Exogenous Reinfection with Multidrug-Resistant Mycobacterium tuberculosis

Active tuberculosis in patients with prior tuberculous infection can occur after endogenous reactivation or exogenous reinfection. Endogenous reactivation results from reactivation of viable tubercle bacilli in dormant foci that persist after primary infection. Exogenous reinfection results from inhalation of new bacilli, causing active disease. Since the publication of Stead's article in 1967 [1], exogenous reinfection has not been considered a significant cause of tuberculosis in individuals known to have had previous tuberculin reaction in the United States and other developed countries.

However, recent reports from the United States have documented exogenous reinfection with resistant Mycobacterium tuberculosis in patients with advanced HIV infection, alcoholism, and malnutrition [2–5]. We describe a diabetic patient with a history of tuberculosis who is receiving treatment for multidrug-resistant tuberculosis (MDRTB) apparently acquired through exogenous reinfection.

A 60-year-old Peruvian man was treated for pulmonary tuberculosis in 1951 with collapse therapy and intramuscular streptomycin. He moved to New York in 1953 and has worked in our hospital's housekeeping department since 1971. In 1974, he underwent a tine test done at the employee health service, which was positive. Other than adult-onset diabetes mellitus, well controlled with oral hypoglycemic agents, he had no other illnesses and took no other medications.

The patient was well until September 1994, when he developed a persistent productive cough and lost 20 pounds over the ensuing 2 months. In November 1994 a chest radiograph revealed patchy nodules in the right lung and left-sided pleural thickening. No previous radiograph was available for review. He denied all risk factors for HIV infection and tested negative for antibodies to the virus. Multiple sputum specimens were smear positive for acid-fast bacilli, and cultures yielded M. tuberculosis that was resistant to seven antitubercular drugs, including all five first-line agents. Restriction fragment length polymorphism (RFLP) analysis revealed that this strain's pattern was identical to that of a strain responsible for many MDRTB cases in New York City (Public Health Research Institute Tuberculosis Center [New York City] strain W) [6].

In January 1997 the patient was completing his 24th month of directly observed therapy, which consisted of daily oral ofloxacin, cycloserine, p-aminosalicylic acid, and pyridoxine; intramuscular capreomycin was included in this regimen during the first 6 months. His compliance with this regimen has exceeded 90%. After he started receiving this therapy, his sputum smears and cultures converted to negative within 2 months, and he had an excellent clinical and radiographic response.

The findings in this case illustrate probable exogenous reinfection of a diabetic man with MDRTB. Despite lack of culture confirmation of our patient's original episode of tuberculosis, much evidence supports prior infection, including his description of a clinical picture consistent with tuberculosis, previous surgical and medical treatment for tuberculosis, and a positive tine test in 1974. In 1994 he had culture-confirmed tuberculosis, probably caused by a strain of M. tuberculosis different from that which caused his initial infection. His job involved cleaning respiratory isolation rooms of patients with suspected and known tuberculosis, including some patients with MDRTB whose isolates had a strain W pattern. Strain W, which apparently dates back to the 1980s, has been recovered primarily in New York City and has caused many cases of MDRTB, including nosocomial outbreaks [6]. This strain first appeared at our institution in November 1992. The RFLP pattern of the isolate from the patient described herein matched the pattern of isolates from other patients seen at our hospital.

This case, as well as those previously reported [2–5], demonstrates that prior tuberculous infection or disease does not provide adequate protective immunity to reinfection with a different strain of M. tuberculosis. These patients were all in groups considered to be at high risk of developing active disease after tuberculous infection [7]. The factors that make such patients more likely to develop disease when they are infected may also put them at greater risk of reinfection when exposed again to M. tuberculosis.

Exogenous reinfection is believed to be a significant cause of tuberculosis in developing countries and other areas where
the risk of tuberculous infection is high [8, 9]. Our patient, and others described in previous reports [2–4], were in environments where they were heavily exposed to M. tuberculosis. In addition to varying degrees of immunosuppression, high levels of exposure to M. tuberculosis likely contributed to their risk of reinfection.

The case described herein illustrates that diabetes may be a risk factor for exogenous reinfection in patients with prior tuberculous infection. To what extent, if any, exogenous reinfection occurs in immunocompetent hosts is unknown. Stead [10] suggested that healthy tuberculin reactors are at very low risk of reinfection when they are again exposed to M. tuberculosis. Shafer et al. [5] presented a case of exogenous reinfection in an immunocompetent woman who had previously used alcohol heavily. However, it is not clear how previous heavy alcohol use affects the immune system.

The number of cases of tuberculosis resulting from exogenous reinfection is undoubtedly underestimated since the cases described to date have involved only reinfection with isolates resistant to multiple drugs. Perhaps, when molecular epidemiological tools are more broadly used to analyze M. tuberculosis isolates, we will have a truer sense of the role reinfection plays in tuberculosis.

**References**


**Recurrent Vancomycin-Resistant Enterococcus faecium Bacteremia in a Leukemia Patient Who Was Persistently Colonized with Vancomycin-Resistant Enterococci for Two Years**

The enterococcus has become a major nosocomial pathogen, particularly in immunosuppressed patients, and has also acquired resistance to all major therapeutic antibiotics including vancomycin. Mortality was high in reported outbreaks of vancomycin-resistant enterococcal bacteremias, particularly in cancer patients [1, 2]. We report the case of a patient with leukemia who had three separate episodes of vancomycin-resistant enterococcal bacteremia over 2 years.

A 40-year-old man with acute promyelocytic leukemia received induction chemotherapy in October 1993 at the University of Maryland Cancer Center. A rectal surveillance culture performed 18 days after admission to the hospital yielded Enterococcus faecium that was resistant to vancomycin (MIC, >256 μg/mL), teicoplanin (MIC, 64 μg/mL), ampicillin (MIC, >256 μg/mL), and streptomycin (MIC, >1,024 μg/mL); in addition, this isolate had high-level resistance to gentamicin (MIC, 1,024 μg/mL). Blood cultures performed during a febrile episode 6 days later yielded an isolate of E. faecium that was identical to the original isolate on the basis of antimicrobial susceptibility tests and pulse-field gel electrophoretic patterns. The isolate was determined to be a vanB1 genotype by PCR.

The patient did not have sepsis on the basis of subsequent vital signs but had severe neutropenia and mucositis. He had received oral vancomycin therapy as bowel prophylaxis and iv vancomycin therapy for a clinically documented catheter exit site infection. His Hickman catheter was removed. The results of subsequent blood and catheter tip cultures were negative. His neutrophil count recovered 6 days later and was associated with remission of his leukemia; he recovered uneventfully without specific therapy.

Over the next 3 months, rectal surveillance cultures continued to yield an E. faecium isolate that was identical to the first one obtained in cultures performed during his first admission; the isolates were determined to be identical on the basis of antimicrobial susceptibility tests and pulse-field gel electrophoretic patterns. In March 1995 his leukemia relapsed for a second time, and he received chemotherapy. A rectal surveillance culture yielded an identical E. faecium isolate. He again became bacteremic with the same E. faecium isolate.