RAPID RISK ASSESSMENT

Louse-borne relapsing fever in the EU

17 November 2015

ECDC threat assessment for the EU

Twenty-seven confirmed cases of louse-borne relapsing fever (LBRF) were diagnosed in EU countries and Switzerland between July and October 2015. These cases, diagnosed among refugees from countries of the Horn of Africa are not unexpected as the disease is present in north-eastern Africa.

The information available indicates that most of the 27 cases are likely to have been exposed to body lice infestations and louse-borne relapsing fever during their journey to Europe. Symptoms of the three cases reported in Sicily occurred shortly after entry, suggesting an infection with *Borrelia recurrentis* near to the time they arrived in Italy. The transmission of *Borrelia recurrentis* to the eight cases reported in Germany is likely to have taken place towards the end of their journey in Libya or upon arrival in Italy. The Netherlands reported cases of LBRF with onset in late spring 2015. These cases used the same migration route through Libya as the German cases, favouring the hypothesis of transmission of LBRF in the countries traversed before arriving in Europe.

In Turin, however, the two affected individuals were living in Italy since 2011 and they denied recent travel to endemic regions. Therefore they are likely to have become infected while being housed in the same overcrowded facility as the newly arrived infected cases. This points to the possibility of locally acquired transmission of LBRF among migrants within the EU.

An increase of refugees from LBRF-endemic areas has been observed in the EU since 2014, indicating that similar importation of cases and subsequent secondary transmission could occur in EU/EEA countries.

These events highlight the importance of early detection and notification, for timely implementation of public health measures in order to reduce the risk of outbreaks. Furthermore, LBRF should be considered in differential diagnosis of malaria and as a potential cause of fever, particularly if recurrent, among refugees using the East African and Central Mediterranean routes.

Body lice infestation is linked to low socioeconomic status, over-crowding and poor personal hygiene. Refugees are vulnerable to body lice infestation due to challenging living conditions during migration, and after entry into the EU due to crowded conditions in temporary shelters. People in close contact with migrants hosting body lice infected with *Borrelia recurrentis* are at risk of being exposed to the disease. Once in the EU, there is a risk of spread from infected individuals infested with body lice to the homeless or other vulnerable population groups sharing the same living environment, in particular temporary housing in crowded environments. The risk of infection for relief workers involved in refugee care is extremely low when appropriate hygiene measures such as wearing gloves during medical examination are observed. Body lice can transmit other diseases (e.g. epidemic typhus and trench fever), and delousing is an effective way to control transmission of louse-borne pathogens.

Suggested citation: European Centre for Disease Prevention and Control. Louse-borne relapsing fever in the EU – 17 November 2015. Stockholm: ECDC; 2015.

Conclusions and options for response

The occurrence of LBRF cases among refugees from countries of the Horn of Africa is not unexpected and additional cases may occur in the EU among these vulnerable groups, in particular among those who travel along the East African and Central Mediterranean routes. The recent report of probable locally-acquired cases in Italy illustrates the potential for autochthonous transmission in overcrowded settings in Europe.

Prevention and control of louse-borne diseases in the EU requires the capacity to detect cases in populations at risk, strengthening surveillance systems and improving communication and collaboration between Member States.

Therefore, options to consider for the prevention and control of LBRF and other louse-borne diseases include:

- where possible, preventing or minimising overcrowding in reception centres for migrants, as well as promoting and enabling adequate hygiene for residents in those facilities
- raising awareness among migrants, particularly at points of entry into the EU, about lice infestation and possible louse-borne diseases
- checking for signs of lice infestation during medical screening of migrants and carrying-out delousing as required. As the detection of lice infestation may not be very sensitive, preventive delousing can be considered
- raising awareness among clinicians of the possibility of LBRF and other louse-borne diseases among refugees
- warning clinicians about the risk of the potentially fatal Jarisch–Herxheimer reaction when treating patients with LBRF with antibiotics, which requires supportive care for monitoring fluid balance
- considering adding cases of LBRF to the routine notification of the public health department in order to identify other exposed persons and apply control measures and treatment in a timely manner.

Source and date of request

ECDC Internal Decision on 10 November 2015.

Public health issue

To assess the public health significance for the EU of cases of louse-borne relapsing fever among refugees reported in 2015 by the EU Member States Germany, Italy, Finland and the Netherlands, and Switzerland.

Consulted experts

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Disease background information

Louse-borne relapsing fever (LBRF) is a vector-borne disease caused by the spirochaete *Borrelia recurrentis,* a human-restricted pathogen transmitted by the body louse *Pediculus humanus humanus* [1-3]. Transmission occurs when the louse is crushed and the infected haemocoel fluid is released onto the human skin [4]. Subsequently, *Borrelia recurrentis* is able to penetrate intact mucosa and skin [2].

The incubation period of louse-borne relapsing fever is usually between four and eight days (range: 2–15). The onset of symptoms is generally sudden, associated with circulation of bacteria in the blood, and includes high-grade fever, malaise, chills and sweats, headache, meningism, myalgia/arthralgia and non-specific gastrointestinal symptoms (nausea and vomiting) [1,5]. The symptoms increase in intensity over five days on average (range: 2–7), then subside as the pathogenic agent disappears from the blood. After a first remission, spirochaetes reappear in the blood and symptoms recur. The relapse occurs over several days to weeks, but fewer than ten relapses are usually observed among untreated patients [1]. Relapses can occur after delousing. The disease can be severe and death may occur in 10–40% of symptomatic cases in the absence of appropriate treatment, and in 2–5% of treated patients [2]. The antibiotic of choice is doxycycline (tetracycline group), although other antibiotic treatments are also effective (penicillin G, erythromycin, chloramphenicol) [6]. A potentially severe or fatal Jarisch–Herxheimer reaction can be induced by antibiotic treatment [1,7,8].

The diagnostic test of choice is the direct identification of spirochaetes in the blood by Giemsa stained blood films , especially during the symptomatic febrile phase [9]. Nucleic acid detection is carried out for species identification and to support the clinical diagnosis [10]. Malaria, typhoid fever, viral haemorrhagic fever, leptospirosis, typhus, tick-borne relapsing fever, non-typhoidal salmonellosis, meningococcal septicaemia and meningitis need to be considered in the differential diagnosis.

Historically, major outbreaks of louse-borne relapsing fever have occurred in Eurasia and Africa [5]. The geographical distribution of louse-borne relapsing fever has shrunk due to improvements in living standards. Currently, the disease is primarily found in limited endemic foci in Ethiopia, but also in Eritrea, Somalia and Sudan [5,11-13]. Antibodies to *Borrelia recurrentis* were detected in homeless populations in Marseille between 2000 and 2003, suggesting that a small, unnoticed outbreak occurred in this particular vulnerable population [14].

Body lice are very sensitive to the temperature and are unable to survive for more than 1 to 2 days off the host. At low temperature, lice are not active which reduces the risk for transmission of infestation to another person. Body lice develop preferentially at 29-32°C and at highest rate at 75% relative humidity. They do not oviposit (lay eggs) when the temperature is below 25°C. The maximum egg survival is 3-4 weeks [15].

Primary prevention of louse-borne relapsing fever relies on measures for avoiding infestation with body lice [2,16]. Such infestations are linked with low socioeconomic status, over-crowding and poor personal hygiene [2].

Detection of a clinical case should lead to source-tracing and it is necessary to investigate and treat infected contact(s). Treatment of clothing for LBRF is necessary as infected lice can remain in them [2].

More information can be found in the ECDC factsheet louse-borne relapsing fever.

Event background information

The Netherlands: Two cases of louse-borne relapsing fever (LBRF) caused by *Borrelia recurrentis* in asylum seekers coming from Eritrea were reported by the Netherlands [17]. Both cases arrived in the Netherlands within one week of each other after passing through Ethiopia, Sudan, Libya and Italy. Both resided in an unofficial street camp in Rome for a few days. The first case was a young adult from Eritrea who was admitted to a regional hospital in northern Netherlands on 4 July 2015 with a five-day history of headache, abdominal pain, myalgia and fever. The case, who was later referred to the University Medical Centre Groningen (UMCG), had entered the EU 14 days earlier and arrived in the Netherlands two days prior to admission to hospital. The second case was referred to UMCG by the physician at the local reception centre for asylum seekers for general malaise, headache, fever and cough. The patient reported symptoms of fever and chills two weeks before referral. For the two cases, initial diagnostic was made by thick and thin blood films examination for malaria diagnostic showing spirochaetes. *Borrelia recurrentis* infection was confirmed by molecular assay for the two patients. They received antibiotic treatment and supportive care as both patients experienced a Jarisch–Herxheimer reaction. The body louse was recovered from the clothing of the first patient only. Following this event, ECDC published a rapid risk assessment on 'Louse-borne relapsing fever in the Netherlands' on 24 July 2015 that proposed options to consider for the prevention and control of louse-borne relapsing fever in the EU [18].

Switzerland: In August, one imported case was diagnosed at the University Hospital Basel [19]. The case was an Eritrean refugee who travelled to Europe approximately two months earlier with stopovers in Sudan (two weeks) and Libya (three weeks), and entered Italy 12 days before being hospitalised in Switzerland. He presented with symptoms of fever lasting for two days, nausea, headache, dysuria and bilateral flank pain upon admission. He reported having had similar symptoms during his journey through Sudan. Similar to the cases reported by the Netherlands, the diagnosis was made by microscopic detection of spirochaetes on blood smears and confirmed by PCR. The patient received antibiotic treatment and did not experience a Jarisch–Herxheimer reaction.

Finland. One case of LBRF was reported in a publication in 2015 [20].

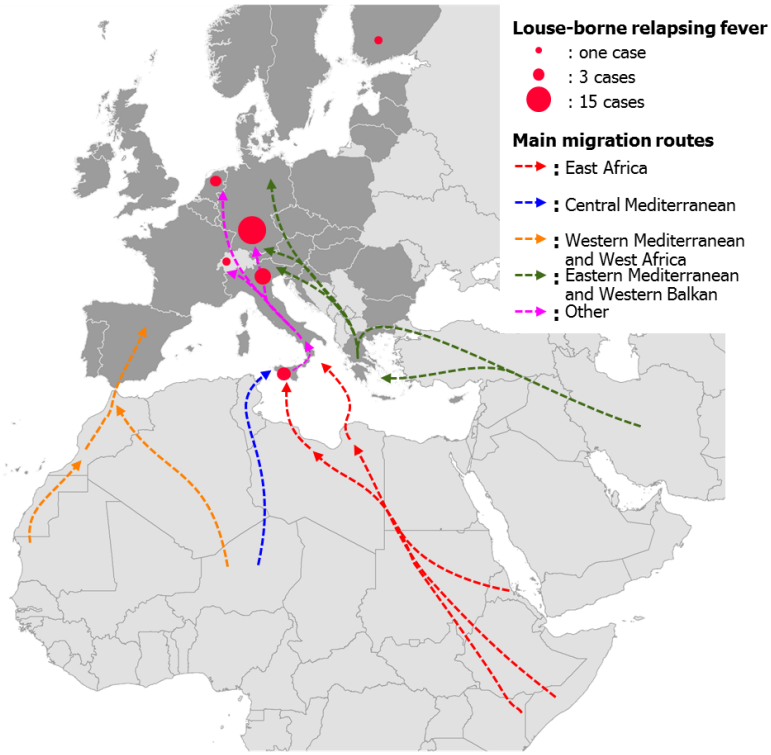
Germany: After reporting three cases among refugees in August 2015, a recent publication acknowledged 15 imported louse-borne relapsing fever cases in Bavaria between July and October 2015 [21,22]. *Borrelia recurrentis* infection was confirmed in fourteen of these cases and one case only presented a Giemsa stained blood film showing spirochaetes. All patients were hospitalised and received antibiotic treatment with doxycycline. One patient died after antibiotic treatment was initiated. Jarisch–Herxheimer reaction to antibiotic treatment was not investigated systematically, but among all patients for whom this information was available, the reaction to antibiotic treatment was observed. Cases occurred among males originating from Somalia (n=12), Eritrea (n=2) and Ethiopia (n=1). Eight of the ten cases with documented onset had onset of disease in the period seven days before or after arriving in Bavaria. Two cases had onset of symptoms more than 20 days before arrival. Through investigations, no previous recurring fever episodes were reported.

Italy: In November 2015, eight louse-borne relapsing fever cases in refugees were reported in Turin (5) and Sicily (3) [23,24].

- In Turin, five confirmed LBRF cases were described among East African refugees from Somalia between 7 June and 26 September 2015 [23]. Three cases recently travelled from Somalia to Italy through Kenya, Uganda, Sudan and Libya. The two other cases were resident in Italy without travel history to endemic foci of LBRF since their entry in Italy in 2011. All cases were diagnosed at the city emergency department to the Infectious Disease Hospital in Turin as they presented a few days history of fever with headaches and chills. The diagnosis was made by microscopic detection of spirochaetes on blood smears and confirmed by PCR. Two out of five patients presented symptoms compatible with Jarisch–Herxheimer reaction after antibiotic treatment.
- In Sicily, three confirmed cases of LBRF were diagnosed among refugees from Somalia after travelling through several countries in Africa [24]. The first case was a three-year-old boy from Somalia with onset of symptoms two days after arrival in Palermo from Libya on 11 July 2015. The second case was a seven-year-old boy from Somalia who presented symptoms on 1 September 2015, six days after his arrival in Lampedusa from Libya on 27 August 2015. The third case was a 17-year-old boy from Somalia who arrived in Trapani on 4 September 2015 after staying five months in Libya. He experienced onset of symptoms three days after arrival. The three patients travelled independently from each other during their journey towards Italy. All cases were diagnosed by a positive blood smear and PCR assay confirming *Borrelia recurrentis* infection. One case presented a Jarisch-Herxheimer reaction a few hours after antibiotic treatment. All patients recovered.

Louse-borne relapsing fever occurred among individuals coming from Somalia, Eritrea and Ethiopia. Most of them were travelling from the Horn of Africa towards Italy through Sudan and Libya using mainly the Central Mediterranean migration route. This has been a major route for entering the EU for almost a decade, and the migration flow have increased substantially over time, especially during the summer months. The Central Mediterranean and the East African migration routes have been used by various African nationalities [25]. For example, Eritreans and Sudanese were ranked as the third and sixth highest nationalities at border crossing points for the second quarter of 2015 [26]. Migrants using the Central Mediterranean migration route usually depart from the northern coast of Libya and more recently Egypt, towards the south of Italy and Malta [25,27] .

Figure 1. Distribution of the 27 cases of louse-borne relapsing fever in Europe by reporting country in 2015, and main migration routes*



Adapted from [25,27]

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Conclusions and options for response

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References

1. Fauci As, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine, 17th Edition. 2008:2754.
2. Raoult D, Roux V. The body louse as a vector of reemerging human diseases. Clin Infect Dis. 1999 Oct;29(4):888-911.
3. European Centre for Disease Prevention and Control (ECDC). Factsheet: Louse-borne relapsing fever [Internet]. 2015 [cited 2015 Nov 10]. Available from: http://ecdc.europa.eu/en/healthtopics/emerging_and_vector-borne_diseases/louse-borne-diseases/Pages/louse-borne-relapsing-fever.aspx.
4. Houhamdi L, Raoult D. Excretion of living Borrelia recurrentis in feces of infected human body lice. J Infect Dis. 2005 Jun 1;191(11):1898-906.
5. Cutler SJ, Abdissa A, Trape JF. New concepts for the old challenge of African relapsing fever borreliosis. Clinical Microbiology and Infection. 2009 May;15(5):400-6.
6. Guerrier G, Doherty T. Comparison of antibiotic regimens for treating louse-borne relapsing fever: a meta-analysis. Trans R Soc Trop Med Hyg. 2011 Sep;105(9):483-90.
7. Coxon RE, Fekade D, Knox K, Hussein K, Melka A, Daniel A, et al. The effect of antibody against TNF alpha on cytokine response in Jarisch-Herxheimer reactions of louse-borne relapsing fever. QJM. 1997 Mar;90(3):213-21.
8. Rahlenbeck SI, Gebre-Yohannes A. Louse-borne relapsing fever and its treatment. Trop Geogr Med. 1995;47(2):49-52.
9. Versalovic J, American Society for M. Manual of clinical microbiology. vol. 1. vol. 1. Washington, D.C.: ASM Press; 2011.
10. Elbir H, Henry M, Diatta G, Mediannikov O, Sokhna C, Tall A, et al. Multiplex real-time PCR diagnostic of relapsing fevers in Africa. PLoS Negl Trop Dis. 2013;7(1):e2042.
11. Elbir H, Raoult D, Drancourt M. Relapsing fever borreliae in Africa. Am J Trop Med Hyg. 2013 Aug;89(2):288-92.
12. Yimer M, Abera B, Mulu W, Bezabih B, Mohammed J. Prevalence and risk factors of louse-borne relapsing fever in high risk populations in Bahir Dar city Northwest, Ethiopia. BMC Res Notes. 2014;7:615.
13. Ramos JM, Malmierca E, Reyes F, Tesfamariam A. Results of a 10-year survey of louse-borne relapsing fever in southern Ethiopia: a decline in endemicity. Ann Trop Med Parasitol. 2008 Jul;102(5):467-9.
14. Brouqui P, Stein A, Dupont HT, Gallian P, Badiaga S, Rolain JM, et al. Ectoparasitism and vector-borne diseases in 930 homeless people from Marseilles. Medicine (Baltimore). 2005 Jan;84(1):61-8.
15. Russel R, Otranto D, Wall R. The Encyclopedia of Medical and Veterinary Entomology CABY; 2013.
16. Médecins Sans Frontières. Refugee Health. An approach to emergency situations. 1997.
17. Wilting KR, Stienstra Y, Sinha B, Braks M, Cornish D, Grundmann H. Louse-borne relapsing fever (Borrelia recurrentis) in asylum seekers from Eritrea, the Netherlands, July 2015. Euro Surveill. 2015;20(30).
18. European Centre for Disease Prevention and Control (ECDC). Louse-borne relapsing fever in the Netherlands. [Internet]. Stockholm2015 [cited 2015 July 24]. Available from: http://ecdc.europa.eu/en/publications/Publications/louse-borne-relapsing-fever-netherlands-rapid-risk-assessment.pdf.
19. Goldenberger D, Claas GJ, Bloch-Infanger C, Breidthardt T, Suter B, Martinez M, et al. Louse-borne relapsing fever (Borrelia recurrentis) in an Eritrean refugee arriving in Switzerland, August 2015. Euro Surveill. 2015;20(32):2-5.
20. Cutler S. Refugee crisis and re-emergence of forgotten infections in Europe. Clin Microbiol Infect. 2015 Oct 20.
21. Robert Koch Institut. EpidemiologischesBulletin [Internet]. Berlin: Robert Koch Institut; 2015 [cited 2015 Aug 15]. Available from: http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2015/Ausgaben/33_15.pdf?__blob=publicationFile.
22. Hoch M, Wieser A, Loscher T, Margos G, Purner F, Zuhl J, et al. Louse-borne relapsing fever (Borrelia recurrentis) diagnosed in 15 refugees from northeast Africa: epidemiology and preventive control measures, Bavaria, Germany, July to October 2015. Euro Surveill. 2015 Oct 22;20(42).

23. Anna L, Filippo L, Cecilia C, Mariaelisabetta S, Rosanna B, Sinibaldo C, et al. Louseborne Relapsing Fever among East African Refugees, Italy, 2015. Emerging Infectious Disease journal. 2016;22(2).

24. Alessandra C, Fabiola M, Francesca di B, Anna G, Giustina V, Piera D, et al. Louse-Borne Relapsing Fever in Young Migrants, Sicily, Italy, July–September 2015. Emerging Infectious Disease journal. 2016;22(1).

25. FRONTEX Risk Analysis Unit. Annual Risk Analysis 2015. Poland: European Agency for the Management of Operational Cooperation at the External Borders of the Member States of the European Union. 2015.

26. FRONTEX Risk Analysis Unit. FRAN Quarterly - Quarter 2 April–June 2015. Warsaw, Poland: European Agency for the Management of Operational Cooperation at the External Borders of the Member States of the European Union. Risk Analysis Unit., 2015 978-92-95205-36-9.

27. I-MAP. Interactive Map of Irregular and Mixed Migration Routes in the Budapest Process, Mediterranean Transit Migration Dialogue and Prague Process Regions [Internet]. 2014 [cited 2015 Nov 11]. Available from: http://www.imap-migration.org/index.php?id=1130&L=0.

28. European Centre for Disease Prevention and Control (ECDC). Factsheet: Bartonella quintana infection/ trench fever 2015 [cited 2015 Nov 10]. Available from: http://ecdc.europa.eu/en/healthtopics/emerging_and_vector-borne_diseases/louse-borne-diseases/Pages/bartonella-quintana-trench-fever.aspx.

29. European Centre for Disease Prevention and Control (ECDC). Factsheet: Epidemic louse-borne typhus [Internet]. Stockholm2015 [cited 2015 Nov 10]. Available from: http://ecdc.europa.eu/en/healthtopics/emerging_and_vector-borne_diseases/louse-borne-diseases/Pages/Epidemic-louse-borne-typhus.aspx.