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Review

Recent advances in understanding the biology, epidemiology and control of chlamydial infections in koalas

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ABSTRACT

The koala (*Phascolarctos cinereus*) is recognised as a threatened wildlife species in various parts of Australia. A major contributing factor to the decline and long-term viability of affected populations is disease caused by the obligate intracellular bacteria, *Chlamydia*. Two chlamydial species infect the koala, *Chlamydia pecorum* and *Chlamydia pneumoniae*, and have been reported in nearly all mainland koala populations. Chlamydial infections of koalas are associated with ocular infections leading to blindness and genital tract infections linked to infertility, among other serious clinical manifestations. Diagnosis can be based on clinical presentation alone, however, it is complicated by the observation that many koala chlamydial infections occur with no overt signs of clinical disease. Instead, accurate diagnosis requires detailed clinical assessment and confirmatory testing by a range of PCR-based assays. Antibiotic treatment for koala chlamydial infection is possible, however, results on its success are mixed. A more practical solution for the protection of diseased populations is the application of a koala *Chlamydia* vaccine, with recent trials indicating promising results. Interestingly, molecular epidemiology studies of koala *C. pecorum* infections and recent comparative genomic analyses of koala *C. pneumoniae* have revealed potential differences in their origin that will have wider ramifications for our understanding of human chlamydial infections and host adaptation of the chlamydiae. This review summarises changes to the taxonomy of koala chlamydial infections and recent advances in our understanding of the epidemiology, diagnosis, treatment, control and evolution of *Chlamydia* infections in this iconic wildlife species.

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1. Koalas: a declining national icon of Australia's biodiversity

The koala (*Phascolarctos cinereus*) is an arboreal herbivorous marsupial and, as the last surviving member of the family *Phascolarctidae*, is an international icon of the rich biodiversity found on the Australian continent. Despite the esteem that is held for this wildlife species, it is generally acknowledged that koala numbers are in a decline across the majority of free-living populations in mainland Australia. Prior to European settlement, the koala's natural range was thought to extend from the eucalyptus forests of North-Eastern Queensland to those of the southern coast of South Australia. Koala populations are now highly fragmented across this range and appear to be declining rapidly in many areas, with one population in South-East Queensland experiencing a 64% decline in the last 10 years and a 51% decline in the last three years (Department of Environment and Resource Management, 2009). Translocation of animals by humans has also led to the establishment of koala populations on islands off the southern and eastern coasts of Australia.

The decline of koala populations across Australia, particularly in previously densely populated habitats along Australia's eastern seaboard, has been attributed to a range of naturally occurring and anthropogenic factors. While bushfire (Lunney et al., 2007) and other factors can impact on koala numbers leading to localised extinctions, the encroachment of human settlement into koala habitats has been estimated to have the most dramatic effect on koala declines. These factors include a loss of habitat due to land clearing (Melzer et al., 2000), motor vehicle traumas (Dique et al., 2003) and dog attacks (Lunney et al., 2007). Of the multiple threatening processes that have been linked to koala declines in peri-urban populations, however, recent modelling has suggested that control of disease is the most important in terms of introducing strategies to bring wild koala populations back to stability (Rhodes et al., 2011). While other pathogens have been reported in the koala, including an endogenous Koala retrovirus (KoRV; Tarlinton et al., 2005; Simmons et al., 2012), and a series of koala and marsupial-specific trypanosomes (McInnes et al., 2011), the most important pathogen of this wildlife species is *Chlamydia*.

Species in the genus *Chlamydia*, like other members of the order *Chlamydiales*, share a biphasic developmental cycle and require growth in a unique host cell membrane-bound inclusion. Paradoxically, despite this unique evolutionary niche, these bacteria are ubiquitous and have adapted to infect and cause a range of significant diseases in domesticated animals including livestock species such as cattle, sheep and pigs and household animals such as guinea pigs and cats, as well as humans. Chlamydial infections of the koala are easily the most intensively studied of any wildlife species and, apart from avian and zoonotic infections caused by *C. psittaci*, of any animal host altogether. As such, koala chlamydial infections serve as an important model for understanding the biology of the host-pathogen interaction, the epidemiology and the impact of chlamydial disease on a native species. Despite this, only a limited number of reviews have been published on this topic (Brown et al., 1987; Whittington, 2001). Recent years have seen major advances in our understanding of the taxonomy and evolution, diagnosis, treatment, control and epidemiology of *Chlamydia* in koalas and these topics and the remaining challenges and future directions in the conservation of these iconic species from chlamydial disease are the subject of this review.

2. The devastating effects of chlamydial disease

Early records indicate that lesions resembling chlamydiosis had been observed in koalas as early as the late 1800s (Mackenzie, 1919, Pratt, 1934, Troughton, 1941). These authors referred to epidemics of disease late in the 1800s and early 1900s, including cystic reproductive tract disease, leading to infertility, and also "ophthalmic disease and periostitis of the skull" (Troughton, 1941). Gordon and McGreevy (1978) suggested that "epidemic disease" was the primary cause of koala population decline in Queensland following the last open season in 1927. Chlamydiae were reported to have been isolated from kerato-conjunctivitis lesions in 1974 (Cockram and Jackson), and from various sites in koalas with kerato-conjunctivitis, rhinitis/pneumonia complex, urinary tract infection, and ascending genital tract infection in female koalas (Brown and Grice, 1984). Although the full range of clinical conditions and syndromes caused by chlamydial infection in koalas has not been comprehensively investigated, the "classical" diseases are relatively well described (Blanshard and Bodley, 2008). These are kerato-conjunctivitis, urinary tract disease, reproductive tract disease, and the rhinitis/pneumonia complex (Fig. 1).

Infection of the mucosal surfaces of the eye results in inflammation, characterised in the early stages by serous discharge, blepharospasm and hyperaemia of the conjunctiva and sclera, progressing to purulent discharge, conjunctival hyperplasia and fibrosis. One or both eyes may be affected. In some severe and chronic cases, the cornea is affected by opacity caused by oedema and pannus with or without pigmentation, and severe end-stage cases may have rupture and collapse of the globe. Clinical presentations are highly variable in severity and chronicity between koalas, and lesions may be active, with copious exudate, or inactive, with no exudate and mature scarring (Wan et al., 2011). Blindness may occur because of the physical barrier to sight caused by bulging and hyperplasia of the conjunctiva, by chronic pathological changes affecting the cornea, such as oedema, scarring and pannus, and in rare cases, by severe ophthalmitis and rupture of the globe. Mild and acute cases respond well to treatment, but the therapeutic efficacy in chronic and severe cases is dependent upon the degree of fibrosis affecting the cornea and conjunctiva. Extensive and advanced fibrosis of the conjunctiva leads to reduction in the size of the palpebral fissure and sometimes entropion, and scarring of the cornea may lead to severe impairment of sight, or blindness. Acute and chronic active cases of kerato-conjunctivitis tend to have higher levels of shedding of chlamydial organisms than chronic inactive cases,