Giardia

Giardia is most common in situations that support a high frequency of transmission, usually as a result of environmental contamination.

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Related terms:

Nested Gene, Bacterium, Infectious Agent, Parasite, Protozoon, Trophozoite, Entamoeba Histolytica, Salmonella, Cryptosporidium

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Microtubules: in vivo

Scott C. Dawson, Susan A. House, in Methods in Cell Biology, 2010

VII Perspectives

Giardia is not known to produce toxins or specific virulence factors; it is the functioning of the giardial MT cytoskeleton that is essentially the etiologic agent of giardiasis. Perhaps the most important function of the giardial MT cytoskeleton is to promote the attachment of Giardia to the intestinal microvilli via the ventral disc. Beyond its role in pathogenesis, the cytoskeleton is critical for motility, intracellular transport, and cell division. MT dynamics are important during interphase, during cell division, and during encystation/excystation. The pivotal role that the MT cytoskeleton plays in pathogenesis highlights the need for a better understanding of giardial cytoskeletal biology (Elmendorf *et al.*, 2003). Future studies on the giardial MT cytoskeleton are sure to include the high-resolution imaging of complex MT structures such as the ventral disc, the identification of proteins and complexes comprising those novel structures, and the analysis of their function in *Giardia*'s complex biology during interphase and during cell division.

Conventional TEM-based analyses of the cytoskeletal architecture in *Giardia* have formed the basis of our understanding of *Giardia*'s complex ultrastructure, yet these analyses were done before modern methods of cryopreservation such as HPF and 3D cryoET without fixation were developed (Baumeister, 2005; McIntosh *et al.*, 2005;

Subramaniam, 2005). Ultrastructural information derived from these older methods may have common TEM artifacts associated with specimen preparation, choice of fixation chemicals, and the process of thin sectioning itself. One new method of 3D imaging—cryoelectron tomography or cryoET—allows the imaging of native hydrated structures at <5 nm resolution in vitreous ice using liquid ethane. When combined with volume averaging (PEET software) of regular repetitive structures (Baumeister and Steven, 2000), this strategy has permitted the unprecedented visualization of hydrated molecular structures at high resolution, including individual tubulin subunits within a MT. 3D cryoET not only offers better resolution of structures but also minimizes fixation artifacts that could lead to misinterpretations of giardial cytoskeletal architecture.

In terms of the molecular identification of components of the cytoskeleton, only about 100 of the roughly 6000 ORFs identified in the 12 Mb giardial genome (Adam, 2000) are known to encode proteins that associate with the MT cytoskeleton (see Table I). The *Giardia* MT cytoskeleton has several novel structures—the funis, the median body, and the ventral disc (Dawson, 2010), and the *Giardia* genome contains many novel proteins. Thus, there could exist many novel MT-associated proteins in this important and widespread parasitic protozoan. Based on the complexity of cytoskeletal structures in *Giardia* like the ventral disc (Dawson, 2010), one would assume a similar complexity of protein composition. For example, over 250 proteins are known to comprise the flagellar axoneme (Ostrowski *et al.*, 2002; Pazour *et al.*, 2005), yet only 10 proteins are thus far known to localize to the complex MT spiral arrays and associated structure of *Giardia's* ventral disc (Bauer *et al.*, 1999; Peattie, 1990; Weiland *et al.*, 2003; Weiland *et al.*, 2005; Nohria *et al.*, 1992; Weiland and McArthur, 2005) (Davids *et al.*, 2008). As binucleate diploid diplomonads are not amenable to classical forward genetic analyses, the use of morpholino-based knockdowns and the overexpression of cytoskeletal proteins with dominant-negative mutations should aid in assessing the function of novel MT-associated proteins in dynamic cytoskeletal movements.

Finally, one can easily argue that by far the majority of eukaryotic cytoskeletal diversity lies in the protists, reflecting their diverse evolutionary status. Fundamental research in cytoskeletal biology is often initiated in protists. "Non-model" once obscure microbial eukaryotes, such as Tetrahymena and Chlamydomonas, have been developed into robust experimental systems that have made profound contributions toward our understanding of cytoskeletal functioning and dynamics (Cande and McDonald, 1985; Gibbons and Rowe, 1965; Greider and Blackburn, 1987; Salisbury *et al.*, 1988) and flagellar biology. While *Giardia* has complex and novel cytoskeletal arrays, other protists mirror this complexity. Thus, the analysis of the giardial MT cytoskeleton should continue to inform basic studies of MTs in other eukaryotes.

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Gene Rearrangement, Eukaryotic

G. Palaguachi, L.A. Katz, in Brenner's Encyclopedia of Genetics (Second Edition), 2013

Karyotype Variability: *Giardia*

Giardia, a microbial eukaryote that has lost many features of eukaryotic cells (i.e., absence of mitochondria, reduced small subunit rRNAs), is a parasite that can cause diarrhea in humans. The number and size of chromosomes (karyotype) that each Giardia isolate possesses in its genome can vary due to the rearrangement and/or duplication of whole and partial chromosomes. For example, in *Giardia lamblia*, the number of chromosomes or ploidy levels can change depending on its life cycle. Since *G. lamblia* has two identical nuclei that are transcriptionally active, the change in ploidy levels can affect gene expression. Furthermore, there seems to be a significant difference in chromosome size in *Giardia* isolates. The lack of a fixed karyotype in *Giardia* might also help enhance its drug resistance due to the change in phenotype as well as avoid the host's immune system.

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Host defenses to protozoa

Peter C. Melby, Gregory M. Anstead, in Clinical Immunology (Fourth Edition), 2013

Innate immunity

Giardia lacks catalase, superoxide dismutase, and glutathione reductase, so it has limited capacity to neutralize reactive oxygen species produced by intestinal epithelial cells. Nitric oxide, produced by both epithelial cells and macrophages, has giardicidal effects; however, Giardia may circumvent this defense by competing with these host cells for arginine uptake.[34] The antimicrobial peptide defensin is produced by Paneth cells and thus can also participate in host defense against *Giardia*. Few macrophages are found in the intestinal mucosa during giardiasis, which suggests they do not play an important role in the innate immune response. The infection is rare in breast-fed infants because breast milk contains free fatty acids lethal to *Giardia* cysts and, in endemic areas, anti-*Giardia* antibodies.

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Immunoassay Applications in Veterinary Diagnostics

Thomas P. O'ConnorJr., ... Erwin Workman, in The Immunoassay Handbook (Fourth Edition), 2013

Classification of organism/pathogenesis

Giardia are protozoan parasites that infect a range of hosts including dogs, cats, and humans. Giardia occur in two forms, the trophozoite and the cyst form. The trophozoite is the motile form found in the intestinal tract and the cyst form is the resistant stage responsible for transmission. Although, most of the cats and dogs shedding Giardia do not show clinical signs of disease, infection can induce illness in some animals. Younger, immunosuppressed animals and those living in crowded environments are at the highest risk of showing clinical disease. The primary clinical signs of infection include chronic diarrhea and weight loss (Scorza and Lappin, 2012).

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Ultrastructural Diagnosis of Infection

Alton B. FarrisIII, ... G. Petur Nielsen, in Diagnostic Pathology of Infectious Disease, 2010

Giardia lamblia

Giardia *lamblia* (Figs. 5-48 and 5-49) consists of pear-shaped trophozoites, alternatively convex dorsally and concave ventrally, measuring 9.5 to 21 μm long and 5 to 15 μm wide, that are normally present free in the small intestine and in cysts in the large intestine. *Giardia* is binucleate, with symmetrically spaced nuclei and a prominent karyosome, and has four pairs of flagella adjacent to an adhesion disc. *Giardia* has a rigid cytoskeleton with evenly spaced microtubules linked by microribbons. It does not have mitochondria, peroxisomes, endoplasmic reticulum, or nucleoli. Morphologic types of *Giardia* can be distinguished ultrastructurally, as can the stage of the life cycle (i.e., free trophozoites in the small bowel and cysts in the large bowel and feces). Mature cysts are 8 to 12 μm long and 7 to 10 μm wide

and have four nuclei, a dense wall, dense cytoplasm with ribosomes and glycogen granules, and peripheral vacuoles or tubules.[1]

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Parasitic infestation

John Walker-Smith MD(Syd), FRCP(Ed), FRCP(Lond), FRACP, in Diseases of the Small Intestine in Childhood (Third Edition), 1988

Prevalence

Giardia lamblia is endemic in most countries of the world, especially in warm climates and countries with poor sanitary practice. Prevalence rates approach 10% in some areas of the USA and Europe (Petersen, 1972) and up to 30% in some areas of the developing world. All members of a cohort of rural Guatemalan children suffered at least one episode of Giardia infestation by the age of 3 years (Farthing *et al*. (1986a, b). Giardiasis is probably the most common water-borne disease in the USA. Contaminated surface water and inadequate water treatment are probably the most important factors in the spread of disease. Epidemiological studies suggest that the beaver and other wild and domestic animals are possible reservoirs of *Giardia lamblia*. Person-to-person transmission is important within families in nurseries, day-care centres and other residential institutions. The prevalence of giardiasis may be very high in children's institutions; for example 40% in one series reported from Australia (Court and Stanton, 1959).

Carswell, Gibson and McAllister (1973) have examined a large group of Glasgow children for *Giardia lamblia*. They studied, first, a control group of inpatients who had no clinical evidence of either giardiasis of coeliac disease; secondly, a group of children with coeliac disease; and thirdly a group of children investigated for coeliac disease but in whom this diagnosis was excluded. There was no difference in the frequency of detection of giardia (16-17%) in the stools of these three groups of children. Giardia was also sought in the duodenal juice and in small intestinal biopsy specimens from children in the second two groups and it was detected in a further 13 children. The protozoon was more common in males and in children from the lower socio-economic groups.

This high prevalence contrasts with the findings at the Queen Elizabeth Hospital in 1973 where on only one occasion out of 115 duodenal intubations was *Giardia lamblia* detected in the duodenal juice. At the Royal Alexandra Hospital, giardia was found on six occasions out of 120 duodenal intubations in 1971. The reasons for

these differences in prevalence in different centres are not clear as identical methods of diagnosis were used in all three centres.

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Giardia—From Genome to Proteome

R.C. Andrew Thompson, Paul Monis, in Advances in Parasitology, 2012

2.3 What is *Giardia*?—Evolutionary Biology and Phylogeny

Giardia has long been considered to be a primitive, early diverging eukaryote due to the apparent lack of typical eukaryotic organelles such as peroxisomes and mitochondria and on the basis of phylogenetic analysis of conserved gene or protein sequences. The early branching of Giardia (and other diplomonads) was first suggested following the characterisation of ribosomal RNAs (Edlind and Chakraborty, 1987; Sogin et al., 1989; van Keulen et al., 1993) and later by analysis of conserved proteins such as the elongation factors (Hashimoto et al., 1994, 1995). However, on the basis of morphology and life history, *Giardia* had previously been suggested to be the most derived member of the order (Brugerolle, 1975). The status of *Giardia* as a "missing link" was further challenged by phylogenetic analysis of the Diplomonadida using morphological characters, which also suggested that *Giardia* was the most highly derived genus in the order (Siddall et al., 1992). Furthermore, the accuracy of the placement of *Giardia* and other diplomonads relative to other eukaryotes has been questioned because of the observed large differences in G + C composition that can bias phylogenetic analysis (Leipe et al., 1993) and due to the possible effects of long branch attraction (Dacks et al., 2002). Lateral gene transfer has also complicated the elucidation of the evolutionary history of *Giardia*, with many genes involved in anaerobic metabolism in *Giardia* having been acquired from prokaryotes (Andersson et al., 2003; Nixon et al., 2002a).

More recent molecular data support Siddall's original proposal that *Giardia* are highly derived, rather than primitive organisms. It is likely that the divergence of the lineage giving rise to *Giardia* was subsequent to the acquisition of introns during eukaryote evolution, following the detection of a spliceosomal intron and eukaryote-specific spliceosomal peptides in *Giardia* (Nixon et al., 2002b). More recent genome sequence data have added further weight to these findings, identifying additional *cis*-spliced introns and also finding novel *trans*-spliced introns, where exons are dispersed throughout the genome and a single transcript is produced by *trans*-splicing (Kamikawa et al., 2011; Roy et al., 2011). Analyses of genomic data have also demonstrated the presence of numerous eukaryotic features, such as sequences

encoding eukaryotic RNA processing machinery (Chen et al., 2011), Scaffold/Matrix attachment regions that are involved in chromatin attachment/DNA organisation in other eukaryotes (Padmaja et al., 2010), the presence of nucleoli (Jimenez-Garcia et al., 2008), meiosis-specific genes (Ramesh et al., 2005) and pathways for RNA regulation such as RNA silencing (Ullu et al., 2004) and microRNAs (Zhang et al., 2009). The presence of mitochondrial remnants, called mitosomes, has been demonstrated in *Giardia* (Tovar et al., 2003) and other amitochondriate protists, as have genes encoding components of Golgi bodies (Dacks et al., 2003). The sequences involved in protein targeting for mitosomes have been shown to be conserved and recognised by the hydrogenosomes of Trichomonas and related to translocases in mitochondria (Dolezal et al., 2005). Phylogenetic analysis of the genes encoding type II DNA topoisomerases found that *Giardia* diverged after mitochondriate kinetoplastids and that amitochondriate protists were polyphyletic, adding further evidence that the *Giardia* lineage diverged after the acquisition of mitochondria by eukaryotes and that secondary loss or alternative evolution of organelles has occurred independently multiple times (He et al., 2005a,b).

A further understanding of *Giardia* evolution has been gained from analysis of genome data. While the genome of *Giardia* is thought to be compact through the reduction or loss of many metabolic pathways, 40% of genes (predominantly variant-specific surface proteins) were found to be duplicates (Sun et al., 2010). Interestingly, phylogenetic analysis of the duplicated genes suggested that expansion of the variant-specific surface proteins coincided with the radiation of placental mammals (Sun et al., 2010). Comparison of predicted small nucleolar RNAs in *Giardia* demonstrated similarity with Dictyostelium, *Plasmodium*, fungi and metazoans, which were all different to those from Euglenozoa, suggesting that the lineage containing *Giardia* diverged later than Trypanosoma and Euglena (Luo et al., 2009). This observation is concordant with earlier analyses using multigene phylogenies, which separated the excavates into three major lineages: Diplomonads, Parabasalids and *Carpediemonas*; *Trimastix* and Oxymonads; Euglenozoa, Heterolobosea and Jakobids, with the lineage including *Giardia* and other Diplomonads closest to the fungi and animals (Simpson et al., 2006). However, a more recent study using phylogenomics suggests that long branch attraction may have affected previous attempts to elucidate the relationships of the excavate groups, and exclusion of the most rapidly evolving genes or species from analyses supports the monophyly of the Excavata (Hampl et al., 2009), leaving the placement of the excavates and the major lineages within it uncertain.

The phylogeny of the Diplomonads has been further elucidated, with *Octomitus* being shown to be a sister taxon to *Giardia* (Keeling and Brugerolle, 2006) and with Spironucleus, *Hexamita* and *Trepomonas* being shown to be a separate lineage from *Giardia*/*Octomitus* (Kolisko et al., 2008). Interestingly, none of the Enteromon-

ads were basal to the Diplomonads (as suggested by Brugerolle, 1975; Siddall et al., 1992) but were instead polyphyletic within the lineage including *Spironucleus*, suggesting either multiple origins of diplokarya or multiple instances of secondary loss of the duplicated nucleus (Kolisko et al., 2008). A genome comparison between *Spironucleus* and *Giardia* found evidence of lateral gene transfer from both prokaryotes and eukaryotes, distinct biases in mutations and polyadenylation signals and differences in codon usage (Andersson et al., 2007). Of more interest, large genomic differences were found between the morphologically indistinguishable species *S. barkhanus* and *S. salmonicida*, including differences in codon usage, the frequency of allelic sequence variation and genome size (Roxstrom-Lindquist et al., 2010). Interestingly, a similar observation has been made for the difference in allelic sequence variation observed between *G. duodenalis* and *G. enterica* (Assemblages A (WB) and B (GS)) (Roxstrom-Lindquist et al., 2010).

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Giardiasis: impact on child growth

M.J.G. Farthing, ... R.A. Kronmal, in Diarrhoea and Malnutrition in Childhood, 1986

Natural and experimental infections in animals

Giardia infection in animals produces a variety of effects on physical growth depending on the species and age of the animal, and possibly the strain of Giardia (*Table 9.5*). Several reports have suggested that natural *Giardia* infections in dogs can result in weight loss and growth retardation, particularly when infection occurs during the first few months of life[1,10]. However, these findings are by no means universal since Bemrick in 1943 reported that his naturally infected mongrel dogs came to no harm during *Giardia* infection[3]. An epidemic of giardiasis recently occurred in young budgerigars in some aviaries in Texas[5]. The infection had a profound effect on growth and development and birds were described by one aviary owner as 'going light' with a mortality of 70–100%.

Table 9.5. Giardiasis and growth retardation—animal studies

Study	Animai	Growth retardation
Natural:		
Bemrick[3]	Dog (mongrel)	–
Barlough[1]	Dog	+
Box[5]	Budgerigar	+
Experimental:		

G. lamblia		
Fantham and Porter[13]	Cat	+
Fantham and Porter[13]	Mouse (adult)	±
Bemrick[3]	Dog (mongrel)	NR
Sehgal *et al.*[40]	Rat (adult)	–
	Rat (weaning)	+
Hewlett *et al.* [22]	Dog (mongrel)	–
Hill *et al.* [23]	Mouse (suckling)	–
G. muris		
Roberts-Thomson *et al.* [37]	Mouse	+

NR = not reported

Some of the earliest experimental *Giardia* infections in animals were produced by Fantham and Porter[13], using cysts from giardiasis sufferers returning from the Eastern Mediterranean war in Gallipoli. They successfully infected six kittens, all of whom failed to gain weight at the same rate as uninfected litter mates. The majority of these animals had severe infection from which they died. These workers also infected adult mice and found that growth retardation was proportional to the severity of the infection. However, a recent study of experimental *Giardia lamblia* infection in suckling albino CF-1 mice produced a self-limiting illness lasting 17–21 days without any effect on growth[23].

Experimental *G. lamblia* infection in adult albino rats also had no effect on body-weight, although infection in weanling animals produced marked weight loss[40]. The authors of two recently described animal models of *G. lamblia* infection in gerbils and rabbits failed to report on the effect of this infection on growth and development[2,39]. Body-weight was reported to have been maintained during experimental infection in mongrel dogs[22], although in infected puppies less than 6 months of age one would have expected weight gain.

Swiss albino mice have also been experimentally infected with the rodent parasite Giardia muris, when it was shown that impairment of growth and development was directly related to the number of cysts used to initiate infection[37]. Weight gain of mice infected with 10000 cysts was reduced by 40% compared with healthy control animals.

Thus there is evidence that *Giardia* impairs growth and development of both naturally and experimentally infected animals, although there are clearly inconsistencies in the reported data. In many of the above studies there are numerous uncontrolled variables such as the genetic background of the animal and the morphological type and strain of *Giardia* used to initiate infection. Despite these difficulties it would

appear that *Giardia* infection does have an impact on growth of young animals, particularly after cessation of breast-feeding.

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Host Defenses to Protozoa

Peter C. Melby, ... Sara M. Dann, in Clinical Immunology (Fifth Edition), 2019

Evasion of Host Immunity

Giardia evades the host humoral immune response by undergoing surface antigenic variation by altering a group of variant-specific surface proteins (VSPs). Selection occurs by an immune-mediated process because switching occurs when intestinal anti-VSP IgA responses are first detected.[30] *G. lamblia* also produces a protease that cleaves IgA. Although Giardia activates dendritic cells for antigen presentation, it also inhibits IL-12 production, in part by enhancing IL-10 release; the net result is the dampening of a local antiparasitical inflammatory response.[30] The trophozoite also releases arginine deiminase, which degrades arginine, making it less available for host NO production.[31]

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Tradition and Transition

Emily J. Jenkins, ... R. C. Andrew Thompson, in Advances in Parasitology, 2013

3.5 Future Impact of Climate and Landscape Change

Giardia is currently well-established in harsh northern climates, where cooler, wetter conditions favour survival and transmission of cysts. It is possible that warming temperatures will decrease environmental survival of Giardia cysts. However, this will likely be offset by increased transmission through changes in regional hydrology.

Among the abiotic ecosystem components, water is the most important in terms of the impact of climate change (Polley and Thompson, 2009). Climate-induced rises in temperature will affect Arctic regions earlier and more severely than elsewhere given the diversity of water sources and this will clearly enhance opportunities for waterborne transmission of *Giardia* (Davidson et al., 2011). Climate change has long been predicted to increase the public health impacts of *Giardia* in the Arctic as a result

of flooding events caused by heavy rain, snowfall, and melting, leading to outbreaks of waterborne infections (Parkinson and Butler, 2005).

Increased precipitation and frequency of severe weather events could overwhelm existing water treatment infrastructure, with a corresponding increase in the frequency and severity of waterborne outbreaks. *Giardia* is the most common cause of drinking water outbreaks in North America, likely as a result of the resistance of the cysts to chlorine treatment. Water treatment infrastructure in northern communities that does not involve filtration or ozonation should be considered vulnerable under current and future environmental conditions.

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