Leptospirosis news: Production effects and public health

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Introduction

Leptospirosis continues to be the most important zoonotic disease in this country. ESR reported that a change in trend among cases became obvious when in 2009, for the first time, the most frequent serovar was *L. borgpetersenii* sv Ballum (33%) followed by *L. borgpetersenii* sv Hardjo (30%), *L. interrogans* sv Pomona (17%), *L. borgpetersenii* sv Tarassovi (13%), *L. interrogans* sv Canicola (2%) and *L. interrogans* sv Copenhageni (2%). Farmers and farm workers tended to be more involved than in previous years. Another emerging group (21%) were from other than highly exposed occupations. Thus, the ecology and risk pattern for leptospirosis appears to undergo change. *Leptospira* circulate continuously through their reservoir hosts where they are found at extremely high endemic level (Table 1).

![Diagram of reservoir hosts, exposure through the environment and co-factors involved in the ecology of leptospirosis in New Zealand](image)

They are shed into the environment mainly by livestock and to a presumably smaller but yet unknown extent, from feral animals. *Leptospira* survive well in temperate and humid climates, accumulate at the surface of water as for example in water logged pasture, ponds, drains or rivers. *Leptospira* can survive in soil and maintain their pathogenesis for up to 74 days even at low humidity levels of 15-31% (Zaitsev et al. 1989). People in contact with animals are increasingly at risk, and this most likely includes veterinarians (Figure 1).
Public health

While human leptospirosis is notifiable, leptospirosis in animals is not. However, all cases of human leptospirosis are considered to be caused by contact with infected animals or their immediate environment. Transmission between humans is highly unlikely. Most human infections are attributed to contact with livestock (cattle, sheep, deer, pig), few with dogs, wildlife or rodents. Dairy cattle have been assumed to be the major source species for transmitting *Leptospira* to humans in the 1970’s and 1980’s. Therefore, vaccination of dairy cattle was introduced in 1979, widely propagated for controlling the disease in people in the 1980s, and followed by a drastic decline of human cases in the 1990s (Marshall and Chereshsky 1996). The other livestock species – deer, sheep, beef cattle – were not regarded as being major sources for human infections. Sheep were even dismissed from being a source for human infections and regarded as an accidental spill over host for *Leptospira* (Blackmore 1982).

However, new evidence generated after 2003, demonstrated a high rate of sheep infection with both, Hardjo and Pomona (Table 1).

<table>
<thead>
<tr>
<th>Year</th>
<th>Farms</th>
<th>HAR</th>
<th>POM</th>
<th>H/P</th>
<th>Animals</th>
<th>HAR</th>
<th>POM</th>
<th>H/P</th>
<th>REF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef cattle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-18m heifers</td>
<td>2006</td>
<td>95</td>
<td>62%</td>
<td>26%</td>
<td>69%</td>
<td>1,265</td>
<td>34%</td>
<td>12%</td>
<td>39%</td>
</tr>
<tr>
<td>Mixed age cows</td>
<td>2009</td>
<td>116</td>
<td>92%</td>
<td>72%</td>
<td>97%</td>
<td>2,308</td>
<td>50%</td>
<td>25%</td>
<td>58%</td>
</tr>
<tr>
<td>Mixed age cows</td>
<td>2010</td>
<td>21</td>
<td>86%</td>
<td>67%</td>
<td>95%</td>
<td>338</td>
<td>45%</td>
<td>19%</td>
<td>55%</td>
</tr>
<tr>
<td>Sheep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slaughter lambs</td>
<td>2004</td>
<td>21</td>
<td>86%</td>
<td>29%</td>
<td>91%</td>
<td>619</td>
<td>16%</td>
<td>4%</td>
<td>19%</td>
</tr>
<tr>
<td>Slaughter lambs</td>
<td>2005</td>
<td>74</td>
<td>27%</td>
<td>7%</td>
<td>31%</td>
<td>2,139</td>
<td>1.7%</td>
<td>0.5%</td>
<td>2%</td>
</tr>
<tr>
<td>Mixed age ewes</td>
<td>2009</td>
<td>161</td>
<td>91%</td>
<td>74%</td>
<td>97%</td>
<td>3,361</td>
<td>43%</td>
<td>14%</td>
<td>51%</td>
</tr>
<tr>
<td>Deer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-30m old deer*</td>
<td>2004</td>
<td>110</td>
<td>68%</td>
<td>20%</td>
<td>74%</td>
<td>2,016</td>
<td>61%</td>
<td>8%</td>
<td>64%</td>
</tr>
<tr>
<td>Mixed age deer</td>
<td>2009</td>
<td>98</td>
<td>60%</td>
<td>49%</td>
<td>76%</td>
<td>1,992</td>
<td>26%</td>
<td>10%</td>
<td>34%</td>
</tr>
</tbody>
</table>

* Deer from non-vaccinated herds; HAR Hardjo, POM Pomona, H/P Hardjo or Pomona, REF references: (1) Dreyfus 2012; (2) Heuer et al. 2007; (3) Sanhueza 2012; (4) Dorjee et al. 2008; (5) Ayanegui-Alcerreca 2006

Table 1. Prevalence by survey year, species and age of livestock in New Zealand

More recent studies revealed the true extent of leptospirosis among dry stock species (Table 1). Farmers, veterinarians, livestock workers and other people with contact to animals were exposed to over 50% sero-positive mixed age sheep and beef cattle, and 34% deer (64% in one study).

Exposure x Infectious dose = Infection

Measuring serology and kidney culture rates in one sheep abattoir revealed the extent of real exposure in workers: during a typical factory day, one slaughter worker was exposed to 3-18 carcasses contaminated with live *Leptospira* in kidneys (Dorjee et al. 2010). Once the rate of exposure was known, the next question was how effective exposure led to infection, i.e. how many workers actually got infected with *Leptospira*. This was measured in 8 abattoirs by sampling workers twice at an interval of one year, and calculating rates of sero-conversion as a measure of infection. This resulted in annual infection rates among abattoir workers processing sheep of 12.3% (n=384). The rate was lower in workers processing cattle (1.5%; n=158) or deer (0%; n=50). The highest sero-prevalence, however, was found in deer plant workers (13-18%), followed by plants processing sheep (6-14%) and cattle (3-4%) (Dreyfus 2012). The high prevalence and low incidence of new infections in deer plants is indicative of a more or less permanent sero-positive state due to past clinical episodes followed by long seropositive periods and/or frequent re-exposure without subsequent illness.

Infection x Pathogenesis = Disease

Even though the awareness of running a high infection risk is certainly not a pleasant thought, infection per-se might not be a worry as long as clinical disease remained absent. The next question therefore was how much illness was occurring and how many illness episodes were likely caused by infection with *Leptospira* – in other
words, how pathogenic Hardjo and Pomona were for freezing workers. In sheep plants, clinical illness associated with influenza-like symptoms was twice as frequent in workers who sero-converted to Pomona or Hardjo, i.e. were infected between two sampling points one year apart (Figure 2): 47% of infected vs. 24% of non-infected workers went down with influenza-like symptoms and four days absence from work. This translates to a 1 in 36 chance of illness due to leptospirosis in 12 months for every worker regardless of work position. If position was taken into account, the slaughter board accounted for a 4-8 fold higher risk being highest at the front (8x) and decreasing towards the end (Dreyfus 2012).

![Figure 2. Path-diagram of the rate of new infections with Pomona or Hardjo in workers of sheep processing plants, and the risk of clinical illness in 2009/10. This related to a total risk of contracting clinical leptospirosis of 1:36 workers (2.7%) within one year](image)

No information is available as yet about comparable risks for farmers, veterinarians and other people with frequent animal contacts in the livestock industries. It is the intention to collect such data in the near future. A study of 311 veterinary students resulted in none being sero-positive (Fang et al. 2012). This result is an ideal base line for inferences on time at work and type of species handled from testing practicing veterinarians.

**Has vaccination cleared *Leptospira* from dairy herds?**

In 2010/11, vaccine efficacy in dairy herds with a history of vaccinating their stock regularly was investigated in an observational pilot study (Parramore et al. 2011). Ten cows were selected for urine sampling in each of 44 dairy herds. Herd managers were asked for timing, schedule, age, booster and regularity of vaccination, type of vaccine, herd size, whether the herd was open or closed, biosecurity measures, previous leptospirosis history, and other animal species on farm. Urine samples were tested by dark-field microscopy (live *Leptospira*) and Real Time-PCR (live *Leptospira* or DNA) and shedding was defined as being positive to either test.

No serological data were available from the sampled animals, information about vaccination inquired from farmers appeared somewhat uncertain, and tests employed may not be 100% accurate. Therefore, the results are preliminary and require confirmation at this stage.

<table>
<thead>
<tr>
<th>Sampled</th>
<th>Shedding</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herds</td>
<td>44</td>
<td>13</td>
</tr>
<tr>
<td>Cows</td>
<td>445</td>
<td>18</td>
</tr>
<tr>
<td>Cows in pos herds</td>
<td>134</td>
<td>18</td>
</tr>
</tbody>
</table>

*Table 2: Dairy herds and cows shedding leptospora testing 10 selected cows per herd (Parramore et al. 2011)*

There was evidence of shedding in 30% of the herds and 13% in animals from positive herds (Table 2). Because animal prevalence was low and only 10 cows were sampled per herd, a number of herds might have been misclassified as ‘not-shedding’. Thus, the true percentage of herds harbouring shedders may well be higher, despite a long standing history of vaccination. On the other hand, PCR may detect small amounts of DNA from live or dead leptospora, thus the DNA-presence per-se may not have indicated that exposure reached an infective dose. Age at first vaccination was the only significant factor associated with the probability of shedding. The
results suggest that *Leptospira* challenge of calves at an early age still exists on dairy farms using vaccines, for example through heifers returning from a contaminated rearing property. Vaccinating already infected animals may not be effective, as it is known that vaccination after natural challenge reduces vaccine efficacy. Neither vaccine type nor the number of serovars included (2 vs. 3) altered the shedding probability.

**Production effects**

In the absence of vaccines for humans, preventing human leptospirosis clearly requires the control of infection in sheep, deer and beef cattle. As publicly funded control programmes for leptospirosis in livestock do not exist, control is voluntary and paid for by producers. A 2009/10 survey showed that 1/162 (0.6%) sheep, 6/99 (6.1%) deer and 21/116 (18.1%) beef breeding farms had their stock vaccinated against leptospirosis (Dreyfus 2012). Farmers afford vaccination primarily to protect themselves, their families and farm workers. An additional motivation for investing in vaccination might be additional production returns. If leptospirosis control resulted in production gains, and the gains were large enough to offset the cost of investment, farmers would probably be more willing to adopt vaccination and other means for control.

This section therefore reviews current knowledge about the production response to infection with *Leptospira* from a population and cost-benefit perspective. While it is known that leptospirosis affects several organ systems and can cause clinical diseases such as kidney or liver failure, studies were only considered in this report when designed to provide a population or economic basis to associations between *Leptospira* infection and production outcomes. Few data are available about the incidence of **clinical disease** whereas most production effects were derived from prevalence or incidence studies about **subclinical disease**.

**Clinical disease** with high fatality generally occurs sporadically and at extremely low incidence. However, outbreaks have been reported following extreme conditions of flooding or extended periods of rainfall with 5-15% lamb loss (Dorjee *et al.* 2005). A recent survey of 1,940 farmers responding to a questionnaire invitation mailed to 7,998 clients of 28 veterinary practices in seven selected regions in early 2009 revealed that 1-5% farms had observed clinical occurrences of leptospirosis in the preceding three years (Table 3). Deer farmers observed clinical disease more frequently than sheep or beef farmers, but the disease was only observed on deer farms that also grazed sheep and the 3-year incidence was 12.5% on these farms, suggesting transmission from sheep to deer. More detailed information is currently being analysed (Dreyfus 2012). Given that few farmers were likely to have deaths investigated by a veterinarian, these data are likely to be under-estimates of the real incidence of clinical leptospirosis. Further, there is likely a low awareness of the clinical manifestation of leptospirosis, including sudden death, contributing to under-diagnosis.

<table>
<thead>
<tr>
<th>Species</th>
<th>Clinical occurrences reported/no. farms</th>
<th>1–3 year incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer</td>
<td>11/233</td>
<td>4.7%</td>
</tr>
<tr>
<td>Sheep</td>
<td>14/1,193</td>
<td>1.2%</td>
</tr>
<tr>
<td>Beef cattle</td>
<td>22/1,061</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

*Table 3. Farmer reported 3-year leptospirosis occurrences of clinical leptospirosis from a mail survey of 1,940 respondents of 7,998 clients of veterinary practices in New Zealand, 2006-8 (Dreyfus 2012)*

Hence, while clinical leptospirosis is known to cause jaundice, kidney disease and haemoglobinuria, this clinical expression of leptospirosis is only seen sporadically in any of the pastoral livestock species in New Zealand.

In contrast, loss due to **sub-clinical disease** was widely believed to be negligible or absent because it was believed that *Leptospira*, despite a high prevalence, had adapted to their reservoir hosts and subsequently lost some or all of their pathogenicity. Subclinical disease was based on either serological prevalence or incidence of sero-conversion. Prevalence or case-control data can at best suggest an association with production loss. Incidence of sero-conversion may allow causal inferences, especially when sero-conversion was preceding or concurrent to the measurement of production outcomes. It was therefore hypothesised that *Leptospira* had retained sufficient pathogenicity to cause sub-clinical production loss in their reservoir hosts.
Prevalence x pathogenesis = production loss

Following this hypothesis in deer, initial observational studies related sero-prevalence to production outcomes and found lower growth rates from weaning to slaughter (-3.7kg) in deer showing evidence of infection during the growth cycle (sero-conversion, urine shedding or kidney culture positive at slaughter), and 11% lower weaning rates of hinds vaccinated for leptospirosis compared with non-vaccinated herd mates. These detrimental effects were substantiated by serious histo-pathological findings in kidney tissues of sero-positive deer (Ayanegui-Alcerreca 2006).

Vaccine efficacy x prevented production loss = financial return

Recent incidence studies in New Zealand measured sero-conversion and production outcomes in within-herd randomised vaccine efficacy studies on five farms. A subsample of weaner animals were randomly allocated to vaccine or control within each herd, isolated for three months and then rejoined with herdmates known to be shedding leptospires. They found higher growth rates in vaccinated vs. non-vaccinated weaners with a mean of up to 6.4kg at 12 months of age in a high prevalence herd (Subharat et al. 2012) and a mean about 6% (range up to 10%) higher weaning rates attributable to annual vaccination of hinds in herds with evidence for moderate-strong natural challenge (Subharat et al. 2011). Since pre-calving checks showed no foetal losses to late October, it appears that vaccination reduced perinatal and/or pre-weaning mortality of progeny. The growth and reproduction responses were sufficient to provide positive financial returns to the investment in about two thirds of herds in an average year, with risk of infection and therefore financial returns higher when the prevalence was high, such as in wet years.

No data are currently available about growth or weaning effects in beef cattle or sheep in New Zealand. Encouraged by the results in deer however, similar NZ-studies are currently underway in sheep flocks and beef breeding herds. Results are expected by mid-2013 (Valle et al. in progress).

In beef cattle, both Leptospira sv Hardjo and Pomona were associated with an increased risk of foetal loss in a population-based case-control study in New Zealand in 2010 (Sanhueza 2012). Conservative estimates from the study indicated that 5% and 4% of foetuses lost were attributable to Hardjo and Pomona, respectively, and were similar to foetal loss attributable to bovine viral diarrhoea virus or Neospora caninum. Such losses may be much higher when susceptible cattle, e.g. returning from a distant runoff, were co-grazed with cattle, deer or sheep when leptospirosis was highly endemic. Similar associations were reported from Spain (Ellis 1978, Atxaerandio et al. 2005). Studies of fetal loss in Canada, US and Ireland estimated 6%, 10% and 50%, respectively, of bovine abortions being associated with serovar Hardjo (Grooms 2006). A study in Victoria, Australia, concluded that L. interrogans sv. Hardjo was NOT associated with abortions in dairy cattle as Leptospira could not be identified by culture in placenta or foetuses from 195 aborting cows despite being isolated from the urine of two infected, apparently non-aborting cows (Chappel et al. 1989). Successful isolation of Leptospira (sero-group Hebdomanis) from these tissues was reported from experimentally infected and aborting cows (Ellis and Michna 1977).

New Zealand data published by Beef&Lamb suggested that pregnancy rates of beef herds was not associated with the sero-prevalence of serovars Hardjo or Pomona (Heuer 2007). Observations about reproductive loss due to Leptospira in New Zealand dairy herds are not available.

In addition to the well evidenced risk of Leptospira infection on abortion in dairy cows overseas, there appears to be a sub-clinical effect on conception rates in dairy cattle. The median time from calving to conception was 34 days longer and one more breeding was required per pregnancy in sero-positive vs. sero-negative to serovar Hardjo first-calving dairy cows in a US-study. A UK study of herds with evidence of exposure to leptospirosis suggested that vaccination against serovar Hardjo potentially increased conception rates and reduced culling (Dhaliwal 1996). This sub-clinical effect was more pronounced in spring calving cows and attributed to conception failure and early embryonic death (Guitian et al. 1999). Calving rates (measured as one minus lactation failure) increased significantly from 81 to 88% in a clinical trial assessing the effect of a L. sv. Hardjo vaccine in beef cattle (Holroyd and Smith 1976). A subsequent study also reported higher weaning rates in vaccinated vs. control cattle (Holroyd 1980). No difference of reproductive performance indicators (pregnancy, calving, stillbirth) were observed in beef cattle of one farm in Brazil between sero-positive and sero-negative at the start of the mating season (DelFava 2004), but the study gave no indication of active challenge during the risk period.
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Conclusions

Since – after a long period of decline – human leptospirosis reached a significant peak in 2003, veterinary and human public health workers have again increased their awareness about this zoonosis. New prevalence data about dry stock warned of a likely very high exposure of people in farming environments, augmented by apparent on-going shedding in dairy herds with a long history of vaccination. Exposure of abattoir workers to Leptospira and the associated incidence of leptospirosis illness suggest that similar information is required for quantifying the risk of exposure, infection and disease that presumably exists for farmers, veterinarians and other occupations.

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