Leptospirosis is an important multi-species zoonotic disease in New Zealand

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McLean and colleagues’ paper in this issue of the New Zealand Medical Journal\(^1\) reports an outbreak of leptospirosis on a dairy farm and illustrates issues in identifying and controlling animal sources. It highlights the practical difficulties in definitively diagnosing each individual case and also shows how increased awareness leads to recognition of additional, milder cases.

Leptospirosis is a globally important zoonotic disease, caused by the pathogenic spirochetes of the genus *Leptospira*. The traditional serological classification, based on agglutinating antigens, classifies *Leptospira* into 20 serogroups and over 300 serovars.\(^2\) Six serovars are endemic in New Zealand: Hardjobovis, Pomona, Ballum, Tarassovi, Copenhageni and Balcanica\(^3\) with the first three of these responsible for the majority of human cases. Apparent correlations between serovars or species and syndromes or severity of human disease are confounded by geographical distribution and other factors.\(^4\)

*Leptospira* serovars have lower pathogenicity for maintenance than for accidental or spill-over hosts, while being similarly infectious. The consequence is that maintenance hosts remain infected and a host-pathogen equilibrium is established by a continued re-/infection cycle balanced by a marginal immune response.\(^5\)

The epidemiological pattern that predominates in New Zealand is occupational, due to domestic species being important maintenance hosts. A 2010 survey of 237 New Zealand farms found serological evidence of exposure to Hardjobovis and/or Pomona in over 50% of adult sheep, 58% of adult beef cattle and in 34% of adult deer.\(^6\)

Therefore, workers other than dairy farmers are also at risk of infection. In a review of 97 notified cases from the Waikato region, dry stock farmers were the occupational group with the highest rates of leptospirosis and dairy farmers formed the second largest group.\(^7\)

In 2010, serovar Ballum emerged as the most frequently notified serovar in human cases\(^8\) and this emergence was coincident with a rise in the proportion of low risk occupations and the decline in affected meat workers.

Traditional maintenance hosts for Ballum are the mouse, black rat and hedgehog.\(^3\) Thus, as pointed out by McLean and her co-authors, an integrated programme that includes vermin control, avoidance of urine splash, use of personal protective equipment and vaccination of domestic species is required.

Infection commences with a leptospiraemic phase of a few days duration. Conjunctival suffusion is common. The second, “immune phase” then supervenes, when antibodies are present; leptospires are cleared from the blood and excreted in urine. These phases are not always distinct.
Classical clinical features include jaundice and renal failure (Weil’s disease) and, in a few cases, pulmonary haemorrhage. Leptospires can be found in the CSF during the leptospiraemic phase. Meningitis is more common in young adults and children and manifests during the immune phase. Other complications can include myocarditis and uveitis.

Pathology is characterised by vasculitis rather than disseminated intravascular coagulation and, unlike in other spirochetal diseases, chronic stages of infection are not recognised.4

Reinfection can occur with different serovars. In animals, infection with non-maintenance serovars can cause clinical disease and subclinical losses. For example, Pomona infection causing sudden death in lamb flocks associated with high rainfall and surface flooding are reported.9,10

Human leptospirosis is uncommon and sporadic, but awareness among rural clinicians and patients is generally good. Diagnosis is erratic because culture and serology are slow and susceptible to early antibiotic treatment, so of limited assistance to the clinician. PCR shows promise11 and we need to better understand which specimens are most informative at each time and the effect of antibiotics.

Serum, CSF or urine may be tested and positive results may be found at unexpected phases of the illness (A. Werno, Canterbury Health Laboratories, Personal Communication, 22 Jan 2014). Serology (microscopic agglutination test, using live leptospires) is the reference standard, but requires paired samples.

Pre-existing titres are not uncommon in rural people, so a rise in titre is sought. Often, it takes 4 to 6 weeks for the acute infecting serovar to become well defined and even then immune reactivity may be blunted by effective antibiotic treatment. In 2013, the Waikato Hospital laboratory tested 612 patients by serology but only 16% had a convalescent serum submitted. Presumably, a large proportion of true cases are not being followed up and the diagnosis is never confirmed, nor included in surveillance notifications.

Preferred oral treatment is either doxycycline or amoxicillin, while ceftriaxone and penicillin may be used intravenously. It is straightforward to cover the possibility of leptospirosis in both general practice and in the hospital setting but, perhaps, at the cost of increased overall antibiotic use if this is not done selectively.

Accurate diagnosis is needed to focus antibiotic use, to elucidate the epidemiology and for ACC purposes. Leptospirosis is an occupational disease in Schedule 2 of the Accident Compensation Act 2001. ACC’s current standard for a diagnosis of leptospirosis is that of a clinically compatible illness and at least one of the following laboratory results:

- Isolation of leptospires from a clinical specimen.
- Detection of leptospiral nucleic acid from a clinical specimen.
- A four-fold or greater rise in leptospiral microscopic agglutination titre (MAT) between acute and convalescent sera.
- Single high antibody titre of $\geq$400 in the MAT.
Protection of dairy and meat workers against leptospirosis has focussed on the use of personal protective equipment, such as aprons, goggles, face masks and gloves. However there are issues with compliance, as these make routine work more difficult.\textsuperscript{12}

In the cross-sectional study of 567 meat workers in New Zealand, in which seroprevalence was 10.9%,\textsuperscript{6} the strongest risk factor among sheep and deer meat workers was working prior to hide removal on the slaughter chain.

Vaccination, advocated by McLean and her co-authors, is feasible in New Zealand because the predominant serovars found in human cases are few and these are maintained in domestic species. However there are many practical and logistical considerations; in New Zealand it is only dairy cattle and pigs that are routinely vaccinated.

Approximately 10\% of beef herds and 9\% of deer herds practice vaccination for leptospirosis and vaccination of sheep is a rarity. Vaccination of deer in sub-clinically infected herds has been shown to improve reproductive and growth outcomes and to be cost-effective for farmers\textsuperscript{13} and this is currently under investigation in sheep flocks and beef breeding herds.

Antibiotic prophylaxis often used elsewhere in the world, during predictable periods of increased disease risk, for example in active outbreaks or in endemic areas post-flooding. A recent Cochrane review reported that the use of weekly oral doxycycline (200 mg) increases the odds for nausea and vomiting with unclear benefit in reducing \textit{Leptospira} seroconversion or clinical consequences of infection.\textsuperscript{14}

Research is key in informing control of human leptospirosis. Leptospirosis has complex interdependence on the interaction between the environment, domestic animals, humans and wildlife and requires a collaborative “one-health” approach.

This editorial and the paper by McLean et al exemplify the synergy of human and animal health clinicians and academics working in clinical practice, district health boards, universities, and laboratories. The current favourable economic situation for dairy, beef and sheep industries and rising expectations in occupational health and safety should support investment in research, diagnostic and control measures.

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\textbf{References:}