If the initial immune system response is not sufficient to clear the bacteria, the bacilli may spread from the initial lesion via the lymphatic and/or circulatory systems to other parts of the body. After a period lasting from 3 to 8 weeks the host develops specific immunity. This is known as cell-mediated immunity (CMI) and delayed-type hypersensitivity (DTH) to the bacilli. Individuals typically show positive results on the TST or interferon gamma release assay (IGRA).

Clinical evidence of an initial infection may include a Ghon focus (a calcified granuloma in the lung), alone, or in combination, with a calcified focus in a draining lymph node (Ghon Complex). The Ghon Focus or Ghon Complex may be demonstrated on chest X-ray, but their absence does not imply absence of TB infection.

In a small proportion of those infected, erythema nodosum (a cutaneous immunologic response to an extracutaneous TB infection) or phlyctenular conjunctivitis (a hypersensitivity reaction) may develop.

Primary TB (Early Disease Progression)

For purposes of disease reporting, everyone with a diagnosis of TB made within 18–24 months of infection is considered to have "primary" disease (about 5% of those infected). Those newly infected people in whom TB does not develop within this period of time will either be left with latent TB infection (LTBI) and will never experience disease (about 90% of those infected) or, after a variable period of latency, they will show late disease progression (about 5% of those infected).

A proportion of those infected with TB will go on to develop active disease within a matter of months. This is especially true in young children and the immunocompromised. A progressive Ghon focus, disseminated (miliary) disease and central nervous system disease may occur as early as 2 to 6 months after infection in infants and the severely immunocompromised. Lymph node disease (which may or may not include respiratory involvement) may also occur.

Latent TB Infection (LTBI)

The majority of those infected will be classified as having a latent TB infection. This means MTB can survive in the granulomas for many years without causing symptoms of active disease. LTBI is usually identified by a positive TST or IGRA.

Reinfection

Studies suggest it takes up to 18 months after the initial infection for cell mediated immunity to mature. During this time, a reinfection carries the same risk of disease as the initial infection, perhaps explaining why disease is much more common in newly infected close contacts of smear-positive cases than it is in newly infected close contacts of smear-negative cases – the former having a greater likelihood than the latter of repeated exposure and reinfection.