OBJECTIVE

Alberta clinicians detect and manage active pulmonary tuberculosis (TB) that poses a public health risk.

While extrapulmonary TB and preventative therapy for latent tuberculosis infection are relevant to primary care, they are outside the scope of this guideline.

TARGET POPULATION

All

EXCLUSIONS

None

RECOMMENDATIONS

DIAGNOSIS (SEE TB DIAGNOSIS ALGORITHM.)

- ✓ Suspect TB in those who exhibit symptoms such as:
  - Sub-acute or chronic cough lasting > two to three weeks
  - Fever
  - Night sweats
  - Anorexia
  - Weight loss
  - Hemoptysis
  - Radiographic findings suggestive of TB

PRACTICE POINTS

High Risk Populations Include:
Immigrant populations
First Nations people
Immunocompromised
Elderly
Inner city populations
Anyone with epidemiologic link to infection

INVESTIGATIONS

- ✓ Physical examination including examination of cervical lymph nodes
- ✓ Chest X-ray
- ✓ Specimen culture for *Mycobacterium tuberculosis*
- ✓ Determine co-morbidities
- X DO NOT use tuberculin skin test (TST) and interferon Gamma Release Assay (IGRA).

MANAGEMENT

PUBLIC HEALTH SAFETY MEASURES

When active TB is suspected:

- ✓ Isolate patient pending further investigations.
- ✓ Notify TB Services (see Notification section).
- ✓ Admit to hospital in a respiratory isolation room if patient has one or more of:
  - Cavitary disease
  - Significant cough
  - High risk profession
  - Children under the age of five
  - Exposure to an immunocompromised person
  - Cannot be home isolated
- ✓ Consider home isolation if:
  - Stable, single family residence
  - No vulnerable household members, i.e., immunocompromised persons or children under five years of age
- ✓ Isolate if resident of a facility:
  - Place patient in a negative pressure isolation room.
    - Place in a single room with door closed until transfer to a negative pressure room is possible.
    - Do not allow patients to leave room except for essential services, i.e., radiologic investigations and bronchoscopy.
- ✓ Ensure appropriate infection control measures are in place for transfer to and from the isolation room including:
  - Staff should wear a high filtration respirator N95 mask during contact with a suspect case.
  - Patient should wear a surgical mask for transport to and from isolation.
  - Alert other facilities to prepare for appropriate precautions, if/when the patient is transferred.
- ✓ Consider alcohol, drug and tobacco withdrawal protocols for all patients in isolation.

NOTIFICATION TO TB SERVICES

Patients living in Edmonton or Calgary:

- ✓ Refer immediately to a TB clinic- located in Edmonton or Calgary:

  http://www.albertahealthservices.ca/services.asp?pid=service&rid=1000852.

Patients living outside of Edmonton or Calgary:

- ✓ There is a virtual TB clinic that works with local community/public health centres to provide service to rural Alberta, including First Nation reserve communities. (See web link above.)

PRACTICE POINT

Your role as an Albertan clinician:
Suspicion of TB
Diagnostics
Determine patient comorbidities
Consider isolation
Call AHS public health prior to positive X-ray or sputum
Ensure patients are not lost to follow-up

BACKGROUND

PREVALENCE

TB is a global public health threat with nine million new cases per year and approximately 1.3 million deaths per year[1]. It is a leading cause of death in high-prevalence regions such as Southeast Asia and sub-Saharan Africa. In contrast, TB is not a common cause of mortality in low-prevalence countries. The incidence of TB in Canada is approximately 4.8 per 100 000, and in Alberta 5.1 per 100 000.[2] The relatively low incidence in our setting poses a challenge to the appropriate and timely detection and management of active TB. Furthermore, for healthcare providers from endemic countries the practices for diagnosis and referral may differ significantly from their previous experience.

The rate of TB in Alberta has increased in the past seven years[3] and delays in the diagnosis of tuberculosis have resulted in increased morbidity and mortality, increased transmission of infection, greater need for prolonged isolation, and higher healthcare costs. In recent years several cases in Alberta with delayed diagnoses have had major public health consequences.

ETIOLOGY

In Canada and Alberta, TB is primarily a condition of immigrant populations and First Nations people. However, the diagnosis should be considered among the immunocompromised, the elderly, inner city populations and anyone who has had an epidemiologic link to infection. Important questions to explore with patients include previous history of active TB or known latent infection, country of birth, aboriginal ancestry, known exposure to TB, travel to an endemic country, time spent in a correctional facility, work in health care, homelessness, and general health status.[4]

Approximately 70-80% of TB in Canada involves the respiratory tract,[2] which includes pulmonary TB, tuberculosis pleurisy, primary TB, TB of intrathoracic lymph nodes, and the upper airway.

SUSPECTING TB

The diagnosis is suspected in those who exhibit symptoms such as sub-acute or chronic cough lasting greater than two to three weeks, fever, night sweats, anorexia, weight loss and hemoptysis.[5] The diagnosis is also more likely in those who are of an epidemiologic risk group such as immigrant populations and First Nations people (see background for more detail) and those who have radiographic (X-ray) findings suggestive of TB. Physical examination is often normal in active pulmonary tuberculosis, although examination of cervical lymph nodes may help detect TB lymphadenitis.

The diagnosis may be suspected on the basis of abnormal chest imaging. The typical findings in active tuberculosis include upper lobe consolidation with or without cavitation. However, in the immunocompromised, pediatric or geriatric population, chest X-ray findings may be atypical. Specifically, lower lobe consolidation may occur, cavitation is less frequent and mediastinal or hilar lymphadenopathy may be a prominent or solitary finding. X-rays may be normal in HIV infected individuals or very early in the TB disease. Other findings suggestive of active TB include pleural effusion, nodular changes, particularly nodularity in a pattern of endobronchial spread.[5] Overall the chest X-ray has limited sensitivity (70-80%) and specificity (60-70%).[6,7,8] There is also a high degree of inter-reader variability in interpretation of chest radiographs.[8]

TB DIAGNOSTIC TESTS

The tuberculin skin test (TST) and Interferon Gamma Release Assay (IGRA) are not recommended for diagnosis of active tuberculosis.[9] Both are useful in diagnosing latent tuberculosis infection, and prior knowledge of a positive TST is helpful in assessing risk of current active TB. However, the TST may be falsely negative in the setting of active infection, and a positive test cannot distinguish latent infection from active disease. The IGRA test is more specific for the presence of TB infection when compared to the tuberculin skin test. However, it too cannot distinguish active disease from latent infection, so its role in the workup of active TB has not been established.[9]

The gold standard for diagnosis of active TB is a positive culture for *Mycobacterium tuberculosis*.[10] In respiratory disease, three spontaneous morning sputa in an individual who is able to produce sputum is the appropriate first step to achieving the diagnosis.[10,11] A health care worker should attempt the initial spot sputum collection and coach the patient on techniques to improve the quality of specimen. At times, sputum induction is necessary to improve the sensitivity of respiratory cultures. This is supervised by a respiratory therapist[2] and involves inhalation of hypertonic saline by nebulizer to help produce a lower respiratory tract specimen.[12,13]

Extrapulmonary specimens may be required to obtain a culture diagnosis for other forms of TB, such as TB lymphadenitis. Biopsy specimens submitted for TB culture should not be fixed in formaldehyde. For details regarding the collection of extrapulmonary specimens, see *the Alberta TB Control Manual 2010 p. 197*. Specimens are first sent for concentrated smear, which determines if the individual has a high burden of organisms and is therefore considered highly infectious. Even if the smear is negative, a patient with a positive respiratory culture for *Mycobacterium tuberculosis* is considered infectious. If the specimen is smear positive, a molecular-based assay identifying the mycobacterial organism as tuberculosis can be performed and is generally reported within 24-48

hours. However, the performance characteristics of these molecular assays are not sufficiently high to rule in or out tuberculosis in the setting of smear negative specimens.[14,15]

Once the concentrated smear is performed, the Provincial Laboratory will hold the specimen for culture. This is positive in active TB within two to four weeks in most cases. However, culture results are only reported as negative after seven weeks of incubation.[5,9] A positive culture is not only confirmatory of active disease, but it also allows for performance of drug susceptibility testing which is very helpful in guiding treatment. When patients are diagnosed clinically without culture confirmation we do not have access to drug susceptibility information.

Public Health Safety Measures

When the diagnosis of active TB is suspected, the individual should be isolated from others while awaiting further evaluation. Patients who have cavitary disease, a significant cough, are in a high risk profession, have children under the age of five, are exposed to an immunocompromised person or cannot be home isolated for another reason should be promptly admitted to hospital in a respiratory isolation room with notification to TB Services.

Home Isolation

Outpatients may require home isolation, which includes avoidance of work and activities involving contact with the public until sputum specimens are obtained and smear results are available. Home isolation may be a consideration for patients who have a stable, single family residence with no vulnerable household members such as immunocompromised persons or children under five.

Facility Isolation

In an institutional setting the patient should be placed in a negative pressure isolation room. If respiratory isolation is not available, the patient should be in a single room with the door closed until transfer to a facility with a negative pressure room is possible. Alcohol, drug and tobacco withdrawal protocols may be considered for all patients in isolation.

Patients should be out of the room only for essential services such as radiologic investigations and bronchoscopy. Appropriate infection control measures for transfer to and from the room should be observed. Staff should wear a high filtration respirator N95 mask when in contact with a suspect case and the patient should wear a surgical mask for transport to and from isolation. Facilities to which the patient is being transferred for further workup should be alerted to the suspected diagnosis so that they can use appropriate precautions.[4]

Notification to TB Services

Patients living in Edmonton or Calgary should be referred immediately to the Edmonton or Calgary Tuberculosis Clinic. If the patient resides outside of Edmonton or Calgary he or she should be sent for urgent chest radiography with notification to Alberta Health Services (AHS) TB services and public health.

REFERENCES

1. World Health Organization. Global tuberculosis report 2013. WHO Press; 2013. Available from:http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf?ua=1.
2. Public Health Agency of Canada. Tuberculosis in Canada 2012 pre-release. Ottawa: Public Health Agency of Canada; 2012. Available from: http://www.phac-aspc.gc.ca/tbpc-latb/pubs/tbcan12pre/index-eng.php
3. Alberta Health and Wellness. Tuberculosis Surveillance Report Alberta 2005-2009. Available from: http://www.health.alberta.ca/documents/CMOH-TB-Alberta-2005-2009.pdf
4. Alberta Health and Wellness. Tuberculosis prevention and control guidelines for Alberta. Edmonton: Government of Alberta; 2010. Available from: http://www.health.alberta.ca/documents/TB-Prevention-Control.pdf
5. Canadian tuberculosis standards. 7th ed.: Canadian Thoracic Society, 2013. Available from: http://www.respiratoryguidelines.ca/tb-standards-2013
6. Daley CL, Gotway MB, Jasmer RM. Radiographic manifestations of tuberculosis: a primer for clinicians. 2nd ed. San Francisco: Francis J. Curry National Tuberculosis Center; 2006. Available from: http://www.nationaltbcenter.edu/products/tbradiographic.cfm
7. Toman K. Tuberculosis case-finding and chemotherapy: questions and answers. Geneva: World Health Organization ; 2004. Available from: http://whqlibdoc.who.int/publications/2004/9241546034_1.pdf
8. Koppaka R, Bock N. How reliable is chest radiography? Toman's tuberculosis: case detection, treatment, and monitoring: questions and answers. 2nd ed. Geneva: World Health Organization; 2004. p. 51-60.
9. Menzies D, Pai M, Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. Ann Intern Med. 2007;146(5):340-54. Erratum in: Ann Intern Med. 2007;146(9):688.
10. Cruciani M, Scarparo C, Malena M, Bosco O, Serpelloni G, Mengoli C. Meta-analysis of BACTEC MGIT 960 and BACTEC 460 TB, with or without solid media, for detection of mycobacteria. J Clin Microbiol. 2004;42(5):2321-5.
11. Mase SR, Ramsay A, Ng V, Henry M, Hopewell PC, Cunningham J, et al. Yield of serial sputum specimen examinations in the diagnosis of pulmonary tuberculosis: a systematic review Int J Tuberc Lung Dis. 2007;11(5):485-95.
12. Anderson C, Inhaber N, Menzies D. Comparison of sputum induction with fiber-optic bronchoscopy in the diagnosis of tuberculosis. Am J Respir Crit Care Med. 1995;152(5 Pt 1):1570-4.
13. Carr DT, Karlson AG, Stilwell GG. A comparison of cultures of induced sputum and gastric washings in the diagnosis of tuberculosis. Mayo Clin Proc. 1967;42(1):23-5.
14. Ling DI, Flores LL, Riley LW, Pai M. Commercial nucleic-acid amplification tests for diagnosis of pulmonary tuberculosis in respiratory specimens: meta-analysis and meta-regression. PLoS ONE. 2008;3(2):e1536.
15. Greco S, Rulli M, Girardi E, Piersimoni C, Saltini C. Diagnostic accuracy of in-house PCR for pulmonary tuberculosis in smear-positive patients: meta-analysis and metaregression. J Clin Microbiol. 2009;47(3):569-76.

SUGGESTED CITATION

Toward Optimized Practice (TOP) Active Tuberculosis Working Group. 2011 November. Diagnosis and management of active tuberculosis clinical practice guideline. Edmonton, AB: Toward Optimized Practice. Available from: http://www.topalbertadoctors.org.

For more information see www.topalbertadoctors.org.

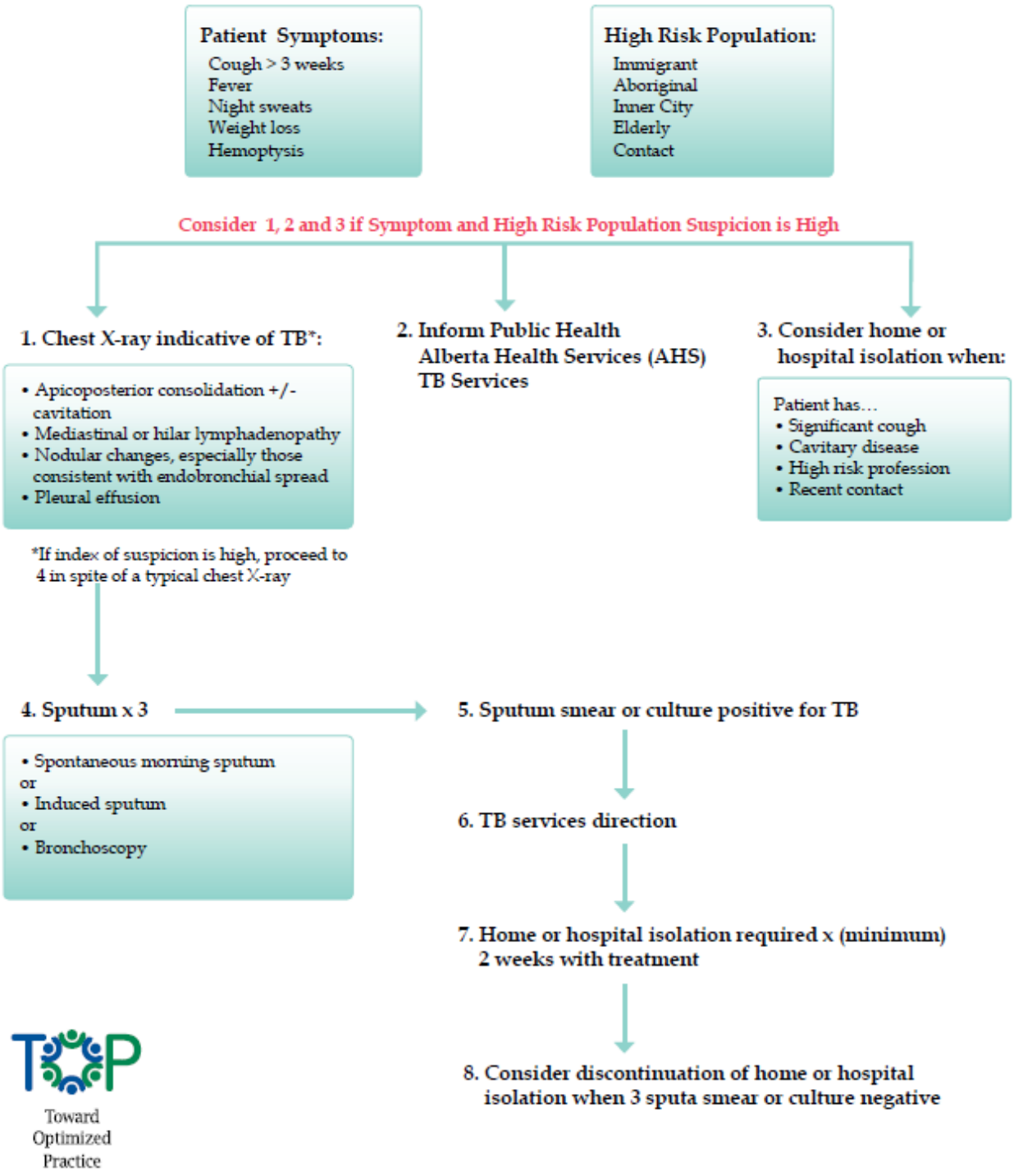
GUIDELINE COMMITTEE

The committee consisted of representatives of internal medicine, community medicine, public health and preventive medicine, infectious disease and nursing.

November 2011
Minor revision May 2014

APPENDIX A

Active Tuberculosis (TB) Diagnosis Algorithm



Toward Optimized Practice