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Review

Chlamydia pecorum infections in sheep and cattle: A common and under-recognised infectious disease with significant impact on animal health

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ABSTRACT

There is a growing recognition that infections of livestock by the obligate intracellular bacterium, *Chlamydia pecorum*, are more widespread than was previously thought. A range of diseases have been associated with this pathogen, with the most important manifestations including infectious arthritis, infertility, enteritis, reduced growth rates, mastitis, and pneumonia. *C. pecorum* infections have also been associated with sub-clinical disease, highlighting our lack of knowledge about its true economic impact on livestock producers.

Diagnosis of *C. pecorum* infection is based on clinical findings, serology and histopathology, which are not necessarily implemented in subclinical or early stages of infection, thus potentially contributing to under-diagnosis and under-reporting of infections associated with this bacterium. Recent molecular epidemiology studies have revealed that *C. pecorum* is genetically diverse and that there may be an association between certain strains and disease in sheep and cattle. Antimicrobial treatment of affected animals has questionable efficacy, justifying development of chlamydia vaccines for livestock. This review summarises current knowledge of the prevalence and impact of *C. pecorum* infections in sheep and cattle and provides an update on attempts to improve detection, management and treatment of infections by this important obligate intracellular pathogen.

Introduction

Chlamydia pecorum is recognised as one of the most widely distributed chlamydial species, with a wide host range that includes production animals such as sheep, goats, pigs and cattle, but also important wildlife species (Giovannini et al., 1988; Francesco et al., 2011), including the koala in Australia (Polkinghorne et al., 2013). In livestock, *C. pecorum* infections are typically associated with arthritis and conjunctivitis in ruminants, as well as encephalomyelitis in cattle (Cutlip et al., 1972; Fukushi and Hirai, 1992; Meagher et al., 1992; Anderson et al., 1996).

McNutt and Waller (1940) first described clinical cases of *C. pecorum* infection, causing encephalomyelitis in cattle. Twenty years later, the first reports of chlamydial polyarthritis were described in feeder lambs (Mendlowski and Segre, 1960) and calves (Storz et al., 1966a, 1966b), both occurring in the USA. In these initial reports, lambs exhibited an insidious onset of lameness associated with serofibrinous synovitis, weight loss and high mortality (Mendlowski and Segre, 1960). A virus-like psittacosis-lymphogranuloma aetiological agent was isolated from infected joints of affected animals and was shown to induce the same disease in experimentally infected lambs (Mendlowski and Segre, 1960).

The first reports of *C. pecorum* infection in calves described severe synovitis with peri-articular and muscle oedema, associated with high mortality in affected herds, 1–3 weeks after birth and a psittacosis-lymphogranuloma agent was isolated from the infected joints and organs (Storz et al., 1966b). This pathogen was later identified as *C. pecorum* (Fukushi and Hirai, 1992; Anderson et al., 1996). While other less common disease manifestations have been associated with this pathogen, more recent studies have reported that subclinical infections likely affect animal and herd productivity (Wehrend et al., 2005; Jaeger et al., 2007; Reinhold et al., 2008; Kemmerling et al., 2009; Poudel et al., 2012), raising concern over the economic impact of these infections worldwide.

Advances in molecular genetic techniques have resulted in several revisions and lack of agreement over the taxonomic classification of *Chlamydia* spp. Page (1966) proposed the genus *Chlamydia* within the family of *Chlamydiaceae* and the order *Chlamydiales*, of which

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only two species were known approximately 50 years ago (*C. trachomatis* and *C. psittaci*). Based on observations in cell culture at that time, *C. pecorum* was referred to as *C. psittaci*, and later re-classified as *C. pecorum*, based on molecular advances (Fukushi and Hirai, 1992). To accommodate nine different species in the family *Chlamydiaceae*, the genus *Chlamydia* was subsequently re-classified to include *Chlamydia* and *Chlamydophila* (Everett et al., 1999; Everett, 2000). Several taxonomic changes later, there are currently 11 species of the genus *Chlamydia* in the family *Chlamydiaceae* (Stephens et al., 2009; Sachse et al., 2014). Thus, for this review, *C. psittaci* serotype 2 and *C. pecorum* will be referred to as *C. pecorum*.

Ongoing development of molecular techniques by a number of research groups is providing insights into the epidemiology of these infections and the genetic diversity of *C. pecorum*. However, diagnosis of *C. pecorum* infection remains problematic, due to limited access to specific diagnostic tests and reliance on serology. In this review, we aim to summarise recent evidence of the prevalence and impact of *C. pecorum* infections in livestock and detail advances in our understanding of the epidemiology and pathogenesis of this important but often under-recognised veterinary pathogen.

Surveillance of *C. pecorum* infections of sheep and cattle

There is growing evidence to suggest that *C. pecorum* infection is endemic in livestock worldwide, particularly in the gastrointestinal tracts of affected animals. However, precise prevalence rates remain unclear, since most veterinary chlamydial diagnostics rely on genus- and not species-specific assays (Sachse et al., 2009).

Sheep

A number of studies have revealed that *C. pecorum* infections are prevalent in healthy and diseased animals worldwide. Australia is the largest exporter of mutton and live sheep,[1] with faecal shedding of *C. pecorum* recently estimated to be present in around 30% of the nation's sheep flock (Yang et al., 2014). This observation was similar to a previous study that demonstrated faecal shedding of *C. pecorum* in 17–50% of healthy and diseased animals (Jelocnik et al., 2013). Elsewhere, studies in the United Kingdom, comparing farms with and without a history of enzootic abortion, found that 25.5% and 11.6% of lamb faecal samples, respectively, were culture positive for *C. pecorum*, although the organism was not detected in any of the adult ewes (Clarkson and Philips, 1997). In Germany, rectal and vaginal shedding of *C. pecorum* appears to be common, with 40.6% of sheep flocks with <1% abortion rates being PCR positive for this agent (Lenzko et al., 2011). Similarly, in Switzerland, one study found that two-thirds of sheep flocks were positive (by PCR or ELISA testing) for *C. pecorum* (Polkinghorne et al., 2009).

Apart from Europe and Australia, surveillance studies for *C. pecorum* in sheep seem to be somewhat limited. One study in Egypt revealed the prevalence of *C. pecorum* infection to be 4.8% in diseased sheep (Osman et al., 2011). The lack of global prevalence data on sheep populations further emphasises our deficiency in knowledge of the prevalence and impact of *C. pecorum* infection.

Cattle

Irrespective of sampling methods employed (e.g. pre-selection based on disease state or random selection) the seroprevalence of chlamydial infections is relatively high in cattle herds worldwide (Reinhold et al., 2011a). Studies in Germany and the USA have shown that herds of healthy dairy cattle can have infection rates of 58.5–100% (Jee et al., 2004; Reinhold et al., 2008). Interestingly, *C. pecorum* shedding can be detected from multiple sites in the same animal (e.g. nasal, faecal, conjunctival and vaginal) and have been regularly found in association with *C. abortus* (Jee et al., 2004; Reinhold et al., 2008). A USA-based study also revealed that 67% of vaginal samples from virgin dairy heifers with mild vaginitis were positive for *C. pecorum* by quantitative PCR (DeGraves et al., 2003).

Elsewhere in Europe, a recent study in Ireland has identified 57% of herds to be seropositive, with an overall prevalence of 4.75% of individuals within a herd demonstrating antibodies to both *C. abortus* and *C. pecorum* by ELISA (Wilson et al., 2012). From a review of the literature, there appears to be no information available regarding the prevalence of *C. pecorum* infections in beef cattle production systems.

Clinical impact of *C. pecorum* infections in sheep and cattle

Polyarthritis and keratoconjunctivitis

C. pecorum isolates from sheep and cattle have mainly been associated with polyarthritis and keratoconjunctivitis in young animals (Cutlip et al., 1972; Storz and Spears, 1979; Andrews et al., 1987). Arthritis in lambs and calves typically affects rapidly growing animals in more than one joint. Clinical signs (Fig. 1) include fever, weight loss, lameness, joint stiffness and are sometimes accompanied by conjunctivitis (Storz and Spears, 1979; Beveridge, 1981; Kemp, 1986; Watt, 2011).

Histologically (Fig. 2), infection results in inflammatory and proliferative changes in the synovial membranes, joint capsules, tendon sheaths, tendons, ligaments, peri-articular connective tissues, and muscles (Shupe and Storz, 1964; Storz and Spears, 1979; Maxie and Youssef, 2007). Chronic changes can include erosion of the articular cartilage, fibrotic thickening of the tendon sheath and articular capsule, with severe inflammation and hyperplasia of synovial villi (Shupe and Storz, 1964; Maxie and Youssef, 2007).

Chlamydial keratoconjunctivitis in ruminants is characterised in the early stages by bilateral epiphora, chemosis and conjunctival hyperaemia, progressing to prominent conjunctival follicle formation and corneal neovascularisation (Smith, 2002). Due to the multi-aetiological nature of ocular disease in livestock, the impact of *C. pecorum*, occurring alone or in mixed infections (e.g. with *Mycoplasma* spp.), on herd health is difficult to assess. Furthermore, there may be interspecies synergism in cases of mixed infections (Gupta et al., 2015).

Weight loss (or failure to thrive) as a result of *C. pecorum* polyarthritis is the primary economic concern for farmers (Mendlowski and Segre, 1960; Storz et al., 1966b; Beveridge, 1981; Kemp, 1986). In Australia, arthritis has been estimated to cost the sheep industry around $30M[2] (Sackett et al., 2006), with 2.1% of lambs and 1.6% of calves at export abattoirs condemned as a result of polyarthritis (Pointon et al., 2008). Similarly, in France, 2.4% of cattle condemnations at abattoir were due to arthritis (Dupuy et al., 2013). However, the specific contribution of *C. pecorum* to these losses remains to be established.

Sporadic bovine encephalomyelitis (SBE)

In young cattle, *C. pecorum* infections can cause fatal SBE, characterised by encephalomyelitis, systemic infection, and polyserositis (Parkinson et al., 2010; Aiello and Moses, 2012). Clinical signs (Fig. 3) include pyrexia, depression, ptyalism, weight loss, limb stiffness, and neurological signs such as staggering, circling and opis-

[1] See: http://www.mla.com.au/Cattle-sheep-and-goat-industries/Industry-overview/Sheep (accessed 21 September 2015).

[2] 1 Australian $ = approx. £0.46, US$0.71, €0.63 at 21 September 2015.