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A cluster of three cases of leptospirosis in dairy farm workers in New Zealand

Margot McLean, Quentin Ruscoe, Terence Kline, Caleb King, Annette Nesdale

Abstract

Aims We report a cluster of three cases of leptospirosis on a New Zealand dairy farm, with regard to clinical, laboratory, and environmental findings. The cluster is discussed against the annual incidence of leptospirosis in humans and cattle, and the vaccination of cattle as one means of preventing human cases on farms.

Methods The three cases were investigated by case interview and review of clinical and laboratory information. A site visit was made to the farm to assess environmental risk. Relevant veterinary information relating to the cattle herds was reviewed.

Results Most of the symptoms exhibited by the three patients were consistent with primary phase leptospirosis. Different methods of laboratory diagnosis were used with each case. However, two cases were confirmed as leptospirosis and in both the causative agent was *Leptospira borgpetersenii serovar (sv) Hardjo*. The third case had a milder illness, received doxycycline early, and was regarded as a 'probable' case as there were no confirmatory diagnostic results. All three cases had worked on the same dairy farm during their incubation period, where the highest risk environment was the milking shed and potential exposure to urine splashes from infected cattle. Also there were inadequacies in the herd vaccination programme.

Conclusions There are options for minimising risk to dairy farm workers in New Zealand. No human vaccine exists in this country. *Leptospira borgpetersenii serovar (sv) Hardjo* (serovar Hardjo) is endemic in New Zealand dairy cattle without causing apparent disease. *L. Pomona* is a sporadic infection but can cause abortions. A cattle vaccine against these serovars was introduced in New Zealand in 1979, after which there was a general fall in notifications of human cases of leptospirosis. This was attributed to the overall decrease in these two serovars among the livestock population.

Vaccination of farm livestock for leptospirosis is an integral factor in preventing human cases. We note the New Zealand initiative to combine vaccination with a risk management programme operated by veterinarians, called Leptosure®, to reduce the risk of human leptospirosis on dairy farms. The efficacy of using doxycycline as a prophylaxis for preventing human infection in trials is reviewed. Other preventative strategies include the use of personal protective equipment to cover the mouth and nose, eyes and all skin breaks, farm workers and rural clinicians being aware of the signs and symptoms of leptospirosis, and prompt treatment of cases with antibiotics.

Leptospirosis is a zoonotic bacterial disease, caused by spirochetes, that affects humans and many other animal species including livestock. It is spread to humans through urine from infected animals.[1,2]

Occupational exposure has been identified as a risk factor for *Leptospira* infection.[3,4] This is true of human leptospiral infection in New Zealand, where a 2002 review found the incidence to be highest among meat processing plant workers and second highest among livestock farm workers.[5]

Dairy workers were found to be the livestock workers most frequently represented. In 2012, "farmers or farm workers" was the occupational group with the highest number of cases.[6]

Dairy cattle infected with leptospirosis may experience abortions and a decrease in milk production, both from acute and persistent infections, resulting in a significant loss of income to the farmer.[7,8]

Leptospira Hardjo is commonly found in cattle and causes disease in humans. In humans, leptospirosis has four possible presentations. They are:

- A mild influenza-like illness (leptospiral or febrile stage);
- Weil's syndrome with jaundice, renal failure, haemorrhage and myocarditis with arrhythmias (icteric stage);
- Meningitis/meningoencephalitis; and
- Pulmonary haemorrhage and respiratory failure.

Human leptospirosis is typically a biphasic disease with the symptoms of the first stage being nonspecific. They are similar to influenza symptoms with headaches, high fevers, myalgia (calves and lumbar region), coughing, vomiting, abdominal pain, diarrhoea and photophobia.

Aseptic meningitis occurs in 25% of acute cases. Conjunctival suffusion is observed in about 30% of cases. Mild cases do not progress past the first phase. Moderate and severe infections progress to a secondary phase. The secondary or icteric phase of the disease is known as Weil's disease. This is a very serious condition with symptoms including jaundice, renal failure, haemorrhage, cardiac arrhythmias, pneumonitis, and haemodynamic collapse and a death rate of 5–15%.[9]

Leptospirosis is a notifiable disease in New Zealand. In 2012, 113 cases of leptospirosis were notified, a rate of 2.5 per 100,000 population, a significant increase from 2011 (1.5 per 100,000, 68 cases).

The highest rates in 2012 were in the Waikato, Hawke's Bay, and MidCentral District Health Boards.[6] The non-specific presentation of leptospirosis means that diagnosis, and determining a true incidence rate, is difficult. [10]

Methods

Three cases of human leptospirosis, from the same dairy farm, were reported by clinicians to the local public health service in August and September 2010. The cases were investigated by case interview, review of clinical and laboratory information, site inspection to assess environmental risks, and review of relevant veterinary information about the cattle herds.

Results

Clinical findings—In August 2010, two male employees from the dairy farm presented with signs and symptoms of illness with onset 1 day apart. The signs and

symptoms included fever, headache, nausea, vomiting, conjunctival suffusion, photophobia, and dark urine.

The two employees worked in the milking shed at the farm. Both required hospitalisation, Case A for three days and Case B for one day. Case A was treated with intravenous fluids for mild dehydration and discharged on 100 mg doxycycline P.O., BD. Case B received flucloxacillin and acyclovir on admission and was treated with IV ceftriaxone/acyclovir while in the hospital. He was discharged without further treatment.

A third male farm worker, Case C, developed symptoms about three weeks after the other two. His symptoms were milder than those of the other two, but knowing about the other employees' illness he saw a general practitioner and was prescribed doxycycline and recovered without any further problems.

The majority of the symptoms exhibited by the three patients were consistent with primary phase (leptospiremic) leptospirosis.

Laboratory findings—Leptospires have a slow growth rate and low metabolic activity making microbiological diagnosis difficult. A faster laboratory diagnosis can be achieved with serological titres using the Microscopic Agglutination Test (MAT) or identification of leptospiral DNA by Polymerase Chain Reaction (PCR).

Different methods of diagnosis were used for each patient (Table 1). Case A had a PCR on serum which was positive for leptospirosis. An acute serum was not done for this patient but a convalescent serum returned a leptospiral MAT value of 800, indicating a recent infection. The causative agent was determined to be serovar *Hardjo.*

Table 1. Laboratory tests performed[1]

Case (date onset)	Leptospiral DNA	Isolation of leptospires	Leptospiral screen IgM	Acute serum MAT	Convalescent serum MAT	Diagnosis	Causative agent	Status
A (25/8)	Detected in plasma (30/8)	Not done	Equivocal (30/8)	Not done	800 MAT (28/9)	Recent infection	Serovar *Hardjo*	Confirmed
B (27/8)	Not detected (1/9)	Not done	Presumptive positive (1/9)	200 MAT (1/9)	1600 MAT (22/9)	Recent infection	Serovar *Hardjo*	Confirmed
C (19/9)	Not done	Not done	Equivocal IgM (21/9)	Negative	Requested but not done	Not confirmed	Not determined	Probable

[1]PCR: nested PCR modified by Canterbury Health Laboratory from the method described in Merien F, Amouriaux P, Perolat P, et al. Polymerase chain reaction for detection of Leptospira spp. in clinical samples. J Clin Microbiol. 1992;30(9):2219-2224

Screening test: Leptospira IgM EIA by Panbio.

The Microscopic Agglutination test (MAT) testing and Leptospiral cultures were done at the Leptospira Reference Laboratory at The Institute of Environmental Science and Research (ESR), Wallaceville as described in: Guidelines for the control of Leptospirosis. WHO publication no.67 1982 S. Faine ED.

A PCR was performed for Case B but leptospiral DNA was not detected. Both acute and convalescent titres were run. The MAT for the acute serum was 200 and for the convalescent serum was 1600. A fourfold or greater increase in titre was indicative of

a current or very recent infection. The causative agent was again determined to be serovar *Hardjo*.

Case C became ill 3 weeks after his co-workers. His symptoms were not as severe. He did not have photophobia or conjunctival suffusion. He was aware of his co-workers' illnesses and sought a general practitioner's care as soon as symptoms developed. He received doxycycline early and his illness was mild. An acute phase leptospiral IgM enzyme-linked immunosorbent assay test (leptospiral screen) gave equivocal results. A convalescent serum MAT was not obtained.

Despite the lack of confirmatory laboratory results Case C was regarded as a "probable" case because of his symptoms and similar environmental exposure to the two co-workers with laboratory-confirmed disease.

Environmental findings—All cases worked on the same dairy farm. A health protection officer visited the farm to assess risks. The highest risk environment was assessed to be the milking shed. The three workers reported exposure to urine splashes from cattle.

Boots, gloves and aprons were worn but not face shields. In addition, there were inadequacies in the herd vaccination programme and 16 cattle of unknown vaccination status had been added to the herd the previous month.

This cluster of human illness was referred to the then Department of Labour (Occupational, Safety and Health Service), for further investigation and action to minimise future risks.

Discussion

In New Zealand, dairy farm workers are at occupational risk of leptospirosis though exposure to the urine of infected cattle. Options for minimising risk include vaccination of animals, animal chemoprophylaxis to reduce the number of animals shedding leptospires in urine, human chemoprophylaxis in outbreak situations, use of personal protective equipment, and greater awareness of symptoms and the need for early medical attention.

Human vaccines do not provide long-term protection, are very reactive and are not commonly used, although they have been effective in some epidemic situations.[11,12] No human vaccine is available in New Zealand.

An assessment of New Zealand dairy herds was conducted in 1975, 1976 and 1977. Sixteen herds that had experienced problems with abortions and five without any history of abortions were studied. Seventy-three percent of the animals that had aborted were found to be positive for *L. pomona*. Nineteen percent of the other cows in the same herds were also positive for *L. pomona.* Cattle from both groups were found to be positive for serovar *Hardjo* but it was not found in any of the cattle which had aborted.[13]

A survey of dairy cattle in the Taranaki region of New Zealand in 1979-1980 found that 62% of the cattle were positive for serovar *Hardjo* by MAT. Serovar *Pomona* was only found in 4% of the cattle.[14] It appears that serovar *Hardjo* is endemic in New Zealand dairy cattle without causing apparent disease, while serovar *Pomona* is a sporadic infection that causes pyrexia and abortion in cattle.

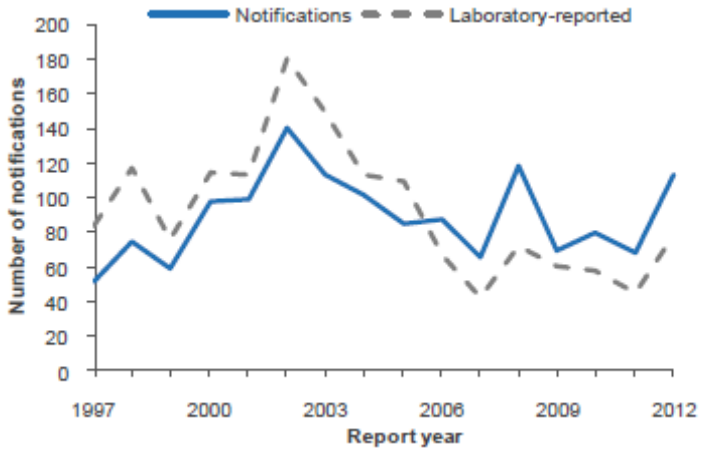
Vaccine is commercially available for cattle, although the level of protection provided may depend on the type of vaccine. Vaccines used in the United States contain serovars *Hardjo, Canicola, Pomona, Grippotyphosa*, and *Icterohaemorrhagiae*. Monovalent vaccines against serovar *Hardjo* were found to be more protective in cattle than a pentavalent vaccine.[15]

Introduction of a cattle vaccine against serovars *Hardjo* and *Pomona* occurred in New Zealand in 1979. Human cases of leptospirosis in New Zealand dropped from 677 in 1979 to 179 in 1982.[16] The decrease in human leptospirosis continued between 1990-1992 and 1996-1998. This was attributed to the overall decrease in serovars *Hardjo* and *Pomona* among the livestock population, although other serovars in wild animals showed an increase in prevalence.[5]

Since 1997 there has been no decline in cases, with the number of notifications fluctuating around 100 cases per year (Figure 1). In 2012, 113 cases of leptospirosis were notified, a rate of 2.5 per 100,000 population, a significant increase from 2011 (1.5 per 100,000, 68 cases).

Of the 80 cases in 2012 with a high-risk occupation recorded, 58 (72.5%) were in farmers or farm-workers. [6] Vaccination of farm livestock for leptospirosis is an essential factor in preventing human cases.

Figure 1. Leptospirosis notifications and laboratory-reported cases by year, 1997–2012



Source: Institute of Environmental Science and Research Limited.

In New Zealand the NZ Veterinary Association and the Society of Dairy Cattle Veterinarians have developed Leptosure®, a unique national risk management programme to reduce the risk of human leptospirosis on dairy farms. The farmer and veterinarian work together to design a specific vaccination programme for cattle, at the same time as including best-practice farm management.

Leptospirosis hazards are identified and a risk management programme established that eliminates, isolates, or minimises significant hazards. Monitoring and risk

management continue on an ongoing basis. There is an annual reassessment to ensure compliance with the programme and to maintain the farm's Protected Leptosure® status.[17] The programme, operated by veterinarians, also includes control of leptospirosis in other species such as sheep, pigs, deer, goats, and farm dogs.

Doxycycline has been used prophylactically for humans to prevent clinical leptospirosis in outbreaks, with good results.[18] A randomised control study looking at the use of doxycycline as a leptospirosis prophylaxis found that while it didn't decrease the infection rate between drug and placebo groups it decreased the number with clinical illness.[19]

A study in US military troops also supported use of ongoing prophylaxis (200 mg doxycycline PO per week) in a specific high-risk environment.[20] Whether doxycycline should be used as prophylaxis following exposure to an infected animal is not known.

The use of personal protective equipment, with special attention being given to covering the mouth, nose, eyes and all breaks in the skin, is recommended for all at risk workers.[21] Meat-processing factories should have written protocols and equipment to minimise risk, as part of an industrial health and safety program.

Individual farmers and farm workers may be at risk because of their inadequate awareness of the risk, variation and compliance with vaccination protocols, and the tendency to vaccinate animals only rather than implement a comprehensive risk management programme.

Vaccination of animals already infected with *Leptospira* does not reduce their shedding of leptospires and consequently does not reduce the risk of exposure to farm personnel. [21] It is important that dairy farmers and farm workers are well aware of the signs and symptoms of leptospirosis as prompt treatment with antibiotics will reduce the likelihood of severe or fatal illness. It is also important for clinicians working in rural areas to be vigilant for signs and symptoms of leptospirosis, as the disease is probably under-diagnosed.

Laboratory confirmation is also complex. Leptospires are only present in the first few days of the illness and are affected by antibiotic use. A study in Colombia compared microscopic diagnosis with PCR. The MAT and PCR both compared favourably with microbiological culture as means of diagnosis.[22]

This cluster of illness was followed up with a community meeting, with participation from farmers and farm workers (including the cases), public health and veterinary staff, to raise awareness and discuss issues relating to the events. Subsequent to this event all cows older than two years of age on the farm were treated with parenteral amoxicillin to eliminate persistent leptospiral infection.

In summary this cluster of leptospirosis is likely to have occurred because dairy farm workers, who were not fully protected by personal protective equipment, were exposed to urine splashes from cattle of unknown vaccination status that were added to the herd in the previous month.

Competing interests: Nil.

Author information: Margot McLean, Medical Officer of Health, Regional Public Health, Hutt Valley District Health Board, Lower Hutt; Quentin Ruscoe, Health Protection Officer, Regional Public Health, Hutt Valley District Health Board, Lower Hutt; Terence Kline, Doctor of Veterinary Medicine, Master of Public Health, Orville, Ohio, USA; Caleb King, Senior Veterinarian, Managing Director, Keinzley Veterinarian Solutions, Carterton, Wairarapa; Annette Nesdale, Medical Officer of Health, Regional Public Health, Hutt Valley District Health Board, Lower Hutt

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Correspondence: Dr Margot McLean, Medical Officer of Health, Regional Public Health, Private Bag 31-907, Lower Hutt 5040, New Zealand. Email: Margot.Mclean@huttvalleydhb.org.nz

References:

1. Vijayachari P, Sugunan AP, Shriram AN. Leptospirosis: an emerging global public health problem. J. Biosci. 2008; 33(4): 557–69.
2. Pappas G, Papadimitriou P, Siozopoulou V, et al. The globalization of leptospirosis: worldwide incidence trends. Int J Inf Dis. 2007;12(4):351–357.
3. Viera ML, Gama-Simoes MJ, Collares-Pereira M. Human leptospirosis in Portugal: A retrospective study of eighteen years. Int J Infect Dis. 2006;10(15):378–86.
4. Vanascoa NB, Schmelinga MF, Lottersberger J, et al. Clinical characteristics and risk factors of human leptospirosis in Argentina (1999–2005). Acta Trop. 2008;107(3):255–8.
5. Thornley CN, Baker MG, Weinstein P, Maas EW. Changing epidemiology of human leptospirosis in New Zealand. Epidemiol Infect. 2002;128(1):29–36.
6. Institute of Environmental Science and Research Limited. Notifiable and other diseases in New Zealand. Annual Report 2012. Available at: http://www.surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2012/2012AnnualSurvRpt.pdf
7. Bennett RM, Christiansen K, Clifton-Hadley RS. Estimating the costs associated with endemic diseases of dairy cattle. J of Dairy Res. 1999;66:455-9.
8. Grooms DL. Reproductive losses caused by bovine viral diarrhea virus and leptospirosis. Theriogenology. 2006;66:624–8.
9. Centers for Disease Control and Prevention. Yellow Book. Chapter 3. Infectious Diseases Related to Travel. Leptospirosis. Accessed on 8 Aug. 2011. Available at: http://www.nc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/leptospirosis.htm
10. International Leptospirosis Society. Human Leptospirosis: Guidance for Diagnosis, Surveillance and Control. World Health Organization: 2003.
11. World Health Organisation. Weekly Epidemiological Record. 4 February 2011 (6);86: 45–52.
12. Adler B, de la Pena Moctezuma A. Leptospira and leptospirosis. Vet Microbiol. 2010: 140(3–4): 287–96.
13. Carter ME, Cordes DO, Holland JTS, et al. Leptospirosis: II. Investigation of clinical disease in dairy cattle in the Waikato district of New Zealand. NZ Vet J. 1982;30(9):136–40.
14. Bahaman AR, Marshall RB, Hellstrom JS. A serological study of bovine leptospirosis in the district of Taranaki. NZ Vet J. 1984;32(8):134–6.
15. Brown RA, Blumerman S, Gay C, et al. Comparison of three different leptospiral vaccines for induction of a type 1 immune response to Leptospira borgpetersenii serovar hardjo. Vaccine. 2003;21(27–30):4448–58.

16. Marshall R, Chereshky A. Vaccination of dairy cattle against leptospirosis as a means of preventing human infections. Surveillance. 1996;23(1):27–8.
17. Anonymous. New Zealand Veterinary Association. Leptosure. Wellington, New Zealand. Available at http://leptosure.co.nz
18. Pappas G, Cascio A. Optimal treatment of leptospirosis: queries and projections. Int J Antimicrob Agents. 2006;28(6):491–6.
19. Sehgal SC, Sugunan AP, Murhekar MV, et al. Randomized controlled trial of doxycycline prophylaxis against leptospirosis in an endemic area. Int J Antimicrob Agents. 200;13(4):249-55.
20. Takafuji ET, Kirkpatrick JW, Miller RN, et al. An efficacy trial of doxycycline chemoprophylaxis against leptospirosis. N Eng J Med. 1984;310 (8):497-500.
21. Keenan BR. Leptospirosis: Reducing the Impact on Human Workplaces. Wellington. Department of Labour;2007. Available at: http://www.dol.govt.nz/PDFs/leptospirosis2007.pdf
22. Hernandez-Rodriquez P, Diaz CA, Dalmau EA, Qintero GM. A comparison between polymerase chain reaction (PCR) and traditional techniques for the diagnosis of leptospirosis in bovines. J Microbiol Methods. 2011;84(1):1–7.