

Extensively Drug-Resistant Tuberculosis, Lesotho

To the Editor: Reports of extensively drug-resistant tuberculosis (XDR TB) in the Republic of South Africa have generated concern in the medical and public health literature (1,2). Given that XDR TB is spread through the air, it is not surprising that cases have been reported in multiple countries throughout the world (3). We report a documented case of XDR TB in Lesotho. This case is closely tied to transnational work in South Africa, thus raising concern about the spread of this disease across highly porous borders and the need for international attention to migrant worker health.

Lesotho is a mountainous nation that is home to 2 million people and completely surrounded by South Africa. It has the third highest rate of HIV in the world; an estimated 24%–30% of the population is infected (4). Lesotho also has a high prevalence of TB with an estimated 695 cases per 100,000 population (5). Ten percent of patients with smear-positive TB are estimated to have multidrug-resistant TB (6). The US Centers for Disease Control and Prevention is undertaking a national reporting registration survey in Lesotho.

In 2007, the Ministry of Health and Social Welfare began working with Partners In Health and the Foundation for Innovative and New Diagnostics, Geneva, Switzerland, to document and treat drug-resistant TB in Lesotho. Hundreds of cases of drug-resistant TB have been reported in the country, and the patient we describe in this letter was reported to have XDR TB.

The patient was a 44-year-old man who had been working in the gold mines in South Africa. He had a history of receiving multiple treatments for TB while he was working in one of

the mines. His condition was declared a treatment failure in July 2007. The patient was discharged from medical care in South Africa with no follow-up plan or medical records and was told, per his report, to “return home.” He traveled by road and bus to Lesotho and easily crossed the border. He was originally seen at a public TB clinic in Lesotho but, given his reports of prior TB treatment, his sputum was sent for culture and drug susceptibility testing. He was followed up at his home with a daily visit from a village health worker trained in the management of drug-resistant TB. When XDR TB was confirmed (in vitro resistance to at least isoniazid, rifampin, a fluoroquinolone, and an injectable agent [7]), he was admitted to the hospital for drug-resistant TB patients in Lesotho and placed in a negative-pressure, single isolation room.

When the patient sought treatment from our program in October 2007, he exhibited severe wasting and dyspnea. An HIV test result was positive; his CD4 count was 36 cells/ μ L. First-line drug susceptibility testing (carried out by the Medical Research Council [MRC], Pretoria, South Africa) showed resistance to isoniazid, rifampin, and pyrazinamide. On the basis of these results, on October 26, 2007, he was empirically prescribed a regimen of second-line drugs: capreomycin, para-aminosalicylic acid, cycloserine, ethionamide, and ciprofloxacin. One month later, second-line drug susceptibility testing, sent by the medical team in Lesotho (none was ever sent during his treatment in South Africa) but carried out at MRC, showed additional resistance to amikacin (MIC 1.0 μ g/mL), capreomycin (MIC 2.5 μ g/mL), and ofloxacin (MIC 1.0 μ g/mL) but susceptibility to ethionamide (5.0 μ g/mL). The patient's regimen was changed to kanamycin, moxifloxacin, ethionamide, para-aminosalicylic acid, and cycloserine. Unfortunately, he died of his disease in December 2007. His known contacts

are being monitored closely for signs and symptoms of TB. Reports have been made to the mine in which he was working, the Ministry of Health of South Africa, and the Ministry of Health of Lesotho. As of the writing of this letter, the South African Ministry of Health has made no formal response regarding this patient.

The report of this case of XDR TB in Lesotho raises many concerns. First, XDR TB was readily found (along with other forms of drug-resistant TB) in this small country that already has high prevalence of HIV. The potential for spread in the community as well as in hospital settings is substantial. The link to working in South Africa is also a major factor. Given the patient's prior treatment while employed by a mining company and the literature reporting XDR TB in South Africa (8), XDR TB likely developed while he was working in the mines, and he brought the disease back to his home in Lesotho. Because South African mines rely heavily on migrant labor from countries such as Lesotho, Swaziland, and Mozambique, transnational spread of drug-resistant TB, including XDR TB, is quite probable and calls for a concerted international approach and institutional collaboration for management and control of this epidemic. Infection control in the mines needs to be addressed, and international efforts to communicate that migratory populations are at risk for XDR TB need to be a priority in controlling the spread of this disease.

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Inquilinus limosus and Cystic Fibrosis

To the Editor: *Inquilinus limosus*, a new multidrug-resistant species, was reported in 1999 as an unidentified gram-negative bacterium in a lung transplant patient with cystic fibrosis (CF) (1). This species was later characterized by the description of 7 new isolates of *I. limosus* and 1 isolate of *Inquilinus* sp. (2). Infections and colonizations by *I. limosus* have been documented mainly in adolescent or adult patients with CF. To date, 8 clinical cases have been described in Germany

(3,4), 1 case in the United States (1), 5 cases in France (5), and 1 case in the United Kingdom (6) (Table). Only 1 isolate of *Inquilinus* sp. has been recovered from blood samples of a patient without CF who had prosthetic valve endocarditis (7).

Because this bacterium is not recorded in all commercial identification system databases currently available, a longitudinal study for *I. limosus* detection with a new real-time PCR assay with a Taqman probe (Applied Biosystems, Foster City, CA, USA), that targets the 16S rRNA gene, has been developed and compared with the culture isolation. Primers *ill*d (5'-TAATACGAAGGGGGCAAGCGT-3') and *ill*r (5'-CACCTCTCTTGGATT CAAGC-3') and probe *il*Probe (6FAM-GGTTCGTTGCGTCAGATGTGAAAG-TAMRA), which were used in this study, were designed on the basis of multisequence alignment of all *I. limosus* 16S rDNA sequences available in the GenBank database.

To confirm specificity, the primers and probe were checked by using the BLAST program (www.ncbi.nlm.nih.gov/blast/Blast.cgi) and also by using suspension of several bacteria recovered habitually in patients with CF. For sensitivity of the Taqman PCR assay (Applied Biosystems), the minimal CFU detectable was 2 CFU/PCR. From January 2006 through June 2007, 365 sputum samples recovered from 84 children and 61 adults with CF and 71 sputum samples recovered from 54 patients without CF were screened blindly for *I. limosus*. By using our real-time PCR, we detected 9 *I. limosus*-positive samples from 4 patients with CF (Table); 8 of these samples were also culture positive. However, all sputum samples from patients without CF were negative. In 1 patient (Table, case 17), *I. limosus* was detected by using real-time PCR 3 months before the culture was positive. Retrospectively, the patient's medical file was rechecked and his clinical respiratory condition worsened briefly at that

stage, which indicates an infection by this bacterium. Thus, in our study, the incidence of *I. limosus* was 2.8% (4.9% for adults with CF and 1.2% for children with CF). The incidence of *Burkholderia cepacia* complex during the same period and in the same patients was 2.1% (3 adults with CF were positive, data not shown).

The genus *Inquilinus* belongs to the α -*Proteobacteria*; the genus *Azospirillum* is the most closely related bacteria (2). This cluster of bacteria contains several strains that are able to grow under saline conditions and in biofilms (8,9). The mucoid phenotype of *I. limosus* may contribute to its colonization and resistance to many antimicrobial drugs. Recently, the exopolysaccharides (EPS) produced by *I. limosus* were studied. The authors indicated that *I. limosus* produces mainly 2 EPSs that exhibit the same charge per sugar residue present in alginate, the EPS produced by *Pseudomonas aeruginosa* in patients with CF. This similarity may be related to common features of the EPS produced by these 2 opportunistic pathogens that are related to lung infections (10). Transmission of *I. limosus* between patients with CF is not known, but in the report from Chiron et al., 1 of the 5 patients with *I. limosus* had a brother who had never been colonized with this bacterium despite living in the same home (5). Schmoltdt et al. reported that 3 patients were treated in the same outpatient CF clinic during overlapping time periods and each patient was infected/colonized by an individual *I. limosus* clone, which suggests that there was no transmission among these patients (4). This bacterium has been recovered mainly from sputum of adolescents (mean age 17 ± 6.47 years, range 8–35), except in our study with a 2-year-old boy, which suggests that this emerging bacterium may be hospital acquired, as recently suggested (7). Because this bacterium is multiresistant to several antimicrobial drugs, particularly colistin, which is widely