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Invited Review

A review of *Theileria* diagnostics and epidemiology

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ABSTRACT

An extensive range of serological and molecular diagnostic assays exist for most of the economically important *Theileira* species such as *T. annulata*, *T. equi*, *T. lestoquardi*, *T. parva*, *T. uilenbergi* and other more benign species. Diagnostics of *Theileria* is considered with regard to sensitivity and specificity of current molecular and serological assays and their use in epidemiology. In the case of serological assays, cross-reactivity of genetically closely related species reduces the use of the gold standard indirect fluorescent antibody test (IFAT). Development of antigen-specific assays does not necessarily address this problem, since closely related species will potentially have similar antigens. Even so, serological assays remain an important line of enquiry in epidemiological surveys. Molecular based assays have exploded in the last decade with significant improvements in sensitivity and specificity. In this review, the current interpretation of what constitute a species in *Theileria* and its impact on accurate molecular diagnostics is considered. Most molecular assays based on conventional or real-time PCR technology have proven to be on standard with regard to analytical sensitivity. However, consideration of the limits of detection in regard to total blood volume of an animal indicates that most assays may only detect >400,000 parasites/L blood. Even so, natural parasitaemia distribution in carrier-state animals seems to be above this limit of detection, suggesting that most molecular assays should be able to detect the majority of infected individuals under endemic conditions. The potential for false-negative results can, however, only be assessed within the biological context of the parasite within its vertebrate host, *i.e.* parasitaemia range in the carrier-state that will support infection of the vector and subsequent transmission.

Contents

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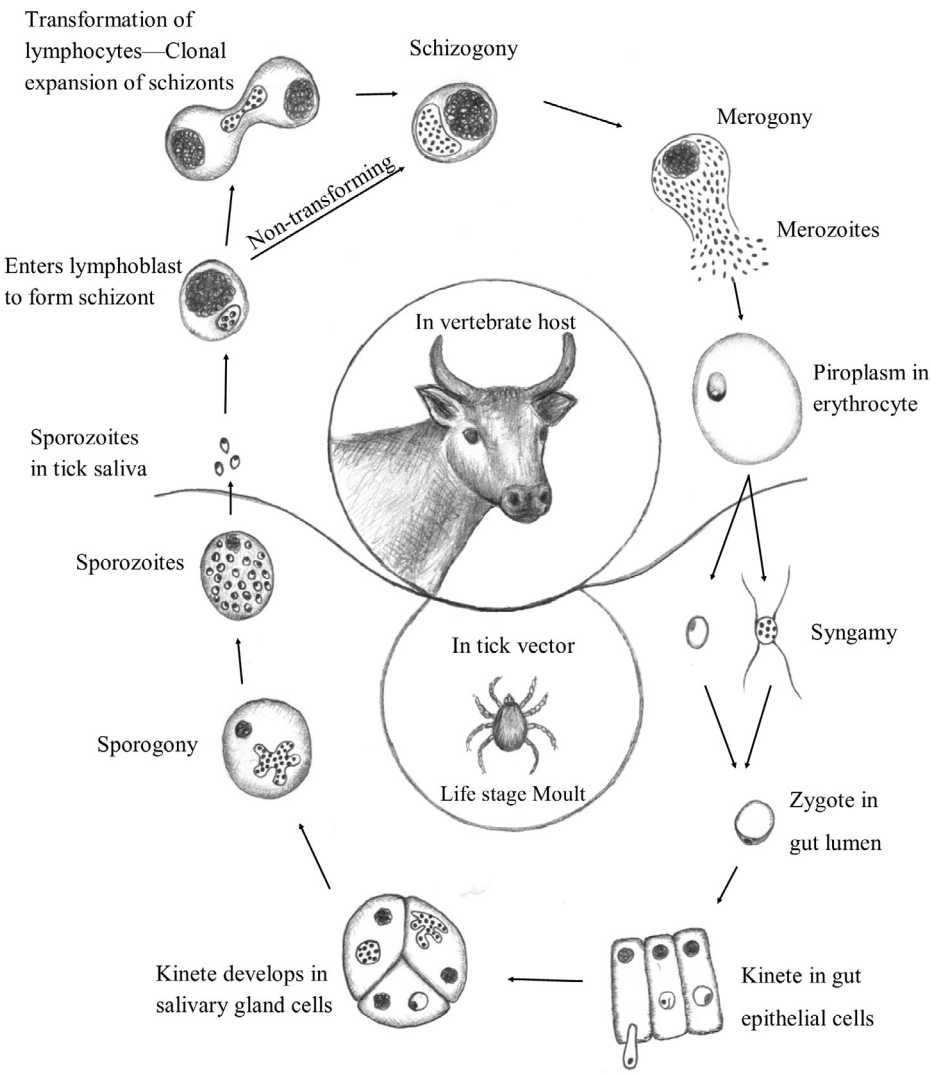

Fig. 1. A generalised lifecycle for the *Theileria* using *T. parva* as example.

1. Introduction

The phylum Apicomplexa comprises a large group of complex eukaryotic organisms known to be obligate parasites of vertebrates and invertebrates. These organisms share a common characteristic of having an apical complex which contains secretory organelles considered to be involved in invasion and/or establishment of the parasite in the mammalian or invertebrate host (Bishop et al., 2004). The phylum is divided into four principal groups; the Coccidia, Gregarinasina (gregarines), Haemosporida (haemosporidians) and the Piroplasmorida (piroplasmids) (Adl et al., 2012). The Piroplasmorida comprises two main genera (*Babesia* and *Theileria*) responsible for the economic important diseases of domestic and wild animals. New species of the piroplasmids are still being discovered and their full biology is not completely documented yet. Many of this order's parasites were formerly classified based on morphology, host cells in which schizogony occurs, the observation of piroplasms in the red blood cells associated with disease manifestation and host-vector specificity (Barnett, 1977; Uilenberg, 2006). The genus *Theileria* is distinguished by infection of leukocytes by sporozoites, maturation of schizonts into merozoites and subsequent infection of red blood cells to form piroplasms (Uilenberg, 2006).

A generalised lifecycle for the *Theileria* genus include secretion of infective sporozoites during tick feeding into the feeding site (Fig. 1). Sporozoites then infect leukocytes and multiply by merogony, after which merozoites are released, which invade red blood cells thereby establishing the piroplasm stage. During a next feeding cycle, larval or nymphal vector ticks ingest piroplasms and the released parasites undergo syngamy in the tick gut, forming a zygote, the only diploid stage. The zygote divides into motile kinetes that infect the tick gut epithelial cells and migrate to the haemolymph and subsequently infect the salivary glands. After moulting and commencement of feeding by the tick, sporogony results in the multiplication of sporozoites in the salivary gland acini before injection into the feeding site by nymphs or adult ticks (McKeever, 2009).

The *Theileria* species infect a wide range of both domestic and wild animals and are transmitted by ixodid ticks of the genera *Amblyomma*, *Haemaphysalis*, *Hyalomma* and *Rhipicephalus*. Most of these ticks are renowned for the large economic losses they cause to the agricultural industry due to disease outbreaks, mortalities, damage to hides and poor production in domestic animals (Bishop et al., 2004). The expansion of wildlife husbandry and conservation has also made *Theileria* of wildlife important subjects of study. The *Theileria* can be grouped into schizont "transforming" and