Letters

Immigration screening for latent tuberculosis infection

To the Editor: The recent article by Denholm brings timely attention to the importance of screening for latent tuberculosis infection (LTBI) in at-risk populations.[1] Currently, screening for LTBI is targeted to patients who are thought to be at highest risk of reactivation, including patients infected with HIV and those receiving immunomodulator therapies. Given that the greatest risk factor for active TB in Australia is immigration from a region where TB is endemic, it seems reasonable to screen immigrants from endemic areas.

The premise of screening is to identify patients who will benefit from isoniazid prophylactic therapy (IPT). However, a number of unresolved issues regarding LTBI screening and management make widespread implementation problematic. First, the lifetime risk of LTBI reactivation is inherently low (2%–7%),[2] meaning that LTBI is innocuous for most patients. Second, current tests are imperfect, with poor positive predictive value for reactivation in low-incidence settings; not all patients with positive test results are at equal risk of reactivation.[3] Moreover, test sensitivity may be adversely affected by factors that increase reactivation risk (eg, immunosuppression). Third, the likelihood that the patient will complete 6–9 months of IPT is limited by drug toxicities.[4] Retrospective data collected from the charts of 57 patients who attended the Brisbane Sexual Health and HIV Service during a 9-year period, from 2002 to 2011, show that IPT was discontinued prematurely for 18 patients, after a median duration of 4 months (interquartile range, 1.25–5 months) (own unpublished data). The reasons for discontinuing IPT are shown in the Box. Severe adverse reactions were uncommon in this group of patients.

Since screening confers an obligation to treat patients with positive test results, a screening program should identify patients who are at the highest risk of reactivation and most likely to complete IPT, and thus most likely to benefit from treatment.

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1 Denholm JT. Immigration screening for latent tuberculosis infection. *Med J Aust* 2013; 198: 524.
2 Marks GB, Bai J, Simpson SE, et. al. Incidence of tuberculosis among a cohort of tuberculin-positive refugees in Australia. Reappraising the estimates of risk. *Am J Respir Crit Care Med* 2000; 162: 1851-1854.
3 Diel R, Loddenkemper R, Nienhaus A. Predictive value of interferon-gamma release assays and tuberculin skin testing for predicting progression from latent TB infection to disease state: a meta-analysis. *Chest* 2012; 142: 63-75.
4 LoBue PA, Moser KS. Use of isoniazid for latent tuberculosis infection in a public health clinic. *Am J Respir Crit Care Med* 2003; 168: 443. ❑

In reply: I thank Griffin and Kelly for elaborating on some practical elements of immigration screening for latent tuberculosis infection (LTBI) in light of their experience with isoniazid prophylactic therapy in a high-risk context.

Any screening program must strike a balance between costs (both the financial costs and the risks associated with screening) and benefits in a specific setting. Accumulating evidence suggests that higher levels of risk are associated with LTBI than previously appreciated, which prompts consideration of a correspondingly larger group who would benefit from treatment. For instance, the estimates of 2%–7% lifetime risk that Griffin and Kelly refer to are based on patients with positive tuberculin skin test results, whereas a considerably higher risk of TB reactivation has been shown by more recent research and analysis based on the results of more specific interferon-γ release assays.[1,2] Nonetheless, many individuals with LTBI (as currently diagnosed) will not develop active disease. While effective screening in appropriately selected populations is possible now, advances in LTBI testing and treatment could be used to further optimise screening programs. In particular, improved ability to predict which individuals are at high risk of reactivation would be welcome, as would treatment regimens that are shorter and better tolerated.

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> Denholm

Reasons for premature cessation of isoniazid prophylactic therapy among patients attending the Brisbane Sexual Health and HIV Service

Reason	Number (n = 18)
Gastrointestinal symptoms	3
Dizziness	1
Hepatotoxicity	3
Peripheral neuropathy	1
Pill burden	1
Tuberculosis-associated immune reconstitution inflammatory syndrome	2
Thrombocytopenia	1
Unknown	6

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