State of Alaska Epidemiology **Bulletin**

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Drug-Resistant Tuberculosis

Case Presentations

A 27-year-old woman had a 40-mm PPD reaction on 6/6/90; chest x-ray (CXR) of 6/11/90 showed nodular lesions in the apices of both lungs. She could not produce sputum for diagnostic evaluation. Nevertheless, her physician prescribed isoniazid (INH) preventive therapy, which she took for 2-3 months. A CXR taken on 2/4/91 showed an increase in the size of the apical nodular masses since 6/11/90. Sputum cultures yielded catalase-negative Mycobacterium tuberculosis, suggesting drug resistance. Treatment with INH, rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) was begun. Antibiotic susceptibility tests confirmed INH resistance. Her disease was cured with a 12-month course of RIF and EMB.

A 41-year-old woman had an 11-mm PPD reaction in 11/89. A CXR of 11/30/89 showed an "increased density at the end of the right 7th rib" which was not further evaluated. A 6-month course of INH preventive therapy was started on 12/2/89; the patient reportedly completed therapy on 7/31/90. In 1/91 she developed a cough and pleuritic chest pain; CXR of 1/8/91 showed a discrete, 3-cm, cavitary right lower lobe lesion. Sputum cultures yielded M. tuberculosis resistant to INH. She was treated with a 12-month course of RIF and EMB.

Discussion

These cases illustrate the hazard of prescribing INH preventive therapy (IPT) for patients with active tuberculosis (TB) disease.

Immunocompetent patients with TB infection have a significant PPD induration reaction without clinical or radiographic signs of disease caused by M. tuberculosis. Use of IPT is based on the presumption that TB-infected persons harbor relatively few tubercle bacilli in their bodies.

Spontaneous mutation conferring resistance to INH occurs in about one per million M. tuberculosis organisms. When a patient's body burden of M. tuberculosis exceeds 10^6, as it commonly does in active TB disease (and particularly in cavitary pulmonary TB), the presence of an INH-resistant mutant is almost certain. Treatment of such a patient with INH alone will kill INH-sensitive organisms but allow INH-resistant organisms to flourish. Both patients described above had abnormal chest x-ray findings whose significance was not understood by the treating physician. Well-intentioned prescription of IPT resulted in the induction of INH-resistant TB (IRTB).

The treatment of IRTB is less often successful (cure rate of about 89-96%) and requires longer therapy (e.g.,RIF and EMB for 12 months, with PZA for at least the first 2 months) than treatment of drug-sensitive TB. Even in the best of hands, the cure rate for TB resistant to both INH and RIF is only about 50-60%. Drug-resistant TB can be fatal.

Drug-resistant TB is uncommon in Alaska. During 1991, only three (5.7%) of the 53 M. tuberculosis isolates tested were drug-resistant; all were resistant to INH alone.

Recent outbreaks of multidrug-resistant TB (MDRTB) on the East Coast and in the Midwest are not due to a new strain of M. tuberculosis but to organisms which have developed resistance to several effective anti-TB drugs as a result of patients' non-compliance with treatment and health-care providers' inappropriate treatment prescriptions. MDRTB is exceedingly difficult to treat and may cause rapidly progressive, fatal disease in immunosuppressed persons.

One can identify a subgroup of patients who are at increased risk of having drug-resistant TB (DRTB). They are patients who: (1) have previously received any anti-TB therapy; (2) are or have been poorly compliant with anti-TB therapy; or (3) are from countries where the incidence of DRTB is high [e.g., east Asia (esp. Korea, Southeast Asia, and the Philippines), Central and South America, Africa].

Recommendations

1. Before prescribing IPT, the health-care provider should always rule out the presence of active TB disease; usually, a CXR is sufficient. Patients whose CXR shows a pulmonary or pleural abnormality must be evaluated further (with sputum mycobacterial cultures and/or other measures) before single-drug preventive therapy is considered.

2. All initial M. tuberculosis isolates should be tested for drug susceptibility; this is done routinely at the State Public Health Laboratory in Anchorage.

3. Patients with active TB disease must be treated with more than one drug (INH and RIF, at a minimum).

4. Sputum cultures (2-3) should be collected monthly from all culture-confirmed pulmonary TB patients until all cultures from a single month's collection are negative.

5. For patients at high risk of DRTB (see above), EMB should be part of the initial drug regimen (usually INH/RIF/EMB or INH/RIF/PZA/EMB) until antibiotic susceptibilities are known.

6. Patients being treated for active TB disease should have close public health supervision to assure completion of prescribed therapy.

To discuss questions about drug-resistant TB, call Tuberculosis Control Program staff at 561-4406.

Adequate medical treatment and close public health follow-up of TB patients will prevent the development of DRTB.

(Contributed by Michael Jones, MD, Section of Epidemiology)