Veterinary Microbiology 181 (2015) 161–169

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Paratuberculosis in sheep and goats

P.A. Windsor

Faculty of Veterinary Science, The University of Sydney, Camden, NSW, 2570, Australia

ARTICLE INFO

Keywords:
Disease control programs
Goat
Health
Paratuberculosis
Sheep
Small ruminants
Vaccination

ABSTRACT

Paratuberculosis is a chronic insidious, often serious, disease of the global small ruminant industries, mainly causing losses from mortalities and reduced productivity on-farm, interference in trading and, in Australia, profound socio-economic impacts that have periodically compromised harmony of rural communities. The pathogenesis, diagnosis, impacts and disease management options for ovine and caprine paratuberculosis are reviewed, comparing current controls in the extensive management system for sheep in wool flocks in Australia with the semi-intensive system of dairy flocks/herds in Greece. Improved understanding of the immune and cellular profiles of sheep with varying paratuberculosis outcomes and the recognition of the need for prolonged vaccination and biosecurity is considered of relevance to future control strategies. Paratuberculosis in goats is also of global distribution although the prevalence, economic impact and strategic control options are less well recognized, possibly due to the relatively meagre resources available for goat industry research. Although there have been some recent advances, more work is required on developing control strategies for goats, particularly in dairy situations where there is an important need for validation of improved diagnostic assays and the recognition of the potential impacts for vaccination. For all species, a research priority remains the identification of tests that can detect latent and subclinical infections to enhance removal of future sources of infectious material from flocks/herds and the food chain, plus predict the likely outcomes of animals exposed to the organism at an early age. Improving national paratuberculosis control programs should also be a priority to manage disease risk from trade. The importance of strong leadership and communication, building trust within rural communities confused by the difficulties in managing this insidious disease, reflects the importance of change management considerations for animal health authorities. Although concerns of vaccine efficacy, safety and issues with diagnosis and administration persist, vaccination is increasingly recognized as providing a robust strategy for managing paratuberculosis, having made important contributions to the health of Australian sheep and the lives of producers with affected properties, and offering a mechanism to reduce risk of infection entering the food chain in ovine and caprine products.

1. Introduction

Paratuberculosis ('Johne's disease') is a chronic bacterial disease of global importance in mainly domestic and wild ruminants, caused by *Mycobacterium avium* subsp. paratuberculosis (Windsor, 2014). The disease was first reported in cattle in Europe in 1895 and has spread throughout the developed and parts of the developing world, particularly in the bovine dairy industries. The infection in small ruminants is also considered of worldwide distribution, diagnosed in sheep and goats in many countries. For ovine paratuberculosis, these include southern hemisphere's Australia, New Zealand and South Africa, numerous northern hemisphere's countries, particularly Great Britain, Norway and Austria, as well as para-Mediterranean countries, e.g., Greece, Spain, Portugal, Morocco and Jordan (Benazzi et al., 2010; Djønne, 2010; Hailat et al., 2010). Caprine paratuberculosis has been diagnosed in Turkey, France, Norway, Switzerland, Croatia, Canada, the USA and Chile (Barkema et al., 2010).

Unlike the clinical signs in cattle, which are readily recognized as profuse watery diarrhea and weight loss, the disease is more insidious in small ruminant flocks/herds, with affected animals eventually displaying progressive weight loss and exercise intolerance termed as 'an increase in the tail to the mob', with soft faeces in some animals (Windsor, 2014). Persistence of the causal organism in the environment and lack of sufficient application of vaccines that are presumed to have less than the desired efficacy, have complicated on-farm control (Sweeney et al., 2012).

E-mail address: peter.windsor@sydney.edu.au (P.A. Windsor).

http://dx.doi.org/10.1016/j.vetmic.2015.07.019
0378-1135/

This paper reviews current knowledge on paratuberculosis in sheep and goats, including pathogenesis, diagnosis and disease impacts, and also discusses the various disease control options that have been successfully used in these species, particularly vaccination and disease awareness extension programs. A change management framework enabling reflection on national control programs in Australia and consideration factors of relevance to improving paratuberculosis control by animal health managers (Windsor, 2014) is briefly discussed, including: drivers and motivation for change, resistance to change, knowledge management, farming systems dimensions and leadership of change management in paratuberculosis control.

2. Pathogenesis of paratuberculosis and aspects of relevance to disease control

Ovine and caprine paratuberculosis involves chronic inflammatory lesions of the intestinal and lymphoid organs, caused mostly by one or other of the 'S' (sheep), 'C' (cattle) or 'Bison type' strains of *M. avium* subsp. paratuberculosis (Windsor, 2014; Kumar et al., 2010). In Australia, the S strain mostly causes paratuberculosis in sheep or fibre-producing goats, the C strain is mostly involved in dairy goat infections and to date the 'Bison strain' has only been detected in Brahman cattle (unpublished observations). This most likely reflects the largely separate geographical locations of the sheep and fibre-producing goat populations from dairy cattle, goat or sheep and tropical beef cattle enterprises farmed in this country. Although sheep are susceptible to the more common C strain and it has been a common finding in sheep in Europe, it has been suggested that distribution and abundance of the S strain may have been underestimated, due to more challenging requirements for mycobacterial culture (Begg and Whittington, 2010). Cattle appear relatively resistant to infection and disease with the S strain, although, in Australia, calves in contact to heavily infected sheep have become infected (Moloney and Whittington, 2008). In a longitudinal evaluation of diagnostic tests in a cattle infection model for paratuberculosis, including determination of adult infection status by post-mortem examination and tissue culture of sheep, goats or cattle infected as young animals, cattle were found to be less susceptible to the C and S strains of the organism than goats and sheep, with goats considered the least naturally resistant (Stewart et al., 2007).

A recent study examining experimental infections of C and S strains in 1.5-month-old Assaf lambs found that specific antibody and interferon gamma (IFNγ) production was significantly greater in animals infected with the C strains, with no consistent IFNγ responses observed in animals infected with S-type strains (Fernandez et al., 2014). Lambs infected with S strains had granulomatous lesions restricted to the lymphoid tissue, with no differences in lesion intensity over time; C strain lesions were more severe at 150 dpi, while at 390 dpi lesions, characterised by well-demarcated granulomas with fibrosis, tending to decrease in severity as infection progressed. It was concluded that the strain of *M. avium* subsp. paratuberculosis has a strong influence over immune and pathological responses developed by the host.

M. avium subsp. paratuberculosis infection mostly results from faceal-oral route exposure, with entry via the intestinal tract then to the lymphatic system, where it resides in M cells overlying Peyer's patches in the ileum. Faceal-oral route exposure may occur as described below.

- Ingestion of faecal material from an infected animal, particularly on the teat of an infected dam, plus exposure to manure contaminated pasture, water, supplements or hay contaminated with faecal material from infected adult animals (Windsor and Whittington, 2010).
- Drinking of contaminated colostrum or milk, as *M. avium* subsp. paratuberculosis is also excreted in the colostrum and milk of cattle (Windsor and Whittington, 2010) or sheep/goats (Lambeth et al., 2004; Nebbia et al., 2006).

Pre-natal infection has also been well described, with prevalence in cows with subclinical or clinical disease estimated to be 9% (95% confidence intervals: 6–14%) or 39% (5% confidence intervals: 20–60%), respectively (Whittington and Windsor, 2009). In a study of 142 late-pregnant ewes and their fetuses from two heavily infected flocks, all five ewes with clinical disease had infected fetuses, but only one of 54 ewes with subclinical disease had an infected fetus, resulting in <1% (95% confidence intervals: 0–5%) of all fetuses diagnosed as infected (Lambeth et al., 2004). There is little information on the consequences of pre-natal infection and whether such animals progress more rapidly to clinical disease, commence shedding of *M. avium* subsp. paratuberculosis earlier, or are relevant to disease management. However, as *in utero* infection may occur frequently in sheep with clinical paratuberculosis, the immediate culling of reproductively active female animals with clinical signs is strongly advised to mange this risk (Lambeth et al., 2004; Whittington and Windsor, 2009; Windsor, 2014).

Culling of clinical cases is also of importance to managing environmental contamination with the causal organism as sheep with clinical paratuberculosis shed huge numbers of the organism in their faeces, estimated at 10^8 organisms g^{-1} of faeces (Reddacliff et al., 2006). This is of concern to disease control programs as *M. avium* subsp. paratuberculosis may persist in the environment, potentially surviving for around one year, although this is dependent on a range of environmental factors, particularly shade (Whittington et al., 2004, 2005). In Australia, the initial paratuberculosis control strategy was regulation and quarantine of infected properties, with destocking of infected sheep properties from the beginning of one summer to the end of the next advocated. This program failed, most likely because of the difficulties of identifying 'clean' replacement stock, despite the early development of a market-assurance scheme to encourage studs to regularly test and provide evidence of their likely uninfected or low risk status (Windsor, 2014).

Of continuing concern has also been the potential zoonotic link between paratuberculosis and human inflammatory bowel diseases, including Crohn's disease. If *M. avium* subsp. paratuberculosis is eventually confirmed as a zoonotic pathogen, it is expected that public confidence in products from bovine and potentially small ruminant dairy industries will very likely decline. With increasing certainty of a role for *M. avium* subsp. paratuberculosis in Crohn's disease, efforts to diminish or remove the organism from the human food chain should be encouraged.

Three distinct forms of paratuberculosis have been observed in sheep: multibacillary disease, paucibacillary disease and asymptomatic infection (Gillan et al., 2010). The multibacillary lesions of chronic granulomatous enteritis and lymphadenitis (particularly involving the mesenteric lymph nodes) in paratuberculosis is characterised by accumulation of epithelioid macrophages containing numerous *M. avium* subsp. paratuberculosis in the lamina propria and submucosa of the intestine. The paucibacillary lesions are typically more lymphocytic in nature with *M. avium* subsp. paratuberculosis being far less numerous (Windsor, 2014). The enteric lesions typically develop within 6–12 months following initial detection of *M. avium* subsp. paratuberculosis infection and although some sheep may develop severe lesions within 12 months of infection, others progress from mild and paucibacillary to severe and multibacillary at variable rates, potentially fluctuating in severity or in the character of the inflammatory infiltrate over a period of years (Dennis et al., 2011). Clinical signs generally become evident in the months following development of severe