

Publication

A cluster of multidrug-resistant *Mycobacterium tuberculosis* among patients arriving in Europe from the Horn of Africa : a molecular epidemiological study

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The risk of tuberculosis outbreaks among people fleeing hardship for refuge in Europe is heightened. We describe the cross-border European response to an outbreak of multidrug-resistant tuberculosis among patients from the Horn of Africa and Sudan.; On April 29 and May 30, 2016, the Swiss and German National Mycobacterial Reference Laboratories independently triggered an outbreak investigation after four patients were diagnosed with multidrug-resistant tuberculosis. In this molecular epidemiological study, we prospectively defined outbreak cases with 24-locus mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) profiles; phenotypic resistance to isoniazid, rifampicin, ethambutol, pyrazinamide, and capreomycin; and corresponding drug resistance mutations. We whole-genome sequenced all *Mycobacterium tuberculosis* isolates and clustered them using a threshold of five single nucleotide polymorphisms (SNPs). We collated epidemiological data from host countries from the European Centre for Disease Prevention and Control.; Between Feb 12, 2016, and April 19, 2017, 29 patients were diagnosed with multidrug-resistant tuberculosis in seven European countries. All originated from the Horn of Africa or Sudan, with all isolates two SNPs or fewer apart. 22 (76%) patients reported their travel routes, with clear spatiotemporal overlap between routes. We identified a further 29 MIRU-VNTR-linked cases from the Horn of Africa that predated the outbreak, but all were more than five SNPs from the outbreak. However all 58 isolates shared a capreomycin resistance-associated *tlyA* mutation.; Our data suggest that source cases are linked to an *M tuberculosis* clone circulating in northern Somalia or Djibouti and that transmission probably occurred en route before arrival in Europe. We hypothesise that the shared mutation of *tlyA* is a drug resistance mutation and phylogenetic marker, the first of its kind in *M tuberculosis sensu stricto*.; The Swiss Federal Office of Public Health, the University of Zurich, the Wellcome Trust, National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), the Medical Research Council, BELTA-TBnet, the European Union, the German Center for Infection Research, and Leibniz Science Campus Evolutionary Medicine of the Lung (EvoLUNG).

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