THINKING ON YOUR FEET

Tuberculosis

Old disease and newcomers

Bashiar Thejeel (Meds 2016), Anthony Chow (Meds 2016)

Faculty Reviewer: Dr Bhooma Bhayana, MD, FCFP (Department of Family Medicine)

MRS MALIK

A physician working at a local emergency department is summoned to see a patient who is complaining of a worsening cough and fever. At triage blood pressure was 118/70 mmHg and heart rate was 72 bpm; the nurse also recorded a temperature of 38.5°C and the patient seemed to be in distress with an elevated respiratory rate of 22 breaths per minute. Mrs Malik presented to the emergency room with a 4-week history of worsening cough, fever and night sweats accompanied by hemoptysis. The triage nurse reports that this patient does not speak English very well and will need an interpreter.

Mrs Malik is a 56-year-old woman of Pakistani descent; she arrived to Canada six months ago as a refugee seeking to start a new life for her family and herself. Mrs Malik does not have a family doctor, which is why she presented to the emergency department when she was feeling ill. She lives with her husband, Khan (age 58), her children, Ahmed (age 18) and Ayesha (age 17), and her mother, Asia (age 79). Mrs Malik does not have a significant medical history; she had two normal vaginal deliveries for her children and no other hospitalizations. Currently she is on no medication and has no known allergies.

Physical examination reveals a productive cough, with bibasilar rales in addition to lymph node enlargement in the distribution of the posterior cervical chain. Mrs Malik seems unwell, as there are signs of respiratory distress. The physician decides to start the diagnostic journey with a chest x-ray, along with a complete blood count and cell differential. The x-ray reveals diffuse pulmonary infiltrates and the blood test shows leukocytosis. Although necessary, these preliminary tests only broaden the differential diagnosis for this patient's condition. Based on these results the pulmonary condition can be infectious, such as pneumonia or tuberculosis; malignant, either a primary lung cancer or a metastasis from a secondary tumor; or autoimmune, such as polyangiitis granulomatosis. All of these conditions are very serious and can result in serious morbidity, so the physician decides to tackle this daunting differential by further working up the patient.

TUBERCULOSIS STATUS OF REFUGEES AND NEWCOMERS

The incidence of tuberculosis (TB) is on a steady decline in Canada over the past 3 decades, but there is disparity among some of the populations living within Canada. These populations include the Aboriginal populations and populations of refugees and newcomers. Every year Canada takes on approximately 10 000 refugees from areas of political, cultural and environmental distress.¹ These refugees are exposed to various pathogens that increase their risk of contracting infectious diseases. Although predeparture screening programs exist, they may not be rigorous or comprehensive due to the conditions and circumstances of regions from which refugees originate. Further, international rules encourage the resettlement of all refugees regardless

of medical illness. This is in contrast to other migrant categories in which individuals may be restricted from immigration to Canada if they have serious health morbidities. In addition despite the existence of rigorous screening for government-assisted refugees, there is no corresponding system for claimants.

One key morbidity relevant to migrants is infection with *Mycobacterium tuberculosis*. Most of these infections are discovered in the inactive phase, meaning the patient is a carrier of the illness and is able to convert into the active state and become symptomatic. The incidence rate of active TB among the refugee population is 20 times that of the Canadian-born non-Aboriginal population, which is currently 5 cases per 100 000 persons.² Individuals with a latent TB infection comprise 30 to 50% of newcomers, which works out to 1.5 million people in Canada who are carriers of the disease and at risk for developing the active infection and passing it on.³

WHAT CONFERS RISK UPON NEWCOMER POPULATIONS?

Many factors influence the risk that a newcomer incurs for TB infection while in Canada. The most important predictors of risk include country of origin, migratory category, other comorbidities and the time since arrival in Canada. Of the 9.2 million cases of active TB worldwide, most are clustered in endemic areas such sub-Saharan Africa and Asia in which the individuals are more likely to be exposed to the tuberculin inoculum.⁴ Further, whether individuals identify as immigrants or refugees is an indicator of their risk for infection; this is due to the fact that refugees come from regions in which TB is of higher prevalence and from relatively poor living circumstances.⁴ In addition, individuals with comorbidities, particularly HIV infection, that reduce the body's ability to fight off infection are at a greater risk. Lastly, time since arrival also correlates with infectivity; individuals who are not diagnosed with TB within the first 5 years of arrival are at lower risk of developing the infection. The risk is highest within the first year and dramatically decreases thereafter.^{4,5} Therefore, based on these criteria, individuals can be stratified into risk groups.

Table 1: Quick Facts: Incidence of Tuberculosis in Countries of Canadian Immigrants^a

COUNTRY	INCIDENCE RATE (PER 100 000 PEOPLE)
Philippines	265
Pakistan	231
India	176
China	73

^a Adapted from Citizen and Immigration Canada and World Health Organization.^{12,13}

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Aware of the aforementioned risks, the physician decides to elicit a comprehensive history from Mrs Malik and her family. Mrs Malik tells the physician that many years ago as a child she had a lung infection that lasted for a very long time but eventually resolved. During her predeparture medical examination she had a positive TB skin test; however, her chest x-ray was negative. Currently, she lives in a one-bedroom apartment along with family. She does not complain of any other symptoms and says that she has been healthy in the past with no other health issues. She does not smoke or consume alcohol. Lab tests for renal function and autoimmune antibodies are negative. This information and the preliminary tests together suggest an infectious process with a high index of suspicion of TB.

Table 3: Quick Facts: Latent Tuberculosis Infection (LTBI)^a

▪ Affects one third of world’s population.
▪ Individuals are asymptomatic and noninfectious but are at risk of developing active disease and becoming infectious.
▪ Risk of reactivation increases with immunosuppression, malnutrition, diabetes and alcohol abuse.
▪ Individuals with LTBI should undergo prophylactic treatment with isoniazid.

^a Adapted from World Health Organization.¹⁴

SCREENING AT RISK POPULATIONS

Attempts are made to screen refugee populations for infective diseases such as TB; however, despite these efforts many individuals migrate to Canada and become ill with TB. All individuals desiring entry into Canada, including refugees, are screened with a chest x-ray. A sputum culture is indicated in those individuals with a positive screening chest x-ray.^{3,6} Individuals with an active infection must be treated and provide proof of treatment and recovery. Most individuals screened with a chest x-ray fall within the category of latent TB infection. These individuals should report to a health care professional within 30 days of their arrival in Canada;⁶ but many individuals with latent TB never make it to a postarrival health care check-up and thus they end up falling through the cracks. In addition, despite the efforts put into the predeparture screening, it is not as efficient as it needs to be, as it identifies only 1% of active TB cases and 3 to 5% of latent cases while refugees and newcomers account for 65% of TB cases in Canada.^{3,7} Furthermore, many issues arise with postlanding management of individuals who are identified as being carriers of the infection. Individuals often fail to complete screening and report for medical evaluation for a positive screen test. Health practitioners also come short when it comes to prescribing chemoprophylaxis and this is often followed by poor compliance due to lack of symptoms and long duration of treatment.⁸ These pitfalls uncover inadequacies in the health care system in terms of providing health care to newcomers.

Mrs Malik is confirmed to have an active TB infection based on a positive stain sputum smear for *Mycobacterium tuberculosis*, which revealed acid-fast bacilli. Along with the history of previous infection, the present symptoms and investigations, the physician confirms the diagnosis of active TB infection and proceeds with the treatment of Mrs Malik. The patient is isolated and admitted to the

respirology service for rigorous treatment. Since this is an active case of TB, the emergency physician goes on to report the case to public health. Furthermore, Mrs Malik is asked to provide a list of contacts.

MANAGEMENT OF NEW CASES OF TUBERCULOSIS IN THE REFUGEE POPULATION

Treatment regimes and protocols have been developed and tested for both latent and active TB. Ideally individuals are identified in the latent infection phase and treated before reactivation. Currently the management for latent TB is a 9-month course of isoniazid.⁹ Many randomized control trials have shown that chemoprophylaxis is more effective than placebo at preventing reactivation.¹⁰ A baseline evaluation of hepatic function must be done before initiation of treatment since there is a risk of hepatic toxicity.¹¹ A large barrier to chemoprophylaxis is monitoring and ensuring patient compliance to the 9-month regimen, which diminishes the efficacy of risk reduction. In patients with active TB, the treatment course is much more demanding as it involves 2 phases of treatment and multiple drugs over an extended duration of time. In addition, during the treatment the patient needs to be kept in isolation to prevent propagation of the infection.

Treatment of active TB includes an initial treatment with isoniazid, rifampin, pyrazinamide and ethambutol for a minimum duration of 8 weeks.⁹ Thereafter a continuation phase is started with isoniazid and rifampin for 26 weeks. At the end of this treatment protocol, investigations such as cultures and x-rays need to demonstrate resolution of the infection. If resolution of the infection is not achieved, the physician will need to investigate as to whether this due to patient compliance issues or a drug-resistant infection. During treatment, hepatic function should be monitored for any signs of toxicity.⁹ Management of an active TB infection extends beyond the infected patient, as the event must be reported to public health. Furthermore, due to the potential for transmission, contact tracing must be performed and contacts must be assessed and treated accordingly. This emphasizes the importance of early detection and chemoprophylaxis.

Canada is internationally recognized for its efforts in resettling refugees from all over the world. Many resources are allocated to ensure the success of the resettlement process. Often times, however, the predeparture process is preferentially resourced, leaving the postlanding procedures without enough support. More awareness needs to be drawn to the heightened TB risk that our refugees are burdened with such that our physicians aren’t left “thinking on their feet”.

Table 3: Quick Facts: World Health Organization Recommendations on Tuberculosis Control Using Direct Observed Therapy (DOT)^a

FIVE COMPONENTS OF DOT

1. Political commitment with increased sustained financing
2. Case detection through quality assured bacteriology
3. Standardized treatment with supervision and patient support
4. An effective drug supply and management system
5. Monitoring and evaluation system and impact measurement

^a Adapted from World Health Organization.¹⁴

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