



Review paper

From *Haemobartonella* to hemoplasma: Molecular methods provide new insights

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Abstract

Hemotropic mycoplasmas (aka hemoplasmas) are the causative agents of infectious anemia in numerous mammalian species. Originally known as *Haemobartonella* and *Eperythrozoon* species, these organisms have been reclassified within the genus *Mycoplasma*. The development of new molecular assays has expanded our knowledge of this heterogeneous group of agents and allowed us to study their epidemiology and pathogenesis. The present review summarizes recently gained insights into feline hemotropic mycoplasmas, formerly known as *Haemobartonella felis*. Besides the two initially identified feline hemoplasma species, *Mycoplasma haemofelis* and *Candidatus Mycoplasma haemominutum*, we discovered a third novel hemoplasma in a Swiss pet cat; preliminary results suggest that the pathogenic potential of the latter agent depends on cofactors. In applying PCR-based assays, feline hemoplasma infections have been documented in domestic cats and wild felids worldwide. Differences between the three hemoplasmas in regard to response to antibiotic treatment and establishment of a carrier status have been reported. Additionally, besides an ostensible vector-borne transmission, direct transmission by aggressive interaction of cats or interspecies transmission might play a role in the epidemiology of these organisms. Based on a potential vector-borne and interspecies transmission, a zoonotic potential of hemoplasmas should be further investigated.

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Keywords: *Haemobartonella felis*; Hemoplasma; *Mycoplasma haemofelis*; *Candidatus Mycoplasma turicensis*; Real-time PCR; Treatment

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1. Introduction

In recent years, there has been growing interest in hemotropic mycoplasmas (aka hemoplasmas), the causative agents of infectious anemia in a variety of mammalian species. Infections with these pathogens can induce acute hemolysis, associated with anorexia, lethargy, dehydration, weight loss and sudden death of infected animals. The inability to culture these agents outside the host has limited the possibilities to investigate hemotropic mycoplasmas. However, the development of specific polymerase chain reaction (PCR) assays for the sensitive diagnosis of hemoplasma infections has allowed us to study the epidemiology and pathogenesis of these agents in more detail.

The present review aims to summarize recently gained insights into feline hemotropic mycoplasmas, formerly known as *Haemobartonella felis*. By applying PCR-based methods, hemoplasma infections in pet cats and wild felids have been diagnosed worldwide. Reviews on two feline hemoplasmas, *Mycoplasma haemofelis* and Candidatus *Mycoplasma haemominutum*, have already been published (Messick, 2003; Sykes, 2003; Tasker, 2006). Thus, the present article aims to give extensive details on the third novel feline hemoplasma, Candidatus *Mycoplasma turicensis*. For comprehensive understanding, data on *M. haemofelis* and Candidatus *M. haemominutum* are also listed, with

focus on new results regarding potential reservoir and transmission routes of the agents and different responses to antibiotic treatment.

2. Phylogenetic analyses and reclassification

The agents formerly known as *Haemobartonella* and *Eperythrozoon* are small (<1 µm), pleomorphic bacteria that attach to red blood cells (RBCs) of various mammalian species. Until recently, they were classified as rickettsial organisms, based on their small size, Gram-negative staining properties, RBC parasitism and proposed transmission by blood-sucking arthropods (Kreier and Ristic, 1984). However, their molecular characterization primarily based on 16S rRNA gene sequencing revealed a closer relationship to members of the class *Mollicutes* (Neimark et al., 2001; Rikihisa et al., 1997). Further supported by some phenotypic characteristics, such as small size of the organisms and their genome, lack of a cell wall and flagella, resistance to penicillin and susceptibility to tetracycline, the genera *Haemobartonella* and *Eperythrozoon* were reclassified within the genus *Mycoplasma* as hemotropic mycoplasmas (Neimark et al., 2001). This new cluster, within the mycoplasmas, is most closely related to the fastidiosum cluster of organisms, which contains glucose-fermenting mycoplasmas from horses (*M. fastidiosum*) and guinea pigs

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