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Cryptosporidium — What is it?

R.C. Andrew Thompson [a,*], Wan H. Koh [a], Peta L. Clode [b]

[a] School of Veterinary and Life Sciences, Murdoch University, South Street, Murdoch, WA 6150, Australia
[b] Centre for Microscopy, Characterisation, and Analysis, The University of Western Australia, Crawley, WA 6009, Australia

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ABSTRACT

Cryptosporidium is a ubiquitous enteric protozoan pathogen of vertebrates, and although recognised as a cause of disease in humans and domestic animals for over 50 years, fundamental questions concerning its biology and ecology have only recently been resolved. Overwhelming data now confirm that, like its close relatives, *Cryptosporidium* is a facultatively epicellular apicomplexan that is able to multiply in a host cell-free environment. These data must be considered in the context of the phylogenetic reclassification of *Cryptosporidium* from a coccidian to a gregarine. Together, they dictate an urgent need to reconsider the biology and behaviour of *Cryptosporidium*, and perhaps help to explain the parasite's incredible genetic diversity, distribution and host range. Improved imaging technologies have complemented phylogenetic studies in demonstrating the parasite's affinities with gregarine protozoa and have further supported its extracellular developmental capability and potential role as an environmental pathogen. These advances in our understanding of *Cryptosporidium* as a protozoan pathogen are examined with emphasis on how they may influence control strategies in the future.

Contents

* Corresponding author.
E-mail address: a.thompson@murdoch.edu.au (R.C.A. Thompson).

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1. Introduction

Cryptosporidium has been an enigma since it was first described by Edward Tyzzer in 1907 in the gastric glands of a mouse (Tyzzer, 1907). He placed it in the coccidian family Asporocystidae reflecting the lack of sporocysts in the oocyst (*i.e.* naked sporozoites) and what were presumed to be the possession of similar life cycle features (Levine, 1988). It is interesting when going back to Tyzzer's morphological description, how atypical it is for a coccidian, in particular the possession of an organ of attachment - a structure that has only recently been given the attention it clearly warrants in terms of considering *Cryptosporidium*'s true affinities.

For the next 70 years following Tyzzer's description, *Cryptosporidium* continued to be viewed as a curiosity. More species were described largely on the basis of host occurrence, but the parasite was always viewed as atypical. This was not only because of its oocyst and attachment organ, but also because of the ability of unshed oocyst to produce autoinfections, and the extracytoplasmic association with its host cell with endogenous developmental stages confined to the apical surfaces of epithelial cells, a characteristic now referred to as epicellular (Barta and Thompson, 2006; Clode et al., 2015; Thompson et al., 2005; Valigurová et al., 2007). However, these fascinating biological peculiarities were overshadowed by the serious public health consequences of opportunistic infections with *Cryptosporidium* that emerged in the 1980's, principally taking advantage of the weakened immune systems of AIDS patients (Checkley et al., 2014). This health emergency brought a sharp focus on the need for chemotherapeutics and quickly confirmed *Cryptosporidium*'s complete insensitivity to anti-coccidial drugs (Tenter et al., 2002; Thompson et al., 2005).

Cryptosporidium's direct life cycle is enhanced by the existence of resistant oocysts that are capable of extended periods of survival in the environment. Thus, apart from person to person transmission by the faecal-oral route, oocysts can be transmitted in water or contaminated food (FAO, 2014; Gajadhar et al., 2015). The emergence of cryptosporidiosis as an opportunistic infection put immense pressure on water utilities to ensure they provided *Cryptosporidium*-free water. The demands of water utilities for improved methods of surveillance to detect but also characterise isolates of *Cryptosporidium* was the main driver for research on the molecular epidemiology of *Cryptosporidium* infections (Cacciò et al., 2005; Thompson, 2003).

As a consequence, the biology and host-parasite relationship of *Cryptosporidium* have not received the attention they should have given the uniqueness of this organism. Recent developments in *in vitro* cultivation, life cycle propagation, phylogenetics, and imaging technologies have served to illustrate the need to re-evaluate many aspects of the biology and ecology of *Cryptosporidium* (Clode et al., 2015; Karanis and Aldeyarbi, 2011).

In this short review, we have tried to highlight the important developments over the last 100 years that have culminated in the recognition that *Cryptosporidium* is: a ubiquitous, pleiomorphic, facultatively epicellular gregarine protozoan, capable of extended existence in the environment, that is elusive, opportunistic and zoonotic with the *potential* to cause disease and death in humans and domestic animals.

2. Transmission — the importance of the environment

Direct transmission *via* the faecal/oral route is likely to be the most common form of transmission, whether zoonotic (see below) or direct person-to-person (FAO, 2014; Checkley et al., 2014). Waterborne outbreaks have been a major issue in the epidemiology of cryptosporidiosis throughout the world and a major financial burden for water utilities in developed countries. The problem has recently been shown to be exacerbated by the potential for biofilms to act as reservoirs of *Cryptosporidium* in which oocysts can not only be trapped and subsequently released into the water supply, but can also act as nutrient-rich environments

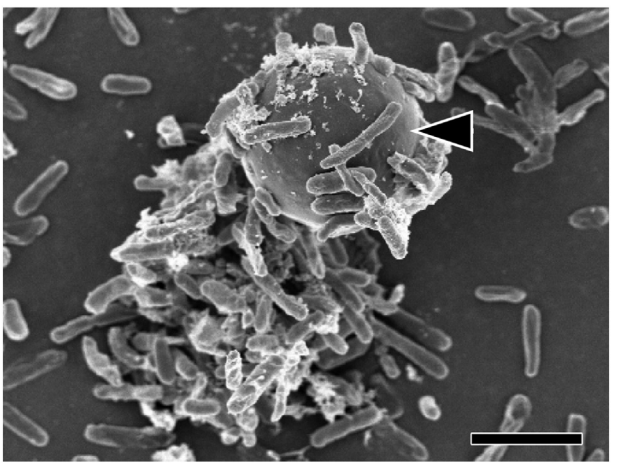

Fig. 1. Scanning electron micrograph of an oocyst of *Cryptosporidium* (arrowhead) within a *Cryptosporidium* – exposed *Pseudomonas aeruginosa* biofilm (see Koh et al., 2014 for methods). Scale bar = 3 μm.

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