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. agilis from amphibians; G. muris from rodents, birds and reptiles; and 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 contaminated 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
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

**Clinical Features**

The prepatent period of giardiasis and the duration of infection are not related to the size of the initial innoculum. 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 lasts 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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<tbody>
<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].
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 a 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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<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>

Figure 4. Trichrome staining of fecal sample containing *Giardia lamblia* trophozoites (courtesy of Lynn Garcia, UCLA Medical Center, Los Angeles, CA).
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 nonviable and cannot be recommended as the only water treatment. In day care centers or other settings with a increased risk of fecal-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 $\leq 2 \mu m$ 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 iodine or chlorine is somewhat less effective but may be an alternative when boiling or filtration is not possible.

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References


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