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Invited review: The economic impact and control of paratuberculosis in cattle

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ABSTRACT

Paratuberculosis (also called Johne's disease) is a chronic disease caused by *Mycobacterium avium* ssp. *paratuberculosis* (MAP) that affects ruminants and other animals. The epidemiology of paratuberculosis is complex and the clinical manifestations and economic impact of the disease in cattle can be variable depending on factors such as herd management, age, infection dose, and disease prevalence, among others. Additionally, considerable challenges are faced in the control of paratuberculosis in cattle, such as the lack of accurate and reliable diagnostic tests. Nevertheless, efforts are directed toward the control of this disease because it can cause substantial economic losses to the cattle industry mainly due to increased premature culling, replacement costs, decreased milk yield, reduced feed conversion efficiency, fertility problems, reduced slaughter values, and increased susceptibility to other diseases or conditions. The variability and uncertainty surrounding the estimations of paratuberculosis prevalence and impact influence the design, implementation, and efficiency of control programs in diverse areas of the world. This review covers important aspects of the economic impact and control of paratuberculosis, including challenges related to disease detection, estimations of the prevalence and economic effects of the disease, and the implementation of control programs. The control of paratuberculosis can improve animal health and welfare, increase productivity, reduce potential market problems, and increase overall business profitability. The benefits that can derive from the control of paratuberculosis need to be communicated to all industry stakeholders to promote the implementation of control programs. Moreover, if the suspected link between Johne's disease in ruminants and Crohn's disease in humans were established, significant economic losses could be expected, particularly for the dairy industry, making the control of this disease a priority across dairy industries internationally.

Key words: paratuberculosis, economics, Johne's disease

INTRODUCTION

Paratuberculosis (also called Johne's disease) can be described as a contagious, chronic, progressive granulomatous infection affecting primarily the small intestine and other organs such as live and mesenteric and hepatic lymph nodes. The disease is caused by *Mycobacterium avium* ssp. *paratuberculosis* (**MAP**), which was first described in 1895 (Johne and Frothingham, 1895; Harris and Barletta, 2001; Salem et al., 2013). The disease primarily affects cattle, sheep, and goats but it has also been reported in horses, deer, alpaca, llama, camels, moose, elk, buffalo, reindeer, pigs, rabbits, stoats, hares, badgers, foxes, and weasels [Beard et al., 2001; CFSPH, 2007; Reyes-García et al., 2008; OIE, 2014]. Epidemiological evidence suggests that domestic ruminants can infect wild animals (Pavlík et al., 2000a) and that wildlife species could be reservoirs for paratuberculosis infection of domestic livestock (Reyes-García et al., 2008).

Paratuberculosis causes inflammation and malfunction of the intestinal tract, with gross pathology showing thickened and edematous intestinal walls (lesions are usually present in the jejunum and ileum). Mesenteric lymph nodes can be swollen and edematous and on occasion, other organs such as liver and hepatic lymph nodes might show lesions. In turn, the intestinal lesions affect the absorption of nutrients and proteins, leading to muscle wasting and lower productivity (Caldow et al., 2001). In addition, IL-10, an antiinflammatory cytokine, suppresses inflammatory immune responses and facilitates the growth of MAP within macrophages (Weiss et al., 2005; Scandurra et al., 2010), which contributes to disease progression. Animals may suffer from diarrhea, submandibular edema, weight loss despite normal appetite, malnutrition, anemia, emaciation, lethargy, and death. This disease may cause substantial economic losses to the cattle industry mainly as a result of increased premature culling, replacement costs, decreased milk yield, reduced feed conversion efficiency, fertility problems, reduced slaughter values, and increased susceptibility to other diseases or

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conditions (Ott et al., 1999; Weber, 2006; Gonda et al., 2007; Richardson and More, 2009). Most infected animals show clinical disease between 2 and 6 yr of age, although clinical manifestations can range from 4 mo to 15 yr (Caldow et al., 2001). An animal in clinical stage has the potential to infect 25 more animals, although disease transmission depends on several factors such as close contact between animals (Whitlock and Buergelt, 1996). The main route of MAP transmission is the oral–fecal route but other infection routes have been proposed, such as intrauterine and aerosol transmission. The MAP bacterium has been detected in dust in cattle facilities housing infected animals, suggesting that aerosol spread of MAP might be possible (Eisenberg et al., 2010). Furthermore, MAP has been isolated from tracheobronchial lymph nodes, supporting the hypothesis of aerosol transmission (Pavlík et al., 2000b). Moreover, there is no effective treatment of cows infected with paratuberculosis (Extension, 2014; NADIS, 2014).

Animals most likely become infected with MAP during the first 6 mo of life; neonates are particularly susceptible to infection (Cocito et al., 1994) and intrauterine infection is also possible. Whittington and Windsor (2009) conducted a meta-analysis and estimated the prevalence of MAP infections in utero to be 39% among cows with clinical disease and 9% among subclinical cows. It has been suggested that MAP infection during adulthood rarely develops into clinical disease (Rankin, 1962). In fact, increased resistance to infection with age has been observed that could be explained by the more fragile immune system in younger animals, which in turn facilitates access of the bacteria to the Peyer's patches (Sweeney, 1996). It can take a few years for animals to develop clinical disease; however, subclinical infections also hamper animal health, productivity, and farm profitability (Johnson-Ifearulundu et al., 2000). Furthermore, animals in subclinical stages may excrete MAP organisms in variable numbers; they are usually low or moderate shedders (shedding fewer than 10^3 colonies/g of feces) but they could also be supershedders and excrete millions or billions of bacteria into the environment (Whitlock et al., 2006).

Infected bulls can excrete MAP bacteria in feces and semen (Larsen et al., 1981; EFSA, 2004; Abbas et al., 2011). Infected cows can excrete MAP in feces, milk, and colostrum. Heavy fecal shedders are more likely to shed MAP in colostrum (Streeter et al., 1995). In fact, MAP infection of young animals can happen via intrauterine transmission or consumption of infected colostrum or milk although it occurs primarily via the fecal–oral route (Clarke, 1997). The bacterium has also been detected in raw milk and therefore could be transferred to humans via milk because MAP might not be effectively inactivated by pasteurization (Corti and Stephan, 2002; Gao et al., 2002; Grant et al., 2002a,b). The disease affects primarily ruminants; however, a potential link between Johne's disease in ruminants and Crohn's disease in humans has raised concerns over the safety of dairy products, prioritizing the control of the disease in ruminants, particularly dairy cattle (Chamberlin et al., 2001; Ghadiali et al., 2004; Naser et al., 2004). The potential link between paratuberculosis in cattle and Crohn's disease in humans forms part of an ongoing scientific debate (European Commission, 2000; Chacon et al., 2004; Ghadiali et al., 2004; Herrewegh et al., 2004; Shanahan and O'Mahony, 2005; Food FSAI, 2009; Juste, 2012). Although there is no definitive evidence to demonstrate that the bacteria causes or contributes to Crohn's disease in humans, MAP has been detected more commonly in patients with Crohn's disease (Scientific Committee on Animal Health and Animal Welfare, 2000; Bull et al., 2003; Naser et al., 2004; Feller et al., 2007). This potential link between Johne's disease in ruminants and Crohn's disease in humans needs to be clarified but the presence of viable MAP in pasteurized milk for human consumption (Ayele et al., 2005; Ellingson et al., 2005) has prompted public health agencies and organizations to advise the industry to prevent MAP from entering the food chain.

The potential zoonotic risk for consumers, the effect on animal health and welfare, and the large financial losses that may be caused by this disease have led to the implementation of disease control programs in many countries. This paper aims to review the most important aspects related to paratuberculosis impact and control in cattle. For this purpose, relevant epidemiological aspects are included to provide context and background information.

DISEASE DETECTION AND PREVALENCE

The tests most commonly used for the identification of infected animals, for estimation of prevalence, and for disease control programs are fecal culture (individual and pooled fecal samples), serum ELISA, and milk ELISA. Fecal PCR may also be used as a confirmatory test (Clark et al., 2008). Individual fecal culture of MAP is considered the reference test (Barrett et al., 2011). The apparent prevalence of MAP will partly depend on the diagnostic test used. In general, the sensitivity of fecal culture and PCR seem to be superior to that of ELISA for the identification of MAP-infected cattle. As an example, a study conducted by Smith et al. (2009) found a prevalence varying from 0 to 4.9% when using serum ELISA and a prevalence of 0 to 13.6% when using liquid fecal culture. The sensitivity and specificity of diverse diagnostic tests for the detec-