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 determined 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, two 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 specimens 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. 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. 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." 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. 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.

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. 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. If the skin test is negative, 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.

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.

6. PCR tests are not recommended.

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