To routinely offer testing for HIV infection in all cases of tuberculosis: a rational clinical approach?

Carol R Emerson and Jeffrey J Post

ABSTRACT

- The strong interaction between the HIV and tuberculosis epidemics has been well described.
- Australian national surveillance data suggest that HIV status is ascertained by clinicians in less than 50% of people with tuberculosis.
- Clinicians are not able to reliably predict which people have HIV infection — risk factor assessment alone is insufficient.
- Because tuberculosis is an AIDS-defining condition and highly effective therapy for HIV infection is available, all patients with *Mycobacterium tuberculosis* infection should be offered HIV testing.

MJA 2008; 188: 162–163

For editorial comment, see page 131

HIV infection affects the natural history of *Mycobacterium tuberculosis* (MTB) infection.[1] Patients with HIV infection are more likely to develop active tuberculosis, develop disseminated disease,[2] reactivate latent MTB infection,[3] become re-infected with MTB,[4] and present with extrapulmonary disease.[5] Tuberculosis can occur at any CD4 count and may not be associated with clinical signs of immunodeficiency. MTB infection may accelerate HIV disease progression.[6-8]

HIV is estimated to account for 9% of all new tuberculosis cases worldwide.[9] Tuberculosis may be the presenting feature of unrecognised HIV infection and is an AIDS-defining condition.[10] Despite this relationship, HIV status is reported in less than half of the notified cases of tuberculosis in Australia.[11] We present an argument for the routine offer of HIV testing to all people diagnosed with, or treated for, MTB infection in Australia.

What is the prevalence of HIV infection in people with *M. tuberculosis* disease in Australia?

The incidence of tuberculosis in Australia has remained fairly stable since 1985 (5.3 per 100 000 population), although there was an increase in extrapulmonary disease in New South Wales between 1975 and 1995.[11,12] The contribution of HIV to this increase is unclear, as only 7% of reported patients had been tested for HIV infection. Between 1999 and 2005, HIV serostatus was reported to the tuberculosis register for only 21% of patients, although this proportion increased to 37% in 2005.[11] This dataset does not capture whether patients were offered or declined HIV testing, and underreporting is possible. The prevalence of HIV infection between 1999 and 2005 was 4.67% (74/1583) in those tested, and therefore at least 1.0% (74/7374) overall.[11]

There are limited other data that can inform clinicians about the likelihood of HIV in tuberculosis patients in Australia. A small study in Sydney in the 1990s found that at least 16% of people with tuberculous lymphadenitis had HIV co-infection.[13] The higher prevalence in the study may relate to the high prevalence of HIV infection in south-eastern Sydney or to selection of subjects with extrapulmonary disease.[5] Interestingly, only a third of these patients were born overseas. The proportion of AIDS cases associated with tuberculosis increased fivefold between 1993 and 2000 (to 2.7% of cases).[14] More recently, between 2003 and 2005, tuberculosis was reported as the AIDS-defining condition in 4.6% of AIDS patients.[15] The absolute numbers have remained relatively stable, but such data rely on physician HIV testing and reporting, as AIDS will not be diagnosed if HIV status is unknown.

What are the current recommendations for HIV testing of people with tuberculosis in Australia?

The current Australian National HIV Testing Policy 2006[16] advises HIV testing on the basis of epidemiological risk factors or patient request. The only recommended clinical indicators are pregnancy or a sexually transmissible infection. It does not specifically recommend testing in the context of HIV-associated clinical manifestations, although they have been well described.[10] It does not specify that tuberculosis is an indication for HIV testing, although the prevalence of HIV infection in people with tuberculosis is at least the same as in people who inject drugs (one of the cited epidemiological risk factors).

The National Strategic Plan for TB Control in Australia Beyond 2000[17] identifies that the overlap between the tuberculosis-infected and the HIV-infected populations in Australia is numerically small. It recommends monitoring the incidence of MTB infection in the HIV seropositive population, but does not recommend HIV testing of all people with tuberculosis.

Where state or territory guidelines for clinicians could be found on an Internet search, they varied from always recommending testing to no recommendation or that clinicians "consider HIV infection in every case of tuberculosis infection"[18] or ask about risk factors and have a "low threshold" for HIV testing.[19]

A range of developed countries recommend testing for HIV infection for all people with tuberculosis.[20-23]

Can clinicians predict which patients with tuberculosis have HIV infection?

North American data suggest that clinicians are unable to predict HIV infection in people with tuberculosis. A study of hospitalised patients with smear-positive tuberculosis revealed that systematic questioning did not identify risk factors for HIV infection in all HIV-infected tuberculosis patients.[24] Disturbingly, they identified that more than half of those with HIV infection had no risk factors identified in the medical record. Another study found rates of HIV infection as high as 18% in people who were considered at low risk and that such patients were significantly less likely to be offered testing.[25]

Is testing likely to be cost-effective?

In the United States, one study found that routine testing is cost-effective even when the prevalence of HIV infection is as low as

0.2%.[26] It is likely that HIV testing of people with tuberculosis in Australia would be cost-effective, as the minimum prevalence is 1.0%.

Are there legal issues that clinicians should consider?

The NSW Supreme Court found a general practitioner negligent in not diagnosing HIV infection in a man with hepatitis B virus infection who transmitted HIV infection to his partner.[27] This precedent could provide legal argument for failure to diagnose HIV infection in the setting of a condition with a strong association with HIV infection (such as tuberculosis, which is an AIDS-defining condition).

How should clinicians act in the face of the current data and recommendations?

HIV testing is appropriate for most people with tuberculosis regardless of identified risk factors. Clinicians are not able to reliably predict which people have HIV infection, as risk factor assessment alone is insufficient. Tuberculosis is an AIDS-defining condition and clinicians have a responsibility to ensure that HIV is excluded, as highly effective therapy for HIV infection is available[28] and HIV transmission can be prevented.

We recommend that all patients with *M. tuberculosis* infection, whatever their perceived risk for HIV infection, be offered an HIV test, with appropriate pre-test discussion.

Acknowledgements

We would like to acknowledge Dr Mark Kelly and Dr John McCaffrey for reviewing the manuscript.

Competing interests

None identified.

Author details

Carol R Emerson, MB BCh, BAO, MRCP(UK), HIV Clinical Fellow,[1] and Conjoint Associate Lecturer[2]
Jeffrey J Post, MB BS(Hons), FRACP, Infectious Diseases Physician,[1] and Conjoint Senior Lecturer[2,3]

1 Department of Infectious Diseases, Prince of Wales Hospital, Sydney, NSW.
2 Prince of Wales Clinical School, University of New South Wales, Sydney, NSW.
3 School of Medical Sciences, University of New South Wales, Sydney, NSW.

Correspondence: jeffrey.post@sesiahs.health.nsw.gov.au

References

1 Post JJ. *Mycobacterium tuberculosis*. In: Hoy J, Lewis S, editors. HIV management in Australia, a guide for clinical care. Sydney: Australian Society for HIV Medicine, 2003.
2 Valway SE, Richards SB, Kovacovich J, et al. Outbreak of multi-drug-resistant tuberculosis in a New York State prison. *Am J Epidemiol* 1994; 140: 113-122.
3 Selwyn PA, Hartel D, Lewis VA, et al. A prospective study of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *N Engl J Med* 1989; 320: 545-550.
4 Small PM, Shafer RW, Hopewell PC, et al. Exogenous reinfection with multidrug-resistant *Mycobacterium tuberculosis* in patients with advanced HIV infection. *N Engl J Med* 1993; 328: 1137-1144.
5 Onorato IM, McCray E. Prevalence of human immunodeficiency virus infection among patients attending tuberculosis clinics in the United States. *J Infect Dis* 1992; 165: 87-92.
6 Whalen C, Horsburgh CR, Hom D, et al. Accelerated course of human immunodeficiency virus infection after tuberculosis. *Am J Respir Crit Care Med* 1995; 151: 129-135.
7 Collins KR, Quinones-Mateu ME, Toossi Z, et al. Impact of tuberculosis on HIV-1 replication, diversity, and disease progression. *AIDS Rev* 2002; 4: 165-176.
8 Goletti D, Weissman D, Jackson RW, et al. Effect of *Mycobacterium tuberculosis* on HIV replication. Role of immune activation. *J Immunol* 1996; 157: 1271-1278.
9 Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med* 2003; 163: 1009-1021.
10 Workman C. Clinical manifestations of HIV disease. In: Hoy J, Lewis S, editors. HIV management in Australia, a guide for clinical care. Sydney: Australian Society for HIV Medicine, 2003.
11 Roche PW, Bastian I, Krause V. Tuberculosis notifications in Australia, 2005. *Commun Dis Intell* 2007; 31: 71-80.
12 Heath TC, Roberts C, Winks M, et al. The epidemiology of tuberculosis in New South Wales 1975–1995. *Int J Tuberc Lung Dis* 1998; 2: 647-654.
13 Wark P, Goldberg H, Ferson M, et al. Mycobacterial lymphadenitis in eastern Sydney. *Aust N Z J Med* 1998; 28: 453-458.
14 Dore GJ, Yueming L, McDonald A, et al. Impact of highly active antiretroviral therapy on individual AIDS-defining illness incidence and survival in Australia. *J Acquir Immune Defic Syndr* 2002; 29: 388-395.
15 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2006. Sydney: National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, 2006. http://www.nchecr.unsw.edu.au/NCHECRweb.nsf/page/Annual%20Surveillance%20Reports (accessed Oct 2007).
16 Australian Government Department of Health and Ageing. National HIV Testing Policy 2006. Canberra: Department of Health and Ageing, 2006. http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm (accessed Oct 2007).
17 Communicable Diseases Network Australia. National Strategic Plan for TB Control in Australia Beyond 2000. Canberra: Department of Health and Ageing, 2002. http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/cda-pubs-other-tb_plan.htm (accessed Oct 2007).
18 NSW Health. Tuberculosis and HIV. Policy directive PD2005_076. http://www.health.nsw.gov.au/policies/PD/2005/pdf/PD2005_076.pdf (accessed Oct 2007).
19 Victorian Government Department of Human Services. Management, control and prevention of tuberculosis. Guidelines for health care providers (2002–2005). Melbourne: Department of Human Services, 2002. http://www.health.vic.gov.au/__data/assets/pdf_file/0006/19986/tb_mgmt_guide.pdf (accessed Oct 2007).
20 Houston S, Schwartzman, Brassard P, et al. Tuberculosis and human immunodeficiency virus. In: Long R, Chernick V, Elwood K, et al, editors. The Canadian tuberculosis standards. 5th ed. Ottawa: Health Canada and the Canadian Lung Association, 2000: 45-65. http://www.phac-aspc.gc.ca/publicat/cts-ncla00/index.html (accessed Oct 2007).
21 Iskander R, Wass T, Jones J, et al. Communicable Diseases Surveillance Centre annual report 2001. London: London Regional Office, 2001.
22 American Thoracic Society, CDC, and Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR Recomm Rep* 2003; 52(RR-11): 1-77.
23 Ministry of Health, New Zealand. Guidelines for tuberculosis control in New Zealand 2003. Wellington: Ministry of Health, 2002. http://www.moh.govt.nz/publications/guidelines (accessed May 2007).
24 Barnes P, Silva C, Otaya M. Testing for human immunodeficiency virus infection in patients with tuberculosis. *Am J Respir Crit Care Med* 1996; 153: 1448-1450.
25 Geduld J, Brassard P, Culman K, et al. Testing for HIV among patients with tuberculosis in Montreal. *Clin Invest Med* 1999; 22: 111-118.
26 Paltiel AD, Walensky RP, Schackman BR, et al. Expanded HIV screening in the United States: effect on clinical outcomes, HIV transmission and costs. *Ann Intern Med* 2006; 145: 797-806.
27 *BT v Oei* [1999] NSWSC 1082.
28 Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV outpatient study investigators. *N Engl J Med* 1998; 338: 853-860.

(Received 5 Jul 2007, accepted 9 Oct 2007) ❑