Outbreak of tularaemia in brown hares (Lepus europaeus) in France, January to March 2011

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We report an outbreak of tularaemia in brown hares (Lepus europaeus) in France, which occurred from January to March 2011 and was characterised by a high mortality rate in the local hare population. In France, hare tularaemia is usually sporadic and does not significantly affect hare populations. The epizootic form of the outbreak reported here led us to reconsider the potential associated risks for hare populations and public health.

Tularaemia is a cosmopolitan bacterial zoonosis caused by *Francisella tularensis*. This gram-negative bacterium contains several highly pathogenic subspecies, whose distribution is ubiquitous in the northern hemisphere [1,2]. Because of its pathogenic potential, tularaemia is a notifiable bacterial zoonosis in France, and is listed as potential bioterrorist weapon. The bacterium has very complex epidemiological cycles, including many wild species, whose epidemiological role is sometimes unclear. Namely, *F. tularensis* has been isolated from more than 250 species, including 190 mammals, 88 invertebrates, 23 birds, three amphibians as well as several species of reptiles and fishes, and two disease cycles, terrestrial and aquatic have been described [3,4]. The interaction between these two cycles remains not well known. In general, the disease cycle involves only few key species in a given region. In the terrestrial cycle in France, the European brown hare plays an important role in the ecology of tularaemia as amplifying host, and it may serve as a significant source of human infection [5]. Hare tularaemia has been reported in most of the departments in France, but endemic areas have been described in the northern part of France. A recent increase in cases in hares has been observed in 2007 and 2008 [6]. At the same time, during the winter, an excess of human cases has been reported (144 sporadic cases from 1 January 2007 to 31 December 2008, including 48 cases in 2007 and 96 in 2008, against a mean of 23 cases per year for the period 2003 to 2006), but the factors responsible for this increase have not be indentified [7].

Although tularaemia is often fatal to hares, hare tularaemia in France is usually sporadic and does not significantly affect hare populations. We report here an outbreak of tularaemia in brown hares in France, which occurred in Pas-de-Calais from January to March 2011 and was characterised by a high mortality rate in the local hare population. The epizootic form of the outbreak reported here raised many epidemiological questions and led us to reconsider the potential associated risks for hare populations and public health.

Outbreak description

In March 2011, 51 tularaemia cases in hares, detected since January near Habarcq, Pas-de-Calais, were reported to the SAGIR network, an outbreak surveillance network that aims at determining the aetiology of wildlife mortalities [8]. About two thirds of the carcasses were recovered from the north-western part of a 110 hectares oak/ash wood, which was therefore considered as the epicentre of the outbreak. The mortality was quickly discovered as the wood is highly frequented by the public and regularly checked by the hunting managers. The outbreak occurred during the mating season in a high-density hare population (estimated at 2.3 per hectare in the wood). The two main reported waves of mortality seem to have coincided with sharp drops in temperature. The first wave occurred around 15 January, after the temperature had dropped by 10 °C in two days around 8 January and increased by 10 °C on 13 January. The second wave occurred around 1 March, after a drop of 8 °C within four days. An emergency investigation was set up to better understand the epidemiology of the outbreak. The timeline of the investigation is shown in the Figure. Information was provided to the local population after the first wave to prevent zoonotic transmission of the disease, which had not been reported in the commune since 1988 (personal communication C. Bethencourt, March 2011). To confirm that tularaemia was responsible of the epizootic, more than 10% of carcasses should be analysed. Eight of the 51 carcasses were found

unaltered, collected (see Figure) and sent for necropsy to the local veterinary laboratory. Infection with *F. tularensis* was confirmed by both bacterial culture and real-time PCR (polymerase chain reaction) [9]. All eight hares were in good body condition, with repleted stomach, confirming the acute nature of their death.

In all of them, macroscopic lesions typical of tularaemia such as splenomegaly, congestion and haemorrhagic lesions of several organs were observed, except that in addition, all hares had signs of tracheitis and sometimes bronchitis. European brown hare syndrome (EBHS) is suspected to be the cause of death when congestion and haemorrhagic lesions of several organs, mainly the tracheal mucosa and the lungs, and hepatitis or a discoloured liver are observed. EBHS, which is also an acute cause of death, was excluded by ELISA.

These findings raise the question of whether several different clinical pictures of tularaemia exist in infected hares, reflecting the route of infection, as is known for tularaemia infections in humans [1,10]. Hares are known to be infected by ticks or mosquitoes, but the upper respiratory tract affection suggests a respiratory route. In Hungary, histological studies lead to the same assumption that hares could become infected via airborne transmission [11].

Epidemiological investigation

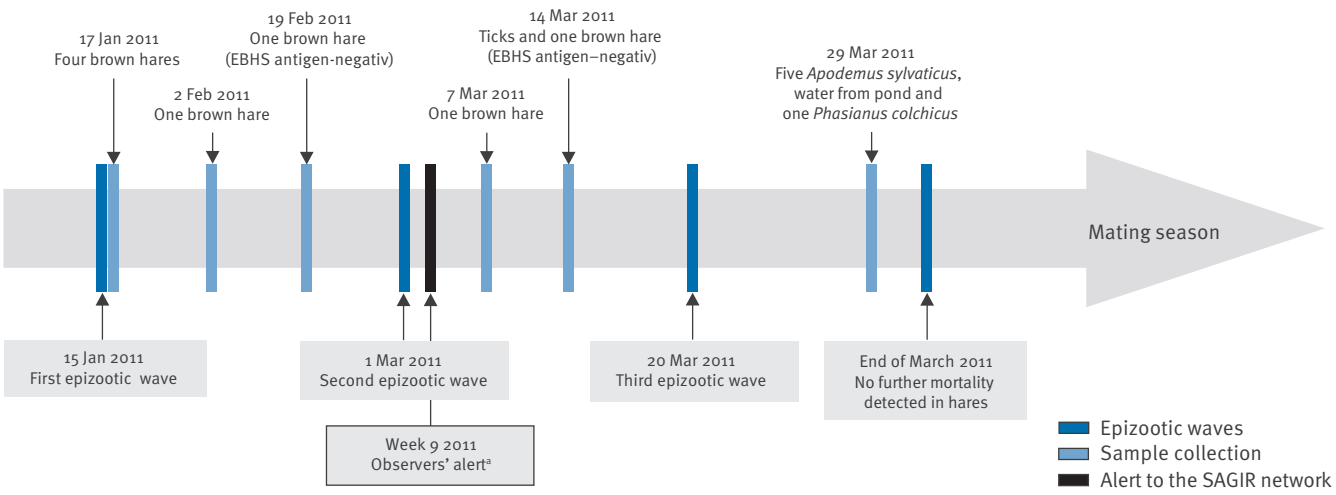
Epidemiological investigations were performed on 14 March in order to collect information about the main potential sources of infection described in the literature, i.e. ticks [12,13], rodents [14] and other small animals, and water ponds [15,16]. Questing ticks were sampled by dragging a white cloth over a part of the ground in the epicentre and the immediate surrounding areas. Only few ticks (n=20) could be collected, which was not surprising because hard ticks do not usually quest for hosts during the cold season. They all tested negative by real-time PCR. Conversely, several ticks collected alive on infected hare carcasses were positive, including one engorged tick and three ticks that did not seem engorged macroscopically but had probably started feeding on their hare host before it died. These ticks likely became infected after feeding on their bacteraemic host, either through their blood meal or through direct contact. A common pheasant (*Phasianus colchicus*) found dead close to the outbreak focus was collected and five wood mice (*Apodemus sylvaticus*) were captured alive and humanely killed. Infection by *F. tularensis* was investigated by testing the brain of pheasant and mice by real-time PCR and bacterial culture. All six animals were negative. Finally, muddy water was sampled from a permanent water pond present in the wood where hares were found dead. *F. tularensis* was not detected in these samples, neither by bacterial culture nor by real-time PCR.

Conclusions

The outbreak ended in late March and the epidemiological field investigations, performed in the middle of March have been unable to identify a source of infection, although they were conducted at a time when hare mortality was still observed. Molecular typing of the isolates recovered from collected hare carcasses and ticks will hopefully help us understand the origin of this outbreak by determining whether it was related to the focus (one case) reported at a distance of 10 km in 2007. Indeed, it is highly important to determine whether the epizootic form of this outbreak was due (i) to the emergence of a novel *F. tularensis* strain, (ii) to the fact that the hare population was unusually abundant, in which case the outbreak may have been a density-dependent phenomenon, or (iii) to particular ecologic circumstances favouring hare-to-hare transmission, since the outbreak occurred during periods of

Figure

Timeline of the epidemiological investigation into the tularaemia in hares, Pas-de-Calais, January–March 2011



EBHS: European brown hare syndrome; SAGIR: Network for the surveillance of wildlife in France

[a] The departmental correspondent of SAGIR alerts the national level when they observe abnormal mortalities.

frost (which may have led the hares to take refuge in the woods) and coincided with the mating season (when hares are immunosuppressed and in close contact with each other). Further studies are planned, including histology and surveillance of ticks and rodents, to gain knowledge on the transmission route and on the maintenance of a disease in the area.

The epizootic focus will be carefully surveyed this year and hunters, people walking in the forest, and physicians will be warned that a potential risk of disease transmission exists in the area, respectively by the departmental federation of hunters involved in the SAGIR network, local authorities, and the regional agency of health. We wish to warn wildlife managers that aggregated cases of hare mortality may be due to *F. tularensis* and that systematic precautions should be taken to make sure that humans do not contract the disease. Human tularaemia is usually sporadic in France even if aggregate cases have been described [17]. Infected ticks like those found alive on dead hares may become a reservoir in the area, thus the potential for human infection is now higher than it was. As the wood is highly frequented, tularaemia should be considered in the area as a diagnosis, particularly in people with contact with hares or ticks.

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