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Tuberculosis (TB)

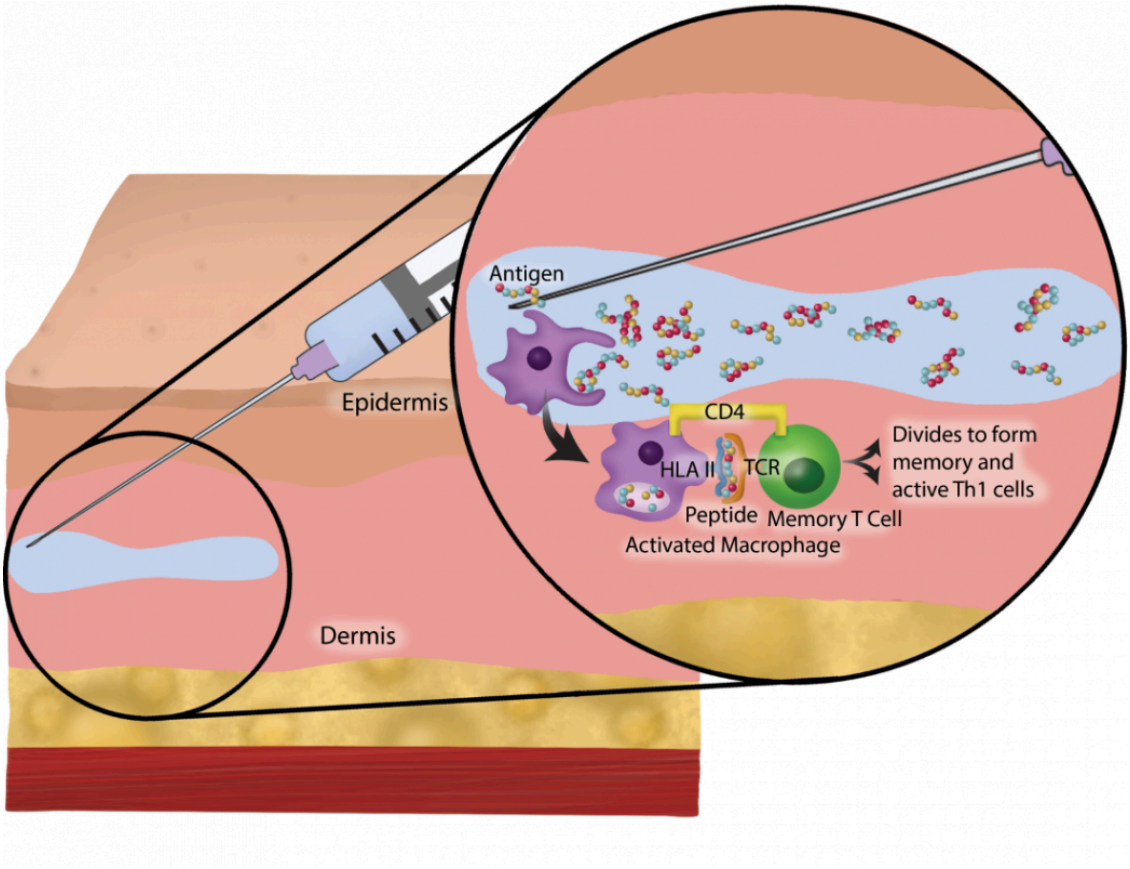
Tuberculosis (TB) is one of the deadliest diseases in the world. TB is caused by an airborne bacteria called *Mycobacterium tuberculosis*. The bacteria have a waxy coat that makes them resistant to acids, bases, detergents, disinfectants, oxidants, complement proteins, and even some antibiotics. Mycobacteria are also unique pathogens in that they can infect an individual without inducing an acute immune response; a condition known as "latency." In fact, the TB bacterium can remain dormant for many years within an individual before becoming an active colonizing bacteria that induces a severe immune response. It has been estimated that over a billion people have been exposed to and may be carriers of the infection; that is, they have a 'latent TB infection.' Fortunately, the United States has experienced a consistent decline for new TB infections since 1993 due to the efforts of many public health programs geared at curtailing this dangerous pathogen. In the US, people with HIV are particularly susceptible to TB. More drug-resistant strains of TB have arisen and this adds to the fear of this pathogen getting a damaging foothold in our communities.

TB is spread by minute, invisible particles called droplet nuclei that are in the respiratory droplets of a person with active TB. This is why it is important to wear appropriate respiratory protection if you are around a person with active TB. A TB infection starts when the *Mycobacterium tuberculosis* bacteria is introduced to the lungs where it is phagocytosed by macrophages (dust cells) in the alveolar sacs. Once inside the macrophage, the bacteria resist lysosomal destruction. Although the macrophages can't kill the intracellular pathogen, they do respond by releasing a host of cytokines that lead to a cell-mediated immune response and a type IV hypersensitivity reaction. Immune cells including T-cells and additional macrophages are recruited. T-helper cells then release chemical signals that increase the ability of macrophages to make and release lytic enzymes. The macrophages thus become more capable of degrading the engulfed bacteria, but end up degrading lung tissue in the process. As T-cells and macrophages become excessively stimulated by the intracellular bacteria, they end up causing more tissue destruction than the actual bacteria do themselves, leading to a type IV hypersensitivity with inflammation and lung tissue damage. Unfortunately, these excessive immune processes do not ultimately clear the lung of TB. Instead, the macrophages and T-cells surround the bacteria and "wall it off" from healthy tissue. This walled off lesion is called a granuloma (or a Ghon focus) and the bacteria within it seem to enter a latent stage. These granulomas can be seen on radiographs even if the patient is symptom free.

Later in a person's life, any primary TB infections that went latent pose an increased risk for resurgence and a secondary infection. Secondary TB involves propagation of the mycobacterium and reactivation of the TB immune responses. Persons with secondary TB may present with fever, anorexia, malaise, and a chronic cough that may produce blood in the sputum. It is not known what triggers a latent TB infection to become active again. Perhaps it is an immune response to another infection, age, a second exposure to TB, or some other reason that causes a person to become immunocompromised.

There are drugs that can work against *Mycobacterium tuberculosis*, but they are most effective if they are delivered early and if the patient is careful to follow strict adherence to the consumption of the drug. They must finish their prescriptions as instructed, even though it may take a long time and they may have no symptoms during the treatment.

The TB skin test is an important resource to help discover if an individual has been infected with TB that might further spread. The TB skin test measures the delayed type IV hypersensitivity response to an intradermal injection of tuberculin, an antigen made by *Mycobacterium tuberculosis*.



TB Skin Test *Image by Becky T. S20*

The image above shows a tuberculin skin test (also called a Mantoux test or Mendel-Mantoux test). This test involves the insertion of tuberculin via a hypodermic needle. Tuberculin is a combination of proteins collected from cultures of *Mycobacterium tuberculosis*. Individuals who have been exposed to this bacteria in the past will have memory cells that can respond to these proteins. The process starts with phagocytosis of the injected tuberculin by resident macrophages which will then present them on their MHC II proteins. Nearby helper T-cells will become activated by interacting with this MHC II receptor and release cytokines that trigger recruitment of immune cells and localized inflammation. Over the next 2-3 days, through a delayed type IV hypersensitivity reaction the excessive response of the helper T-cells will cause a red bump to increase in size around the injection site. A medical professional trained in the observation of these areas will determine if the spread of the inflammation suggests previous exposure to TB.

There is a vaccine for TB called the Bacillus Calmette-Guerin (BCG) vaccine. This vaccine is recommended in countries where TB is common. It is not currently routinely given in the US. The vaccine is a bit controversial as some studies show it has low to no protective effect, while other studies show it has protective effects. It is not known why the data is so inconsistent. The vaccine continues to undergo study and analysis for effectiveness. It is important to note that individuals who have had the vaccine may have a false positive Mantoux test.

1. Deutsch-Feldman M, Pratt RH, Price SF, Tsang CA, Self JL. Tuberculosis — United States, 2020. MMWR Morb Mortal Wkly Rep 2021;70:409–414. DOI: http://dx.doi.org/10.15585/mmwr.mm7012a1external icon