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Zoonotic Enteric Protozoa

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Abstract

A growing number of enteric protozoan species are considered to have zoonotic potential. Their clinical impact varies and in many cases is poorly defined. Similarly, the epidemiology of infections, particularly the role of non-human hosts, requires further study. In this review, new information on the life cycles and transmission of *Giardia*, *Cryptosporidium*, *Entamoeba*, *Blastocystis* and *Balantidium* are examined in the context of zoonotic potential, as well as polyparasitism and clinical significance.

Keywords: Enteric protozoa, Zoonoses, Transmission, Foodborne, Polyparasitism, Clinical significance, *Giardia*, *Cryptosporidium*, *Entamoeba*, *Blastocystis*, *Balantidium*.
1. Introduction

Humans are susceptible to infection with numerous species of protozoa that colonise the intestinal tract. An increasing number of these protozoa are being shown to have zoonotic potential although their clinical significance varies. Apart from *Entamoeba histolytica* and *Balantidium coli*, they do not invade the mucosal tissues or other organs. *Cryptosporidium* has an epicellular association with the host cell, principally in the mucosal epithelium, but cannot be considered to be invasive. In most cases, the pathogenesis of most enteric protozoa is poorly understood and with some species, such as *E. coli*, opinions vary as to whether they should be considered as parasites.

In this review, we update the latest information on individual species of enteric protozoa, and then examine transmission, polyparasitism and clinical significance on a broad scale.

2. The parasites

2.1. *Giardia*

The molecular characterisation of *Giardia* isolates from different species of mammalian hosts throughout the world has confirmed the existence of host specific species and two species with broad host ranges and which are zoonotic (Table 1). A revised taxonomy has consequently been proposed which largely reflects the species
nomenclature reported by early workers in the field (Monis et al., 2009; Thompson and Monis, 2011).

The application of multilocus genotyping to *Giardia* from human and other mammalian hosts in different parts of the world has clearly demonstrated the occurrence of zoonotic species in human and non-human hosts (dogs, cats, livestock and wildlife) in the same geographical areas supporting the potential for zoonotic transmission (rev. in Thompson, 2011; Leonhard et al., 2007). Although such studies do not provide evidence of actual zoonotic transmission, a number of studies in defined endemic foci have provided convincing evidence involving dogs and humans (Traub et al., 2004; Inpankaew et al., 2007; Salb et al., 2008). Although the focus of these studies has been on the dog as a reservoir of human infection, several reports demonstrate that ‘reverse zoonotic transmission’ (zooanthroponotic) is an important factor that must be considered in understanding the epidemiology of *Giardia* infections. Humans are considered to be the source of infection in non-human primates and painted dogs in Africa, marsupials in Australia, beavers and coyotes in North America, muskoxen in the Canadian arctic, house mice on remote islands and marine mammals in various parts of the world (Graczyk et al., 2002; Sulaiman et al., 2003; Moro et al., 2003; Appelbee et al., 2005, 2010; Kutz et al., 2008; Dixon et al., 2008; Teichroeb et al., 2009 Thompson et al., 2009, 2010b, 2010; Ash et al., 2010; Johnston et al., 2010). These reports raise important issues for conservation. This is because we do not understand the impact *Giardia* may have on what are possibly naïve hosts that may have been exposed to the parasite relatively recently as a consequence of habitat disturbance and human encroachment (Thompson et al 2010a; Johnston et al., 2010). In contrast, in Aboriginal communities in isolated regions of
northern Australia, reverse zoonotic transmission undoubtedly occurs between
humans and dogs but the fact that the dogs are frequently infected with their own
host-adapted species of *Giardia, G. canis*, demonstrates that competitive interactions
likely limit opportunities for zoonotic species to establish in dogs (Hopkins et al.,
1997, 1999; Thompson and Monis, 2004). However, the fact that dogs have contact
with young children passing *Giardia* cysts, as well as discarded nappies/diapers,
means that dogs are likely to act as mechanical transmitters of zoonotic *Giardia* since
their coats are likely to be contaminated with cysts.

Although competitive interactions between different species/assemblages of *Giardia*
has been proposed to explain the predominance of single assemblage infections in
both dogs and cattle, this may reflect the consequences of mixed infections in
endemic foci where the frequency of transmission is very high. In other situations
where transmission is sporadic mixed infections may co-exist and have been
increasingly reported from multilocus studies in several countries in humans, dogs
and cattle (e.g., Hussein et al., 2009; Sprong et al., 2009; Dixon et al., 2011; Covacin
et al., 2011).

The two zoonotic species/assemblages of *Giardia* are geographically widespread and
as more isolates are genotyped some patterns are emerging on host occurrence.
Recent studies in dogs have shown that it is not possible to extrapolate from one
geographical region to another in terms of the prevalence or species/assemblage
composition of *Giardia* infections in dogs (Ballweber et al., 2010; Covacin et al.,
2011). Until recently, comprehensive data on the assemblage distribution of *Giardia*
in dogs in the USA was not available, and studies in Europe had suggested that
assemblage B has a predominantly human distribution (Sprong et al., 2009).

However, a recent study of dogs infected with *Giardia* in the USA found a higher frequency of infections with assemblage B than assemblage A, which has not been reported elsewhere (Covacin et al., 2011). This suggests that in North America at least, we cannot assume that assemblage A is the most common of the zoonotic assemblages found in non-human hosts. Indeed in wildlife, assemblage B often predominates (e.g., Johnston et al., 2010) whereas in cattle, assemblage A is most often reported (Sprong et al., 2009). However, there is extensive genetic sub-structuring within assemblage B, and it is possible that some subgroups are commonly associated with zoonotic infections than others. As regards *Giardia* infections in humans, there is some evidence of geographic sub-structuring (Wielinga et al., 2011) and assemblage B may be more common in isolated and/or community settings where the frequency of transmission is high (Thompson 2000). Under such circumstances, the parasite is likely to be exposed to greater selection pressure in terms of exposure to anti- giardial drugs and competitive interactions which might explain why evidence of recombination in *Giardia* is mostly confined to assemblage B isolates (Lasek-Nesselquist et al., 2009; Thompson and Monis 2011).

It is still not yet clear whether the different species/assemblages of *Giardia* are associated with differences in pathogenesis. Although differences have been reported in human populations infected with assemblage A vs B, no clear picture has emerged (Thompson and Monis 2011). This may be particularly relevant to the two main disease syndromes of diarrhoea and failure to thrive. Similarly, it is not known whether there is any difference in the clinical outcome in dogs infected with the zoonotic assemblages or *G. canis*.
2.2. Cryptosporidium

Current evidence indicates that the main reservoirs of zoonotic Cryptosporidium remain livestock, with the potential transmission of C. parvum (= C. pestis [see Slapeta 2011]), including the so-called cervine genotype, to humans via contaminated water or through direct contact with livestock (Robertson et al 2010; Gormley et al., 2011). Sub-genotyping continues to reveal genetic sub-structuring within C. parvum but whether this is reflected in variation in host specificity and zoonotic potential remains unclear. The recent demonstration of zoonotic transmission to humans in the U.K of a newly described genotype of Cryptosporidium from rabbits (Chalmers et al., 2009) has raised concerns that humans may be at risk of Cryptosporidium infection from rabbits in other geographical areas, as recently proposed in Australia where the rabbit genotype has been identified (Nolan et al., 2010). Although given a new species name, C. cuniculi, by Robinson et al (2010), it is genetically very close to C. parvum and C. hominis and thus it may be prudent to reconsider the taxonomic status of all three ‘species’ in the future, particularly given the intra-specific genetic variability that has been described. In contrast, available evidence suggests that the evolving nomenclature for what appear to be host specific forms in different species of domestic and wild animals, is likely to be stable and largely reflective of the early taxonomy (see O’Donoghue, 1995) proposed before the advent of molecular characterisation.

Phylogenetically, Cryptosporidium has been shown to have closer affinities to gregarine protozoa than the coccidians (Barta and Thompson 1996; Borowski et al.,
2010). This is reflected in the life cycle, developmental biology, metabolism and host parasite relationship of *Cryptosporidium* and will require a reappraisal of its biotic potential, particularly in terms of survival, particularly in aquatic environments.

2.3. *Entamoeba*

Of the zoonotic amoebae, *Entamoeba histolytica* is undoubtedly of most clinical significance and is considered by some authorities as the only amoeba parasitic in the human intestine (Schuster and Visvesvara, 2004). However, the public health risk from zoonotic transmission of *E. histolytica* would appear to be minimal. Dogs can be a potential source of human infections following coprophagy of human faeces, although this reverse zoonosis is unlikely to result in significant environmental contamination since *E. histolytica* rarely encysts in dogs (Eyles et al., 1954; Barr, 1998). Similarly, *E. histolytica* is found in non-human primates (Schuster and Visvesvara, 2004) but the risk to public health would appear to be minimal as such infections appear to again reflect reverse zoonosis.

A number of other potentially zoonotic species of *Entamoeba* have been reported in humans including *E. coli*, *E. polecki* and *E. hartmanni* (Meloni et al., 1993; Stensvold et al., 2011). They have generally been considered to be ‘non-pathogenic’ and ‘commensals’ but increasing evidence of their widespread and common occurrence, particularly as co-infections with other enteric protozoa and helminths, warrants a re-evaluation of their potential clinical significance. Of the three species, *E. coli* is one of the most commonly reported enteric protozoa in human surveys (Chunge et al., 1991; Ouattara et al., 2008; Youn, 2009; Boeke et al., 2010), and apart from non-human
primates (e.g. Howells et al., 2011) has been recovered from dogs and marsupials (Campos Filho et al., 2008; Youn, 2009). It also exhibits extensive genetic diversity with at least two major subtypes. Although previous reports have considered *E. polecki* to be zoonotic (Barnish and Ashford, 1989), recent molecular studies suggest this species is restricted to humans whereas *E. hartmanni* is potentially zoonotic with infections reported in non-human primates (Stensvold et al., 2011).

2.4. *Blastocystis*

*Blastocystis* is an emerging pathogen in terms of its association with disease and zoonotic potential (Vassalos et al., 2008; Boorom et al., 2008; Parkar et al., 2010). Now that robust molecular tools are available to detect and characterise *Blastocystis*, it has been shown to be both more common and genetically diverse than previously envisaged (Parkar et al., 2010). *Blastocystis* is a ubiquitous parasite of humans usually associated with chronic infections, the prevalence of which increases with age. In addition to humans, *Blastocystis* is common in numerous species of wild and domestic animals (Parkar et al., 2007, 2010; Yoshikawa et al., 2008). As has been shown with *Giardia* and *Cryptosporidium*, *Blastocystis* comprises a genetically variable complex of interspecific and intraspecific variants and a stable taxonomy has yet to be established. Humans are susceptible to infection with a variety of genetically distinct subtypes some of which have also been reported in domestic and wild animals (Parkar et al., 2007, 2010; Yoshikawa et al., 2008). Studies in defined endemic foci, such as zoos, have provided convincing evidence of zoonotic...
transmission (Parkar et al., 2010). However, the frequency of zoonotic transmission
and risk factors have still to be clearly defined.

2.5. Balantidium

This is the only ciliate known to cause infections in humans and is considered to be
zoonotic with pigs as the asymptomatic natural reservoir, although other domestic
livestock such as cattle may be infected in some areas (Bilal et al., 2009). Non-human
primates are also susceptible to infection (see Howells et al., 2011) but their role in
zoonotic transmission is likely to be minimal.

Balantidium is most common in tropical and subtropical regions (Zaman, 1998;
Farthing et al., 2003; Owen, 2005) and the risk of infection in humans is in
communities that have a close association with pigs (Schuster and Ramirez-Avila
2008). However, infection in humans is rarely reported (Farthing et al. 2003; Schuster
and Visvesvara, 2004; Conlan et al. 2011). The parasite is invasive in humans and can
cause serious disease but cases are reported sporadically (Schuster and Visvesvara,
2004; Conlan et al., 2011). The low reported prevalences, even in pig rearing
communities (Owen 2005; Kirkoyun Uysal et al., 2009) would suggest that even if
cysts are ingested from the environment, the parasite rarely establishes ‘patent’
infections. However, the only reported waterborne outbreak originating from
contaminated pig faeces, resulted in 110 people infected (Walzer et al., 1973 [in
Farthing]). This would suggest that sporadic and/or isolated infections usually go
unnoticed or that sojourn in water may enhance infectivity to humans in some way.
3. Transmission

3.1. Pathways of transmission

Specific transmission pathways for enteric protozoan parasites can be difficult to determine though some routes are more common than others. Direct transmission via the faecal/oral route is likely to be the most common form of transmission, whether zoonotic (see above) or direct person to person. However, indirect transmission, where infection results through the mechanical transmission of oo/cysts on, for example, flies (Szostakowska et al., 2004) or other animals such as dogs or livestock, or by the contamination of food or water sources (Smith et al., 2007; Karanis et al., 2007; Nyarango et al., 2008), poses a significant threat particularly in the developing world. Quantifying the level of protozoan parasite infection using commonly applied metrics such as the DALY (eg Pruss et al., 2002) is impractical unless gross non-specific estimates are required as distinguishing between all possible sources of infection and the confounding impact of polyparasitism is rarely if ever possible (Payne et al., 2009; King 2010). Epidemiological analysis of focal point contaminations such as water or specific food contamination events can provide good estimates of the spread and impact of parasite infection, but on a global scale, due to the uncertainty caused by the scarcity of data (Payne et al., 2009) the impact of these occurrences remains poorly understood.

3.2. Enhancing transmission
Children are a particularly high risk group for infection with enteric protozoan parasites although the relative risk for infection with different parasites varies between different geographic regions of the world (Figure 1). Interestingly, based on a major review of the number of reports in the scientific literature (Smith and Thompson, unpublished report, Food Safety, Zoonoses and Foodborne Diseases, World Health Organization, Geneva) the risk of infection appears greater within rural environments than within urban areas; presumably because of the increased opportunity for both direct and indirect transmission to occur in areas with poor sanitation and higher contact rates with wildlife and domestic animal reservoirs of infection.

Poor hygiene has been shown to be a crucial factor in enhancing the transmission of enteric protozoa (Ang, 2000; Alvarado and Vasquez, 2006; Diaz et al., 2006; Balciogul et al., 2007; Azian et al., 2007). However, the term ‘poor hygiene’ is broad and does not fully describe the range of risk factors involved.

*Blastocystis, Cryptosporidium, Giardia, Entamoeba* spp, and *Balantidium* can all be transmitted in water, including drinking water sources, recreational water, as well as lakes and streams. The impact of infection obtained from lakes and streams varies greatly depending on geographic location as there exists significant variation in the use of such water bodies throughout the world as well as within regions depending on socioeconomic status. For example the predominant use of lakes and streams in Europe is recreational whereas in Africa or Asia there is a much greater reliance on these water sources for drinking and in the preparation of food and personal hygiene.

Waterborne transmission of parasites in the developed world is therefore more likely...
to be the result of contamination, or a process failure within water utilities, industry or in public places such as swimming pools (Welch, 2000; Stuart et al., 2003; Dawson, 2005; Shields et al., 2008). In the developing world in particular, areas which are prone to flooding face an increased risk of waterborne infection particularly where basic sewerage systems such as long-drop latrines are common. The risk is further increased in those communities and societies where the keeping of animals (pets and livestock) within or near the home is common and the risk of infection with specific parasites including concurrent infections will vary culturally depending on the species of zoonotic reservoir involved (Hunter and Thompson, 2005).

3.3. Foodborne transmission

Cases of foodborne transmission have until recently been difficult to determine, and linking infection to a contaminated food source remains so for the majority of scenarios. Small scale outbreaks, where the point of initial contamination may be the result of poor hygiene by an individual resulting in localised foodborne transmission to family members or the immediate community, are extremely common particularly in the developing world. Transmission resulting from contamination of food or drink that leads on to larger scale infections, such as an outbreak of cryptosporidiosis in the USA in 1993 arising from the consumption of infected fresh-pressed apple cider is a relatively much rarer event (Millard et al., 1994). Again, according to reports published in the primary scientific literature, the risk of becoming infected with Blastocystis from contaminated food appears low, although infection arising through poor hygiene practices of food handlers has a potentially much higher infection rate. For example, a survey of 150 apparently healthy food handlers in Bolivar State,
Venezuela, showed that 25.8% (n = 107) were in fact positive for *Blastocystis* (Requena et al., 2003), whereas a review of 103 published reports concerning *Blastocystis* infection between 1990 and 2008 showed that none were able to conclusively ascribe infection to conventional foodborne transmission (Smith and Thompson, unpublished report, Food Safety, Zoonoses and Foodborne Diseases, World Health Organization, Geneva). However, other enteric parasites are readily transmitted on food and in some regions of the world farming and agricultural practices such as the use of human waste for fertilisation and inefficient or absent pasteurisation techniques positively enhance transmission. None the less, the majority of indirect transmission from contaminated food arises from more proximate sources of infection such as infected food handlers and poor hygiene, often resulting from overcrowded living conditions where clean running water is scarce, and also from children and adults with little or no health education.

Foodborne transmission, whether arising as a result of agricultural practices or poor hygiene within households, or by food handlers, is undoubtedly responsible for a significant number of infections every year. Preliminary estimates derived from a literature review of published reports and case notes for *Cryptosporidium* and *Giardia* occurrence, suggest that the number of cases of foodborne transmission resulting in infection by *Giardia* range from 13 million in the WHO derived Eastern Mediterranean region (EMR) to 76 million in the Western Pacific Rim (WPR) region (Fig 1). Similarly, preliminary estimates for *Cryptosporidium* suggest there may be as many as 6 million cases of foodborne transmission annually in the EMR region and up to 27 million in the African region. However, these estimates must be interpreted with extreme caution as the majority of publications upon which most estimates are
based simply do not, or cannot, ascribe infection to a particular source or event such as contact with contaminated food. Transmission between humans, either involving intermediate vessels such as contaminated food or water, or via direct contact, is ultimately responsible for most reported cases, with zoonotic parasites and parasite strains as well as zoonotic sources of human strains also a major source of infection in many parts of the world (Thompson 2000; Feltus et al., 2006; Ng et al., 2008; Thompson et al., 2008).

4. Polyparasitism

The clinical impact of zoonotic enteric protozoan infections is greatest in the developing world where inadequate sanitation, poor hygiene and proximity to zoonotic reservoirs, particularly companion animals and livestock are greatest. In such circumstances, it is not surprising that infections with more than one species of enteric protozoan is common, and in fact single infections are rare (see above).

Unfortunately, the impact on health of such concurrent/co-infections has not been adequately taken into account. Awareness of the significance of polyparasitism (concurrent/concomitant infections) in terms of malaria, schistosome infections and more recently gastrointestinal (GI) helminths, is now well established (Cox, 2001; Pullan and Brooker, 2008; Midzi et al., 2008; Koukounari et al., 2010; Supali et al 2010). However, the impact of polyparasitism in the context of enteric protozoan infections has not been considered (Ouattara et al., 2008).

Enteric protozoan infections are components of a complex ecological system, shared with helminths and bacteria. As such, we should not study the components of such an
ecological system in isolation (e.g., see Rohani et al., 2003) especially when considering their impact on disease dynamics (Jolles et al., 2008). Polyparasitism will lead to the stimulation of different components of the immune system that may act synergistically, lead to competitive interactions and/or alter pathogenic behaviour of one or more species (Thompson and Lymbery, 1996; Cox, 2001; Mideo, 2009; Koukounari et al., 2010; Supali et al., 2010). These may have an additive and/or multiplicative impact on nutrition and pathogenicity (Pullar and Brooker, 2008) leading to an increase or decrease in clinical severity, and/or interfere with normal gut microflora.

Current measures of determining the impact on health of parasitic disease (DALY) do not take into consideration the “co-morbidities of polyparasitism” (Payne et al., 2009). Payne and colleagues suggest a new approach where co-infections with more than one infectious agent are defined as a specific disease, for example malaria, hookworm, malaria + hookworm etc. This would appear a logical approach and should be readily achievable with diseases such as malaria and hookworm where the pathogenic mechanisms of the individual aetiological agents are reasonably well understood. This would be much more of a challenge with most of the enteric protozoa since their pathogenesis is still poorly understood, particularly in chronic infections. However, it is an area of future epidemiological research that should be given priority.

Available survey data, mostly from rural areas of developing countries, that provide data on the prevalence of mixed infections with enteric protozoa show that they are the rule rather than the exception and that children are at most risk with the majority of the populations studied infected with at least two species of protozoan (Chunge et
al., 1991; Ouattara et al., 2008; Nematian et al., 2008; Nguiu et al., 2009; Aly and Mostata, 2010). The most commonly represented protozoa in concurrent infections are *Giardia*, *Blastocystis*, and *Entamoeba coli*, which are usually also found with the cestode *Hymenolepis nana* (Chunge et al., 1991; Meloni et al., 1993; Ouattara et al., 2008; Nematian et al., 2008). Chronic helminth infections could have a significant influence over the immune response and hence susceptibility to other pathogens (Rodriguez et al., 1999). This was concluded in the context of GI nematode infections but consideration should also be given to *H. nana* which is rarely found on its own in developing areas of the world and usually co-infects with one or more enteric protozoan species. Depending on the endemic area, *E. histolytica* and *E. dispar* may also occur in mixed infections. In addition, other potentially zoonotic protozoa, such as *Chilomastix mesnili* and *Endolimax nana* that may have been dismissed as having no clinical consequence and not reported, are also probably common (e.g. Chunge et al., 1991) and in the context of polyparasitism should be considered.

5. Clinical significance

The clinical impact of *Entamoeba histolytica* and *Cryptosporidium* in humans are well understood. They have clearly defined individual effects on the host and the resulting morbidity will be worsened in an additive way when other enteric protozoa are present. The severity of *Cryptosporidium* infections is greatest in individuals with an impaired or deficient immune system. Much less is known about the clinical impact of other enteric protozoa particularly in chronic and mixed infections.
The symptoms associated with *Giardia* infections vary greatly but have mostly been documented on the basis of individual infections with the expression of short-lasting diarrhoea the most common manifestation (Eckmann, 2003). However, there is increasing realisation that the clinical impact of *Giardia* is greatest in children, particularly in developing countries or disadvantaged communities where poor hygiene and the proximity of animal reservoirs favour a high frequency of transmission and the establishment of chronic infections (Thompson, 2009). In such situations, nutrition may be suboptimal and *Giardia* infections contribute to poor growth and development (‘failure to thrive’), zinc and iron deficiency, as well as predispose to the development of allergic diseases (Muniz-Junqueira and Queiroz, 2002; Muniz et al., 2002; Nematian et al., 2008; Hesham et al., 2005; Savioli et al., 2006; Thompson, 2008; Boeke et al., 2010; Duran et al., 2010; Quihui et al., 2010). Importantly, diarrhoea is not necessarily a symptom in such chronic infections (Nash et al., 1987; Chunge et al., 1991; Flanagan 1992; Rodriguez-Hernandez et al., 1996; Troeger et al., 2007), which are often shared with enteric parasites that contribute to the syndrome of failure to thrive, such as *Entamoeba coli, Blastocystis* and *Hymenolepis nana* (see above). Reports from around the world suggest there are differences in the clinical outcome in humans of infections with assemblage A (*G. duodenalis*) and assemblage B (*G. enterica*) (Thompson and Monis, 2011). However, it is difficult to directly compare between reported studies because of differences in design and populations sampled. It has been suggested that infections with assemblage A are usually short lasting, acute infections often associated with diarrhoea whereas infections with assemblage B are more common in community settings or localised endemic foci where the frequency of transmission is high.
resulting in chronic infections that may contribute to poor growth (Thompson and
Monis, 2011).

There is now increasing recognition that *Blastocystis* is pathogenic, at least in
humans, although the circumstances and mechanisms associated with disease are not
understood (Boorom et al., 2008). Similarly, the spectrum of disease manifestations
associated with *Blastocystis* infections have yet to be clearly defined. Many of the
documented symptoms are non-specific and may be overlooked but the realisation
that *Blastocystis* is most often associated with chronic infections and that prevalence
increases with age, demonstrates that such symptoms may be indicative of a range of
disorders, often sporadic, not necessarily associated with an enteric pathogen, for
example inflammatory bowel disorders (Boorom et al., 2008). As with *Giardia*, it is
possible that some ‘strains’ of *Blastocystis* are more often associated with overt
disease than others (Boorom et al., 2008). The developmental cycle of *Blastocystis* is
not completely understood. It comprises a range of morphologically pleiomorphic
stages and it is not clear whether all are always represented and whether some are
more pathogenic than others.

Most attention on the clinical effects of zoonotic enteric protozoa has focussed on
infections in humans. Comparatively little is known about the clinical consequences
of infections in domestic animals and livestock.

Although infections with *Giardia*, and to a lesser extent *Cryptosporidium*, are
common in dogs and cats, infections are usually asymptomatic (Thompson et al.,
2008). *Giardia* infection in ruminants is also often asymptomatic, but may also be
associated with the occurrence of diarrhoea and ill-thrift in calves (O’Handley et al., 1999; Geurden et al., 2006), as well as production losses (Olson et al., 1995). In this respect, the effects of polyparasitism, with *Giardia* as one member of an often diverse parasite community in livestock (O’Handley and Olson, 2006), requires further study. Infections with *Cryptosporidium* in calves can be clinically significant with profuse diarrhoea, depression and anorexia, and is often life threatening in housed animals where stress associated with overcrowding may predispose to disease (Thompson et al., 2008).

The impact of enteric protozoa on wildlife is not known, but there is evidence of an association with clinical disease of infections with *Giardia* and *Balantidium* in primates (Graczyk et al., 2002). The stress associated with captivity may further predispose to disease, particularly in the case of infections of *Cryptosporidium* in wildlife. This incredible diversity of species and ‘strains’ of *Cryptosporidium*, *Giardia* and *Balantidium* in wildlife clearly warrants further study in terms of their potential impact on wildlife health. Habitat loss as a result of human encroachment can lead to a variety of stressors (e.g. increased competition for food, mates and refuge, as well as greater exposure to predators) that may exacerbate the clinical consequences of infection with enteric protozoa in wildlife (Thompson et al., 2010a; Johnston et al., 2010; Howells et al., 2011).

6. Conclusions

Although tremendous advances have been made in the development of molecular epidemiological tools, their practical potential in terms of controlling
enteric protozoan infections has yet to be realised. In both developed and
developing countries there has been little progress in identifying risk factors for
infection and understanding the outcomes of infection. This is particularly so for
the developing world where these infections are most common and the
frequency of infection very high. In such environments, the epidemiology of
diseases caused by enteric protozoa is poorly understood in terms of
transmission dynamics and sources of infection. Importantly, we must not
consider enteric protozoan parasites in isolation in terms of impact on their
hosts. A child or dog, on good planes of nutrition, harbouring a single infection
with *Giardia* in a developed country represents a very different host parasite
relationship to that in a developing country where *Giardia* rarely occurs as a
single infection but is accompanied by several other protozoa, nematodes and
cestodes in an environment usually deficient in some way, in terms of nutrients
available to the host. Unravelling the interactions and impact on their hosts in
such circumstances is an important challenge for the future.

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### Table 1.

Proposed and existing species in the genus *Giardia*

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<th>Species</th>
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<tbody>
<tr>
<td><em>G. duodenalis</em> (=Assemblage A)</td>
<td>Wide range of domestic and wild mammals including humans</td>
</tr>
<tr>
<td><em>G. enterica</em> (=Assemblage B)</td>
<td>Humans and other primates, dogs, some species of wild mammals</td>
</tr>
<tr>
<td><em>G. agilis</em></td>
<td>Amphibians</td>
</tr>
<tr>
<td><em>G. muris</em></td>
<td>Rodents</td>
</tr>
<tr>
<td><em>G. ardeae</em></td>
<td>Birds</td>
</tr>
<tr>
<td><em>G. psittaci</em></td>
<td>Birds</td>
</tr>
<tr>
<td><em>G. microti</em></td>
<td>Rodents</td>
</tr>
<tr>
<td><em>G. canis</em> (=Assemblage C/D)</td>
<td>Dogs, other canids</td>
</tr>
<tr>
<td><em>G. cati</em> (=Assemblage F)</td>
<td>Cats</td>
</tr>
<tr>
<td><em>G. bovis</em> (=Assemblage E)</td>
<td>Cattle and other hoofed livestock</td>
</tr>
<tr>
<td><em>G. simondi</em> (=Assemblage G)</td>
<td>Rats</td>
</tr>
</tbody>
</table>
Fig. 1. Estimated prevalence of Blastocystis, Cryptosporidium, Giardia and Entamoeba within children from rural and urban regions for each of the World Health Organisation (WHO) defined regions of the world: European Region (EUR), South-East Asian Region (SEAR), Western Pacific Region (WPR), African Region (AFR), Region of the Americas (AMR) and Eastern Mediterranean Region (EMR).