We report on the first documented extensively drug-resistant tuberculosis (XDR-TB) case in Austria, diagnosed this year. The term XDR-TB was used for the first time in March 2006, in a report jointly published by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) to describe a disease caused by Mycobacterium tuberculosis that was resistant not only to isoniazid and rifampicin (i.e. multi-drug resistant tuberculosis, MDR-TB), but also to at least three of the six classes of second-line anti-TB drugs – aminoglycosides, polypeptidines, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid (1,2). As this definition was dependent on unstandardised drug susceptibility testing (DST) methodologies and did not necessarily distinguish the most difficult-to-treat cases using the current drug armamentarium, it was eventually modified in October 2006 [1].

XDR-TB is now defined as: resistance to at least rifampicin and isoniazid, in addition to any fluoroquinolone, and to at least one of the three following injectable drugs used in anti-TB treatment: capreomycin, kanamycin, and amikacin [3].

Case report
In May 2008, a 45-year old male Romanian presented to a pulmonology centre in Vienna, Austria, complaining of fatigue, constitutional symptoms and weight loss. The patient was afebrile (37.5°C) with an oxygen saturation of 91.3% on air room, not associated with haemoptysis or night sweats, but presenting with a productive cough yielding large amounts of yellowish-greenish sputum. The patient reported having been treated with an injectable medication in the aetiology of drug-resistant disease. On examination, the patient was 1.70 m tall but weighed only 53 kg. Auscultation revealed bilateral crepitations. Chest X-ray examination showed a reduced volume of the left lung with alveolar infiltrations, and cavitory lesions on the left side. Blood tests showed leukocytosis (neutrophil count of 13.63 x 10⁹/l) and an elevated C-Reactive Protein (37 mg/l; local cut-off value 12 mg/l). Ziehl-Neelsen staining of sputum smear showed abundant acid fast bacilli (AFB 3+). Therapy with terizidon, ethambutol, linezolid, moxifloxacin and capreomycin was re-established, based on the results from the sputum cultures from Sweden. Under therapy, the patient’s condition improved, he gained 7 kg in weight and the load of AFB in sputum smears fell to 1+. Isolates from sputum samples taken in Austria yielded M. tuberculosis of spoligotype T1 (111111111111111111111111111111000011111111111). On 18 July DST showed in-vitro resistance against isoniazid, rifampicin, pyrazinamide, amikacin, ofloxacin, capreomycin, rifabutin, cycloserine, and protonamide, and susceptibility to streptomycin, ethambutol, para-aminosalicylic acid and linezolid. Accordingly, capreomycin therapy was terminated, and para-aminosalicylic acid and streptomycin were added to the treatment regimen.

The patient is presently isolated in a TB ward at a pulmonology centre in Vienna. We have no information on results of contact tracing performed for this patient.

Discussion
While this is the first published report of a case of XDR-TB in Austria it does not preclude the possibility that other cases had occurred or transited the country previously. This study illustrates some key public health concerns very pertinent to TB in the world today, including disease chronicity, its association with low-resource settings, the mobility of infectious patients and the role of improper medication in the aetiology of drug-resistant disease.

By June 2008, 18 countries in the European Union (EU) and Western Europe - including Romania - and six in the former Soviet Union had officially reported XDR-TB cases [4]. Four of these countries (Czech Republic, Germany, Italy, and Slovenia) share a border with Austria. A large part of the drug-resistant TB caseload in Europe occurs in the countries of the former Soviet Union [5]. The XDR-TB case in Austria originated from Romania, a resource constrained country at the eastern border of the EU. Our case shows only too well that XDR-TB is not confined by state borders. Schmid et al. have recently also described an outbreak of MDR-TB among HIV-seronegative refugees in Austria [6]. As the reporters of the first XDR-TB case in Ireland concluded in a recent article, we expect to have further cases from amongst nations of countries with a high burden of drug-resistant TB [7].
The available evidence shows that XDR-TB results mainly from poor clinical practice [1]. Poor adherence to treatment, inappropriate prescription, irregular drug supply, and poor drug quality are the main reasons for acquiring resistance in TB [8]. Once XDR-TB is acquired the prospects of successful chemotherapy remain low. In one series from Western European countries the mortality among non-HIV patients was reportedly 36% [8]. This makes the implementation of appropriate public health measures to prevent further spread all the more crucial. The occurrence of XDR-TB in Austria should serve as a wake-up call to strengthen the national TB control programme by implementing evidence-based measures to regulate the monitoring of TB treatment and contact tracing.

References


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