



Tuberculosis: 10. Prevention

Dick Menzies, MD, MSc; Terry Nan Tannenbaum, MD, MPH;
J. Mark FitzGerald, MD

Tuberculosis (TB) can be prevented by means of 2 major strategies. The first is to prevent transmission from patients with active, contagious forms of the disease to uninfected people; this strategy will prevent new infections. The other strategy aims to prevent development (called reactivation) of disease after infection. Prevention is possible if the person has undergone BCG (bacille Calmette–Guérin) vaccination before exposure, because although BCG vaccine cannot prevent the acquisition of infection, it will (to a variable extent) prevent the development of disease. Prevention of disease after infection can also be accomplished by antibiotic treatment before active disease develops. This strategy relies on the identification of people with latent or dormant infection, usually by means of the tuberculin skin test.

Preventing transmission

The most important and effective means of preventing new infections is to eliminate the sources of transmission.^{1,2} Therefore, the first priority of TB control programs is to ensure that active disease is diagnosed as early as possible (a process called case-finding) and that patients are treated with an effective antibiotic regimen until they are cured (which is called case-holding). A TB control program should not embark on other activities such as screening until it has achieved the benchmark of 90% successful completion of therapy for all patients with active disease.

Prevention of transmission requires prompt respiratory isolation of people with suspected pulmonary or laryngeal TB. Such isolation is most effectively carried out in hospital (see upcoming article in this series on nosocomial disease). If a patient cannot be admitted to hospital or must be discharged while still contagious, the treating physician must ensure that the patient remains in quasi-isolation at home. Such patients cannot return to work or school, nor can they engage in their usual social activities. They must avoid any contact with people who are highly susceptible to TB, particularly very young children and people infected with HIV. Because transmission of TB occurs primarily in indoor environments, patients must avoid all indoor public places, such as cinemas and shops. These measures must continue until the patient is no longer contagious, although it is difficult to precisely define the duration of this state, and there is some controversy about this issue. By the most conservative — that is, the safest — definition, initially smear-negative but culture-positive patients remain contagious until the end of 2 weeks of therapy, whereas initially smear-positive patients are contagious until conversion of the smear to negative,³ which takes at least 2 weeks of full antituberculosis therapy but may take much longer, up to 2 or 3 months in some patients with extensive disease.

Once therapy has started, the most important determinant of continued contagiousness is degree of compliance with treatment.^{1,3} Various strategies are available to help patients complete their therapy, and mechanisms to identify and correct suboptimal compliance must be established by the treating physician, in collaboration with public health authorities, *before* treatment is prescribed. It is no longer considered acceptable medical practice to simply prescribe therapy for active TB and assume that the patient will comply. At a minimum, the physician must notify public health authorities, see the patient

Education

Éducation

Dr. Menzies is Associate Professor of Medicine and of Epidemiology and Biostatistics, Respiratory Epidemiology Unit, McGill University, Montreal, Que.; Dr. Tannenbaum is Assistant Professor of Epidemiology and Biostatistics, McGill University, and is also with the Direction de la santé publique, Régie régionale de la santé et des services sociaux de Montréal-Centre, Montreal, Que.; and Dr. FitzGerald is Associate Professor of Medicine, University of British Columbia, Vancouver, BC.

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

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frequently and assess compliance at each visit; in addition, a recall system must be in place to alert the physician if the patient misses an appointment. Compliance should be estimated from several indicators, such as punctuality with follow-up visits, urine testing for isoniazid metabolites as well as visual examination for the orange-red discoloration caused by rifampin, and pill counts.⁴ When compliance is suboptimal, the local or regional public health unit should become involved, to develop a coordinated management strategy. Such a strategy might include intensive patient education, simplification of the treatment regimen, a greater number of visits to the physician, home visits by a nurse or other health care provider, and enlisting the help of family members. Directly observed therapy may be instituted. In extreme cases, legal measures may be needed to enforce treatment, but this occurs only rarely.

Key points

Preventing transmission of tuberculosis (TB)

- A person with suspected pulmonary or laryngeal TB should be placed in respiratory isolation, preferably in hospital
- If hospital isolation is not possible, the person must be kept in quasi-isolation at home, staying home from work or school and avoiding social situations, particularly indoor public places (e.g., shops)
- Contact with those susceptible to TB must be avoided
- Compliance with therapy must be ensured through frequent visits to the physician, urine testing and pill counts
- If necessary, public health or legal authorities may become involved

Preventing disease after infection

The risk of development of active TB after infection can be reduced if the person has undergone BCG vaccination before exposure. The BCG vaccine is a live attenuated vaccine first developed from *Mycobacterium bovis* by 2 French microbiologists, Calmette and Guérin. The vaccine is usually given intradermally at a dose of 2×10^6 bacilli for infants and $4-5 \times 10^6$ for older children and adults. The vaccine usually causes a local reaction characterized by induration (swelling) that may progress to necrosis and local ulceration with drainage for 2 to 6 weeks after the vaccination. Regional lymphadenopathy occurs infrequently, and in 1% to 2% of all vaccines the regional lymph nodes will suppurate and drain.⁵ These adverse effects are usually self-limiting, and no specific therapy is required in most infants⁵ (unpublished data). These complications are much less frequent in

older children and adults. The only significant contraindication to BCG vaccination is severe immunodeficiency, either inherited or acquired; dissemination of BCG, which can be fatal, may occur in infants with these disorders.⁶ In communities where BCG is routinely given to newborns and HIV prevalence is rising, the policy of BCG vaccination should be reconsidered; if after reconsideration the policy is continued, prenatal HIV testing is essential.

At present, BCG vaccination is used almost worldwide. The World Health Organization has estimated that 88% of all infants born receive this vaccine. In countries or communities where the annual risk of TB infection is greater than 1%, BCG should be given to newborns because it is effective in preventing TB meningitis and miliary TB in the first few years of life.⁷ Without the vaccine, severe, life-threatening forms of TB meningitis and miliary TB can develop rapidly in infants who become infected early in life. In some instances, the first indication of an adult with active pulmonary TB has been the presentation of an infant with one of these severe forms.

However, the role of BCG vaccination in TB control in Canada remains controversial, partly because of the declining incidence and changing epidemiology of TB; thus, the need for BCG vaccination must be re-evaluated periodically. In addition, the reported efficacy of BCG vaccination in preventing pulmonary forms of TB in adolescents and young adults has been highly variable, ranging from 0% to more than 80%.^{8,9} There is no satisfactory explanation for these contradictory results, although many theories have been advanced.^{7,9-11} Furthermore, because BCG does not prevent infection but rather acts to limit the spread of bacteria after infection, interpretation of the tuberculin skin test in those who have been vaccinated is more difficult, although by no means impossible (a positive result may reflect the presence of the BCG or it may indicate true infection).

Adults who can anticipate exposure to multidrug-resistant strains of *Mycobacterium tuberculosis* through work or travel should also undergo vaccination, because there is no antibiotic therapy of proven benefit for preventing TB associated with these strains. BCG vaccine works equally well for drug-sensitive or drug-resistant strains and is therefore the only preventive therapy of proven benefit.

Treating latent infection

Step 1: Identify latent infection with the tuberculin skin test

The tuberculin skin test is a simple, yet highly sensitive test for detecting latent or dormant infection, although false-negative results may occur because of immunosuppression. Administration of the test is relatively simple, although errors in technique can lead to false-positive or false-negative results. The Mantoux technique is strongly recommended, because it is more reliable than multipuncture techniques.¹²⁻¹⁴ The Mantoux technique involves intra-



dermal injection in the forearm of 0.1 mL of liquid containing 5 tuberculin units of purified protein derived (hence the term "PPD") from *M. tuberculosis*. People with prior mycobacterial exposure will have a localized reaction, the tuberculin reaction, which begins within 24 hours, reaches maximal size in 48 to 72 hours and subsides slowly over the next 1 to 2 weeks. Usually redness (erythema) and swelling (induration) occur. The erythema should be ignored; instead, the transverse diameter of the induration (in millimetres) is the most reliable indicator of TB infection. Approximately 1% to 2% of patients with a positive tuberculin reaction experience blistering; in this situation, the area should be kept clean with a dry dressing. Topical steroids are frequently used to treat the reaction, but were of no benefit in one randomized controlled trial.¹⁵ Reading tuberculin reactions requires training and experience, and even among well-trained individuals, tuberculin test readings will vary by 2 to 3 mm.

A tuberculin test should be administered to people who may have been exposed to patients with active, contagious forms of TB and those with medical conditions that increase their risk of reactivation of disease if they are infected (e.g., HIV infection, diabetes, renal failure or immunosuppression because of medications). Screening may be proposed for high-risk groups, such as recent immigrants from countries where TB is endemic and health care or prison workers, who may have significant risk of occupational exposure.

Step 2: Interpret the tuberculin skin test

The interpretation of the tuberculin test result consists of more than measurement of the reaction. Interpretation has 2 stages. The first is relatively simple: "When do I consider the test result positive and refer the patient for further assessment?" As shown in Table 1, in most circumstances in Canada, the result is considered positive if the diameter of the reaction measures 10 mm or more. Any patient considered to have a positive result should be referred for medical and radiographic assessment. However, he or she should not undergo any further tuberculin testing, because positive reactions may wane and even become negative again or they may remain positive. There is no epidemiologic basis for interpreting the results of such follow-up tests (i.e., it is unknown if the risk of active TB is higher for a person with persisting positive tests than for someone whose tuberculin reaction has waned). Therefore, although the dictum "once positive, always positive" may not apply to the tuberculin skin test, the corollary "once positive, no longer useful" is true. An exception is people who have undergone tuberculin testing after BCG vaccination; in this situation, a positive postvaccinal reaction usually wanes, and tuberculin testing may be useful some years later.

The second step of the interpretation of the tuberculin tests is a decision regarding management following a detailed medical evaluation. Assessment of those with a positive result should include chest radiography, a review of the

symptoms and a medical history, to exclude active disease and to identify factors that are associated with true-positive or false-positive results or that increase the risk of TB reactivation in infected people. Management depends on the relative likelihood of a true-positive or a false-positive result and the likelihood of disease compared with the likelihood of adverse effects from therapy.

False-negative results occur largely because of anergy. In clinical series of patients with newly diagnosed TB disease, between 20% and 30% initially had false-negative tuberculin test results, but the results were positive once their acute illness had resolved.^{16,17} Among HIV-infected patients with documented past history of active TB, false-negative tuberculin test results are seen in 20% of those with CD4 cell counts greater than $500 \times 10^9/L$ and in 80% to 100% of those with CD4 cell counts less than $200 \times 10^9/L$.^{18,19} Patients taking corticosteroids at daily doses equivalent to 20 mg of prednisone or more may have false-negative results. Similarly, patients with renal failure or malnutrition, concurrent viral illness such as infectious mononucleosis or measles, and recent live-virus vaccination (such as for measles or mumps) may have temporary anergy and a false-negative tuberculin test result.²⁰

The 2 main causes of false-positive results are infection with nontuberculous mycobacteria and BCG vaccination. Many nontuberculous mycobacteria occur in the soil and water in tropical and subtropical climates,^{21,22} and sensitivity to these bacteria is common among people living in these areas and may lead to false-positive tuberculin test results through cross-reactivity. The importance of sensitivity to nontuberculous mycobacteria as a cause of false-positive results depends on the relative prevalence of these organisms and the true level of TB infection in the population. For example, in the southern United States, TB infection is much less prevalent than sensitivity to nontuberculous mycobacte-

Table 1: Canadian criteria for a positive tuberculin test result

Population	Diameter of reaction considered positive, mm
People with very-high-risk conditions	
HIV infection*	
Contact of active case of TB	
Signs of inactive TB on chest radiography	5
People with high-risk conditions	
Injection drug use	
Diabetes or renal failure	
Steroid medication or malnutrition	
Silicosis	10
High-prevalence populations	
Foreign-born people	
Aboriginal people	
Health care workers	
Urban poor	10
Low-prevalence populations	
	10†

Note: TB = tuberculosis.

* In some HIV-infected populations with a high prevalence of TB infection (e.g., people born outside Canada and injection drug users), reactions of 0 to 4 mm diameter are considered positive.

† Criterion differs from that in the United States, where a diameter of 15 mm is recommended because nontuberculous mycobacteria, which cause false-positive results, are common.



ria.²³ Therefore, these organisms are an important cause of false-positive reactions in this region. In contrast, new Canadians who have immigrated from tropical and subtropical countries commonly show sensitivity to the antigens of nontuberculous mycobacteria, but TB infection is also much more common in these immigrants, so nontuberculous mycobacteria are relatively unimportant as a cause of false-positive results.²⁴ Because of the cold Canadian winters, nontuberculous mycobacteria occur relatively rarely in the environment. Therefore, even though true TB infection is uncommon in Canadian-born residents, nontuberculous mycobacteria are even less common and are therefore not an important cause of false-positive reactions. As a result, 15 mm is recommended as the cut-off point for a true positive test for those born in United States, whereas 10 mm is the recommended maximum cut-off point for all Canadians.²⁵

Almost everyone who undergoes a tuberculin skin test within 2 or 3 months after BCG vaccination will have induration of 10 mm or more, but such reactions diminish over time. Virtually all children who received BCG in infancy and who undergo a tuberculin skin test after the age of 2 years will have a reaction less than 10 mm in diameter.²⁶⁻²⁸ Among those who received BCG in primary school or adolescence, 15% to 25% have positive reactions up to 20 years later.²⁶ In most countries of Africa, Asia, Latin America and the Caribbean, TB infection is common and is more likely the cause of a positive test result than BCG

vaccination. Therefore, a reaction of 10 mm or more in foreign-born people from these areas can be considered a true-positive result, regardless of BCG vaccination status.²⁴

Step 3: Treat the infection (prophylaxis)

The decision to administer antibiotic therapy takes into consideration the size of the reaction, the likelihood of false-negative and false-positive reactions, and the risk of disease if the person is actually infected. The risk of disease increases with the size of the reaction, at least in the range 5 to 20 mm. However, deciding to give therapy solely on the basis of the size of the reaction is an oversimplification of a complicated management decision. In general, the cut-off point should be lower if the patient's risk of disease on the basis of other factors is higher, as in patients with HIV infection, recent contact with active disease or abnormal radiographic findings consistent with inactive TB. In immunocompetent populations, more than 98% of those with TB infection have reactions of 5 mm or greater, and more than 90% have reactions of 10 mm or greater, but only 50% to 60% have reactions of 15 mm or greater.²⁹ Therefore, increasing the cut-off point from 5 mm to 10 or 15 mm reduces the sensitivity, although it may improve specificity by reducing the number of false-positive reactions. If the tuberculin reaction is a true positive, the likelihood of active disease depends on the interval since infection was acquired, the age of the infected person and the presence of associated medical conditions. The risk of active disease is higher if the infection is recent^{30,31} or if the person is very young or very old.³² HIV infection is the most important risk factor for development of active disease. Other conditions that predispose to reactivation include other immunosuppressing conditions or immunosuppressant therapy, pulmonary silicosis, renal failure (especially that necessitating dialysis), diabetes mellitus, malnutrition and abnormal radiographic findings consistent with inactive TB.

The decision to treat infection must balance the future risk of disease with the present risk of side effects, which are serious, if rare. Most randomized controlled trials and clinical practice experience have involved the drug isoniazid. In randomized clinical trials, isoniazid taken for 6 months was associated with subsequent incidence of active TB 69% lower than among patients who received placebo;³³ active TB was 93% to 97% lower than in the control group if the drug was taken with good compliance for 1 year.^{33,34} Problems associated with isoniazid therapy include the need for daily therapy over a prolonged period, the occurrence of gastrointestinal upset in 5% to 10% of patients, acne (in adolescents and young adults) and non-specific symptoms such as fatigue. The most important problem is drug-induced hepatitis, which is rare in those under 20 years of age and occurs in 0.3% of those 20 to 35 years of age,³⁵ in 1.2% of those 35 to 50 years of age,³⁵ in 2.3% of those aged 50 to 64 years of age³⁵ and in 5% or more of those 65 years of age and older.³⁶ In 2 studies, the

Key points

Treating latent TB infection

Step 1: Identify latent infection by administering the tuberculin skin test to the following groups

- anyone exposed to patients with contagious forms of TB
- anyone with a medical condition increasing the risk of reactivation of TB (e.g., HIV infection, diabetes, renal failure, immunosuppressive therapy)
- high-risk groups (e.g., immigrants from countries where TB is endemic, health care or prison workers)

Step 2: Interpret the tuberculin skin test

- determine whether the reaction is positive
- refer for medical and radiographic assessment
- do not repeat tuberculin skin test in those with a positive reaction
- be aware of potential for false-negative and false-positive results

Step 3: Treat the infection

- make decision to treat on the basis of size of reaction, likelihood of false-negative or false-positive reaction, and risk of disease
- balance future risk of disease against present risk of side effects



mean number of deaths from drug-induced hepatitis was 14 per 100 000 treated.^{33,37} Death was more likely in patients who had clinical jaundice and continued to take the medication, a particular problem in those given enough drugs for several months at one time and those who stopped therapy and then the same drug was given again.^{35,37} However, increased awareness of this risk and more careful follow-up has reduced the number of deaths from drug-induced hepatitis.³⁷

Because of the potential for serious adverse effects, several cost-benefit and risk-benefit analyses of isoniazid have been performed.³⁸⁻⁴⁰ These analyses have produced inconsistent results and contradictory conclusions, primarily because of differences in the assumptions on which they were based. These studies have left the general impression that the use of isoniazid is controversial. However, all of these studies focused exclusively on the so-called low-risk reactors, young adults from low-prevalence countries without other risk factors and with normal results on chest radiography. In most clinical situations the use of isoniazid is not controversial (Table 2).

Despite the high efficacy of isoniazid demonstrated in clinical trials, the actual benefit of this drug is often substantially lower because of poor compliance. Several surveys have shown that compliance with preventive therapy has ranged from 40% to 60% under program conditions,⁴¹⁻⁴³ although it is better in clinical trials.^{33,34} The adverse effects, though serious, are relatively uncommon and constitute a minor reason for noncompliance. Much more important are the beliefs of the patient (and, all too often, the provider) that the risk of disease is low, that the therapy is not helpful and that the side effects are serious. In some jurisdictions, directly observed preventive therapy has been given to particularly high-risk groups such as patients with dual HIV and TB infection. Another approach is to use shorter courses of therapy with 2 antimycobacterial agents. To date, the results of clinical trials have shown that all regimens involving isoniazid and rifampin or rifampin and pyrazinamide for 2 to 3 months yield inferior results to those of isoniazid alone for 6 months and are substantially worse than isoniazid alone for 12 months.⁴⁴⁻⁴⁶ However, compliance is much better with shorter regimens, so under

program conditions the effectiveness of the shorter regimens may in fact be equivalent to that of the longer isoniazid regimens.

There are few data from clinical trials on which to base recommendations if a person has been exposed to a patient with drug-resistant TB. However, empiric recommendations⁴⁷ are to use rifampin if the index or source case involves organisms resistant to isoniazid and pyrazinamide plus a quinolone (ofloxacin or ciprofloxacin) if the organisms are resistant to isoniazid and rifampin (i.e., multidrug-resistant TB).

Identifying infected people: contact investigation

After case-finding and case-holding, the next priority in TB control is contact investigation, as people who have been in contact with active disease represent a group at particularly high risk. At the time of initial contact investigation, active disease is already present in 2% to 3% of an infected person's close contacts. In addition, contact investigation identifies those with new infection, in 5% to 12% of whom the disease will develop within the next 2 years.^{30,31} The responsibility for contact investigation usually falls to public health officials. In some instances, the treating physicians will assess the closest contacts, particularly for highly contagious index cases in which the patients are admitted to hospital. If so, the assessment should be done in consultation with the public health unit. More extended contact investigations, such as at school or work, are beyond the capacity of most treating physicians and are almost always the responsibility of the public health unit.

Case

A 30-year-old man immigrated to Canada from a country where TB is endemic at the beginning of May 1996. He arrived with 3 siblings between 25 and 35 years of age and moved in with another sibling, a sister who had arrived in Canada in 1990. The sister had 3 small children, all born in Canada. In late June 1996 the man presented to the emergency department of an acute care hospital with cough, fever and weight loss, and was found to have smear-positive cavitary disease; *M. tuberculosis* was later confirmed. He was admitted and placed in respiratory isolation. Contact investigation was undertaken. All of the children were tuberculin positive, as were the 4 siblings. In addition, one of the siblings had abnormal findings on chest radiography. Sputum induction was performed; microscopic examination of a direct sputum smear was negative, but *M. tuberculosis* was isolated 2 weeks later.

This case history illustrates many of the issues in contact investigation, which involves assessment of contagiousness of the index case, the environment in which exposure occurred and tracing of transmission in ever-widening circles of contacts.

Table 2. Indications for isoniazid (INH) preventive therapy

INH definitely recommended

Low-risk reactor,* age < 20 yr

Recent contact or conversion (all ages)

Associated medical condition, including steroid medication, renal failure, malnutrition, silicosis, HIV infection, diabetes (all ages)

Abnormal chest radiograph findings consistent with inactive TB (all ages)

Use of INH controversial

Low-risk reactor, age 20-35 yr

INH definitely not recommended

Low-risk reactor, age > 35 yr

*Person with positive tuberculin test result, normal chest radiograph results and no risk factors for reactivation.



Step 1: Evaluate the contagiousness of the index case

Extrapulmonary (nonrespiratory) TB is seldom contagious, although in selected cases, household contacts may be assessed. For those with pulmonary disease, the simplest, most practical and most valuable index of contagiousness is the result of direct microscopic examination of a sputum smear for acid-fast bacilli. Contagiousness is 4 to 6 times greater in smear-positive than in smear-negative cases.⁴⁹ Other factors that increase contagiousness include younger age, more frequent cough and more extensive radiographic abnormalities including cavitation. Laryngeal involvement, or TB laryngitis, is a highly contagious form of respiratory tract TB.⁵⁰ It is important to consider all factors together, because a young person who coughs frequently but who is smear negative may be more contagious than an elderly person who rarely coughs but is smear positive. In the case history described here, the index case was highly contagious, because it involved a young smear-positive person with extensive disease visible on chest radiography who coughed frequently.

Step 2: Evaluate the environment in which exposure occurred

TB is transmitted through the air and is usually not very transmissible, because the number of airborne bacteria generated by a person with active respiratory TB is relatively low. Transmission does not occur outdoors, where the concentration of bacteria diminishes rapidly; the bacteria are also killed by sunlight. However, in indoor environments that are small, crowded, poorly ventilated, dark and damp the concentration of bacteria in the air is generally higher and their survival is prolonged.^{51,52} The patient described in the case history lived with many contacts in a small apartment, a situation with a high risk of transmission.

Step 3: Identify the most exposed and most susceptible contacts

The most exposed contacts constitute the "first circle" of infection. The most susceptible contacts are young children and people with HIV infection. Transmission occurs most frequently to contacts who have spent prolonged periods in a closed environment with the index case, generally speaking, people who live and sleep in the same household. Close friends and colleagues at work or school who have had prolonged exposure should also be included in the first circle. Ideally, the first circle will consist of 8 to 10 people who, under normal circumstances, would be expected to be tuberculin negative, such as Canadian-born people and young children. Tuberculin testing is performed on all close contacts identified, unless they have a history of prior therapy for TB or documented prior positive result for a tuberculin skin test. Any reaction of diam-

eter 5 mm or greater is considered positive (Table 1), and these people are referred for medical and radiographic assessment. Apart from rapid identification and assessment of those most exposed, the other objective of this step is to determine the actual contagiousness of the index case, on the basis of evidence of transmission. Transmission is judged to have occurred if there are any secondary cases of active disease or if any of those who should be tuberculin negative are actually positive. In the case described above, there were 3 young Canadian-born children who were tuberculin positive and a secondary case of active disease within the first circle of contacts, which indicates significant transmission.

Steps 1, 2 and 3 should be performed as soon as possible after the TB is first diagnosed. If the diagnosis is suspected on the basis of a positive smear, testing should be limited to close contacts until the diagnosis is confirmed by culture or amplification testing such as polymerase chain reaction. In the past, physicians have sometimes undertaken extensive contact investigation in smear-positive cases, only to learn that the index case involved nontuberculous mycobacterial disease. Amplification tests can be helpful in confirming *M. tuberculosis* rapidly, before the contact investigation is initiated.

Step 4: Extend contact investigation to the "second circle"

If there is evidence of transmission within the first circle, then contact investigation should be extended to those who are in regular but less frequent contact with the index case. The decision to extend the contact investigation to this second circle may also be made if the index case was highly contagious for a prolonged period. The second circle usually includes contacts at work, school or regular social activities (e.g., church). When a contact investigation is conducted in these settings, the reaction may be one of near panic. Therefore, those who conduct the investigation should be experienced, must provide adequate information to those involved, and must ensure that testing is well organized and follow-up is rapid. There must be clear and effective communication between those conducting this phase of the contact investigation and the treating physician(s). The results must be collected systematically to allow evaluation of the extent of transmission. In addition, great care must be taken to maintain the confidentiality of the index case to avoid social ostracism. In some instances, despite every effort to educate those involved, the person loses his or her job or has to change schools. One innovative way to maintain confidentiality is to wait and conduct the contact investigation after the index case has returned to work or school. When all of the contacts in the work or school setting are tested, a sham skin test (using normal saline) is performed on the index case (with their knowledge and consent). They will in fact appear to have a negative skin test.



Step 5: Extend investigation to the “third circle,” if necessary

It may be necessary to extend the contact investigation to an even larger circle if there is evidence of transmission in the second circle (judged in the same way as for the first circle) or if the index case involves a highly contagious form of the disease, such as TB laryngitis.

Step 6: Retest tuberculin-negative contacts

Tuberculin conversion occurs 3 to 7 weeks after infection.^{53,54} Therefore, the result may be negative if tuberculin testing is performed within 6 weeks after the end of exposure, yet the person may become positive shortly afterward; this situation indicates very recent infection, just before the end of exposure. Therefore, contacts who are initially tuberculin negative should be retested 8 to 12 weeks after the contact is broken. A change from a negative reaction to a reaction of more than 5 mm may be interpreted as indicating recent infection.⁵⁵

Screening for TB

Screening for active disease

Screening for active disease (active case-finding) by mass miniature radiography used to be common practice in many countries. However, this type of screening program has been abandoned because of low yield and high cost. Radiographic screening of refugees or immigrants before or on arrival in Canada is currently recommended to identify prevalent active cases. This procedure also identifies people with abnormal radiographic findings consistent with inactive TB who are at substantially greater risk of reactivation in future.⁵⁶⁻⁵⁸ These people should be offered preventive therapy after arrival in Canada or placed under surveillance.

Screening for infection

Screening of people with clinical risk factors is the highest priority because the numbers are relatively small, the risk of disease is substantial, and generally both the patient and the physician realize the importance of preventive therapy if a positive tuberculin reaction is found. Screening should be performed at the time of diagnosis of the associated risk factor; if the result is negative, the test need not be repeated unless the person remains at high risk of infection (e.g., through occupational exposure or travel to countries where TB is endemic or because of a known contact). HIV-infected patients who are tuberculin negative, particularly if their CD4 count is less than $500 \times 10^6/L$, may be considered for further assessment, including chest radiography and even preventive therapy, given the high rate of false-negative tuberculin tests in this group.¹⁸⁻²⁰ Screening in high-risk settings, such as acute care hospitals, shelters for the home-

less and prisons, is currently recommended⁵⁹ because of the increased risk of transmission in these settings.

Screening of populations with a high prevalence of infection, such as schoolchildren who have immigrated from countries where TB is endemic, will probably yield large numbers of positive reactions. However, the benefit of such screening cannot be realized unless follow-up is carefully planned^{43,60} so that all reactors are assessed

Key points

Contact investigation

Step 1: Evaluate the contagiousness of the index case

- form of TB
- result of testing for acid-fast bacilli
- age
- frequency of cough
- extent of radiographic abnormalities

Step 2: Evaluate the environment in which exposure occurred

- crowded, poorly ventilated indoor environments are conducive to transmission

Step 3: Identify the most exposed and most susceptible contacts and test them

- those who live and sleep in the same household
- close contacts at school or work

Steps 4 and 5: Extend contact investigation as appropriate

- provide adequate information
- ensure that testing is well organized
- ensure that follow-up is rapid
- maintain confidentiality of index case

Step 6: Retest contacts who were tuberculin negative on the first test

- to catch infections that occurred shortly before index case was diagnosed and may not have shown a reaction on initial testing

promptly and, where appropriate, isoniazid preventive therapy is offered. Common problems in screening programs are that many of those eligible for screening do not participate, those with tuberculin reactions do not report for further assessment, and their physicians may not agree with the need for screening and therapy. Finally, only about half of those given preventive therapy actually complete at least 6 months of therapy.^{60,61} As a result, less than one-fifth of tuberculin reactors in the target population will be identified and assessed and will receive a prescription for and complete an adequate course of isoniazid preventive therapy. Without high participation in the screening, thorough follow-up of all reactors detected and prescription of isoniazid for all those for whom it is indicated, the public health impact of such screening will be far less than anticipated.



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Reprint requests to: Dr. Dick Menzies, Respiratory Epidemiology Unit and Montreal Chest Institute, McGill University, 1110 Pine Ave. W, Montreal QC H3A 1A3; fax 514 398-8981; menzies@meakins.lan.mcgill.ca