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Tuberculosis - Traps and Tips

On June 8, 1994 a 28-year-old woman from South America was evaluated at a medical facility in Alaska. A tuberculin skin test applied on June 22 was examined 2 days later and found to have 20 mm of induration. A chest x-ray obtained on June 27 was normal; a second chest x-ray on July 12 was read as "old granulomatous disease." Although the patient denied fever, weight loss, cough, or night sweats, three sputum specimens collected for smear, culture, and polymerase chain reaction (PCR) testing were sent to an out-of-state commercial clinical laboratory. Each of the three smears was reported as negative for acid fast bacilli. However, two of the three specimens had a positive PCR test for *Mycobacterium tuberculosis*. At the time of this report, none of the three sputum cultures had any growth after 4 weeks of incubation, final results were pending.

Polymerase chain reaction is a technique used to identify and amplify specific nucleic acid sequences which are considered unique to a given organism.¹ PCR has been applied to a variety of clinical specimens including blood, cerebrospinal fluid, sputum, and bronchoalveolar washings to test for the presence of suspected pathogens. **PCR methodology for detection of *M. tuberculosis* in clinical specimens has not yet been approved by the U.S. Food and Drug Administration.**

A recent report from the California Department of Health Services noted that commercial clinical laboratories in both that and other states were offering detection of *M. tuberculosis* in specimens by use of "home brew" PCR tests which had been developed in-house.² The California report concluded, "until these products have been thoroughly evaluated as to their sensitivity, specificity, predictive values, and correlations to clinical conditions, we recommend that laboratories and clinicians continue to rely on established techniques for the diagnosis of tuberculosis."²

The experience at a New York hospital is consistent with this recommendation: Physicians there conducted traditional laboratory and diagnostic procedures (sputum smear and culture, chest roentgenography, bronchoscopy, biopsy, etc) as well as a PCR test of sputum or bronchoscopy washings for 65 patients undergoing diagnostic evaluation for pulmonary disease.³ Among 37 patients with a positive PCR for *M. tuberculosis*, 15 (41%) had no evidence suggesting that they had active tuberculosis (TB).

Furthermore, among patients for whom active TB had been ruled-out using standard diagnostic tools, 55% had a PCR-positive sputum (e.g., specificity of PCR of sputum for active TB = 45%). The report recommended that PCR "should not be part of the routine initial evaluation of patients with suspected pulmonary TB."³

The cardinal symptoms of pulmonary TB include cough, fever, weight-loss, and night sweats. For most patients, an evaluation for possible TB is simple and straightforward.⁴ Patients with more complex problems may require additional tests.

The Section of Epidemiology recommends the following simplified approach:

1. If TB is suspected, a tuberculin skin test should be done.
2. The diagnosis of TB can be excluded if the skin test is negative **unless** anergy or overwhelming infection is suspected.
3. If the skin test is positive, a chest x-ray should be obtained. A negative chest x-ray usually excludes the diagnosis of pulmonary TB unless the patient is anergic.
4. If the chest x-ray suggests TB (or if unusual circumstances or the presence of symptoms suggest a patient with a normal chest x-ray has TB), sputum for acid fast bacilli smear and *M. tuberculosis* culture should be collected on 3 separate days.
5. As a general rule, antituberculosis medications should not be started until three sputum specimens have been collected. Initial treatment with four drugs (isoniazid, rifampin, ethambutal, and pyrazinamide) is strongly recommended.⁵
6. PCR tests are not recommended.

The Section of Epidemiology provides medical consultation to health-care providers and fills prescriptions for anti-tuberculosis medications at no cost. Contact investigations are conducted by public health nurses with assistance from the Section of Epidemiology. State Public Health Laboratories in Juneau and Anchorage provide, at no charge, sputum smears and cultures as well as susceptibility testing of *M. tuberculosis* isolates. **Health-care providers should report any patient who is suspected to have TB to the Section of Epidemiology at 561-4406.**

References:

1. Eisenstein BI. The polymerase chain reaction: a new diagnostic method of using molecular genetics for medical diagnosis. *N Engl J Med* 1990;322:178-83.
2. California Department of Health Services. Detection of *Mycobacterium tuberculosis* by "home brew" nucleic acid amplification methods. *Calif Morb* 1994;23/24:June 17.
3. Schluger NW, Kinney D, Harkin TJ, Rom WN. Clinical utility of the polymerase chain reaction in the diagnosis of infections due to *Mycobacterium tuberculosis*. *Chest* 1994;105:1116-21.
4. Schluger NW, Rom WN. Current approaches to the diagnosis of active pulmonary tuberculosis. *Am J Respir Crit Care Med* 1994;149:264-7.
5. American Thoracic Society. Treatment of tuberculosis and tuberculous infection in adults and children. *Am J Respir Crit*

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