Epidemiology and Transmission

Giardiasis is cosmopolitan, but infection rates vary regionally from 1% to more than 25%. Rates are higher in warmer climates and in crowded unsanitary environments. Men and women are affected equally, but age is a risk factor. Children under age 5 years are 3 times more susceptible to infection than adults, and prevalence of cyst passage in

Introduction

Definition

Giardiasis is gastroenteritis caused by the flagellate protozoon *Giardia intestinalis* (syn. *Giardia lamblia*) of the order Diplomonadida, family Hexamitidae.

Synonyms

Synonyms for *G. intestinalis* include *Giardia duodenalis*, *Giardia lamblia*, *Giardia enterica*, *Lamblia intestinalis*, *Cercomonas intestinalis*, and *Megastoma enterica*. The name *G. duodenalis* is sometimes followed by the name of the animal from which the parasite was obtained. Lamblia- sis and lambliosis are also synonyms for giardiasis.

General Considerations

Until the early 1940s, *G. intestinalis* (syn. *G. lamblia*) was considered a harmless commensal. It is now recognized as a major cause of waterborne enteric disease throughout tropical and temperate regions. In 1682 Leeuwenhoek briefly described an organism that was probably *G. intestinalis*. In 1859 Lambl gave the first comprehensive description of the trophozoite stage, followed by Grassi’s description of the cyst stage in 1879. In 1915 Stiles established the name *Giardia lamblia* in honor of Giard, a French biologist and parasitologist (1846-1908), and Lambl.

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Figure 6.1

Multiple piriform *Giardia intestinalis* trophozoites (arrows) in lumen of duodenum demonstrating paired nuclei. x400
**Giardiasis**

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**Supplementary Notes**
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children under 3 years can reach 50%. In the United States, although underreporting is likely, approximately 19,000 cases were reported yearly between 2006 and 2008.1,2

Humans are infected by ingesting water or food contaminated with *Giardia* cysts or by fecal-oral transmission. Waterborne outbreaks of giardiasis have been linked to unfiltered water from shallow wells, persistent contamination of communal drinking water sources, and ingestion of water from recreational sources such as swimming pools. In the United States, most cases of giardiasis are reported in late summer and early fall, the peak seasons for recreational water sports. Foodborne outbreaks are well-documented, as is person-to-person transmission among homosexual men and among children and staff in day care facilities. The cyst wall of *G. intestinalis* is resistant to chlorine. Before water treatment standards in the United States became more stringent, waterborne transmission of *G. intestinalis* accounted for an estimated 25% of reported cases of giardiasis. In 2002 giardiasis became a nationally notifiable disease in the United States. Enactment of the Surface Water Treatment Rule and the Ground Water Rule by the EPA has decreased the number of ground water associated giardiasis outbreaks.1

The importance of giardiasis as a zoonotic disease is controversial, although there has been documented evidence of the zoonotic transmission of *Giardia* sp. Many studies on genotyping of various zoonotic *Giardia* sp have shown that the genotypes found in the zoonotic species (C through G) have not been found in humans. Although there has been documented evidence of *Giardia* sp transmission from animals to humans and humans to animals, zoonotic transmission is generally considered to be of minor consequence.3-6

**Infectious Agent**

**Morphologic Description**

*Giardia intestinalis* exists in 2 stages: trophozoite and cyst. Trophozoites, the only stage seen in biopsy and autopsy specimens, are pear-shaped and bilaterally symmetrical. Trophozoites range in size from 10 to 20 µm long, 5 to 15
μm wide, and 2 to 4 μm thick (Figs 6.1 to 6.3). There are 2 nearly identical ovoid nuclei, each having a central karyosome (Figs 6.2 & 6.4 to 6.6). A large adhesion disk is conspicuous on the anterior ventral surface (Fig 6.7). Pairs of axonemes give rise to 8 long flagella that stain poorly and are rarely observed. Trophozoites typically contain 2 curved rods, called median bodies, that lie posterior to the nuclei near the center of the cell (Fig 6.8). Trophozoites reproduce by longitudinal binary fission and can be cultured from duodenal aspirates (Fig 6.9).

The cyst stage of *G. intestinalis* is usually recovered from stool specimens. Cysts are ovoid to ellipsoid and measure 8 to 12 μm by 5 to 10 μm (Figs 6.10 & 6.11). The cyst wall is 0.3 to 0.5 μm thick. Mature cysts contain 4 nuclei, usually located at one end of the cyst, with each typically containing a spherical karyosome (Figs 6.10 & 6.12). Cysts also have median bodies, an adhesion disk, and retractile flagella in axonemes that appear as fibrils (Fig 6.13).

**Clinical Features and Pathogenesis**

As few as 10 to 25 cysts can cause infection in humans. The incubation period can be as long as 10 weeks, but is usually 1 to 2 weeks. Gastric acid and pancreatic enzymes induce excystation of trophozoites. These trophozoites colonize the small intestine, especially the duodenum, by attaching to enterocytes, possibly by specific receptor ligands.

The mechanism by which *G. intestinalis* causes gastrointestinal dysfunction is not completely understood. The number of trophozoites adhering to the gut mucosa directly affects the proper absorptive and enzymatic functions of the intestine. Immune-mediated mechanisms, competition for essential nutrients within the intestinal lumen, bacterial overgrowth, and the formation of a physical barrier to absorption are proposed mechanisms. There may be a significant decrease of brush border enzymes and malabsorption of fat, vitamins A and B12, disaccharides, and protein.

Clinical presentation of giardiasis ranges from asymptomatic infections to fulminant diarrhea, malabsorption and severe malnutrition. In asymptomatic infections only the passage of cysts in stool indicates the presence of parasites. Symptomatic giardiasis can be acute or chronic. The acute stage of infection is marked by the sudden onset of explosive, watery, malodorous diarrhea. Epigastric cramps are accompanied by bloating, flatulence, sulfuric belching,
malaise, weight loss, anorexia, and nausea. Continuous or intermittent diarrhea is the cardinal clinical complaint. Stools may be fatty but typically do not contain mucus, blood, or pus. The acute stage lasts from a few days to 2 or 3 months. White blood cell counts are normal and there is no eosinophilia. Persistent symptoms may mimic hiatal hernia, ulcer, or gallbladder disease. Many patients with recurrent diarrhea after treatment are actually experiencing temporary lactose intolerance, not a relapse of infection.

Humoral, cellular, and mucosal responses play a role in immunity to giardiasis. The intestinal IgA response to acute infection is critical, as are the proliferative responses of the mesenteric lymph nodes and Peyer’s patches. Nitric oxide synthesized by the intestinal epithelial cells is antiparasitic.

Although asymptomatic infections are more often seen in children, chronic childhood giardiasis can cause malabsorption, weight loss, retarded growth, and zinc deficiency. Persistent diarrhea can produce hypokalemia, especially in elderly hospitalized patients. Rare extraintestinal manifestations such as hepatobiliary disease, and allergic reactions including urticaria, angioedema, and arthropathy have been reported. Patients with AIDS may develop a giardiasis refractory to treatment if they are severely immunosuppressed.

Pathologic Features

Most patients with giardiasis have normal duodenal mucosa (Fig 6.14). It is important to look for *G. intestinalis* in endoscopic biopsies that show normal small intestinal mucosa. Organisms do not invade tissue but are located in the lumen or attached to the epithelial surface of the villi. Laterally oriented organisms, especially when scant, may be easily overlooked (Fig 6.15). Reported cytologic and architectural changes include epithelial cell damage, loss of the brush border, villous atrophy, crypt hyperplasia, increased goblet cells, intraepithelial lymphocytes, increased inflammatory cells within the lamina propria, nodular lymphoid...
hyperplasia, acute inflammation, and crypt abscesses.\textsuperscript{18-20}

Some of these features may be seen in small intestinal biopsies from patients with giardiasis and other concomitant diseases such as cryptosporidiosis (Fig 6.16), Whipple’s disease (Fig 6.17), or hypogammaglobulinemia (Figs 6.18 and 6.19). The histologic features of giardiasis are similar in immunocompromised and immunocompetent patients. Gastric biopsies from patients with chronic atrophic gastritis with intestinal metaplasia may reveal giardiasis\textsuperscript{21}, and trophozoites may rarely colonize the biliary tree and gall-bladder.

**Diagnosis**

Definitive diagnosis is made by demonstrating *G. intestinalis* in stool specimens, duodenal contents, or intestinal biopsy specimens. In most patients, microscopic examination of 3 consecutive stool specimens collected 2 days apart is sufficient to establish or eliminate a diagnosis. Stool specimens usually contain cysts only, but trophozoites may be found in stools from patients with severe diarrhea (Fig 6.8). The parasite can be seen on wet mounts stained with trichrome (Fig. 6.10), iodine (Fig 6.11), or iron hematoxylin (Figs 6.12 & 6.13). In some patients, when stool examination is negative, motile trophozoites may be observed in Giemsa-stained smears of duodenal fluid, collected by the string test or aspiration.

Endoscopic biopsy can reveal other upper intestinal parasites (*Cryptosporidium* (Fig 6.16), *Cyclospora*, or microsporidia) and detect other causes of malabsorptive diarrhea such as celiac disease. *Giardia intestinalis* trophozoites, most numerous in the lumen of the duodenum and upper jejunum, are usually adequately demonstrated in histologic preparations of biopsy specimens stained with hematoxylin and eosin (Figs 6.1, 6.2, & 6.16). Special stains such as
M ovat, Brown and Hopps (Fig 6.5), and Wilder’s reticulum (Fig 6.6) may accentuate the paired nuclei. Trophozoites may be demonstrated cytologically by a touch preparation of fresh biopsy specimen stained with Giemsa.

Numerous commercial antigen detection assays are available commercially and are reasonably reliable when compared with stool examination. Immunochromatographic dipstick tests (ICT), direct fluorescent antibody (DFA) assays, and enzyme immunoassays (EIA) are available. Molecular techniques are sensitive and specific but not widely available.

Treatment and Prevention

Giardiasis is most commonly treated with metronidazole, tinidazole or nitazoxanide. Paromomycin may be used to treat pregnant women as it is poorly absorbed. Alternative medications are albendazole, paromomycin, furazolidone, and quinacrine. Extended treatment may be necessary for immunocompromised patients. A combination of metronidazole and quinacrine has been used in refractory cases.

The key to the prevention of giardiasis transmission lies in preventing fecal contamination of food and water, and preventing direct transmission. Drinking untreated water should be avoided. Control measures include removing Giardia cysts from water by filtration, flocculation, and sedimentation. Chlorination alone is insufficient. Avoid eating food prepared with untreated water. Adequate personal hygiene, including hand washing, can prevent fecal-oral transmission. Keeping young children with diarrhea away from day care type settings and public recreational water facilities can help prevent waterborne transmission. The proper use of protective barriers during anal-oral sex will prevent sexual transmission of Giardia.

References