

OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

TUBERCULOSIS IN OREGON: GOING BUT NOT GONE

During the winter of 2007-08, a call center employee with cavitary pulmonary tuberculosis (TB) coughed among >1000 co-workers for more than four months, sparking one of the state's largest TB contact investigations. TB is a rare and declining disease in Oregon, with 94 cases in 2007 (incidence=2.5/100,000 population); however, several recent outbreaks resulting from infectious cases with delayed diagnoses show that TB can still be a major public health issue in our state. In this issue of the *CD Summary*, we review pathogenesis, clinical characteristics, and diagnosis of TB, and identify factors contributing to delayed diagnosis.

**THE PROBLEM**

Anyone with active pulmonary TB sitting for >4 months in close contact with co-workers is likely to spread TB effectively. This contact investigation blossomed as increasingly distant concentric rings of co-workers around the index case continued to have high rates of TB skin test conversion. In the year since diagnosis, this investigation has reached across multiple counties and states in search of the relatively mobile workers. More than 900 contacts have been tested, of whom 91 (10.1%) have been diagnosed with latent TB infection (LTBI). Currently, four subsequent cases of active TB disease have been linked by strain genotyping, and another two cases share epidemiologic links. This outbreak has several important characteristics: highly infectious index case, congregate work/living setting, long delay to diagnosis despite seeking medical care, and a local health department stretched thin by the enormous scale of the resulting contact investigation.

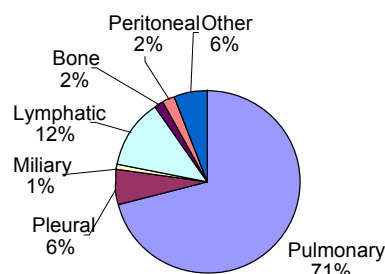
**PATHOGENESIS AND CLINICAL PRESENTATION**

Tuberculosis is caused by *Mycobacterium tuberculosis* (MTB). Infection results when a person with pulmonary TB disease coughs and releases

bacteria into the air, which are inhaled by a susceptible individual. Host and organism factors then converge to determine the outcome. The organism may be walled off in the lung by primary immune defenses resulting in LTBI. Although this containment is relatively effective, it will 'break-down' to cause disease in about 10% of people with LTBI sometime during their lifetime. Alternatively, local defenses may be overcome after initial infection, producing primary lung disease, dissemination throughout the body via the blood stream, or both. Thus, although pulmonary disease is the most common presentation of TB (and the main form contagious to others), TB has an almost endless array of presentations, from adenopathy to skin nodules, pancreatitis to Pott's disease (bone), meningitis to uveitis. This diversity of presentation can make the diagnosis hard to pin down and can delay diagnosis and treatment.

In Oregon, pulmonary TB disease (including miliary) accounts for 72% of the cases (figure). Cavitary lesions and sputum smear positive disease significantly increase infectivity; of the pulmonary cases, 29% involve cavitary lesions and 49% are sputum smear positive. Patients are symptomatic in 81% of the pulmonary cases, with cough (88%), weight loss (61%), night sweats (50%) and fever (48%) the primary symptoms. Only 28% of pulmonary cases report hemoptysis.

**Figure: Clinical type of TB disease in Oregon, 2003-2007**



Extrapulmonary TB is diverse, with lymphatic, peritoneal and pleural disease being the main sites. However, because the vast majority of extrapulmonary disease started in the lungs, (the exception is transplant-associated TB) many extrapulmonary cases continue to have pulmonary disease and pose a risk of transmitting their infection to others.

**MAKING THE DIAGNOSIS**

Clearly, very few people with prolonged cough in Oregon have TB. Clinical suspicion and a thorough history are key to placing TB in the right place on the differential diagnosis list.

Start by asking about TB risk factors. Between 2003 and 2007, two-thirds of Oregon's TB cases were born outside the US (table). While people born in Latin America account for the largest number of Oregon cases, those born in Africa and SE Asia have the highest rates of disease.

**Table: Risk factors for TB disease in Oregon, 2003-2007**

Risk Factor*	% Cases
Foreign-born	66.7
Alcohol Use	13.3
Homeless	8.8
Drug Use	8.0
Previous Diagnosis of TB	5.5
HIV	4.7
Health Care Worker	3.7
Corrections (inmates and employees)	1.6

\* Multiple risk factors can be present in a single individual

Other risk factors include a history of alcohol or drug use, homelessness, or incarceration; the call center case had several of these risks. Medical risk factors for developing disease among persons with LTBI include: HIV infection, diabetes, chronic renal failure, silicosis, solid organ transplant, gastrectomy, and use of immunosuppres-



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sive medications such as chemotherapy, steroids, and TNF-alpha inhibitors.

MTB can be seen by light microscopy in sputum smears stained for acid fast bacteria (AFB). However, this method is both insensitive (40–60% of culture positive cases will be smear negative) and non-specific (also detects non-tuberculous mycobacterium.) We recommend collecting three sputum specimens 8–24 hours apart, with at least one being an early morning sample. Definitive diagnosis of TB disease is made by laboratory isolation of MTB in culture, or more rapidly by detection of MTB DNA using a nucleic acid amplification test (NAAT). Neither test provides immediate results, so clinicians should consider presumptive treatment of highly suspect cases while awaiting definitive diagnosis.

Because laboratory samples are not always available and culture methods are not always successful (18% of US cases are culture negative), the diagnosis can also be made clinically. The following clinical criteria suggest the possibility of culture-negative TB: 1) evidence of TB infection by either a positive tuberculin skin test or Quantiferon-gold blood test (immunocompromised patients may be an exception); 2) clinical presentation consistent with TB; 3) clinical or radiographic response to anti-TB therapy; and 4) a complete diagnostic work-up ruling out alternate explanations.

#### **DELAYED DIAGNOSIS**

Prolonged illness before diagnosis can lead to large numbers of contacts being exposed. Delayed diagnosis of TB can involve both patient and pro-

vider factors; patients may wait to seek medical consultation while providers may not initially suspect TB or may wait for cultures to start treatment. The onset of symptoms to the start of antibiotic treatment is one way to estimate time to diagnosis. Examining Oregon case data, we found that patients who delayed seeking care for  $\geq 1$  month after symptom onset were more likely to be older than >65 years (OR = 10.5) or homeless (OR = 3.5). Foreign-born people tended to seek care early (OR = 0.6; 95% CI: 0.32, 1.03) possibly reflecting greater knowledge of TB.

To examine provider factors in diagnosis delay, we analyzed the time from initial patient contact to the start of TB treatment. Time to diagnosis greater than the median (16 days) was considered provider delay. Female patient gender (OR = 3.2) was the only factor that significantly predicted provider delay in diagnosis. Although we are unsure of the reasons for this finding, it has been noted in other studies.<sup>1,2</sup>

#### **Clinical Pearl**

20% of active TB cases are skin test negative. A negative TST or Quantiferon does not exclude the possibility of TB disease.

#### **THE ROLE OF PUBLIC HEALTH**

As a reminder, suspected and confirmed TB disease is reportable to your local public health department within one working day. Timely reporting facilitates contact investigations to identify and treat new infections and cases of disease. The local health department also serves as a valuable re-

source for patient management by assisting with diagnosis (collection and forwarding of sputum smears to the Oregon State Public Health Laboratory (OSPHL), chest X-ray reimbursement for uninsured patients to rule out active disease); treatment (medications and Directly Observed Therapy); and case management (patient agreements to treatment and isolation, assistance with social, cultural and financial barriers to care). The OSPHL processes sputum smears, cultures and sensitivities, and forwards samples to the CDC for genotyping and cluster analysis. In addition, the Oregon TB Control Program can provide timely clinical advice via our expert TB physician consultant.

#### **THE BOTTOM LINE**

TB exists in Oregon and delayed diagnosis is costly. While most patients with chronic cough will not have TB, think TB in patients who are foreign-born, have a history of homelessness or incarceration, or medical risk factors such as immunosuppression. As always, we are happy to discuss TB diagnosis and treatment with you. Call your local health department, or the state TB Control Program at 971-673-0174.

#### **REFERENCES**

1. Rodger A, Jaffar S, Paynter S, et al. Delay in the diagnosis of pulmonary tuberculosis, London, 1998–2000: analysis of surveillance data. *BMJ* 2003; 326: 909–10.
2. Diez M, Bleda MJ, Alcaide J, et al. Determinants of health system delay among confirmed tuberculosis cases in Spain. *Eur J Pub Health* 2005; 15(4): 343–9.