Tularemia Transmission to Humans, the Netherlands, 2011–2021

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Our use national registry data on human cases of Francisella tularensis subspecies holarctica infection to assess transmission modes among all 26 autochthonous cases in the Netherlands since 2011. The results indicate predominance of terrestrial over aquatic animal transmission sources. We recommend targeting disease-risk communication toward hunters, recreationists, and outdoor professionals.

Francisella tularensis subspecies holarctica bacteria are the main causative agent of tularemia in Europe (1). The pathogen can be transmitted to humans from animals, vectors, food and water, or the environment, through broken skin or via conjunctival, oral, or respiratory routes. The clinical manifestation of tularemia in humans can be ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic, or typhoidal. The bacterium has a complex ecology and 2 interconnected lifecycles: a terrestrial lifecycle associated primarily with lagomorphs, small rodents, ticks, and tabanids; and an aquatic lifecycle associated with mosquitoes, semiaquatic animals such as beavers, contaminated water, and mud (1). The relative contribution of these lifecycles to human tularemia varies among countries (1).

In the Netherlands, no autochthonous human cases were reported during 1953–2010 (2), even though notification was mandatory during January 1976–April 1999. However, since 2011, multiple autochthonous human tularemia cases caused by F. tularensis subsp. holarctica infection have been detected.

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and high volumes, especially during large waves of infection. We urge laboratories to confirm unusual mutation findings by repeating libraries and sequencing or by using alternative protocols, or both, to avoid artifacts and ensure accurate sequences in databases such as GISAID, which are used by the global scientific community.
(2–5) and systematically registered; mandatory notification was reinstated in 2016. In addition, the bacterium has been detected since 2013 in European brown hares (Lepus europaeus) and Eurasian beavers (Castor fiber), as well as in surface water (6–8). No wildlife cases were reported during 1953–2012 (6).

To target preventive measures and communication regarding human tularemia requires insight into the main transmission modes and identification of the lifecycle. We assessed the distribution of transmission modes in autochthonous human tularemia cases in the Netherlands, using the national registry of tularemia cases. We extracted data from all autochthonous human cases from 2011–2021 from the National Public Health Institute database. Public health authorities identified the most probable transmission mode of each case at the time of diagnosis on the basis of the clinical presentation of the disease combined with information on exposure, either occupational or nonoccupational, obtained from standardized interviews with each patient https://lciring.nl/sites/default/files/2018-10/LCI-richtlijn%20Tularemie%20-%20bijlage%202018-10/LCI-richtlijn%20standardized interviews with each patient https://lci.nlv/sites/default/files/2018-10/LCI-richtlijn%20standardized interviews with each patient. We aggregated cases per transmission mode and allocated them to either the terrestrial or aquatic lifecycle of F. tularensis subsp. holarctica. We considered the transmission mode confirmed if the source was an animal carcass that tested positive for F. tularensis subsp. holarctica by quantitative PCR or culture; otherwise, the mode remained probable. We included clinical manifestations and basal clade data of cases in the overview if available.

In total, we analyzed 26 human cases from across the country, all but 2 in male patients. Median age was 52 (range 1–78) years. In 23 cases, the source was confirmed (n = 2) or probable (n = 21). Of these, 16 cases were allocated to the terrestrial lifecycle, and 7 to the aquatic lifecycle. In 3 cases, the transmission mode was unclear; we excluded these cases from further analysis (Table).

Occupational exposure was likely in 4/23 cases: 1 case-patient was probably infected while tending to cattle in pasture, the other 3 while performing vegetation maintenance, and 2 of those 3 had the pneumonic tularemia, which was reported in no other patients (Table). The strain from 1 pneumonic case-patient had been characterized previously as belonging to F. tularensis subsp. holarctica B.6-B.11.

Table. Overview of autochthonous human tularemia infections reported in the Netherlands, 2011–2021

| Life cycle | Transmission mode | Probable or confirmed mode | Year | Occupational exposure | Clinical manifestation | Basal clade | Reference |
|------------|-------------------|----------------------------|------|-----------------------|-----------------------|-------------|-----------|
| Terrestrial | Aerosols from contaminated vegetation | Probable | 2016 | Yes | Pneumonic | B.6-B.11 | (4) |
| | Contact with (or consumption of) infected hare carcass | Probable | 2017 | Yes | Pneumonic | ND | |
| | | Probable | 2014 | No | Ulceroglandular | ND | (3) |
| | | Confirmed | 2014 | No | Glandular | B.12-B.20 | |
| | | Probable | 2016 | No | Ulceroglandular | ND | |
| | | Probable | 2017 | No | Ulceroglandular and oropharyngeal | ND | |
| | | Probable | 2019 | No | Glandular | ND | |
| | Mouse bite | Probable | 2021 | No | Glandular | ND | |
| | Tick bite | Probable | 2021 | No | Ulceroglandular | B.6-B.11 | |
| | | Probable | 2019 | No | Glandular | ND | |
| | | Probable | 2020 | No | Glandular | B.12-B.33 | |
| | Insect bite while on land | Probable | 2013 | No | Ulceroglandular | B.6-B.11 | |
| | | Probable† | 2016 | No | Glandular | B.12-B.33 | |
| | | Probable | 2021 | Yes | Ulceroglandular | B.6-B.11 | |
| Aquatic | Contact with contaminated water/mud | Probable† | 2016 | No | Glandular | ND | (5) |
| | | Probable | 2016 | No | Ulceroglandular | ND | |
| | | Probable | 2016 | No | Ulceroglandular | ND | |
| | | Probable † | 2015 | No | Ulceroglandular | B.6-B.10 | |
| | Contact with contaminated water or insect bite | Probable | 2021 | No | Ulceroglandular and oropharyngeal | ND | |
| | | Probable | 2021 | No | Ulceroglandular and oropharyngeal | ND | |
| | | Probable | 2011 | No | Ulceroglandular | B.6-B.11 | (2) |
| Unclear | Unclear | Probable | 2016 | No | Glandular | ND | |
| | | Probable | 2018 | No | Ulceroglandular | B.6 | |
| | | Probable | 2018 | No | Glandular | B.6 | |

*Data are for 26 infections caused by Francisella tularensis subspecies holarctica. ND, not determined.
†Water, sampled within 6 weeks from waterbodies in the area where infection was assumed to have occurred, tested positive for F. tularensis subsp. holarctica by quantitative PCR, indicating presence of the bacterium in the local environment around the time of infection and highlighting the interconnection between lifecycles (7).
basal clade B6 (4), supporting previous associations found between pneumonia and basal clade B6 in both humans and hares (8,9).

Nonoccupational exposure through contact with infected terrestrial mammals was likely in 9 cases. Of those, 8 were assumed or confirmed to be infected by contact with infected hares, mainly through skinning and rarely through consumption. These case-patients were mostly hunters (n = 7) who showed diverse clinical symptoms; 2 cases were related to the same hare (Table). The ninth case concerned an ulceroglandular infection from a mouse bite (Table), a mode previously described in Switzerland (10). Nonoccupational exposure through arthropod bites, contaminated water, or mud was likely in the remaining 10 case-patients, who contracted tularemia while performing recreational outdoor activities in a terrestrial (4/10) or aquatic environment (6/10) (Table).

These results support the need for ongoing tularemia risk and prevention communication to hunters, and they identify a need for communication to outdoor (water) recreationalists and to professionals such as grounds maintenance workers and foresters. Physicians must be aware of these risk groups and the diversity of clinical presentations for early identification and treatment.

The relative importance of the terrestrial lifecycle as a source of human infections in the Netherlands is consistent with the rare and sporadic occurrence of cases; human tularemia cases from aquatic sources are more likely to occur as large outbreaks (1). Nevertheless, local disease ecology can change over time, and the Netherlands is a low-lying, water-rich country in which favorable conditions for F. tularensis, such as floodplains and meandering waterways, are promoted to buffer excess rainfall due to climate change. It is therefore relevant to continue monitoring the transmission routes in human tularemia cases for early detection of shifts in tularemia lifecycle contributions, which may require adaptation of risk and prevention communications.

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