

I understand that there is a lot of confusion and therefore anxiety about numerous issues of tuberculosis. Most of this is because it is an extremely complicated organism and disease process – one of the most complicated that we will teach in this class. However, you hopefully appreciate that it is one of the most important bacterial diseases worldwide and that it will definitely impact your medical practice – it's not an esoteric topic. There are three areas of confusion/controversy so far – site of initial infection, location of the Ghon complex and secondary reactivation; reading a PPD; and treatment. I will summarize my understanding of these things. But more than anything else, please note that I, as the person who writes most the exams and ultimately approves them, am aware of these issues!

1. Location, location, location! Where is the site of primary infection? Ask yourself, how do people encounter Mtb and where do the bacteria enter the body. Answer – direct inhalation into the lungs, as opposed to initial colonization of the upper respiratory tract (no matter how you define it) followed by aspiration or extension. Therefore, THE INITIAL SITE OF INFECTION IS ANYWHERE INHALED PARTICLES SMALL ENOUGH TO AVOID THE MUCOCILIARY ESCALATOR WILL END UP. This will be alveoli and is clearly not restricted to the apices of the lung. At these sites, the organisms will be engulfed by resident macrophages which will be unable to completely kill the organisms. However, there will be an immune response to wall off the infection, and this leads to calcified lesions with caseating necrosis – the Ghon lesions. The infected macrophages will migrate to the draining lymph nodes, which will undergo an inflammatory response that cannot completely kill the bacteria. The combination of the lesions in the lung and the lymph nodes is the Ghon complex. In fact, in many people, the infected macrophages and the bacteria themselves get into the bloodstream and see about every tissue of the body, where they eventually are walled off and held in check. That is why people can have reactivation TB just about anywhere in the body. However, as you are well aware, these bacteria prefer high oxygen levels. This does not affect the site of primary infection, per se. That was determined by where they were inhaled to. However, this predilection for oxygen does determine where reactivation occurs since the bugs must replicate to high levels to cause disease. Hence, reactivation in the lung – the cavitory lesions and major CXR events – are in the apices, and the reactivation systemic sites are those where the oxygen tension is high – even though the bacteria have seeded all over the body.

2. PPD test – The PPD test simply shows if someone has been infected with TB at some point in their lives. I don't like saying "exposed" because if I am in a room with someone with TB and they cough, I technically have been exposed. But if the bacteria don't get in my body and replicate enough, I won't make the cell-mediated immune response that causes the positive PPD. So, you should know that the PPD is detecting a cell-mediated immune response, i.e., infiltration of lymphocytes, to the site of injection of mycobacterial antigens – a recall response. That is why you measure induration and not erythema. Does BCG vaccination cause a positive PPD reaction? It can, but it does not always.

How do you read a PPD as positive or negative? That depends on the patient and your level of sensitivity as to the danger or likelihood of the patient either having or progressing to active infection. For immunocompromised people (e.g., AIDS), the diameter is smaller since you are more concerned about their health if they progress and because they are less likely to produce a full blown "positive reaction" because they have defective CMI. In fact, they may have an active, symptomatic infection, but not produce any induration. People with no risk factors who live in areas where they may be exposed to cross-reactive organisms, like in Florida, have the widest zone for "positive". They are less likely to have a real infection, they are more likely to have a false positive, and they are less likely to experience serious illness quickly if you make a mistake. Then there's everyone else who has an intermediate radius for being positive. Remember that there are at least 2 reasons for using the PPD. 1) It can help diagnose an active infection (reactivation, etc.). 2) If someone is otherwise healthy and they are PPD+, you must decide if you are going to give them antibiotic prophylaxis to prevent their potential reactivation. A consideration in this decision is when you think they were infected. Why? Because half of people who will reactivate do so in the first two years after initial infection. According to Dr. Islam, since people who received the BCG vaccine are generally coming from endemic areas and since the vaccine is not 100% effective, you cannot be sure that a positive PPD+ from a vaccinated person is simply a reaction from the vaccine. So you must decide if they will receive prophylaxis. NOTICE THAT I HAVE INTENTIONALLY NOT WRITTEN ONE NUMBER FOR MEASUREMENT FOR READING A PPD!

3. Treatment. You must know the antibiotics that are used and their mechanism of action, if known. There are two purposes for treatment. Obviously, if someone has active infection (miliary, reactivation, etc.), you must treat them. That is a multiple drug regimen because of existing resistance and the likelihood that spontaneous mutations will arise in the very large numbers of bacteria typically present in these symptomatic people. How many, which drugs, for how long – that's all detail that you can learn later.

Second – if someone is PPD+ but asymptomatic, you need to decide if you are going to treat them to clear their infection to reduce the probability that they may be part of the 10%-15% who will eventually reactivate later in life. This is a simpler regimen. Since they have a smaller number of bacteria, the likelihood of resistant mutants is lower (unless they got infected with an already resistant mutant).