

Dr. Sunanda Guar

Good afternoon, I'm delighted that I'm able to address you all here today. I'm the only pediatrician in the entire group and I feel like I need to the pitch for pediatrics. We were able to have a section on infectious diseases and I'm very happy about that but I'm hoping that the next time we do this we will have a section on pediatrics as well, because there are many, many issues that relate to South Asian children that really have not been touched on in today's conference.

I'm now going to move on to tuberculosis and touch on a few key issues that relate to South Asians and the issue of tuberculosis. This slide shows the reported total number of TB cases every year in the United States over a period of time. As you can see, the total number of people with tuberculosis as of the year 2003, has gone down. While the total number of cases are going down, in the last couple of years the rate of decline, which is on average about 5% a year, is now about 3 or 4 percent a year. So there has been a decline in the rate of decline, but overall TB numbers have gone down. The next slide shows you the breakdown by race and ethnicity of the TB cases in 2003. And as you can see, Asians comprise 33% of the TB cases that were reported. By the way, of the Asians, 90+ percent are foreign born. So the majority of new cases that are occurring in the Asian population are among people that are foreign born. The other point I want to make is that in terms of just looking at the proportions of different Ethnic populations, Asians are highly over-represented. So TB is clearly an issue in this population.

Now let us focus on foreign born versus US born and the cases of TB in the United States. As you can see in this slide, if you look from 1993 to 2003, over this ten year time frame, the cases of TB among US-born has clearly declined. But if you look at the foreign born cases, it's been steady, maybe even a slight increase over the last few years among the foreign born. So much so that as of 2003, and the recent data from 2004 as well, the greater majority, over 54% or so, of TB cases are among people that have been foreign born. So clearly the existence of tuberculosis in the United States now is disproportionately high among people who are foreign born.

Next slide shows you a little about the percentage of TB patients among foreign borns by state. And New Jersey is actually in the purple, which is a state that has more than 50% of TB cases among foreign born. As a matter of fact, in New Jersey, 70% of cases of TB are in foreign born. Next slide shows you the country of origin. And as you can see, Mexico and Philippines are among the top two. India is in 8%. The other South Asian countries are lumped together under "other" countries. Country specific data for tuberculosis is available. If you add all South Asian cases along with cases from India, South Asian countries rank number 3, i.e. Vietnam. So clearly it is an issue.

As the CDC is beginning to focus on how to eliminate tuberculosis in the United States, it is becoming clear that a lot of the tuberculosis that we're seeing now is among foreign born individuals. One of the things that CDC is looking at is when in their travels, coming from their countries to immigrate to the US, when do they get to the TB? So the length of stay in the US prior to TB diagnosis has been a focus of the CDC. This slide shows data from 2003. As you can see, about half of the TB cases occur in people that have been in the country for less than five years. There seems to be two groups. There are those that have recently arrived that present with tuberculosis and those that have stayed for some time and they're now presenting with later onset or reactivation of disease. One of the theories is that the reason we see so many recently arrived people showing up with active tuberculosis has to do with incubating disease. They recently acquired disease before they came. Perhaps the stress of travel and stress of immigration, may play a role. This is something that the CDC is focusing on in terms of what we can do about it. How can we prevent this and are there other preventive ways to deal with this issue to try to reduce the incidence of tuberculosis.

The other point that I want to make is that among foreign born persons that present with tuberculosis there is an increased incidence of resistant tuberculosis, because of where they are coming from. Because they are coming from countries with high levels of resistance, such India or other South Asian countries. In the US born cases the incidence of finding TB resistance is about 6-7 percent whereas in the foreign born people it's about 12 or 13 percent. This is important for two reasons, one is to pick the right medications to treat them, because INH in this case does not work and in some cases they have multiple resistance, so-called MDR TB. So you need to be familiar with which drugs to treat them with. And secondly, our communities need to understand how resistance occurs, that with TB it's very important to complete the treatment as is recommended in order to reduce the emergence of resistant TB. And many people still don't understand that. And I've seen this many times. I treat children and I've seen that in children as well. The child comes in with TB, you start the treatment and the child starts to feel better and once he starts to feel better, he thinks, well why do I still have to take all these medications. That lack of treatment is completion is what leads to resistance. This is something that we need to communicate to the South Asian community.

CDC has come up with a six step plan to reduce incidence of TB in the US. The plan particularly focuses on foreign born populations because the prevalence of TB is pretty high in that population. And one of the main things that the plan emphasizes is early diagnosis and treatment in this group which has gained priority. So what do we do about early diagnosis? There's a lot of confusion among folks in general, and also amongst physicians, regarding what is latent tuberculosis versus what is TB, the disease. And it is important to understand that. This is a figure showing you the process of

how TB occurs. So basically, it's a person who has TB in lungs, and is coughing up these TB germs and the second person inhales it in, and these TB bacteria then go and set up a site of infection in the person number two. In the normal series of events the body's immune system then comes into play and limits this infection. It sort of holds the infection in place and doesn't let it become disease and disseminate and cause problems for the person. So this person that has acquired this infection and has now been able to contain the infection in this little sphere right here, and is "asymptomatic". He has no symptoms. He is going around feeling completely normal. But he has latent tuberculosis infection; has infection in the lungs. It hasn't caused any problems for that person. Okay, so why do we worry about that? So be it. So let the infection be there. Well, the problem is that at some other time during the lifetime, and there is a lifetime risk of 3-5 percent of this thing happening whereby these bacteria that were laying dormant and contained in the lungs then activate themselves and actually reactivate and spread more into the lungs and cause disease that will go to other areas of the body. And that is tuberculosis. So it can be just limited to the lung TB or it could be disseminated TB to the entire body. That is tuberculosis. And this reactivation, what causes it? It could be immunosuppression of some sort; stress; sometimes it's pregnancy. Other factors can also lead to this reactivation. And the idea of treating early infection is to treat early during latent infection, before it goes there i.e. tuberculosis. In the person with latent TB, the one with the contained infection, usually the chest x-rays is negative. Usually there are no symptoms of TB, whereas when you have disease the chest x-rays most likely would be abnormal and there would be symptoms that would suggest disease, such as fever, cough, night sweats, etc. And these people, when you culture the sputum of these people, will often be positive for the bacteria. So how do we diagnose TB infection in order to institute early treatment? We need to diagnose early. And you all are probably familiar with the tuberculin skin test. It's called the TST or the PPD test. You inject the PPD antigen under the skin and then, in 48 to 72 hours later you read this and you can see a positive response, that's a positive PPD and there are cut offs that are considered to be a positive response. A positive test means is that the person has been infected with the TB bacteria. It doesn't mean that the person has TB. All it means is that the infection has occurred. The diagnosis of active versus latent TB is based on presence or absence of signs of the disease.

This is important, as we talk about preventive treatment. Before I go to the preventive treatment issue let me mention a new test. It's called the Quantiferon TB test, that has recently been approved by the FDA to detect TB infection. So instead of doing a skin test you can do a blood test. And this blood test will measure the gamma interferon production from lymphocytes that have been incubated with the PPD antigen. People that are infected with TB, will produce a certain level of

gamma interferon in response to the PPD, which will lead to a positive test, meaning that they are infected with TB. The reason I bring this is up is because it will be important in the diagnosis once it becomes available. This test is recently approved. It's very expensive. It's not yet offered by most laboratories. But once it does become widely available, it will be a nice resource to have whereby you can do a blood test. Hopefully it won't be too expensive. It's particularly important for the South Asian community, people that have traveled from India, because some of the people have been vaccinated by the BCG vaccine. And when you have BCG vaccine, the interpretation of the PPD skin test can be sometimes problematic. When we have this test it will make that interpretation a little bit easier.

Goal of treatment is to treat latent tuberculosis as early as possible. In persons that have latent TB there is an annual risk of developing active TB, and if we treat with INH for nine months that progression to active disease can be quite substantially reduced. CDC particularly emphasize guidelines to identify and treat latent TB in recent foreign arrivals. I would now like to touch on the BCG vaccine, because this is an issue with many beliefs and myths within the community, especially as it relates to children, because many of the children that are coming over who have been born in India have been vaccinated with the BCG. BCG is a vaccine against tuberculosis. It's efficacy is 50-80 percent but it's important to remember that it does not prevent primary localized disease. It only prevents the dissemination of TB. So because you have BCG vaccine doesn't mean you're not going to get tuberculosis infection. Many people think, in our community, that if you have the BCG vaccine you're protected against TB. That is not the case. It is recommended for infants born in countries with high TB prevalence such as South Asian countries. The issue with BCG that comes up very often is when you do a skin test to diagnose early TB infection in someone who is BCG vaccinated the skin test can be falsely positive. The BCG vaccine induced skin test, it's maximal size is at two years or so after the BCG and then it decreases progressively after that. The BCG vaccine induced positive PPD skin test is rarely more than 10 millimeters. So if you do have someone who has 10 millimeter positive skin test most likely they are infected with TB and not because they have the BCG vaccine.

I'll now move to HIV and the Asian population. This slide shows that the proportion of AIDS cases in the US in the different ethnicities, and as you can see, that all of the HIV/AIDS data is collected as Asian Americans and Pacific Islanders. And about one percent of patients are among this group in the US. The other important point is that the rate of rise of HIV AIDS cases among the Asian Pacific Islanders group is much higher than other ethnicities. It's one of the highest rising groups. So that is an important emerging problem in the community. There is lack however of South Asian

specific data. We tried to get South Asian specific data from New Jersey, it's just not possible. Apparently California does collect specific data for South Asians.

I would now like to present a case to you. This is a recent patient we saw in our clinic at Robert Wood Johnson. It's a 29 year old South Asian American woman who was evaluated for persistent diarrhea and weight loss in the United States. She underwent an extensive workup, but, no diagnosis was reached. Several months later she visited India where stool studies revealed cytosporidium. This led to HIV testing and she was diagnosed to be HIV positive while she was in India. Her two year old child was found to be HIV infected as well. Her husband was tested and was negative for HIV. The point that the case makes is that HIV diagnosis was not considered in the United States at all, because she did not have any "risk factors" for HIV. That is a missed opportunity. I think people need to remember "sexual activity" itself is a risk factor for HIV. And particularly in South Asian populations, "marriage" itself is a risk factor for HIV. It certainly needs to be considered, this woman could have been diagnosed early, and perhaps – had she been diagnosed early, particularly in her pregnancy, the infection to her child could have been prevented because basically, perinatal HIV is now an essentially preventable illness. In this conference we have a poster in which we are presenting data over the past five years. We've been seeing an increasing number of South Asian women in our HIV clinic. So far luckily only one child is infected and the rest of the children of these seven mothers, are uninfected. We clearly need increased data collection, South Asian specific HIV education, awareness, and support groups for patients of South Asian origin with HIV/AIDS. Thank you very much for listening.

Dr. Mahal: Okay, are there questions for Sunanda?

Q: Just a point of clarification. Your point, we do not have sufficient data on tuberculosis in South Asian. Now going back, you made a statement, a lot of instance of to the recent migrant landed. And they have an active tuberculosis. Two points of clarification. Number one, most of them landed and began land here in New Jersey or in the United States. The one who would have likelihood of having tuberculosis, active stages is the older age, are grandparents, parents and mother-in-laws, father-in-law. But when they start from the country of origin, they do not, they're not issued visas, they are fully screened by []. My doubt is how come they land here with an active tuberculosis? Second question. If the landed immigrant is not an older age, they are the younger group, most of them are cleared. They have, we say, BCG done. The second thing they have a full two times, three times, x-ray of lungs taken. So how come they are skipped tuberculosis activity and they land with tuberculosis in

the United States? Because I fear, then, we say such statement, there is some pinpointing. Saying South Asians are usually the one who land here with the tuberculosis, which is untrue even though I'm too naïve in this specialty. I'd like you to comment on that.

Dr. Gaur: I think one of the issues is that of PPD testing before travel. When you apply for visa, it's recommended but it's not for all types of visas, from what I understand. So some people are traveling without any PPD testing before they come.

Q: [inaudible]

Dr. Gaur: But you know, x-rays will not always pick up TB. You have to have a skin test. And the skin test is not always done.

Q: [inaudible]

Dr. Gaur: So that's where the issue comes up, does the BCG vaccine truly give a positive PPD.

Q: [inaudible]

Dr. Gaur: X-rays, but the PPD test is not routinely done and that will pick up more cases.

Q: I have [] that the pregnant ladies who are traveling to India, how should we do for selecting malaria medication?

Dr. Kapila: That's a difficult question. There's no doubt Mefloquine still has been used. However, avoid everything in the first trimester, absolutely. Stay at home. If you have to go then take all the other precautions and make sure that you put on the long sleeves. Make sure you put on a little DEET or whatever is necessary to prevent mosquito bites. Otherwise not only is there higher risk of tuberculosis but also the risk of dengue, and as I said there's no prevention or treatment for dengue. I just want to make a comment on the age groups. We now know that it used to be that 35 was a cutoff point for preventive therapy. In the last year or so the CDC has looked at that data clearly and no matter what the age, if the PPD is more than 10 millimeters it's mandated that you give preventive therapy. Initially the evaluation was 35 or below, three, over 35, watch and wait. But there's no doubt

that that is rapidly changing and the concept hasn't sunk in still. I've talked with so many doctors now, Nobody seems to be doing it. So if you have anybody that you know of that has a greater than 10 millimeter PPD, and there are some contraindications as such. But most of the time you will have to give preventive therapies in that setting. And as I said, in the other question that you asked, there's really not much you can do. Malorel has also been used, as you know. This is a drug that has atamoform and proguanil combined and that is suggested also. But it has to be taken on a daily basis dimethicin has to be taken on a weekly basis. We always take the risk versus the benefit and I would say that that there is no data at this time pertaining to associated problems with pregnancy, taking these medications in the first trimester.

Dr. Gaur: I just wanted to add in terms, also, of the preventive techniques [inaudible]. In some of the preventive treatment, just add to what Dr. Kapila said, no matter whether the BCG has been given or not, because BCG is used, PPD positivity doesn't last for years and years. And that's the myth that's been circulating, that if you've had BCG you cannot do PPD testing. This is not the case.

Q: A couple of quick questions pertaining to TB, what is the, you know, we were just discussing that case, if they had done a full travel PPD that could have been picked up. So should everyone have a pre and post travel PPD?

Dr. Gaur: I think pre is not essential but post travel, I would recommend, especially for children. Let Dr. Kapila comment on the adults, but the children we do recommend post travel.

Dr. Mahal: We've been given only two more minutes for answers.

Dr. Kapila: If you're PPD negative to begin with and you think you've had significant exposure in India then I think it's almost mandated that you test yourself. Especially if you develop symptoms, the symptoms – low grade fever, may or may not have much of a cough. But I think it depends on your clinician. You need to see a doctor and let him make a decision. I don't think it should be routine but if there's any doubt it should be done.

Dr. Gaur: And once you're positive then you're positive. You cannot use that test again.

Q: You mentioned about the meningococcal epidemic in India, so I was giving the vaccine this year to everybody? But is this a thing that everyone is doing?

Dr. Kapila: I think, really again, it depends on exposure. As I said, most of us the [] occurred in the old Delhi slums. And maybe, and also now it has spread to other areas. I would say if you have young children, and if you suspect that there [] exposure, yes. You see the problem in India is there is no exclusiveness of the socioeconomic. You always have servants. And there's no doubt, exposure to people who don't wash their hands and they feed you, there is a high risk of typhoid, no matter how careful you are with consuming bottled water. So there is no doubt that you may have a typhoid Mary in your mother's home who has been cooking for her for the last ten years, and these are really very difficult issues to discuss. But I think it's better to be safe than to be sorry. And many [] disease. And as I've already told you that the CDC has suggested that young adults, especially when they're going to college and living in dorms be protected against meningococcal. So why not do that at that age and hope that it won't be necessary to bear the consequences of.