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Pediatric TB for the Private Provider #4

Treatment and Control of Pediatric TB

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This transcription is from the question and answer session which immediately followed the original presentation and is best read within that context. Only minor edits have been made to facilitate learning and understanding.

1 – When can you reliably discontinue window period prophylaxis in an infant who is less than 6 months of age?

A child can progress from infection to disease in a matter of weeks. The window period is the time from exposure to the time a reactive TST will be produced if infected. During this time if a child has been exposed, and they have a negative TST we are not sure if they are truly uninfected. The younger they are, the more likely they will progress to active disease so we put them on INH until we can be assured that they don't actually have LTBI.

If a child is less than 6 months of age the skin test will probably be negative because they have some degree of anergy. I take these situations on a case by case basis. I recommend that you treat them as you would another child for window prophylaxis.

Regarding the second TST, sometimes we will wait more than the 8 weeks which is recommended by CDC. The previously recommended time to repeat a TST was 12 weeks. In an infant there may be a better chance of having a reliable TST if the repeat test is delayed 12 weeks until they are a little older. We know from studies, and I know from experience, that infants this young with LTBI or TB can certainly have a reactive TST, so doing the test and repeating it 8-12 weeks after exposure is useful even in this age group.

If that second TST is negative, and we've made sure that the index case is no longer contagious, I feel comfortable stopping the window prophylaxis. If I suspect that the exposure was significant, and I can not personally examine the infant, I may request another chest x-ray just to reassure myself. Most of the time you can rely on the TST result if that's all you have. Hopefully, in the future with the QuantiFERON® test, we will have an answer. As long as that child is being followed periodically, and most children are during their first year of life, I think you are pretty safe stopping the INH.

2 – In a daycare or school, where a child has TB, the adults who were with that child should be evaluated. If they are negative, do the other children need to be screened for TB?

The question is, "A child who has TB is in a daycare setting or a school setting; once we've excluded disease in those communal settings then is it okay to stop looking for other cases?" I will separate the school setting form the daycare.

In the daycare setting, children are normally young and in general will have hilar adenopathy and not have a contagious form of TB. They should not have spread TB to the other children. If you ask the right questions, and do the TST and you still do not find a case of contagious TB, it is not required that you skin test the rest of the daycare (the children). If you screen all of the daycare workers with a TST and you don't ask for symptoms you may miss someone with active TB.

Once you have a child with TB on therapy for a couple of weeks, he/she can return to daycare. At this point, further source case investigation begins. The most likely culprit is, of course, in that child's environment, the household environment.

Now, I will add a caveat to that. Sometimes it is not necessarily science or experience or evidence-based guidelines that guide this process (source case investigation). It's more anxiety. Everyone who has worked with tuberculosis has had to deal with situations where anxiety, liability issues or parental concerns drove the investigation. In certain situations, the children at the daycare are investigated with a TST to address these anxieties. It is not wrong to request such an investigation if there is any question of potential transmission from the child with disease or an unknown source case.

School situations are a little bit different. If it is a young child we use the same rules as the daycare. However, adolescents can have cavitary disease or extensive pulmonary disease. They are very good at coughing and they are also very good at not covering their mouths. If they are old enough to cough or old enough to have extensive disease then I would investigate the classroom for possible transmission. I typically use 10 as an arbitrary age for contagiousness. The household should be tested also. Again, when anxiety and other parental issues exist a health department may have to investigate the entire school.

3 – Do you recommend doing source case investigations for children who have LTBI?

That is a very good question and has been addressed fairly recently by the CDC. The conclusion that the CDC has come to is that if a child actually has infection, we know that some adult in their environment has infected the child. It is as sentinel an event as a case of disease because that child got the infection from an adult in his environment. It is important to look, at least briefly, for who the source might be.

But, in terms of resources the CDC has decided that we do not have to do an exhaustive source case investigation for children with LTBI. Most health departments are deciding how to interpret that. In North Carolina, if a child is extremely young, say 2, and has LTBI we may want to look for the source case. If they are older, if you have looked in the household you don't need to go any further. The CDC recommends that you don't spend any TB resources on looking for source cases of children who have LTBI.

4 – If you have a child who is on window prophylaxis, and later you find that they have progressed to active disease, is there a concern for drug resistance?

The short answer is yes. If a child has been placed on window prophylaxis they should always have had a chest x-ray first. I point this out to all the pediatric residents I work with. If you have a child who has been exposed to TB and you test them during the course of a contact investigation, and their TST is

nonreactive you must always do a CXR before putting them on INH for window prophylaxis. The skin test may be negative but it could be a false negative and the last thing you want to do is put a child with disease on just one drug, especially if they have extensive disease. You always want to get that chest x-ray on a child before initiating window prophylaxis.

If you have a negative TST and a chest x-ray that is normal you can begin them on window prophylaxis. You then repeat the TST. If it is reactive you will do a CXR again. Ninety to 95% of children, who have been compliant with INH, are not going to develop disease. However, we all know how difficult it is to assure that children are taking their medicine. If they end up with a reactive TST and an abnormal CXR, or a negative TST and symptoms of disease, this is when you will suspect resistance. However, it's never as clear cut as this.

If you have a child who has a source case identified and you know the organism, you don't have to culture for the child's organism and you don't have to admit them for gastric aspirates. In a situation where you may suspect resistance, you will have to evaluate the child further (with gastric aspirates or sputum). If they are old enough, have them produce sputum, or do a bronchoscopy or whatever is indicated. At the very least, if you suspect resistance, I would make an attempt at isolating the organism. If you get the organism and you find out that it is INH resistant then you know what you are dealing with. If it is not drug resistant then you now have a drug that you can use. If you couldn't get an organism, and you know that the source case was fully susceptible and now you would assume that the child is INH resistant, you may start therapy with Rifampin, Ethambutol and PZA.

5 – How much elevation of liver enzymes can be tolerated in babies who are taking INH during window prophylaxis?

Elevation of liver enzymes is not that uncommon. We know from old studies that they may have some viral infections going on and, that the elevation may not just be the INH. In general, 10% of adults can go up to 5 times normal. I use 4 times normal in babies as the point that I would definitely stop the INH. Twice normal I would tolerate if they were asymptomatic. I would make them aware of signs and symptoms of toxicity. I would ask them to call about any development of symptomatology. Twice normal I would tolerate, 3 times normal I would start to get worried, and 4 times normal I would stop treatment.

These are not guidelines that you will find in the CDC guidelines. If a child becomes symptomatic at any time then I would certainly stop. The important thing is to be vigilant in terms of follow-up. Instead of seeing that patient once a month you may see them more frequently and repeat their liver enzymes every 2-4 weeks.

6 – When should the second skin test be repeated in a contact investigation? Is it wrong to wait 12 weeks considering the new CDC guidelines say 8 weeks is enough?

It's not wrong. As we discussed earlier, sometimes I do wait 12 weeks because it gives a young infant another month to grow and make sure that they are not going to be anergic.

We have known for years that the delayed hypersensitivity to make a reactive TST can take up to 12 weeks. If you look at some of the older literature it actually only took 8 weeks which is why CDC has improvised their guidelines. It allows for 4 weeks less of exposure to INH. Twelve weeks is not wrong

and the truth is no one is exactly on an 8 week schedule. By the time you get them in the second test is pushed to 9-10 weeks. I do occasionally use 12 weeks; 8 weeks just makes it a little bit easier for the patient and it may improve adherence for the patient. It also makes it easier on the health department to not have to monitor the patient for that extra month. You always worry about toxicity of INH if taken too long. In children that risk is so low that I wouldn't worry about that aspect of it if they are otherwise doing well.

It is also important to remember that their window period is determined by their last exposure to the infectious TB case and not the last time you did the TST.

7 – Do you routinely repeat x-rays on children who are on treatment for LTBI?

No, once they are diagnosed with LTBI with a positive TST, have a normal chest x-ray and are compliant with the INH, I don't. Once they are treated I normally don't. Children are put on DOT to ensure that all medication is taken. We try to avoid the word prophylaxis because INH really is a treatment. Rather than have the parents administer the medication to their children, we give children twice weekly INH by DOT using a health department employee. This way we are comfortable that the children are getting their full course of treatment.

If you have a family who lapses in therapy, for example, you've given them the medicine for a month and somehow there is a delay in starting the medication, or you suspect that they aren't giving the child the medicine and there may be an adherence issue, it may be beneficial to repeat the CXR somewhere during the course of therapy, not at the end of therapy.

We know, through studies and through experience, that most of the time children do fine, even if they are not 100% adherent to medication. The original studies, which looked at the efficacy of INH, found that it was very efficacious. We were not doing DOT during that time those studies were done.

8 – Is there any problem with using Tylenol when the patient is on INH? Is there an increased risk for liver toxicity?

There is evidence that would suggest that this could be an issue. In some of these studies it showed that there was more toxicity than what would be expected from the INH alone. Some of the studies were done in certain areas where Hep A is very common, like India. So the question then is, was it because of viral hepatitis?

I explain that Tylenol can cause liver toxicity and Motrin can cause renal toxicity. If the child has a fever during a course of INH I recommend that they use Motrin rather than Tylenol. Now, nephrologists don't like me saying that because they would rather preserve the kidneys. I do tell the families, that from a personal standpoint, I prefer Motrin.

There is not a lot of evidence where we have studied that "X" amount of Tylenol will cause liver toxicity. We really don't know how much will matter. If people use it here and there, we really can't record that. I tell my patients who are on LTBI (CDC doesn't say this) that certainly anything used in moderation is normally fine. Again as long as they're not using it for a long period of time they should be fine.

I'm sorry that this is not a clear cut "yes" or "no" answer. I warn families from the beginning that Tylenol could interact with INH because when the child gets sick it is often over the weekend and they use the Tylenol over several days in a row before they reach me.