RAPID RISK ASSESSMENT

Multidrug-resistant tuberculosis in migrants, multi-country cluster

First update, 19 December 2016

Conclusions and options for response

An international whole genome sequencing cluster involving 16 cases of multidrug-resistant tuberculosis (MDR TB) in asylum seekers has been detected. The first seven cases were identified in Switzerland between February and August 2016. Their countries of origin are Somalia (5 cases), Eritrea (1) and Ethiopia (1). Whole genome sequencing (WGS) showed no difference among isolates in four cases and differences of one allele in the three others. Based on the WGS results, the strains belong to a single molecular cluster. The same genetic clone with the same and so far unknown drug resistance profile was detected in nine additional cases from Somalia, six of them diagnosed in Germany, two in Austria, and one in Sweden.

Further multi-country outbreak investigation is focussing on identifying exposure risk factors, including the travel itinerary and the history of possible contacts among patients in this single-strain outbreak of MDR TB. Although the limited number of cases detected so far suggests that there is only a limited risk of this outbreak becoming a widespread event, more cases may occur in association with this cluster. Sharing WGS-based typing information between affected countries on outbreak-related cases is important to the further delineation of the extent of the outbreak.

Improving understanding of this outbreak – including identifying any other potential cases and contacts – will allow targeted prevention and control measures. It will be important to perform epidemiological investigations, which would comprise contact tracing, source case investigation, and investigation of possible epidemiological links, as well as to ensure early case finding of active TB and drug susceptibility testing, especially in newly arriving migrants from the Horn of Africa, in order to identify and treat active cases and to provide preventive treatment or monitoring for those diagnosed with latent tuberculosis infection.

Source and date of request

ECDC internal decision, 7 December 2016.

Public health issue

This first update provides information regarding the risk of EU transmission of an MDR TB clone initially detected in seven asylum seekers from the Horn of Africa who currently reside in Switzerland. Recommendations are given to improve the understanding and the public health impact of this outbreak for the EU.

Consulted experts

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Disease background information

Multidrug-resistant tuberculosis (MDR TB) is defined as tuberculosis (TB) disease caused by a *Mycobacterium tuberculosis* complex strain resistant to at least rifampicin and isoniazid [1]. MDR TB is an urgent public health priority in Europe, with significant health and cost implications associated with the expensive and prolonged treatment often required [2]. Inadequate or incomplete TB treatment is the main risk factor for the development of resistance among TB cases, and is usually associated with intermittent drug use, errors in medical prescription, poor patient adherence and low quality of TB drugs [2].

Options for prevention of TB infection among contacts of MDR TB cases are limited and require an individual risk assessment, taking into consideration:

- the risk of progression to TB disease;
- the drug susceptibility pattern of the source case; and
- the risk of adverse drug events [4, 5].

Migrants seeking refuge from conflict or deprived areas may be at increased risk of TB and MDR TB because of the collapse of health service infrastructure in these contexts. Some migrant groups, including refugees, refused asylum seekers, victims of trafficking, and undocumented migrants may be at particularly high risk of (MDR) TB due to exposure to destitution, poor social conditions (e.g. overcrowding, poor living conditions, incarceration or detention, and homelessness), exposure to other migrants from high-incidence countries affected with MDR TB along their migration route or after entry in the host country, or co-infection (e.g. with human immunodeficiency virus) [2].

Tuberculosis burden in high-income countries disproportionally affects the foreign-born migrant population, and transmission is documented to predominantly occur within migrant communities or native communities, and less between migrant and natives [2, 6] [7]. Active disease occurs in five to ten percent of those infected within a few months to many years after infection and, in up to ten per cent per year, in HIV-positive people.

Event background information

Seven cases of multidrug-resistant tuberculosis (MDR TB) were diagnosed in Switzerland between February and August 2016 with a strain that was resistant to rifampicin, isoniazid, ethambutol, pyrazinamide and capreomycin, but fully sensitive to amikacin and fluoroquinolones. All cases were males aged 15–19 years who had sought asylum at different points in time between December 2015 and June 2016. Their countries of origin are Somalia (5), Eritrea (1) and Ethiopia (1).

Sputum smear microscopy for acid-fast bacilli was positive in three patients, negative in one, and not done or unknown in three. One of the cases was diagnosed four months after a contact with one of the cases with negative sputum smear microscopy. No other epidemiological link has been identified so far. Whole genome sequencing (WGS) of the cases diagnosed in Switzerland showed identical isolates in four cases and differences of one allele in the other three. Based on WGS analysis, the seven strains are genetically highly related and are likely to be part of a single molecular cluster. The MIRU-VNTR 24 loci profile of the strains is 2-2-4-2-4-3-3-3-2-4-2-4-2-2-5-1-4-3-3-3-4-3-2-2.

The Swiss National Reference Laboratory for Mycobacteria requested information from laboratories in Austria, France, Germany, Italy, the Netherlands and the United Kingdom. As of 19 December 2016, six cases in Germany are of the same genetic clone. The patients are asylum seekers from Somalia. Two cases from Somalia with the same WGS profile were detected in Austria (2), one with the same drug susceptibility pattern; for the second case, drug susceptibility testing (DST) is ongoing. In addition, one isolate with the same MIRU-VNTR 24 loci pattern, the same drug susceptibility pattern, and the same WGS pattern has been identified in Sweden in a patient from Somalia.

Based on MIRU-VNTR 24 loci typing data on 2 828 MDR-TB cases reported to ECDC, covering the period 2003–2015, this outbreak type is rare, with only two MDR TB cases with the same MIRU-VNTR 24 loci pattern reported from Belgium: one case was diagnosed in 2011 (country of origin: Somalia), the second one in 2013 (country of origin: Djibouti). These cases from Belgium are not considered part of the recent transmission chain, but the findings indicate the presence of this genotype in the Horn of Africa. Further comparisons of WGS profiles of these and outbreak-related strains should clarify their ancestral relationship and make it possible to find a probable date of divergence for the outbreak strain.

ECDC requested information from all EU/EEA Member States on whether they identified cases with an MDR TB strain showing the same MIRU-VNTR 24 loci pattern. The pattern could not be identified in Bulgaria, Croatia,

Cyprus, Denmark, Estonia, Hungary, Greece, Italy, Latvia, Luxembourg, Malta, Poland, Portugal and Romania. ECDC is still waiting for responses from the Czech Republic, Iceland, Liechtenstein, Lithuania, Slovakia, Slovenia and Spain.

Of the responding countries, two countries reported a total of three cases from the Horn of Africa with the same MIRU-VNTR pattern and drug susceptibility pattern. In addition, eight cases from Somalia with similar MIRU-VNTR results and various antimicrobial susceptibility patterns have been reported from four countries. The dates of isolation of these strains range from 2009 to 2014, or are unknown.

ECDC threat assessment for the EU

According to data published in the latest WHO TB report, the estimated incidence of TB in Somalia was 274 per 100 000 in 2015. According to the same source MDR TB was estimated in 8.7% of new TB cases and in 47.0% of previously-treated TB cases in Somalia. According to IOM, 2.1% of the refugees in Europe, i.e. about 10 000 people, are coming from Somalia. The available information on near-identity of whole genome sequence of the infecting strains in this recent cluster, suggests a possible recent transmission. The genotypically clustered patients who come from different countries, are likely to have become infected either in their country of origin or in a place along their migration route to the country of destination.

Infected persons who do not have active TB are not infectious. However, they are at risk of developing active TB disease and becoming infectious. The lifetime risk of reactivation TB for a person with documented latent TB infection (LTBI) is estimated to be 5 to 10%, with the majority developing TB disease within the first five years after initial infection [8].

Although TB in a foreign-born population does not have a significant influence on TB in the native population in the EU/EEA, there is a risk of transmission for both migrants and the native population [2].

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