

Tuberculosis in the 21st Century: Challenges in Diagnosis, Treatment, and Global Control

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Abstract

With an estimated 10 million cases and over one million fatalities annually, TB is still one of the most significant infectious illnesses affecting worldwide public health, mostly in low- and middle-income nations. Mainly affecting the lungs (pulmonary TB), Mycobacterium tuberculosis is a slow-growing, acid-fast bacillus that causes tuberculosis. However, it may also affect other organs, such as the lymph nodes, bones, central nervous system, and genitourinary tract. Due to a number of variables, including delayed diagnosis, poor treatment adherence, the emergence of drug-resistant strains, and socioeconomic determinants including poverty, malnutrition, and HIV co-infection, tuberculosis (TB) continues to be a major cause of morbidity and death even though it is preventable and treatable. Bacterial evasion mechanisms and the host immune response interact intricately in the pathophysiology of tuberculosis. Latent tuberculosis infection (LTBI) can result from M. tuberculosis remaining dormant in macrophages for years after inhalation.

Unless they are immunocompromised, only 5–10% of infected people experience active illness at some point in their lives. Serious obstacles to tuberculosis control and eradication have arisen as a result of the development of extensively drug-resistant tuberculosis (XDR-TB) and multidrug-resistant tuberculosis (MDR-TB), which have further complicated treatment procedures. Although recent developments include nucleic acid amplification tests (NAATs), such as GeneXpert, and interferon gamma release assays (IGRAs) for the identification of latent infections, the diagnosis of tuberculosis still mostly depends on sputum smear microscopy, chest X-rays, and culture techniques. The necessity for novel, shorter, and more efficient medication regimens is highlighted by the fact that drug-resistant TB necessitates lengthy and sometimes hazardous second-line treatment. The BCG vaccine, early case diagnosis and treatment, and public health initiatives aimed at high-risk groups are the main components of prevention programs. Because of ongoing inequalities in health care, delayed diagnosis, and poor access to and adherence to treatment, tuberculosis eradication is still a long way off, despite international efforts through programs like the WHO's End TB Strategy.

Keywords: Pulmonary tuberculosis, sputum microscopy, infectious disease, TB epidemiology, interferon-gamma release assays

Introduction

Mycobacterium tuberculosis is the bacteria that causes TB. The disease can be transmitted by people who have active TB in their larynx or lungs. The germs are dispersed through the air by the small droplets they emit. Sneezing, coughing, laughing, singing, and chatting can all cause this. Inhaling these droplets might result in infection. People who spend a lot of time together inside are more prone to spread the sickness. As a result, it spreads quickly in areas where people frequently live or work together. Additionally, it spreads more readily in crowded places. therapy, most people who are receiving medicine to treat active TB are unable to spread the illness. Certain types of TB germs are becoming resistant to drugs. This indicates that drugs that used to treat the illness are no longer working. Natural genetic alterations in bacteria are partly to blame for this. For the whole prescribed term, take all drugs as prescribed (Tuberculosis et al., 2002). Use these precautions to keep people safe: Remain at home. Avoid going to school or work. At home, isolate yourself. The Bacille Calmette-Guérin (BCG) vaccination is frequently administered to infants in nations where TB is prevalent. Infants and young children, who are more susceptible to

active TB in the fluid around the brain and spinal cord, are protected by this vaccination. The stage known as latent TB infection often follows the original infection. The cells of the immune system envelop the lung tissue that harbors the TB bacteria. (Dutta et al., 2014) The bacteria can no longer do damage if the immune system controls them. But they live. A latent TB infection has no symptoms. When an infection is out of the immune system's control, active TB illness develops. Disease in the lungs or other bodily parts is brought on by the microorganisms. Although it often happens months or years after a latent TB infection, active TB illness can manifest right after the first infection. A bacterial infection is the cause of tuberculosis (TB). Although the lungs are frequently affected, other bodily components, including the spine, brain, or kidneys, may also be impacted. (Satta et al., 2022) Not all TB infections result in illness. Asleep, or latent, TB stays within the body. In the US, up to 13 million people have latent tuberculosis. (Mancuso et al., 2016) A latent TB infection can last a lifetime in certain people without causing symptoms (active TB). However, if the immune system deteriorates, TB may become active. Bacterial growth may be unabated by a compromised immune system. It will take longer to finish therapy, though.

Pulmonary tuberculosis

Although it mostly affects the lungs, this illness can extend to other organs. Anyone exposed to MTB has the potential to get the infectious illness TB. Although TB, as it was once known, is no longer a major cause of mortality in the US, multidrug-resistant TB epidemics are still present in other nations and among some vulnerable or homeless populations in the US. Although the majority of individuals recover from their initial TB infection, the virus can linger for years inactively. Secondary TB occurs when a latent TB infection reactivates, generally but not always in an immunocompromised individual. It is possible to avoid tuberculosis. A positive skin test indicates that you have been in touch with the TB germs, not that you have active TB or are contagious. Many persons who have been exposed to TB at some point—not necessarily recently—test positive. For a few months, latent TB infection is treated with just one or two drugs, which stops the illness from becoming active and eliminates the need for longer-term therapy with additional medications. For at least six months, a combination of many drugs is always used to treat active TB. Several tablets taken throughout the day are necessary for successful regimens,

even for ordinary TB. Drug regimens get more complicated if drug-resistant TB is detected. Conversely, preventive treatment could just include taking one or two medications daily for a shorter amount of time. A medical practitioner may need to keep an eye on prescription medicine consumption if there are concerns that they are not taking all of their prescriptions as prescribed. We refer to this method as directly observed treatment (DOT). In this situation, a doctor may prescribe medicine to be taken twice or three times a week (Andreu et al., 2004).

Sputum microscopy

The lungs create a form of viscous mucus called sputum, sometimes referred to as phlegm. A higher quantity might be a sign of lung illness, although this can also be normal. Pneumonia or other bacterial infections are typically indicated by this. Cystic fibrosis patients also frequently have yellowish-green sputum. Mucus accumulates in the lungs and other organs in people with the hereditary condition cystic fibrosis. This is typically seen among smokers. Additionally, it is a typical symptom of black lung disease. Long-term exposure to coal dust can cause black lung disease, a dangerous illness. This may indicate ancestry. Inhaling dust, other brown materials, or poisons can also cause it. This may indicate pulmonary edema, a disorder where the lungs accumulate too much fluid. People who suffer from heart failure frequently have pulmonary edema. This might be a lung cancer early warning indication. P The physician will ask you to take a deep breath and then cough into a designated receptacle. A medical practitioner will urge you to take a deep breath and then cough into a designated receptacle. To aid in the removal of sputum from lungs, the doctor may tap the chest. D Doctors might advise taking a saline solution to help cough more deeply (Steingart et al., 2006).

Infectious disease

Conditions known as infectious illnesses arise when microscopic organisms infiltrate the body and proliferate. Disease-causing organisms include bacteria, viruses, fungi, and parasites. Our bodies are home to numerous creatures. Their size prevents them from being seen by the unaided eye. Also, they are frequently innocuous or even helpful. The cause of the infection affects the symptoms of infectious disorders. However, they frequently involve exhaustion and fever. Mild infections can be cured with rest and natural

therapies. Other infections, however, have the potential to be fatal, and hospitalization may be necessary for treatment. Vaccines can prevent a number of infectious illnesses, including chickenpox and measles. Additionally, receiving a vaccination may lessen the severity of other illnesses, such as COVID-19. Additionally, regular and thorough handwashing helps shield against the majority of infectious infections. In severe cases, it can be lethal. Additionally, handling animal excrement might make you more susceptible to illness. Cleaning a cat's litter box, for instance, without using disposable gloves or washing afterwards, might expose you to parasites. The illness, known as toxoplasmosis, is especially dangerous for pregnant women and those with compromised immune systems. The fetus may be exposed to microorganisms that cause infectious illnesses from the pregnant woman. The organ that gives the fetus oxygen and nutrition, the placenta, is susceptible to some bacteria. During birth, the newborn may potentially be exposed to vaginal germs. Additionally, there is a little chance that breast milk might spread pathogens. Breastfeeding a child with someone else's breast milk or purchasing breast milk online from a milk-sharing website increases this danger. (McNab et al., 2015)

TB epidemiology

A significant global public health issue, tuberculosis (TB) is projected to have caused 8.6 million new cases and 1.3 million deaths in 2012, despite a gradual but consistent drop in incidence over the previous ten years. Without a doubt, tuberculosis is a disease linked to poverty, largely afflicting the most vulnerable people in the world's poorest nations. One of the main obstacles to TB control is the existence of multidrug-resistant strains of *M. tuberculosis* in the majority of nations, with high incidence in specific areas. This might possibly impede recent progress, especially in some contexts. Early TB case identification is still difficult, particularly in areas with low resources and among disadvantaged communities, as well as an estimated 3 million individuals who are mistreated, unreported, and undiagnosed. Even though TB incidence, prevalence, and death have been declining over the last ten years, the illness is still difficult to eradicate globally and will cost a significant amount of money. The poorest, most vulnerable, and disadvantaged demographic groups are disproportionately affected by tuberculosis (TB), a disease linked to poverty. Furthermore, without putting in place an efficient surveillance system to track the progression of the epidemic and evaluate how control measures affect the illness, TB

control is impossible. Because of this, national TB programs need to invest a lot of money in disease-specific reporting and recording systems. (Glaziou et al., 2013)

Interferon-gamma release assays

With between 8 and 10 million cases annually, tuberculosis (TB) is still one of the most common infectious causes of morbidity globally, despite the World Health Organization (WHO) declaring it a global health emergency more than 15 years ago. Our methods for detecting and preventing tuberculosis are over a century old and unable to contain the pandemic, despite this rising threat to global public health. Nonetheless, new developments in the detection of latent tuberculosis infection (LTBI) hold great potential for significantly enhancing TB control. The reservoir of latently infected people, which is thought to comprise one-third of the global population, is far more than the number of active TB cases, which sets the epidemiology of TB apart.

TB and not depend on the presence of BCG. This idea has been employed in a number of research studies to evaluate the diagnostic accuracy of the TST and IGRAs in contact tracing and epidemic investigations, especially when it comes to children. 22–27 Despite the fact that the ELISpot test has a stronger body of data than the ELISA, it is generally agreed upon from this research that both IGRAs correlate with levels of TB exposure, regardless of BCG status, either as well as or better than the TST. This was best illustrated in a large school epidemic research with 535 pupils, where the ELISpot showed a considerably stronger correlation with exposure to *M. tuberculosis* than the TST based on exposure time and proximity to the index case.

The substantial correlation between the ELISpot and exposure to TB has also been validated by several studies conducted in a range of low, moderate, and high prevalence settings. (Mandalakas et al., 2011)

Conclusion

Despite decades of medical advancements and focused control efforts, tuberculosis continues to be one of the most persistent hazards to public health globally. Numerous biological, environmental, and social variables, including poverty, overcrowding, malnutrition, and restricted access to high-quality treatment, interact intricately to

contribute to the persistence of TB. In low- and middle-income nations, where the disease burden is greatest, these factors not only contribute to the spread of *Mycobacterium TB* but also impede prompt diagnosis and efficient treatment. Even though the BCG vaccination and the development of efficient anti-TB treatments have greatly decreased the death rate from tuberculosis over the past century, there are still many obstacles to overcome. A significant concern to the security of global health is the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of TB, which necessitate more costly, time-consuming, and toxic treatment regimens with inconsistent outcomes. About 25% of the world's population is afflicted by latent tuberculosis infection (LTBI), which is a huge worldwide reservoir that impedes eradication attempts.

References

- Andreu, J., Caceres, J., Pallisa, E., & Martinez-Rodriguez, M. (2004). Radiological manifestations of pulmonary tuberculosis. *European Journal of Radiology*, 51(2), 139-149.
- Dutta, N. K., & Karakousis, P. C. (2014). Latent tuberculosis infection: Myths, models, and molecular mechanisms. *Microbiology and Molecular Biology Reviews*, 78(3), 343-371.
- Glaziou, P., Falzon, D., Floyd, K., & Raviglione, M. (2013). Global epidemiology of tuberculosis. In *Seminars in Respiratory and Critical Care Medicine* (Vol. 34, No. 01, pp. 3-16). Thieme Medical Publishers.
- Mancuso, J. D., Diffenderfer, J. M., Ghassemieh, B. J., Horne, D. J., & Kao, T. C. (2016). The prevalence of latent tuberculosis infection in the United States. *American Journal of Respiratory and Critical Care Medicine*, 194(4), 501-509.
- Mandalakas, A. M., Detjen, A. K., Hesselting, A. C., Benedetti, A., & Menzies, D. (2011). Interferon-gamma release assays and childhood tuberculosis: Systematic review and meta-analysis. *The International Journal of Tuberculosis and Lung Disease*, 15(8), 1018-1032.
- McNab, F., Mayer-Barber, K., Sher, A., Wack, A., & O'Garra, A. (2015). Type I interferons in infectious disease. *Nature Reviews Immunology*, 15(2), 87-103.
- Satta, E., Alfarone, C., De Maio, A., Gentile, S., Romano, C., Polverino, M., & Polverino, F. (2022). Kidney and lung in pathology: Mechanisms and clinical implications. *Multidisciplinary Respiratory Medicine*, 17(1), 819.
- Steingart, K. R., Ng, V., Henry, M., Hopewell, P. C., Ramsay, A., Cunningham, J., Urbanczik, R., Perkins, M. D., Aziz, M. A., & Pai, M. (2006). Sputum processing methods to improve the sensitivity of smear microscopy for tuberculosis: A systematic review. *The Lancet Infectious Diseases*, 6(10), 664-674.
- Tuberculosis Trials Consortium. (2002). Rifapentine and isoniazid once a week versus rifampicin and isoniazid twice a week for treatment of drug-susceptible pulmonary tuberculosis in HIV-negative patients: A randomised clinical trial. *The Lancet*, 360(9332), 528-534.