Leptospirosis: today a rare occurrence, in the future more prevalent?

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Abstract
We report two cases of leptospirosis with multi-organ failure after fishing for carp in fresh water. One patient died of progressive liver failure, while the other patient recovered fully. Leptospirosis is the most common zoonosis in humans, with a potentially fatal outcome. We expect an increase in the near future due to global warming and societal changes.

Introduction
Leptospirosis is a potentially fatal zoonosis, infecting both animals and humans. The disease is endemic in the tropics with an incidence approximately tenfold higher than in temperate regions, although it does occur worldwide. In most cases leptospirosis is mild and self-limiting; however, the mortality rate increases to 52% in ICU patients.[1] In the Netherlands there has been an increase of leptospirosis over the last few years with an estimated 40 cases a year during the period 1925-2008, increasing to up to 80 diagnosed cases in 2015.[2] In this case report we describe two patients who were admitted to our ICU within one week with severe systemic leptospirosis and multi-organ failure.

Case reports
Case 1
A 58-year-old man presented to the emergency department with fever, myalgia of the legs, dyspnoea and abdominal pain. His occupation was rat breeding and one week before presentation he had been fishing for carp. Based on the suspected relationship between the fishing and the start of symptoms, leptospirosis was presumed. A positive polymerase chain reaction (PCR) confirmed the diagnosis. Despite maximal respiratory and haemodynamic support, renal replacement therapy, corticosteroids and broad-spectrum antibiotics, which were changed to penicillin after confirmation of the diagnosis, he died of progressive liver failure and haemodynamic instability.

Case 2
A 54-year old man presented to the emergency department with progressive weakness of the muscles of his upper legs, nausea and vomiting. A week before he had been fishing and swimming in a lake. Afterwards he developed a headache and general weakness, which resolved spontaneously. Shortly before presentation he developed progressive muscle weakness of the upper legs. Leptospirosis was suspected, which was confirmed by PCR. He was treated with penicillin and supported by mechanical ventilation and renal replacement therapy. Corticosteroids were not given. Laboratory results showed elevated liver enzymes, but no signs of acute liver failure. A couple of days after extubation he developed a haematothorax without trauma, which was thought to be associated with the leptospirosis, because no other cause could be found. After a couple of weeks the patient could be discharged home with improving liver enzymes and independent of haemodialysis.

Discussion
Leptospirosis is caused by the spirochete Leptospira spp. Diagnostics in leptospirosis are difficult because laboratory findings are non-specific. In the Netherlands, PCR is the most common method, which is positive in blood up to a week after presentation.[3,4] About a million infections of leptospirosis are estimated to occur worldwide annually.[5] The acute phase is due to toxin release by spirochetes. The most common symptoms are headache, jaundice, myalgia, fever, and conjunctival oedema, which is specific for leptospirosis. Symptoms may worsen after initiation of therapy due to a Jarisch-Herxhimer reaction, in which there is a significant increase in toxin release due to killing of the spirochetes.[6-8] In our patients a Jarisch-Herxhimer reaction did not occur. In the convalescent phase, symptoms are immune-related and can usually be attributed to vasculitis. Renal failure and bleeding, mainly respiratory (severe pulmonary haemorrhage syndrome), is specific for
Leptospirosis although acute respiratory distress syndrome, liver failure, bleeding in other sites and aseptic meningitis may occur as well. All symptoms may be reversible after treatment of the infection, which consists of antibiotic treatment (penicillin) and supportive treatment. The role of corticosteroids is not specified yet, though they are generally given as a last resort in severely ill patients. Most cases of leptospirosis are self-limiting. Mortality rates vary widely in the literature, increasing to 52% when admission to ICU is necessary.

Environmental considerations
Leptospirosis is a zoonosis, transferred by contaminated surface water, with small animals being a reservoir for the disease, excreting the spirochetes with their urine. Leptospirosis is endemic in resource-poor countries, where water is more likely to be contaminated than in the Western world. Because of global warming and an increase in outdoor activities the number of leptospirosis epidemics is increasing, transferring from the Third World to more developed countries. The risk of getting infected is thought to be greater with higher concentrations of spirochetes in the ground water. Examination of the contaminated water itself by culture is thought to be useless, because no difference between non-pathogenic and pathogenic spirochetes can be seen. However, differentiation by PCR is possible, but is not performed on a large scale due to lack of protocols, the high costs and a lack of highly sensitive and specific tests. Therefore, identification and eradication of rodent hosts is thought to be more useful. Vaccination against leptospires is widely available for animals, although in humans it has generally been restricted to individuals in high-risk occupations. Human vaccination is possible after determination of the accountable serovars, although vaccination is accompanied with local pain and general discomfort. Fewer side effects were reported in a chemically defined medium, but efficacy was low and therefore it is not used. According to the literature weekly doxycycline as prophylaxis can be given to individuals at high risk of exposure in endemic areas.

Conclusion
We report two cases of severe systemic leptospirosis with septic shock and multi-organ failure. Even though this severe clinical course is uncommon in the Netherlands, we expect an increase in the near future due to global warming, which will cause expansion of the (sub)tropic region where leptospira are endemic. Furthermore we expect an increase due to the concomitant increase in outdoor activities. We doubt whether the current strategy of rodent extermination will be adequate in the future. We advocate for a more proactive rodent control and optimising protocols on microbiological examination of water by PCR in popular outdoor natural swimming areas.

Disclosures
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