Giardia: Overview and Update

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Giardia is a protozoan flagellate that was first observed by Van Leeuwenhoek in 1681 and more fully described by Lamb in 1859. It was initially thought to be a commensal in humans, but it is now clearly recognized as a common cause of diarrhea and malabsorption. Giardia infects millions of people throughout the world in both epidemic and sporadic forms. It is transmitted through ingestion of contaminated water and food, person-to-person contact in child care centers, and male homosexual activity.

The Life Cycle

Morphological classification schemes have placed Giardia in the Phylum Zoomastigophora, Class Zoomastigophorea, and Order Diplomonadida. More recently, Sogin et al. [1] placed Giardia as one of the most primitive eukaryotic organisms (by means of molecular classification with use of small subunit rRNA). Three species of Giardia have been described on the basis of differences discernible by light microscopy; these species are G. ardeae from herons; G. lamblia (also called G. intestinalis or G. duodenalis) from various mammals. Two additional species that are indistinguishable from G. lamblia by light microscopy, G. ardeae (from herons) and G. psittaci (from psittacine birds), have been identified on the basis of morphological differences observed on electron microscopic examination [2, 3]. G. lamblia is found in domestic animals such as cats and dogs, as well as a variety of wild animals including beavers, which have been implicated in waterborne outbreaks of giardiasis [4, 5].

The life cycle of Giardia is composed of two stages: the trophozoite and the cyst. The cyst is the infectious form of this protozoan and is relatively inert and environmentally resistant. After ingestion, excystation occurs in the duodenum as a result of exposure to the acidic gastric pH and the pancreatic enzymes chymotrypsin and trypsin, producing two trophozoites (vegetative stage) from each cyst [6, 7]. The trophozoites replicate in the crypts of the duodenum and upper jejunum and reproduce asexually by binary fission. Some of the trophozoites then encyst in the ileum, possibly as a result of exposure to bile salts or from cholesterol starvation [8, 9] (figure 1).

The cysts can be round or oval and measure 11–14 × 7–10 μm (figure 2A). They each have four nuclei and contain axonemes and median bodies. The trophozoites measure 10–20 μm in length by 5–15 μm in width and have the shape of a teardrop when viewed from the dorsal or ventral aspects (figure 2B). There is a ventral, concave sucking disk bearing four pairs of flagella, two axonemes, and two median bodies. The trophozoites have two nuclei that are identical by all criteria that have been studied and that are both transcriptionally active. Giardia contain five chromosomes and are polyploid. Mitochondria, peroxisomes, smooth endoplasmic reticulum, and nucleoli have not been identified, consistent with the suggestion that Giardia is a primitive eukaryote [10]. The ventral disk acts as a suction cup, allowing mechanical attachment to the surface of the intestine (figure 3).

Epidemiology

Infections may result from the ingestion of 10 or fewer Giardia cysts [11]. Under favorable conditions of temperature and humidity, such as water at 4–10°C, the cysts may remain viable for several months [12]. The cysts are relatively resistant to chlorination and to disinfection by ultraviolet light. Boiling is very effective for inactivating Giardia cysts, but some cysts may survive after freezing for a few days. Most human infections result from ingestion of contaminated water or by direct fecal-oral transmission, such as that occurring in child care centers. Less commonly, transmission may occur via food contamination by food handlers. Male homosexual sexual contact is another route of transmission [6].

G. lamblia is found worldwide and is especially common in areas where poor sanitary conditions and insufficient water treatment facilities prevail. Seasonality of giardiasis has been reported, with a peak incidence during late summer in the United Kingdom, the United States, and Mexico, but no seasonal pattern has been observed in day care situations. The prevalence of Giardia in stool specimens submitted for ova
The prepatent period of giardiasis and the duration of infection are not related to the size of the initial inoculum. The incubation period for people with symptomatic infection is 1–2 weeks but varies from 1 day to 45 days. In the majority of infected individuals (~60%, depending on the population), the infection remains asymptomatic. Asymptomatic infections may be more common in children and in people with prior infections. For example, in an outbreak of giardiasis at a ski resort [15], residents of the area were less likely to develop symptoms than were visitors to the ski resort despite the fact that there was no difference in exposure.

**Symptoms.** Symptomatic patients have diarrhea with loose, foul-smelling stools; there are increased amounts of fat and mucus in fecal samples. Flatulence, abdominal cramps and bloating, and nausea are common, as are anorexia, malaise, and weight loss. Blood is not present in stools. Fever is occasionally present at the beginning of the infection. In contrast to most other forms of infectious diarrhea, *G. lamblia* infection results

![Figure 1](image1.png)  
**Figure 1.** Life cycle of *Giardia lamblia*. A: Cysts are excysted in the duodenum, and trophozoites are released and multiply by binary fission. B: Cysts and trophozoites are excreted with feces to the environment. C: Water and food are contaminated with infectious cysts favored by moist and cool conditions.

and parasite examination is 2%–5% in industrialized countries and 20%–30% in developing countries. Seroprevalence studies of Peruvian children showed that 40% of children had been infected before 6 months of age, with reinfections occurring frequently [13]. The majority of cases are asymptomatic, but some children develop chronic diarrhea. However, travelers to these areas of endemicity are at high risk for contracting symptomatic giardiasis. For example, studies of travelers to St. Petersburg, Russia, have demonstrated symptomatic giardiasis in as many as 95% of travelers. Hikers and campers are also at increased risk for giardiasis, since *Giardia* cysts, often of animal origin, can be found in freshwater lakes and streams. The prevalence of *Giardia* can be as high as 35% among children attending child care centers. Although these children are frequently asymptomatic, they may transmit symptomatic giardiasis to family members [10].

For the waterborne outbreaks of diarrhea in which the etiologic agent was identified, *Giardia* has consistently been the most commonly identified agent (table 1). Waterborne transmission is commonly a result of inadequate water treatment or contamination of drinking, well, or surface water with sewage. Giardiasis has also been associated with exposure to contaminated recreational water such as swimming pools. *Giardia* cysts can be inactivated by exposure to ozone and halogens; however, the concentrations of chlorine used for drinking water are not enough to inactivate *Giardia* cysts. Filtration is an effective means for removal of the cysts from water; however, some municipal water supplies are not treated by filtration [6].

**Clinical Features**

The prepatent period of giardiasis and the duration of infection are not related to the size of the initial inoculum. The
mechanisms for the diarrhea produced include disruption of the brush border or immunopathologic processes [10].

*Giardia* antigens continuously stimulate the intestinal mucosa–associated lymphoid tissue during the course of infection. Giardiasis in patients with hypogammaglobulinemia (and possibly those with isolated IgA deficiency) is more severe than in immunologically normal patients, suggesting a prominent role for the humoral immune response in the control of giardiasis. Animal studies have confirmed the importance of the humoral immune response in giardiasis; this immune response is T cell dependent in animals. In addition to humoral immunity, macrophages, neutrophils, nonimmune factors involving the intestinal mucosa, intestinal motility, and human breast milk (for infants) may also contribute to protection from symptomatic giardiasis.

Despite the apparent importance of the antibody-mediated immune response, the diarrhea caused by *Giardia* frequently persists for weeks. The reason for the chronicity of giardiasis is not clear. One potential reason is antigenic variation, which has been documented in *G. lamblia*. Another possibility is that the antibodies are limited in their efficacy because of the intralumenal location of the trophozoites. Despite the limits of the immune response, there is some evidence that antibodies provide protection against newly acquired infection or reinfection. For example, protection against infection following passive transfer of antibodies has been observed for *G. lamblia*–infected gerbils. In addition, studies of children in India have indicated lower infection rates for those children whose mothers had giardiasis, a finding that suggests a protective role for maternally acquired antibody [17].

**Diagnosis**

The diagnosis of giardiasis is most commonly established by identification of cysts or, less frequently, trophozoites in fecal specimens that are stained with trichrome or iron hematoxylin (figure 4). Stool samples can be concentrated by formalin-ethyl acetate or zinc sulfate concentration methods. The passage of cysts is somewhat sporadic, and if the first specimen from a patient with suspected giardiasis is negative, the sensitivity can be improved by repeating the examination once or twice.

**Table 1.** Recently reported outbreaks of giardiasis caused by contaminated drinking water.

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>No. of outbreaks/(no. of cases)</th>
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<tr>
<td>1984</td>
<td>6 (879)</td>
</tr>
<tr>
<td>1985</td>
<td>3 (741)</td>
</tr>
<tr>
<td>1986–1988</td>
<td>9 (1,169)</td>
</tr>
<tr>
<td>1989–1990</td>
<td>7 (697)</td>
</tr>
<tr>
<td>1993–1994</td>
<td>34 (3,994)</td>
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</tbody>
</table>

NOTE. Data are from [14].

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**Figure 3.** Longitudinal cross section of a *Giardia lamblia* trophozoite showing the suctorial disk (S), as demonstrated by transmission electron microscopy. (Bar = 1 μm.)
than giardiasis. Despite the value of duodenal biopsy or aspiration for the diagnosis of giardiasis, it should be emphasized that biopsy supplements stool examination: biopsy is less sensitive than stool examination but will identify patients for whom the diagnosis cannot be ascertained by stool examination alone [19, 20].

Serodiagnosis can not be used to differentiate between present and prior infection and is therefore not useful for the diagnosis of giardiasis. The sensitivity of PCR for diagnosing giardiasis is relatively low because inhibitors of PCR are present in fecal specimens.

**Treatment**

A number of effective treatment alternatives exist for patients with symptomatic giardiasis (table 2). Most patients respond to a single course of treatment, especially when metronidazole or quinacrine is used [6]. In refractory cases, multiple or combination courses have occasionally been required. Quinacrine HCl has long been considered the treatment of choice, but side effects such as toxic psychosis and hemolysis sometimes occur in patients with glucose-6-phosphate dehydrogenase deficiency. Quinacrine has been supplanted by metronidazole in the United States and is no longer commercially available. Although there was initial concern about the carcinogenicity of metronidazole in rats, a detectable risk for cancer in humans has not materialized. Metronidazole is generally free of major toxicity, but the development of nausea is frequently a barrier to its use. It also has an disulfiram-like effect, and patients should be warned not to ingest ethanol while taking metronidazole. Tinidazole, another nitroimidazole, is widely used throughout the world, and a single dose is effective for treatment of giardiasis. However, it has not yet received approval for use in the United States.

Furazolidone is somewhat less effective but is commonly used to treat children. It is ironic that furazolidone is now the only drug approved by the U.S. Food and Drug Administration for treatment of giardiasis in the United States. There has been less clinical experience with albendazole, but several recent clinical studies have shown that this agent has efficacy comparable to that of metronidazole and that it is associated with fewer side effects when given in a daily dose of 400 mg for 5 days [21]. Paromomycin, a nonabsorbable aminoglycoside, is ineffective for treatment of giardiasis or other protozoal forms of diarrhea (e.g., cryptosporidiosis, isosporiasis, or cyclosporiasis). Crohn’s disease, or lymphoma, that may also present as diarrhea and malabsorption. Abnormalities will also be seen in patients with tropical or nontropical sprue, but such abnormalities are not diagnostic of these entities.

Conversely, completely normal biopsy results for a patient with diarrhea and weight loss would suggest diagnoses other than giardiasis. Despite the value of duodenal biopsy or aspiration for the diagnosis of giardiasis, it should be emphasized that biopsy supplements stool examination: biopsy is less sensitive than stool examination but will identify patients for whom the diagnosis cannot be ascertained by stool examination alone [19, 20].

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**Table 2. Effective drugs for the treatment of giardiasis.**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Metronidazole</td>
<td>250 mg t.i.d. × 5 d (15 mg/[kg·d])</td>
</tr>
<tr>
<td>Quinacrine HCl</td>
<td>100 mg t.i.d. × 5 d (6 mg/[kg·d])</td>
</tr>
<tr>
<td>Furazolidone</td>
<td>100 mg q.i.d. × 7–10 d (6–8 mg/[kg·d])</td>
</tr>
<tr>
<td>Paromomycin</td>
<td>25–30 mg/[kg·d] in 3 doses × 7 d</td>
</tr>
<tr>
<td>Albendazole</td>
<td>400 mg/d × 5 d</td>
</tr>
<tr>
<td>Tinidazole</td>
<td>2 g (single dose)</td>
</tr>
</tbody>
</table>
less effective than the other agents but is commonly used for the
treatment of pregnant women because of theoretical concerns
regarding potential teratogenic effects of the other available
agents [6].

Prevention

G. lamblia is most often transmitted by contaminated water
or by the fecal-oral route. Therefore, efforts at prevention
should focus on these routes of transmission. Drinking water
sources associated with outbreaks of giardiasis have generally
been surface water or shallow wells. Filtration is quite effective
for removing Giardia cysts from water. On the other hand,
chlorination is relatively ineffective at rendering the cysts non-
viable and cannot be recommended as the only water treatment.
In day care centers or other settings with a increased risk of
fetal-oral transmission of enteric pathogens, special care should
be taken by washing hands frequently and rigorously and by
disposing of soiled diapers appropriately.

Since G. lamblia is frequently found in lakes and streams—even
in remote areas—hikers and backpackers should be
warned to boil or filter water prior to ingestion. Cysts are
rapidly rendered noninfective by boiling. Simply bringing the
water to a brisk boil is sufficient, even at higher altitudes.
Filtration with a pore size of ≈2 μm is also very effective but
does not remove viral pathogens unless an adsorptive surface
is included. Contamination of the wrong side of the filter with
pretreated water must also be avoided. Halogenation with io-
dine or chlorine is somewhat less effective but may be an
alternative when boiling or filtration is not possible.

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