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Monitoring an epidemic of *Theileria*-associated bovine anaemia (Ikeda) in cattle herds in New Zealand

A.M.J. McFadden[a,*], D. Vink[a], D.J. Pulford[a], K. Lawrence[b], E. Gias[a], A.C.G. Heath[c], C.B. McFadden[d], P. Bingham[a]

[a] *Ministry for Primary Industries, PO Box 40742, Upper Hutt 5018, New Zealand*
[b] *Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand*
[c] *Agresearch Ltd., c/o Hopkirk Research Institute, Private Bag 11008, Palmerston North 4442, New Zealand*
[d] *Epi-consulting, Normandale, Lower Hutt 5010, New Zealand*

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ABSTRACT

Monitoring an epidemic of an emerging vector-borne disease can be problematic; particularly in a country where vector-borne disease has previously had minimal impact on livestock. This paper describes methods of past and current surveillance of the *Theileria*-associated bovine anaemia (Ikeda; TABA) epidemic in New Zealand, and the resulting inferences made.

Over the three year period of the TABA epidemic a portfolio of surveillance methods has been used: case reporting (with subsidised PCR testing), syndromic surveillance, sentinel surveillance, testing convenience samples for herd infection, as well as specific active surveillance initiatives to understand the tick vector distribution. Surveillance data have shown that the number of affected cattle herds has continued to increase over time with seasonal peaks in spring and autumn coinciding with peak activity of nymph and adult ticks respectively. In spring 2014, the epidemic extended south into areas that were previously considered to be unsuitable for the tick vector. As a result a survey was initiated that showed that ticks were present in areas outside of the known distribution.

Testing pooled blood samples from cattle herds across New Zealand showed there still remained a significant percentage of herds where only non-Ikeda type infections were present, indicating that these herds were at risk of future TABA (Ikeda) outbreaks. For some regions there had been a noticeable increase in the percentage of herds infected, yet with only a small increase in the number of outbreaks compared with the previous year. Thus, outbreaks had either gone unobserved or had not been confirmed by testing. In these regions extensive low-input beef farming could explain the non-detection observed. There was a close relationship between the number of syndromic reports of anaemia and the number of confirmed cases of TABA (Ikeda), ($P < 0.01$, adjusted R-squared = 0.74).

Active monitoring of the epidemic for a three year period has provided valuable insight into seasonal nature of the disease and its continuing impact. Information from multiple surveillance sources can help build up an understanding of the epidemiology, even when data from each individual surveillance stream are limited. The TABA (Ikeda) epidemic in New Zealand represents a useful case study of long term monitoring where disease is caused by an emerging pathogen.

1. Introduction

Theileria orientalis is a protozoan of cattle that is transmitted by *Haemaphysalis* species of ticks, vectors that are essential for the completion of its life cycle (Lawrence, 2004). *Haemaphysalis longicornis* is the only biological vector of *T. orientalis* present in New Zealand (Heath, 2016) although means of mechanical transmission have been suggested (Heath, 2013). *T. orientalis* was first reported in New Zealand in 1982 (James et al., 1984). However, until recently, *Theileria*-associated bovine anaemia (TABA) in New

Abbreviation: BVD, bovine viral diarrhoea; HCT, haematocrit; MPI, Ministry for Primary Industries; NZVA, New Zealand Veterinary Association; TABA, *Theileria* associated bovine anaemia.

* Corresponding author. Fax: +64 48945611.
E-mail address: andrew.mcfadden@mpi.govt.nz (A.M.J. McFadden).

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Zealand was considered to be a sporadic event that only affected cattle debilitated by another condition (Fairley, 1992; Black and Orr, 1999). In 2009, an outbreak of haemolytic anaemia occurred when non-infected cattle from the South Island were introduced to a Northland herd where both *H. longicornis* and *T. orientalis* were endemic. In this case, the Chitose type of *T. orientalis* was identified as the cause of anaemia (McFadden et al., 2011) and showed that the Chitose pathogen is capable of causing clinical disease in cattle that were not necessarily debilitated by another disease.

In the early stages of the epidemic, from late August 2012 to late April 2013, there were 38 outbreaks of TABA in dairy and beef cattle herds located in multiple regions across the upper North Island, New Zealand, reported to the Ministry for Primary Industries (MPI, Wallaceville). This number compared with only 12 notifications for the period 2000–2012 i.e. approximately one report per year. From late 2012, a number of affected herds were found to have a high prevalence of animals with anaemia, in comparison to the historic reports where there was generally only one animal affected, often debilitated by other disease. The outbreaks tended to follow the same pattern described by McFadden et al. (2011); that is, disease in presumed naïve cattle, subsequent to mixing with affected animals grazed in areas with suitable tick habitat. However, this was not the case in all circumstances, with TABA occurring in dairy-cow herds with limited animal movements as well as disease occurring in beef calves that had been born onto Northland properties. As a result of the temporal clustering observed further investigation was carried out aimed at understanding the cause.

Genotyping of *T. orientalis* was carried out on samples collected from herds experiencing outbreaks early in the epidemic and one of the types was identified as *T. orientalis* (Ikeda) (Pulford et al., 2016a,b). Analysis of data from the New Zealand outbreaks showed that there was a greater likelihood of *T. orientalis* Ikeda type being present in cattle from herds experiencing outbreaks of anaemia compared to non-outbreak herds. In addition, individual animals within an affected herd were more likely to be anaemic if the Ikeda type was present, compared with animals with endemic strains of *T. orientalis* such as the Chitose type (McFadden et al., 2013a; Lawrence et al., 2013, 2014). As a result, *T. orientalis*, in combination with other unknown risk factors, was considered to be the aetiological cause of the New Zealand outbreaks (McFadden et al., 2013a; Lawrence et al., 2013, 2016).

The Ikeda type has been determined to have been responsible for recent outbreaks of anaemia in cattle in Australia (Eamens et al., 2013). The first cases of TABA were observed in Australia in 2006 with identification of the Ikeda type reported in 2010 (Izzo et al., 2010; Kamau et al., 2011). The Ikeda type is widely distributed throughout Asia (Ota et al., 2009; Kakuda et al., 1998; Khukhuu et al., 2011) and has also found to be responsible for anaemia in cattle (Kawamoto et al., 1991; Yagi et al., 1991). On affected properties the impact can be quite variable, ranging from low prevalence infections with few clinical cases to those with high morbidity (McFadden et al., 2013a; Lawrence et al., 2013, 2016; Vink et al., 2016). The long-terms effects on milk production and reproduction performance have been variable; although there have only been a small number of studies carried out on single farms (Yamane et al., 2001; McDougall et al., 2014; Perera et al., 2014).

Since the initial diagnosis of TABA (Ikeda) MPI has continued to monitor the New Zealand epidemic through various surveillance initiatives. Monitoring has been important to inform on risk, and understand the epidemiology and impact of the disease. Monitoring an epidemic of an emerging syndrome can be problematic, particularly where vector-borne disease has previously had minimal impact on livestock. This paper describes methods of past and current surveillance, and the resulting inferences made from this data.

2. Materials and methods

2.1. Case reports

Initially, surveillance of TABA (Ikeda) involved veterinarians and veterinary pathologists reporting suspect outbreaks to MPI using a hotline for exotic and emerging disease. Investigation of these early cases involved testing anaemic cattle with a PCR for *T. orientalis* using the methods described by Pulford et al. (2016a) as well as a standard battery of tests to exclude other causes of regenerative anaemia (copper deficiency, post-parturient haemoglobinuria, leptospirosis, acute facial eczema). Small on-farm studies were carried out to determine the intra-herd prevalence of anaemia, together with risk tracing to determine any association with other infected farms (McFadden et al., 2013a,b; Lawrence et al., 2016; Pulford et al., 2016a).

To improve *T. orientalis* diagnostic precision and speed, a set of new quantitative PCR (qPCR) assays were developed and validated using characterised bovine whole blood samples obtained from TABA clinical and non-clinical field samples (Pulford et al., 2016b). Furthermore, the new qPCR assays were also validated for use with serum samples to provide passive surveillance data to report the spread of *T. orientalis* during the TABA epidemic (McFadden et al., 2015, 2016). Following validation, all surveillance has been conducted using an Ikeda-specific TaqMan qPCR, either used with a *T. orientalis* qPCR that used high resolution melt analysis of amplicons to define genotypes, or from 2014 using a multiplex TaqMan qPCR test that produced specific and sensitive results for Buffeli, Chitose and Ikeda genotypes in the same test (Pulford et al., 2016b).

In late 2013, as the number of cases increased, the capacity of the MPI Animal Health Laboratory (Wallaceville) to service farmers and veterinarians by testing blood samples from cattle by qPCR for *T. orientalis* Ikeda was put under pressure. As a result, molecular diagnostic work was transferred to the private regional veterinary laboratories (New Zealand Veterinary Pathology, Hamilton, N.Z, and Gribbles, N.Z). A subsidy from MPI to the regional veterinary laboratories was put in place to compensate for the cost of molecular diagnostic tests where specific criteria for a suspect case were met. A suspect case was defined as where one or more clinically affected cattle had a haematocrit (HCT) of less than or equal to 0.24 and theilerial piroplasms observed in a blood smear. The primary objective of the subsidy from MPI was to ensure the cost of testing was not a barrier for sample submission to laboratories, and in doing so was aimed at increasing both the sensitivity and specificity of surveillance for TABA (Ikeda). At the same time AsureQuality (Auckland, New Zealand) was employed to collect data related to the affected farm, including the geographical location and the type of farm affected e.g. beef, dairy or dry stock. A standardised analysis (epidemic curve, spatial mapping of cases) developed by MPI epidemiologists was carried out and reported to disease control experts and field veterinarians.

2.2. Syndromic reports

The surveillance strategy was revised for the North Island in January 2015 as the disease became increasingly widespread, and the value of identifying individual cases diminished. In addition, as exposure of herds to the Ikeda type increased, finding the presence of Ikeda in cattle with clinical signs of anaemia was no longer specific to cattle affected by TABA (Ikeda). As a result, the strategy for the North Island was changed to monitoring syndromic data from regional veterinary laboratories where case submissions from veterinarians to the laboratory indicated that affected cattle had anaemia as part of the presenting syndrome i.e. cases not necessarily confirmed as being TABA (Ikeda) by qPCR. Data were removed from analysis where a specific aetiological diagnosis had