

POLICY RECOMMENDATION: LATENT TUBERCULOSIS INFECTION SCREENING AND TREATMENT IN CHILDREN IN IMMIGRATION DETENTION

Vicki Krause and the National Tuberculosis Advisory Committee

Background

Latent tuberculosis infection (LTBI) is a sub-clinical infection with *Mycobacteria tuberculosis* complex without any clinical, bacteriological or radiological evidence of manifest TB disease.¹ LTBI results from contact with an infectious case of TB. It is characterised by the presence of mycobacterial T-cell responses, assessed by either the tuberculin skin test (TST) or more recently, interferon gamma release assays (IGRAs).²

The World Health Organization estimates that one-third of the world's population is latently infected.³ The diagnosis and treatment of LTBI is an important strategy for TB control and elimination, especially in low incidence countries where most adult cases result from reactivation of latent infection.⁴

Children with LTBI have an increased risk of developing active TB disease without treatment.⁵ Children under 4 years of age are at highest risk.² In this age group the incubation or latency period is briefer and the disease more lethal, with invasive forms of the disease such as meningeal or miliary disease being more common.⁶ Progression to active TB has been reported in up to 40% of infected infants.⁷ Other children at particular risk for TB include those who are immunocompromised, malnourished or living in high TB burden areas.² A recent population-based study of TB in children across 20 United States of America (USA) jurisdictions during 2005–2006 found that, compared with TB rates among USA-born children with US-born parents, rates were 32 times higher in foreign-born children and 6 times higher in US-born children with foreign-born parents.^{8A}

In Australia, screening for TB infection is targeted at those at high risk of recent infection (e.g. contacts of persons with TB disease or recently arrived foreign-born migrants), those at high risk of progression because of underlying conditions (e.g. HIV or disorders requiring immune-modulating drugs) or those with signs of possible past untreated TB disease.⁹ The two currently available tests for LTBI in Australia are the TST and the QuantiFERON-TB Gold test, the only commercially available IGRA in Australia.

While the use of IGRAs for the detection of infection with *M. tuberculosis* among adults has shown promising results, the evidence base is still lacking in children. A recently published review on diagnostic approaches for LTBI in children found that studies assessing IGRA performance in children are limited.² Several studies have shown a higher percentage of indeterminate results in young and or immunocompromised children.² A position statement endorsed by the National Tuberculosis Advisory Committee in 2012 stated that IGRA should not replace TST for detection of LTBI in children.¹⁰ However, IGRA may have additional value over TST in children that received bacille Calmette-Guérin vaccination after the first year of life.¹⁰

Whatever the diagnostic test, according to the US Pediatric Tuberculosis Collaborative Group, any child with LTBI should receive treatment.¹¹ This is because young age is a major risk factor for progression to active disease and infection in children is likely to have been more recent (another risk factor for reactivation of infection). Moreover, children have more years ahead of them to develop active TB. Preventive therapy should also be given to a child under 5 years of age (even if TST or IGRA negative) who is in close contact with an infectious adult until re-evaluation sometime after first contact, as this age group are most at risk of progression to active disease.²

Recommendations for the treatment of LTBI in children vary among countries; Australian guidelines for first line treatment of LTBI suggest 6–12 months of isoniazid monotherapy.^{12,13}

Latent tuberculosis infection treatment in children in immigration detention

Children in immigration detention are at increased risk of both active TB disease and latent TB infection as they mostly come from high incidence countries and prior experiences may have included poverty, overcrowding and poor access to clinical and public health services.¹⁴ By virtue of being in detention in a congregate setting, they are also at increased risk of exposure from adults with active TB. Between 2010 and 2012 the Northern Territory and Western Australia TB Units notified 57 cases

of tuberculosis among Irregular Maritime Arrivals in Australian immigration detention facilities (unpublished data).

In this context, ideally all children would be screened and treated for LTBI. Prioritisation, however, should be given to those at greatest risk of disease progression (e.g. contacts of active TB cases) and to those children attending school, as a public health initiative.

Recommendations

1. The following children (aged 6 months–18 years) in immigration detention should be screened for TB infection:
 - a. All contacts of TB cases (priority should be given to contacts of cases who have smear positive pulmonary TB cases and/or extensive lung involvement);
 - b. All children attending school (this should be undertaken optimally prior to attending school but at the latest, within one month of starting school);
2. The screening test for LTBI is the TST.
3. All children who have a positive TST and/or have symptoms or signs of TB should have a detailed history, clinical examination and chest X-ray performed to rule out active TB. This should preferably be carried out at a specialised TB Unit.
4. Children diagnosed with LTBI or children under 5 years of age who have had close contact with TB should be offered preventive treatment as per jurisdictional guidelines. Children under 5 years of age who have had contact with TB and who are TST negative should have another TST performed 3 months after their first contact. If this second test is negative, then preventive treatment can generally be ceased.
5. Children who are released from immigration detention and have not been screened for LTBI (i.e. they were not contacts or attending school) should be referred to a local TB Unit to be screened and managed according to local guidelines.

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National Tuberculosis Advisory Committee members (in alphabetical order): Associate Professor Anthony Allworth, Dr Ral Antic, Dr Ivan Bastian, Mr Philip Clift, Dr Jo Cochrane, Dr Chris Coulter (Chair), Dr Paul Douglas, Dr Justin Denholm, Dr Steve Graham, Clinical Associate Professor Mark Hurwitz, Dr Vicki Krause, Mr Chris Lowbridge, Ms Rhonda Owen, Dr Richard

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Author details

Corresponding author: Dr Vicki Krause, Director, Centre for Disease Control, Department of Health, Northern Territory Government, Ground Floor, Building 4, Royal Darwin Hospital, TIWI, NT 0810, PO Box 40596 Casuarina NT 0811. Telephone: +61 8 8922 8510. Email: vicki.krause@nt.gov.au

References

1. Tadolini M, Migliori GB. Chapter 18. The WHO strategy for TB control and elimination. *European Respiratory Monograph* 2012;58:242–253.
2. Amanatidou V, Syridou G, Mavrikou M, Tsoia MN. Latent tuberculosis infection in children: diagnostic approaches. *Euro J Clin Microbiol Infect Dis* 31(7):1285–1294.
3. World Health Organization. *Global tuberculosis report 2013*. Geneva: World Health Organization; 2013.
4. Diel R, Nienhaus A. Chapter 6. Prevention of TB in areas of low incidence. *European Respiratory Monograph* 2012;58:72–83.
5. Rutherford ME, Hill PC, Triasih R, Sinfield R, van Crevel R, Graham SM, et al. Preventive therapy in children exposed to *Mycobacterium tuberculosis*: problems and solutions. *Trop Med Int Health* 2012;17(10):1264–1273.
6. Munoz FM, Starke JR. Tuberculosis in children. In: Reichman LB, Hershfield ES, eds. *Tuberculosis: A Comprehensive International Approach*. New York: Marcel Dekker, Inc; 2000. p. 553–586.
7. Marais BJ, Gie RP, Schaaf HS, Hesselting AC, Obihara CC, Starke JJ, et al. The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era. *Int J Tuberc Lung Dis* 2004;8(4):392–402.
8. Pang J, Teeter LD, Katz DJ, Davidow AL, Miranda W, Wall K, et al. Epidemiology of tuberculosis in young children in the United States. *Pediatrics* 2014;133(3):e494–e504.
9. National Tuberculosis Advisory Committee. The strategic plan for control of tuberculosis in Australia: 2011–2015. *Commun Dis Intell* 2012;36(3):E286–E293.
10. National Tuberculosis Advisory Committee. Position statement on interferon- γ release assays in the detection of latent tuberculosis infection. *Commun Dis Intell* 2012;36(1):125–131.
11. Targeted tuberculin skin testing and treatment of latent tuberculosis infection in children and adolescents. *Pediatrics* 2004;114(Suppl 4):1175–1201.
12. Victorian Government Department of Health. Tuberculosis management, prevention and control of tuberculosis: Guidelines for health care providers 2002–2005. 2013. Accessed on 25 November. Available from: <http://ideas.health.vic.gov.au/diseases/tuberculosis-management-guide.asp>
13. Northern Territory Department of Health, Centre for Disease Control. Guidelines for the control of tuberculosis in the Northern Territory. Darwin: Centres for Diseases Control, Department of Health; 2008.
14. Kimbrough W, Saliba V, Dahab M, Haskew C, Checchi F. The burden of tuberculosis in crisis-affected populations: a systematic review. *Lancet Infect Dis* 2012;12(1):950–965.