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Testing healthcare workers for latent tuberculosis: Is it evidence based, bio-plausible, both or neither?

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Testing healthcare workers for latent tuberculosis

The Centers for Disease Control recommend that all US healthcare workers be tested for active and latent tuberculosis (TB) infection upon hire, and annually for those working in medium-risk settings.¹ Latent TB infection refers to a dormant state in which infection is asymptomatic, noncontagious, but may reactivate. The guidelines recommend that asymptomatic healthcare workers who test newly positive for latent TB infection be treated preventively.¹

Medium-risk institutions include those that may host patients with active TB or laboratories with clinical specimens that may contain TB. Healthcare settings with less than 3-6 TB patients/year are considered low-risk facilities, although annual testing may be implemented based on state or institution-wide regulations. All healthcare workers in medium-risk institutions exposed to patients or specimens are required to be tested annually. The US is considered a low-burden country whose rates of TB have consistently fallen over the past decade,² yet it engages in widespread screening and subsequent treatment of identified latent TB infection cases with no direct evidence showing that such campaigns improve health outcomes for staff or patients. Moreover, the indirect rationale behind such campaigns is questionable in the modern era. Here, we explore this issue.

No direct evidence screening provides benefit

Although healthcare workers have an increased risk of latent TB infection, there is no direct evidence from RCTs that show that screening for and treating latent TB infection in this population is effective at reducing active TB rates. A 2016 systematic review by the US Preventive Services Task Force (USPSTF) found that there were no RCTs comparing screening versus no screening assessing the benefits of screening for latent TB infection on clinically meaningful outcomes such as rates of active TB, mortality, or transmission.¹ Their recommendation was based on indirect evidence of (a) TB test accuracy and (b) the efficacy of treatment. It must be noted that similar indirect evidence exists for many screening strategies that failed when tested directly, such as chest radiography for lung cancer and transvaginal ultrasound and CA-125 screening for ovarian cancer.³

Evidence gaps in case for screening
First, let’s consider the recommended screening test for healthcare workers, TB skin tests. TB skin tests indirectly test for TB by measuring immune sensitization to *Mycobacterium tuberculosis* antigens. The most common TB skin test administered to healthcare workers uses purified protein derivative to elicit immune reactions. After 48-72 hours, indurations are measured and reactions > 5-15 mm (depending on risk factors) are diagnosed as positive.²

TB skin tests frequently result in false positives due to the Bacillus Calmette-Guérin vaccine (BCG, a TB vaccine common in high-risk countries) and nontuberculous mycobacteria. Those receiving BCG vaccinations may elicit reactions from purified protein derivative for 10 plus years after vaccination and therefore positive results cannot conclusively indicate that they have latent TB infection.² Similarly, nontuberculous mycobacterial infections commonly produce false positives. A 2001 study on purified protein derivative testing in US-born healthcare workers and medical students found that up to 50% of TB skin test results measuring 5-14 mm were due to nontuberculous mycobacteria.⁴ A longitudinal study on TB skin tests and alternative IFN-γ assays for latent TB infection in healthcare workers found that most conversions from negative to positive tests were false positives, with 53.7% of positive TB skin test results reverting back to negative six months later.⁵ IFN-γ assays had similar conversion reversions at 56.8% and 63.9%. False positives among HCW can lead to misdiagnoses and unnecessary treatment.

Second, the USPSTF found only one high-quality RCT that tested the efficacy of the recommended treatment regimen for preventing active TB.¹ The 1982 International Union against Tuberculosis trial compared isoniazid antibiotic treatment with placebo in adults with pulmonary lesions but no active TB. A 6-month regimen of isoniazid, the recommended treatment, was shown to reduce incidence of TB from 15.0 to 4.7 persons/1000 at risk.¹ The USPSTF noted that the relevance of the trial is questionable due to its age and focus on subjects with pulmonary lesions, potentially overestimating benefits of latent TB infection treatments in current low-risk countries.

Potential treatment benefits may be eclipsed by the medications’ adverse effects. A systematic review on adverse effects of latent TB infection drugs found that a median of 36.1% patients experienced adverse events from isoniazid, with 8.2% experiencing grade 3-4 adverse events with a 6-month regimen.⁶ Adverse events in patients receiving other drugs ranged between 11.5% and 29.7%. For those who test positive for latent TB infection, treatments and regimens vary depending on guidelines and settings, but each has risks of events such as hepatotoxicity, neurotoxicity, and acquired antibiotic resistance, with toxicity risk increasing with comorbidities.¹
Third, risk of reactivation remains low in healthy healthcare workers. The CDC estimates that around 4% of the US population has latent TB infection and those with latent TB infection who are otherwise healthy have an annual risk of 0.1% for reactivation. ² A recent review of TB worldwide noted that: (1) most cases of active TB present soon after infection, and disease rarely manifests more than two years after infection, and (2) most TB cases do not result in major disease outbreaks, likely due to effective public health practices.⁷ Furthermore, an epidemiological study comparing healthcare workers in low and middle-income versus high-income countries found that while latent TB infection was associated with occupational exposure in low and middle-income countries, it more commonly associated with non-occupational factors in high-income countries.⁸ Among healthcare workers latent TB infection risk is low, likelihood of contracting latent TB infection from healthcare settings is low, and likelihood of TB reactivation is low.

Conclusion

WHO guidelines for high income, low incidence countries suggest that systemic testing and treatment for latent TB infection be considered, yet this is a conditional recommendation with low to very low quality of evidence.⁷ Efforts to eliminate TB through prevention are valuable, but widely screening and treating healthcare workers may be an inefficient strategy. There is no high-quality evidence to prove its efficacy, screening tests have poor specificity, treatments have substantial toxicities, and prevalence and risks of reactivation are low. Annual TB testing has shown to be cost-ineffective for North American healthcare workers and no better than targeted screening and post-exposure screening in revealing new active TB cases.⁹ Targeted testing for those with clinically high risks and post-exposure is a less expansive step, and one-step further would be to only test healthcare workers with symptoms. Annual testing of healthcare workers may be distracting TB elimination efforts and adding unnecessary burdens to already burdened healthcare workers. We believe that current policies of universal healthcare worker screening are unjustified and likely poor use of limited healthcare resources.
References


