Clinical basics

Tuberculosis: 13. Control of the disease among aboriginal people in Canada

J. Mark FitzGerald, Lei Wang, R. Kevin Elwood

Case 1

A 36-year-old aboriginal woman has a 12-mm-diameter reaction to a tuberculosis (TB) skin test, done as part of a community survey. She was vaccinated with BCG (bacille Calmette–Guérin) at 6 weeks of age. There is no documented history of contact with TB, and no skin tests were carried out previously. The woman's family doctor wonders about the significance of the result.

Case 2

A 27-year-old aboriginal man presents with a 6-week history of cough and fever and recent onset of hemoptysis. He has recently completed 2 courses of antibiotics, but there has been no improvement in symptoms. Chest radiography shows right upper lobe pneumonia. A further course of antibiotics is prescribed. What investigations should be completed next?

Case 3

The mother of a 2-day-old aboriginal infant asks for advice about the benefits of BCG vaccination. She is confused about the side effects of BCG and its effectiveness.

Tuberculosis (TB) remains a major public health problem for aboriginal people in Canada.[1] Although incidence rates for this segment of the population have declined in many parts of the country,[2] they remain unacceptably high. These rates tend to be highest in more northerly and remote areas, communities that were the last to be exposed to TB as European settlers moved across Canada.[3] In 1996 annual incidence rates for status Indians were highest in Saskatchewan, at 105 per 100 000 population, and lowest in the Atlantic region, where no cases of active disease were recorded. The annual incidence rate for status Indians for 1996 (35.8 per 100 000 population) greatly exceeded that for Canadian-born people of nonaboriginal descent, for whom the rate was less than 2 per 100 000 population, and for the population as a whole, for which the rate was 6.5 per 100 000 population.[2] The prevalence of tuberculous infection is much higher in aboriginal communities[4] than among Canadian-born nonaboriginal people, and it is therefore likely that TB will remain a major problem in these communities for the foreseeable future. A reduction in rates will likely be achieved only with improvements in socioeconomic status and community involvement in disease management combined with comprehensive medical surveillance and treatment programs.[5] With such high rates of infection, the potential for an increase in rates of disease is real, especially if control efforts are relaxed or there are significant changes in risk categories.

Management of TB among aboriginal people

As with all TB programs, the priority for TB control in aboriginal populations is prompt diagnosis and initiation of antituberculous therapy, particularly for smear-positive infectious cases. The high prevalence of disease in these communities means that there should be a low threshold for considering the possibility of TB in aboriginal people. Therefore, patients with respiratory tract symptoms who continue to be symptomatic after a course of antibiotics should undergo chest radiography as well as sputum smear and culture for acid-fast bacilli. The classic apical distribution of TB[6] will be found in most cases.

Review

Synthèse

From the BC Centre for Disease Control Society, Vancouver, BC

Series editor: *Dr. Anne Fanning, Division of Infectious Diseases, University of Alberta, Edmonton, Alta.*

CMAJ 2000;162(3):351-5

For a complete list of the articles in this series, see the final page of this article.

There are a number of differences in presentation and prior history between aboriginal people and the general population. For example, aboriginal people are less likely than members of the general population to have lymphadenopathy (5.9% v. 16.4%), more likely to have pleural disease (21.3% v. 16.4%) and more likely to have a prior history of contact (53% v. 17.9%).[7] Similarly, cavitary disease is twice as common among aboriginal people as in the general population (18.9% v. 9.3%).[7]

Only about half of all cases of pulmonary TB are smear positive, and there is no difference in the proportion of aboriginal and nonaboriginal subjects with smear- or culture-positive disease.[7] Therefore, in the presence of suggestive radiographic findings and despite the presence of a smear-negative sputum sample, empiric antituberculous therapy is warranted while awaiting culture results and a potential radiologic response.[7] This combination of radiologic and clinical responses may be the only proof of disease in the 10% to 15% of cases that are not bacteriologically proven. The converse is also true. Although its results were unusual, a recent study from Saskachewan[8] reported that in 25 of 518 consecutive cases of pulmonary TB, chest radiography results were normal but disease was proven bacteriologically. Thus, in the presence of symptoms, sputum should be assessed for the presence of acid-fast bacilli even if chest radiography results are normal.

Although smear-positive cases have priority, it should be recognized that people with smear-negative, culture-positive TB can also transmit the disease.[9] Among aboriginal people, there is an added dimension to the need for prompt initiation of therapy to render cases noninfectious, because of the significant risk of clustering (occurrence of 2 or more cases of TB with the same genetic fingerprint, determined by restriction fragment length polymorphism analysis[10]).[11] Data from western Canada indicate that 42% of cases among aboriginal people are due to recent infection (i.e., the effects of clustering), whereas the proportion among the rest of the population is less than 12%[12] (the remainder of active cases are due to reactivation of prior infection).

Although controversial,[13,14] directly observed therapy (DOT) has been recommended as a standard of care by the World Health Organization and endorsed by many other agencies. In Canada, DOT is currently the standard of care for all regions where the Medical Services Branch of Health Canada is responsible for TB control policies on reserves. This accounts for the majority of TB control activities for on-reserve status Indians. As its name implies, DOT requires the direct observation of the ingestion of medication by a health care worker or surrogate.[15] Such a program must be implemented with sensitivity and must include frank discussion with the patient of the difficulty he or she may experience in maintaining the motivation to take the medications over a prolonged period, particularly when, after the initial acute phase, he or she may be essentially asymptomatic. Nonadversarial implementation of DOT with a well-informed patient is usually seen as an opportunity not only to ensure that the patient receives the medication, but also to assist the patient in prompt recognition of adverse reactions. A systematic review of randomized controlled trials of strategies to promote adherence to TB treatment showed that the best results were achieved with a combination of patient incentives and health education. Compared with traditional administration of therapy, patients who were given incentives and education were more likely to complete their course of medication (odds ratio 2.4, 95% confidence interval 1.5 to 3.7).[16] It is important to acknowledge the cultural and social issues related to implementing DOT among aboriginal people. Hunting and community ceremonial events may interfere with such a program, so some flexibility is needed. For example, if a patient goes into the bush to hunt, a buddy system could be provided whereby a friend or family member would assume responsibility for supervising medication. The effectiveness of DOT relative to self-administered therapy has not been formally evaluated among aboriginal people, but our experience in using directly observed chemoprophylaxis[17] indicates that this method is associated with better rates of completion of therapy.

Overall completion rates for treatment of Canadian aboriginal people living on reserves ranged from 82.1% in Ontario to 97.3% in Saskatchewan for the period 1991 to 1996.[2] These completion rates are equivalent to or better than those for the general population.

BCG vaccination

There is controversy about the role of BCG vaccination in TB control. A recent meta-analysis suggested that BCG confers a protective effect of nearly 90% against TB meningitis and miliary TB.[18] The protective effect against pulmonary TB is less dramatic, probably in the range of 50%.[18] BCG is generally well tolerated, although when given half the usual adult dose (the current standard dose for infants), approximately 2% to 3% of infants have a local reaction.[19] In the early 1990s those responsible for the TB vaccination program in British Columbia recognized that these adverse reactions, although occurring in only a small minority of patients, were a disincentive to the use of BCG; they therefore started using a quarter of the usual adult dose, and the rate of local reactions has declined significantly (J.M.F., unpublished data). This policy differs from that in the rest of the country. The original dosing recommendation was based on limited data and as reduced doses are associated with less adverse reactions, this is a reasonable compromise. Data for vaccine efficacy with the reduced dose are not known.

More recently, a greater concern with regard to the use of BCG in aboriginal infants is the potential for immunization of infants with unrecognized HIV infection and subsequent development of what is known as disseminated "BCG-itis." BCG-itis is the occurrence of fever and a clini-

cal pattern similar to that of miliary TB after administration of BCG to an immunocompromised person[20] (or, in rare instances, use of BCG as a treatment for bladder cancer). Therefore, when considering administration of BCG to infants it is important to first determine that they are not infected with HIV. Because HIV testing is now recommended for all pregnant women, antenatal recognition of HIV infection should allow appropriate antiretroviral prophylaxis to be given to the mother, but as the newborn infant may still be infected with HIV it is recommended that careful follow-up be done and that caution be used before BCG is given. In addition, there have been recent reports in Canada of disseminated BCG-itis associated with severe combined immune deficiency syndrome.[20] The use of BCG against this background is presently being reviewed by the Medical Services Branch of Health Canada; however, on the basis of a decision analysis it is likely that BCG use will continue to be recommended in the foreseeable future (Dr. Theresa Jordan: personal communication, 1999).

Vaccination with BCG may affect the results of subsequent purified protein derived (PDD) skin testing. In general, BCG given in infancy is unlikely to lead to a positive PDD response (induration of greater than 10 mm diameter) in later life. Thus, a positive PPD test result in a BCG-vaccinated person probably indicates concurrent or previous TB infection.[21] Nonetheless, people who have been vaccinated with BCG pose special problems in the investigation of possible contacts of a person diagnosed with TB. In a recent study of a large group of contacts of several active cases of TB, we showed that ignoring BCG history may lead to overuse of chemoprophylaxis.[22] Of 732 non-BCG contacts, 134 (18.3%) were offered chemoprophylaxis, whereas 169 (43.8%) of 386 contacts who had received BCG were offered chemoprophylaxis ($p < 0.001$).

Despite the proven efficacy of BCG,[18] its use varies across the country. In Ontario the proportion of aboriginal infants who receive the vaccine ranges from 1% and 98.5% in different regions of the province (several different programs implement BCG vaccination in Ontario); in British Columbia 90% of aboriginal newborns living on reserves receive BCG, in Alberta the proportion is 60%, in Saskatchewan it is 50%, in Quebec it is 35% and for Canada as a whole the proportion is 35%.[2] Concerns about side effects and efficacy as well as potential interference with subsequent TB skin testing, rather than concerns about cost, appear to be the major impediments to its use. If rates of TB continue to fall, the role of BCG will likely diminish, but before it is withdrawn completely, it will be necessary to have in place an appropriate surveillance mechanism for TB. For aboriginal communities this is especially important if, as part of health transfer (see below), TB control becomes decentralized. Criteria for discontinuation of BCG vaccination have been defined.[23] Although individual communities may fulfill these criteria, overall the decision has been made that BCG vaccination should continue for now.

Chemoprophylaxis

Chemoprophylaxis has been dealt with in detail earlier in this series.[24] However, several aspects of chemoprophylaxis in aboriginal populations should be emphasized. As the number of TB cases in aboriginal communities declines, there will be an increasing need for active surveillance to ensure appropriate intervention with chemoprophylaxis when warranted, particularly if BCG vaccination is discontinued. Aboriginal people have a significantly higher prevalence of tuberculous infection than the general population (approximately twice as high) and chemoprophylaxis will be a key component of TB elimination in this group.[2] Chemoprophylaxis, which is given to prevent future development of active disease, is a challenge because it requires that the patient take medication even though he or she is asymptomatic. However, directly observed chemoprophylaxis has been associated with greater rates of completion of medication than self-administered chemoprophylaxis (50.9 v. 36.6%).[17] It is likely that the risk of hepatitis infection was overstated in previous studies; a more recent study from the United States showed an extremely low rate of hepatotoxicity in a large cohort of patients followed in Seattle County[25]: among 11 141 consecutive patients starting therapy with isoniazid, 0.01% of those starting and 0.15% of those completing the therapy had hepatotoxic reactions. There was no routine monitoring using liver function tests.

Recent publications showing the benefit of ultra-short-course chemoprophylaxis in the context of dual HIV and TB infection[26] suggest that this approach may be useful for chemoprophylaxis among aboriginal people. The short-course regimens may be associated with a slightly increased risk of hepatotoxicity, but the possibility of having to complete only 8 weeks, rather than 12 months, of chemoprophylaxis is appealing.

When administering isoniazid prophylactically, physicians must be aware of its potential use as a means of suicide. In our recent case series,[17] one person in the self-administration group committed suicide with isoniazid. Therefore, this medication should not be prescribed for self-administration to those at risk of suicide. Issues related to suicide and isoniazid administration are discussed in greater detail elsewhere.[17]

TB control and substance abuse in the inner city

Aboriginal people form a disproportionate group of the poor and deprived residents of Canada's inner cities. For example, among injection drug users in Vancouver, approximately 30% are thought to be aboriginal.[27] Among participants in the Vancouver Injection Drug Users Study, 25% had tuberculous infection and 23% were infected with HIV.[28] These high rates of disease bring with them the risk of clustering and the potential for significant deterioration in efforts to control TB. In addition, we have identified a significant increase in HIV-related TB in Vancouver,

mainly among young aboriginal women who are injection drug users.[29] Surveillance efforts will be successful only if they are undertaken in tandem with appropriate measures to improve housing and provide better substance abuse programs and greater involvement with community agencies.

Health transfer

Across Canada many aboriginal bands are now assuming responsibility for control of their members' health. This decentralization of health care, termed "health transfer," is to be welcomed, but caution is needed in terms of TB control. TB control was decentralized in the Northwest Territories (now the Northwest Territories and Nunavut) in the mid-1980s, when rates of disease had declined significantly.[2] Recently, however, there has been a major resurgence of TB in this part of the country, and a major obstacle to disease control is the lack of central coordination. TB control in high-prevalence communities brings with it unique challenges, which are further magnified by the movement of people from the reserve to local communities and inner city locations (and vice versa). This mobility of patients has been identified as a major risk factor for defaulting from treatment (relative risk 5.5, 95% confidence interval 4.1 to 7.4).[30] TB control in this decentralized environment necessitates education for health care providers such as public health nurses, community health representatives and lay drug dispensers. These people will be required to work within a coordinated program to manage active TB cases, investigate outbreaks and carry out surveillance. Such a program must also address deficiencies in knowledge about TB, such as those identified in recent surveys.[31]

Conclusions

TB control among aboriginal people in Canada, both those living on reserves and those residing in the inner city, continues to pose a major public health problem. The potential for a significant worsening of the situation is real, especially for the marginalized inner-city population with a background of substance abuse. Major efforts, involving targeted surveillance, DOT and chemoprophylaxis, will be needed to prevent such a deterioration.[28] In addition, attention must be paid to social issues such as housing and programs to reduce substance abuse. These goals must be achieved in a culturally sensitive manner with a greater degree of community partnership than has been seen in the past.[32]

Resolution of the cases

Case 1

The positive result for the skin test is probably not related to the BCG received in infancy; it is more likely related to tuberculous infection and indicates that the woman has a 10% lifetime risk of active TB. Isoniazid chemoprophylaxis taken for 12 months will reduce this risk by 90%.[33] The risk of hepatitis related to the chemoprophylaxis has probably been overestimated in previous studies[25] and is probably less than 0.5%. In the general population, age is often a factor in the decision of whether to prescribe isoniazid, with people over 35 years of age not receiving the drug. However, in a high-risk population such as aboriginal people, use of isoniazid has been recommended for patients of any age.[34] Therefore, this woman should be given the chemoprophylaxis, even though she is over 35 years of age.

Case 2

A chest x-ray shows a small cavity in the right apex and sputum is positive on smear for acid-fast bacilli. Contact investigation is initiated after more detailed history-taking reveals that the man has assisted in ceremonies at the community's longhouse (a ceremonial building used for aboriginal cultural events) over a 6-month period. After extended follow-up in the community, a total of 20 cases of active TB are diagnosed.

Case 3

The protective effect of BCG against disseminated miliary TB and TB meningitis is explained to the mother (a meta-analysis has shown that the protective effect of BCG against these life-threatening forms of TB is close to 90%,[18] although protection against pulmonary TB is less definitive, likely in the range of 50%[18]). Recently, there have been occasional reports of disseminated BCG-itis in Canada associated with HIV infection or severe combined immune deficiency syndrome. However, the mother's HIV status was assessed antenatally, and her serum was nonreactive. The mother is also told that local adverse reactions to BCG may also occur (the risk being 1% to 2% at most), and the usual benign evolution of these reactions is explained to her. She agrees to have the infant vaccinated.

Dr. Wang was funded by the World Bank.

Competing interests: None declared.

References

1. Young TK, Casson RI. The decline and persistence of tuberculosis in a Canadian Indian population: implications for control. *Can J Public Health* 1988;79:302-6.
2. Medical Services Branch. *Tuberculosis program and epidemiologic review*. Ottawa: Minister of Public Works and Government Services; 1999. Cat no H34-96/199E.
3. Gaudette LA, Ellis E. Tuberculosis in Canada: a focal disease requiring distinct control strategies for different risk groups. *Tuber Lung Dis* 1993;74:244-53.
4. Division of Tuberculosis Control, BC Centre for Disease Control Society. *Annual report 1998*. Vancouver: BC Ministry of Health; 1998.
5. Schluger N, Ciotoli C, Cohen D, Johnson H, Rom WN. Comprehensive tuberculosis control for patients at high risk for non-compliance. *Am J Respir Crit Care Med* 1995;151:1486-90.
6. Joseph K, Korzeniewska-Kosela M, Müller N, FitzGerald JM. Radiologic features of pulmonary tuberculosis: an assessment of 188 cases. *Can Assoc Radiol J* 1994;45:101-7.
7. Wang L, Noertjojo K, Elwood RK, FitzGerald JM. Tuberculosis among Aboriginal and non-Aboriginal persons in British Columbia [abstract]. *Int J Tuberc Lung Dis* 1998;2(Suppl):S149.
8. Marciniuk DD, McNab BD, Martin WT, Hoeppner VH. Detection of pulmonary tuberculosis in patients with a normal chest radiograph. *Chest* 1999;115:445-52.
9. Behr M, Warren SA, Salamon H, Hopewell PC, Ponce de Leon A, Daley CL, et al. Transmission of *Mycobacterium tuberculosis* from patients smear-negative for acid-fast bacilli. *Lancet* 1999;353:444-9.
10. Kulaga S, Behr MA, Schwartzman K. Genetic fingerprinting in the study of tuberculosis transmission. *CMAJ* 1999;161(9):1165-9.
11. FitzGerald JM, Black WA, Kunimoto D. Evaluation of non-HIV related, drug sensitive cluster outbreaks of TB with PCR based DNA finger printing.

Can Respir J 1996;3:317-21.
12. FitzGerald JM, Kunimoto D, and Canadian Molecular Epidemiology of TB Study Group. Molecular epidemiology of TB in Canada [abstract 75]. *Clin Invest Med* 1997;20:4.
13. Garner P. What makes DOT work? Directly observed therapy. *Lancet* 1998;352:1326-7.
14. Moore RD, Chaulk CP, Griffiths R, Cavalcante S, Chaisson RE. Cost-effectiveness of directly observed self-administered therapy for tuberculosis. *Am J Respir Crit Care Med* 1996;154:1013-9.
15. Hershfield E. Tuberculosis: 9. Treatment. *CMAJ* 1999;161(4):405-11.
16. Volmink J, Garner P. Systematic review of randomized controlled trials of strategies to promote adherence to tuberculosis treatment. *BMJ* 1997;315:1403-6.
17. Heal G, Elwood RK, FitzGerald JM. Acceptance and safety of directly observed versus self-administered isoniazid preventive therapy in aboriginal peoples in British Columbia. *Int J Tuberc Lung Dis* 1998;2:979-83.
18. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, et al. Efficacy of BCG vaccine in the prevention of tuberculosis: meta-analysis of the published literature. *JAMA* 1994;271:698-702.
19. FitzGerald JM, Duclos P. The reporting and management of adverse reactions to bacillus Calmette-Guérin (BCG) vaccination. *Can Dis Wkly Rep* 1991;17(19):98-100.
20. Disseminated bacille Calmette-Guérin infection: three recent Canadian cases. *Can Commun Dis Rep* 1998;24-9:69-75.
21. Menzies RI, Vissandjee B, Amyot D. The effect of remote BCG vaccination on tuberculin reactivity. *Am Rev Respir Dis* 1992;145:621-5.
22. Noertjojo K, Wong L, Elwood RK, FitzGerald JM. The impact of BCG on PPD skin test results: results from a large number of contacts identified in cluster outbreaks [abstract]. *Int J Tuberc Lung Dis* 1998;2:S149.
23. International Union Against Tuberculosis and Lung Disease. Criteria for discontinuation of vaccination programs using bacille Calmette-Guérin (BCG) in countries with a low prevalence of tuberculosis. *Tuber Lung Dis* 1994;77:179-80.
24. Menzies D, Tannenbaum TN, FitzGerald JM. Tuberculosis: 10. Prevention. *CMAJ* 1999;161(6):717-24.
25. Nolan CM, Goldberg SV, Buskin SE. Hepatotoxicity associated with isoniazid preventive therapy: a 7-year survey from a public health tuberculosis clinic. *JAMA* 1999;281:1014-8.
26. Watson F, Dahl N, Remple S, Elwood RK, FitzGerald JM, and VIDUS Group. Use of directly observed chemoprophylaxis among intravenous drug users with a high prevalence of HIV infection [abstract]. *Int J Tuberc Lung Dis* 1998;2:S139.
27. Halsey NA, Coberly JS, Desmormeaux J, Losikoff P, Atkinson J, Moulton LH, et al. Randomised trial of isoniazid versus rifampicin and pyrazinamide for prevention of tuberculosis in HIV-1 infection. *Lancet* 1998;351:786-92.
28. FitzGerald JM, Patrick D, Strathdee S, et al. Prevalence of tuberculous infection in a population of intravenous drug users [abstract]. *Am J Respir Crit Care Med* 1997;155(Suppl):A561.
29. Blenkush MF, Korzeniewska-Kosela, Elwood RK, Black W, FitzGerald JM. HIV-related tuberculosis in British Columbia: indications of a rise in prevalence and a change in risk groups. *Clin Invest Med* 1996;19:271-8.
30. Cummings KC, Mohle-Boetani J, Royce SE, Chin DP. Movement of tuberculosis patients and the failure to complete anti-tuberculosis treatment. *Am J Respir Crit Care Med* 1998;157:1249-52.
31. Broder S, Elwood RK, Clifton J, FitzGerald JM. Knowledge, attitudes and beliefs towards tuberculosis in two Aboriginal communities [abstract 550]. *Clin Invest Med* 1997;20:4.
32. MacMillan HL, MacMillan AB, Offord DR, Dingle JL. Aboriginal health. *CMAJ* 1996;155:1569-78.
33. IUAT Committee on Prophylaxis. Efficacy of various durations of INH preventative therapy for tuberculosis: five years of follow-up in the IUAT trial. *Bull World Health Organ* 1982;60:555-64.
34. Standards Committee, Canadian Thoracic Society (FitzGerald JM, editor). *Canadian tuberculosis standards*. 4th ed. Ottawa: Canadian Lung Association; 1996.

Reprint requests to: *Dr. J. Mark FitzGerald, BC Centre for Disease Control Society, 655 W 12th Ave., Vancouver BC V5Z 4R4; fax 604 660-1950; markf@interchange.ubc.ca*

CMAJ's tuberculosis series

This series is now complete.