelines are published by the CDC about how to prevent transmission in healthcare settings; so I'm not going to talk about that. I'm just going to touch quickly on the general principles of this.

The fundamentals of infection control include administrative controls, environmental controls, and respiratory protection.

Fundamental controls of infection include administrative controls. These are things that we do to reduce the risk of exposure via an effective infection control program. The infection control program is supposed to assign the responsibility of the facility; conduct annual risk assessment of the facility; institute an infection control plan to identify TB suspects, isolate them, evaluate them, and treat them; ensure that a facility has the recommended laboratory services; and that the healthcare workers and the patients and visitors are educated, trained, and counseled about TB.

The environmental controls prevent the spread and reduce the concentration of the droplet nuclei. And these include primary controls and secondary controls. Primary controls are usually the ventilation issues and the use of AII rooms. Secondary controls include HEPA filters and ultraviolet germicidal irradiation.

Characteristics of AII rooms are: single-patient rooms with a private bathroom; negative pressure relative to the hallway; all the air is sent outdoors or HEPA filters; and the exchanges are six or more air changes per hour; and the visitors to the patients in those rooms should wear N95 respirators.

There are respiratory protection controls to further decrease the risk of exposure in special areas or circumstances. These consist of using personal protective equipment in areas with increased risk of exposure. So this equipment should be used by persons entering the rooms of patients that have suspected or confirmed TB, and wherever there are procedures that can produce cough or aerosolized organisms. The protective equipment includes N95 respirators, and these need to be fitted because there are different sizes and features. And so each person that works in a healthcare center that has any risk of TB should have a fitting process for the N95 respirators. These are worn by the healthcare workers, not by the patients.

The patients wear a surgical mask, and the purpose of this is to stop the droplet nuclei from being spread, exhaled by the patient. These should not be worn by the healthcare worker.

So in deciding infection control in a hospital, you need to take into account risk factors for infectiousness: the presence of a productive cough; the presence of cavitation or extensive upper lobe disease; positive AFB in the sputum or involvement of the larynx; failure to cover the mouth or nose with cough; and the presence of procedures that generate aerosols that could contain the bacilli.

Based on those risks, adult patients that are admitted to the hospital with TB or suspected TB should have airborne infection isolation. That means that they should be placed in negative pressure rooms, what we call the AII rooms; and all of the healthcare workers and the visitors entering the room should wear N95 masks. And the isolation is discontinued if it's a suspect case when another diagnosis is found that can explain the symptoms and exclude TB, or if three negative AFB sputum smears are negative.

If there is confirmed TB, the isolation can be discontinued when there is effective therapy and clinical improvement and three negative smears.

The isolation of patients that are children – it's a little bit different. And I want to make a point, stop here a little bit to explain this a little bit more. Like I said before, children with TB, if they're less than 10 years of age, are rarely infectious. Nosocomial transmission in pediatric settings is extremely rare. However, adults that are accompanying the children into the hospital may be the source case, and they could potentially be infectious. So the emphasis on infection control when children less than 10 are admitted to the hospital should be in the adults, not as much in the kids.

So the general recommendation is to isolate the children until their infectiousness is excluded, but also until the adults that are accompanying the patients have been evaluated and infectiousness is excluded from them. A chest x-ray is a critical component of the evaluation. And until that evaluation is complete, we should limit the visitation, or visitors should wear masks not only the room – actually, they don't need to wear masks in the room if they are parents or people that have already been living with the patient. But they should wear masks in the common areas of the hospital until they are cleared that they are not infectious.

And this is not something that is done routinely. Some hospitals do – whenever there was a survey to see how many of the children's hospitals do this, this survey is old; and at that time, only 42% of the hospitals were actually evaluating adults accompanying children with suspected TB that were admitted to the hospital.

In 2002, Dr. Starke and his group published a study that they did at the Children's Hospital in Texas, where they actually screened adults that were caretakers of children admitted with suspicion of TB. And actually the adults had to be screened prior to the admission; the chest x-ray was part of the screening. And if there was any delay in evaluating the adults, then they put the kids in airborne isolation.

But if the children were young and did not have any of the high-risk categories, like cavitation or laryngeal TB or any procedures that could aerosolize the bacilli, they were actually not isolated. As long as the kid was considered not infectious or contagious and the adults accompanying the kids were not contagious, they decided not to do airborne isolation on them. So when they look at their study period, they were 59 children that were identified as admitted with suspected TB; and once they applied their criteria, only 8 children required isolation. And they screened 105 adults and actually found 15% of them had abnormal chest x-rays compatible with TB, and they did not know that they had it.

So this study really brings up and highlights the importance of actually having a process to screen adults who are accompanying children when they get admitted in our hospitals for suspicion of TB. And just to highlight the fact that children rarely transmit disease. In this particular study, they also looked at if there was a conversion rate that changed in regard to before the study period and during their study period to see if there were more healthcare workers that converted TST; and their rate did not change.

They even went ahead and tried to see if any of the healthcare workers had converted in TST. They evaluated if any of them had been in touch or had contact with these kids that were admitted, and none of them had. All of the healthcare workers that had positive TST did not have contact with these particular children. So in their study period, which took several years, they did not find any conversion associated with the pediatric case. So again, it's just to highlight the importance of placing emphasis more on the adults than on the actual kids.

The next section that I want to review is something that I get a lot of questions about, and it is usually when there is a baby – newborns – that have mothers that have some TB of different stages. If the mother has LTBI, meaning the mother has a reactive TST or IGRA and a normal x-ray and is asymptomatic – so no cough or fever or anything suggestive of TB – then no separation is necessary. The mother should be treated for LTBI; so the mother should be referred to the Health Department to be treated for LTBI after the initial postpartum period.

The newborns need no further evaluation. But it's recommended that other household members should be evaluated for TB infection or disease. However, we should not hold the babies from discharge waiting for the household evaluation. But it should be strongly recommended. And these mothers can breastfeed their infants without any hesitation.

The next case scenario is if the mother has suspected TB. This is a mother that has clinical signs and symptoms or an abnormal chest x-ray consistent with TB disease. So in this case, the mother should be evaluated as soon as possible; and we recommend to separate the mother from the infant until the evaluation is complete. If TB is suspected or confirmed, we recommend to separate them until the mother is receiving adequate therapy, and she wears a mask and understands and is willing to follow infection-control measures.

So if the mother, let's say, is suspected to have or confirmed to have TB, then she needs to be on treatment, wear a mask, and understand the infection control measures; and at that point, you can reunite them. The mother can breastfeed the infant after two weeks of adequate treatment, if she is then at that point considered not contagious.

If the mother has TB disease, then we need to evaluate the infant, the baby, for congenital TB. And that includes chest x-rays, TST – actually, we recommend to do TST on the babies even if they're a newborn. This can be hard to interpret, so you can interpret a positive but you cannot interpret a negative. They have chest x-ray; sometimes they have evaluation, LP, and all that. In general, if the congenital TB is excluded, then we begin INH on the baby and then repeat the TST when the baby is three to four months old. If the repeat TST is negative, we can discontinue the INH. If the TST is positive, we'll reevaluate for TB disease; and if there is no disease, then we complete nine months of INH therapy as LTBI.

Once the baby is evaluated and start on INH, separation is no longer necessary unless there is a suspicion for MDR TB. So if the mother has disease and there is a suspicion for MDR TB or proven MDR TB – so, basically, once the mother has the diagnosis of TB disease, then the next question is: Could this be MDR TB?

And of course for that, you have to remember the risk factors for MDR TB: They're foreign-born, coming from countries where MDR is more prevalent than in the United States. Is there a history of previous treatment for TB and now has active disease? Those are things that you need to consider. And if there is any suspicion that it could be MDR, then we recommend to separate the mother and the infant until the mother is considered no longer contagious.

If they cannot be separated – so they have to be together for social reasons, there's nobody to keep the baby, those kinds of things – then strong consideration should be given to give BCG vaccination to the infant if there is no risk for HIV and, as I said, the separation is not possible. This is one of the few indications for BCG vaccine in the United States.

Now, if the mother has an abnormal chest x-ray but on evaluation has no evidence of TB disease, then separation is not necessary. The mother should still receive treatment for LTBI, and the recommendation should be to investigate the household; but the baby does not need any further evaluation.

So prevention of transmission in the community – in child care, as we said, children that attend daycare are usually not contagious, even if they have TB; so they can continue attending. But it's important to identify a source case because then if their source case is a worker from the daycare center, other

children need to be evaluated. And remember that a child with TB is not contagious unless they have adult-type disease.

In the school setting, it's a little bit different. Children that are diagnosed with TB can attend school if they are receiving appropriate therapy. And if they have adult-type disease, then they need to be proven not contagious or have adequate treatment for at least two weeks and have three negative smears. Any children that have adult-type disease that have attended school, then a contact investigation should be done in the school setting.

Just to finish, I want to summarize the take-home messages. The diagnosis of TB in a child is a sentinel event representing recent transmission of TB in the community. A source-case investigation should be considered when a young child is diagnosed with TB. We start with the household, but it can be expanded to non-family caregivers, like grandparents or older nannies or daycares.

Contact investigations are an essential component of TB prevention. Daycares represent a high priority for contact investigation. Young children are rarely contagious, but the source case is; so that's again importance of source-case identification and the importance of using window prophylaxis in young children.

I list here the main references that I used, and you will have it in your handout. And now we'll open the panel for questions.

Thank you.

Hello, this is Connie Haley Can you hear me?

Yes.

I want to thank you so much for that wonderful, wonderful discussion. As always, it was very clear and had so many good points in terms of some questions that I get a lot when I take calls from community providers that fill out the health permit. If you're ready, I'd like to ask you some questions that have been posed through our question line.

Sure.

One of them is going back more specifically to your patient that you described during the presentation. And the question was asking about the high school contact. How many of those 48 high school contacts completed LTBI treatment? Do you know that information?

I don't know the exact number, but I know that most of them did. I was involved in that investigation, and we followed them pretty closely; and so most of them did. I can't guarantee that all of them did, but it was a pretty high rate of completion.

And maybe just a quick follow-up to that to talk a little bit about ways that you might help improve treatment completion among high school students who are sometimes difficult to get ahold of and are busy. Could you just talk briefly about how to facilitate completion in a pediatric setting?

Yes, we are actually right now in Jacksonville going through this. This case that I'm describing here was many years ago. But last year, we had a case of pretty contagious TB in a high school. And we're still in the process of evaluating all of the students. And many of them also have LTBI. So what we decided to do this time around, which is different from what we did several years ago, is actually treat them – instead of doing INH for nine months, we decided to do rifampin for four months. And that's because shorter duration is more likely for them to complete.

We see them every month. We see them in the clinic every month and try to assure that they take their medication. And so we're still in that process, so I can't tell you the success rate of that; but at least we feel like we have a better control over that making it shorter.

Yes, thank you. There were a few more questions regarding a similar topic. Regarding the contacts that are less than five years old, someone has asked: If you repeat the skin test and it's positive, but the patient is asymptomatic, do you then recommend a chest x-ray?

No, basically if they started treatment – the window prophylaxis – and they remain asymptomatic, if they convert, we don't repeat the x-ray or do anything else, just continue the therapy basically to complete nine months. So only if they become symptomatic or, for example, in one particular case, there was a kid that was identified kind of late. So we had a little bit of doubt if we had started the window prophylaxis early enough. So that kid actually ended up getting a repeat chest x-ray, and it was negative; but we were just not sure if we had started the window prophylaxis early enough.

One point in here to remember is that when these kids are identified, they need to be evaluated soon. And by "soon," we're talking about like the same week or so. We also have another case where there was a delay in the evaluation; and by the time we saw the kid, he had developed miliary TB. We knew he was a contact; it's just that there was a delay in the evaluation. So when these kids less than five years are identified as contacts, they need to be evaluated promptly – like within that same week.

Great, okay, another question that we've received: In a situation of daycare with so many young children, say you have a number of initial positive tests, do you ever consider putting all the children on window prophylaxis regardless of the age, even children who might be above the age of five?

No, I mean we did put all of the children less than five on the prophylaxis; and most of them in the daycare were young. There were like, I'm thinking, maybe two or three kids that were a little bit older, and they were not in the daycare the whole time. They were just going there after school, and so their time in the daycare was less; and they were a little older. But we did do TSTs on them and repeated the TSTs. But because they were older, we did not put them on window prophylaxis, and none of them developed TB disease.

So you really took it case by case, patient by patient, even though there's a high rate of transmission in that setting?

Right, right.

Okay, another question is really good; it's about the hospital infection control topic. And that is: What is the procedure of getting visitors in N95 masks without prior evaluation and fit testing? How is that handled?

Well, that depends on the hospital actually; each hospital has its own policies/procedures for infection control. In the study that I described that they did in Children's Hospital in Texas, the Infection Control program actually paid for the chest x-rays of all the adults. And these efforts were done at any time; some of them were done at the Health Department, some of them were done actually in the hospital, and some of them were actually read overnight because they wanted to rule out disease pretty early, so they were pretty aggressive on that. But I'm sure that not all hospitals are willing to pay for x-rays for all the adults.

So what we do here is we assess symptoms of the parents or any adults accompanying the kids and ask them if they have been tested for TB before or any risk factors for TB, that kind of thing. And we ask them to go to the Health Department the following day, and we evaluate it there. We don't evaluate them in the hospital. But if there is anybody that has any potential symptoms related to TB, we ask them either not to come to the hospital, or we do ask them to wear a mask in between – like from the entrance to the room. When they're in the room with the kid, they don't need to wear a mask because of course they've been living together; so there's no point in isolating them then.

But as I said, sometimes that is tricky. And that's why I wanted to highlight that because I think that more children in hospitals need to be aware of that and try to include some of these recommendations into their policies.

Okay.

One of these questions is talking about if you have a mother who has confirmed tuberculosis and is given standard therapy with rifampin, INH, pyrazinamide, and ethambutol, the question is actually: Is the rifampin safe in breastfeeding? But perhaps you can go ahead and talk about the safety of all four medications in breastfeeding, and then also whether or not the baby would require any kind of supplementation with Vitamin B6 or a polyglycine-type thing.

That's a very good question, and we get asked that too. In general, a couple of the drugs are secreted in the breast milk; but the concentration of the drug in the breast milk is very, very low, so it's not considered a contraindication to breastfeeding and it's not considered to be in a concentration that could potentially be toxic to the baby. So it's not a contraindication.

So the mom can be on the four drugs and can still breastfeed. And because the concentration in the breast milk is so low, nobody should feel that the baby is getting medicine through the breast milk and that we'll protect them because it's too low to be protected for the baby. For example, these babies that go home with the moms that are on TB treatment are started on INH on their own. So besides what they get in the breast milk, they actually are started on their own dose of INH. And for these babies, we do recommend to do Vitamin B6 on those babies too – the ones that are on INH.

Could you tell us what this would be for the Vitamin B6? Is it based on weight? Is there enough in a standard vitamin?

Yes, it is based on weight; but I don't have the actual dose handy. Usually, I have to look it up.

Okay, we can maybe send that information out later.

Yes.

Another question, someone was asking if rifampin therapy is used in young children. The question is asking: Is the rifampin therapy six months instead of four when you're talking about LTBI, and what would be the age cutoff for using the six months over the four months? At what point could a child be able to take the standard four months of rifampin therapy for LTBI?

Yes, that's a good question also – all of the questions are good. We use, basically, puberty instead of age. So basically, post pubertal adolescence, we use the four months; and if they're pre pubertal, we do six months of the rifampin.

Great, the question about BCG in the newborn, since that's not used in our country for most situations I think many of us would like more information on. Someone was actually asking about physiology and pharmacokinetics. I'm not sure it's fair to ask you that question; answer it if you can. But maybe you could talk a little bit about practical aspects of BCG in this situation, if you have a child with exposed indurate TB and there's not an appropriate LTBI prophylaxis you can get, how hard is it to get it in a typical hospital setting? How old should the child be to get it? Are there any other details like that you could talk about how that would work?

Yes, I don't know all the pharmacokinetics. But BCG, in the countries with a high prevalence of TB, is given at birth. So obviously, they can get it at any time; so that's not an issue. That's approved at birth basically. And how easy it is to get it, I don't know personally because to tell you the truth, after being here for so many years and doing TB for a long time, I've never had to use it. As a matter of fact, the only time I had to separate a mother from the baby was because there was a high index of suspicion for MDR; but we were able to find a place for the baby with another family member that was living separate; and we

were keeping the mom separated until she was considered not contagious. So we did not have to give BCG.

Basically, you only give BCG if there is a suspicion for MDR and you cannot separate them. So if there a suspicion for MDR but you can find another placement for the baby until the mom is on effective treatment, then that's the way to go. But if you cannot separate them before that, then basically do BCG. And I think you can get it through the CDC, if I'm not mistaken. It's not like the hospitals all have it; usually the hospitals don't have it or the clinics don't have it but can get it I think it's through the CDC, but I can do a little bit of finding out the exact details if somebody wants to know.

And I think it's important to just reiterate that the BCG is not going to necessarily prevent them from infection or treat them, but it may help to avoid disseminated more severe forms of TB if the baby does acquire tuberculosis.

Exactly, so those kids that get BCG are not completely out of the woods; but at least we offer them the protection from serious illness when they're a baby.

And also to remind the families that these skin tests will no longer be an accurate test in that young child because of its cross reactivity with BCG vaccine.

Well, if they get BCG, then we cannot TST to rule out infection on the baby; but if a baby gets BCG, after we say about maybe four or five years, then you can interpret the TST regardless of BCG vaccination.

Great, I'm going to ask one more question kind of combining a few that I see here. There are a few more questions about window period prophylaxis. Could you maybe summarize again the appropriateness of window prophylaxis, particularly for patients with HIV, and when you will be willing to use it – what situations you would use it in?

Okay, so window prophylaxis basically you have to rule out disease first of all. So those patients in your county that are in window prophylaxis are the high-risk patients, either because of age – so the very young – and then our patients that have conditions that predispose them to develop TB disease – so HIV, but also like all of the list of medical conditions: immunosuppressant therapies, and certain types of cancer, diabetes, all of those.

So the ones that have the very severe immunosuppressant conditions – so HIV, the transplant patients, and the ones with tumor necrosis, alpha antagonists – those three, it is thought the result of the IGRA or the TST are a little bit questionable. In HIV, I'd say depending on their CD4 count; if their CD4 count is really good and they've been on therapy for a long time, you can interpret the TST or the IGRA. But if they are immunosuppressed, then you don't know if the IGRA or the TST is negative because of the immunosuppression. So in those, you don't really even do window prophylaxis; you treat them anyway. You assume that they potentially got infected; and because you cannot rule it out, you treat them for nine months or six months or four months of rifampin, depending on their age. But you don't repeat the TST.

The other conditions – less than five years of age – and the other conditions that increase the risk but are not the severe immunosuppression, those you do window prophylaxis after you rule out disease. So those patients need to have TSTs and x-rays and full evaluations before you put them on INH as window prophylaxis. And then they get a repeat either IGRA or TST 8 to 10 weeks after their last exposure to the case. And then if that test is negative, then you can stop the INH or the rifampin. Is that clear?

Thank you so much; that was an excellent summary of that.

Thank you again for a fabulous presentation. It was so clear, and we really appreciate all those extra points and addressing questions.

And I'll just remind you that Ana also can be reached through our NCD hotline: 1-800-4TB-INFO. So if you have questions regarding specific investigations of pediatric patients, you can also reach Ana or one

of her colleagues through our region. And I believe the other regions also have a pediatric consultant. But I know Ana would be very glad to help you with specific questions in the future.