Interest in the intestinal parasitic protozoa that comprise the genus *Giardia* has increased considerably in the last quarter century. One reason for this has been the gradual recognition that *Giardia* organisms in humans are potentially pathogenic: while most frequently they occur in the absence of symptoms, they are sometimes capable of causing a mild, self-limiting intestinal syndrome, and even more rarely are responsible for serious disease. In the past the prevailing medical opinion was that *Giardia* were commensal parasites of humans and that their ability to cause disease was questionable (1). *Giardia* currently are the intestinal parasites most frequently identified in public health laboratories in this country (2) and in the United Kingdom (3).

This review was prompted by a number of recent developments which affect our understanding of the epidemiology of giardiasis. These, to be discussed, include recognition that:

1) *Giardia* may occur in epidemic, as well as endemic, form, acquired by the ingestion of cysts in drinking water;
2) the *Giardia* cyst, the transfer form of the organism, may remain viable in cold water for upwards of two months;
3) humans may be infected not only by *Giardia* from other humans, but also by *Giardia* from other animal species as well;
4) giardiasis may be spread by sexual activity, particularly among homosexuals; and
5) immunodeficient individuals are particularly likely to have severe symptoms of the disease.

**THE QUESTION OF GIARDIA SPECIES**

There is no general agreement regarding those characteristics which define species in the genus *Giardia*. Characteristics which have been used to date have been host specificity, body shape and dimensions, and variations in the morphology of median bodies, microtubular structures which occur inside *Giardia* and whose function is presently unknown.

A number of early workers assumed that *Giardia* were highly host specific; partly on this basis at least 40 different species were described (4). Recent work suggests that, while the *Giardia* from some animals may exhibit an apparent high degree of host specificity, other...
Giardia are capable of infecting more than one host species (5, 6). Similarly, the suitability of relying on Giardia dimensions as a means of speciating these parasites has been questioned. While Giardia size and shape are known to vary with organisms from certain hosts, it is also true that Giardia isolated from a number of different hosts are morphologically indistinguishable.

Filice (7) challenged the concept that Giardia body dimensions can be used as species criteria by statistically comparing the measurements he had made of organisms obtained from a number of different animal species. He was unable to differentiate Giardia from different host species on this basis. For this reason, and because Giardia size may vary with time in a given host, with varying diet (8), and perhaps for other reasons, Filice recommended discarding the concept.

Filice (7) proposed recognizing only three Giardia species, based primarily on median body morphology, as follows: 1) G. agilis, organisms encountered in tadpoles and frogs, with long, teardrop-shaped median bodies; 2) G. muris, parasites occurring in rodents, with two small rounded median bodies; and 3) G. duodenalis, a species found in a great variety of warm-blooded vertebrates including humans and rodents, with median bodies which resemble the claw of a claw hammer. This issue, however, has not yet been resolved. There have been arguments in the literature recently supporting Giardia measurements and host specificity as species criteria (9, 10). The application of physiologic, biochemical or immunologic criteria, which have been used in the speciation of other protozoan species including Leishmania, Trypanosoma and Plasmodium, might well help resolve this issue.

**GIARDIA INFECTION AND GIARDIA DISEASE**

**Nomenclature and definitions**

A variety of genus and species names are used to describe these parasitic protozoa. In the western hemisphere and western Europe, G. lamblia is the name usually employed for these protozoa causing human infections; in the Soviet Union and eastern Europe, these same organisms are commonly called Lamblia intestinalis and the infection that they cause is termed "lambliasis."

Unless otherwise indicated, the term Giardia used in this review refers to organisms of the G. duodenalis type as designated by Filice (7). We consider "giardiasis" to simply signify infection of the human host by Giardia, whether or not symptoms have resulted. We use the term "reservoir host" in the sense used by Brown (11), to refer to animals that harbor the same species of parasites that humans do. Such hosts may ensure the continuity of the parasitic life cycle and act as additional sources of human infection.

**Life cycle**

The life cycle of Giardia in humans is diagramed in figure 1; it includes a trophozoite and cyst form. The usual habitat of the flagellated, binucleate trophozoite (figure 2) is the epithelial brush border of the upper two-thirds of the small intestine (duodenum and jejunum), where the organism attaches by a ventral adhesive disk (see figure 3); there the parasite reproduces by binary fission.

Some of these vegetative forms detach from the brush border for unknown reasons and enter the fecal stream. In the small intestine encystment begins (12) with the trophozoite rounding up and elaborating a cyst wall; the resultant cyst is excreted with the feces. As cysts these organisms survive passage outside the host, and a new host acquires infection by ingesting these cysts.

Each of the two nuclei in the cyst undergoes a single division, so that the mature cyst contains four nuclei. At the time of excystation a quadrinucleate
trophozoite in the process of division emerges from the cyst wall (13), and promptly completes the division process, yielding two binucleate trophozoites.

Sometimes the transition in the intestine from trophozoite to cyst fails to occur. This may happen, for example, in instances of rapid intestinal transit where sufficient time is not available for cysts to form. Diarrheic specimens from patients with giardiasis thus are particularly likely to contain trophozoites. The trophozoite to cyst transformation apparently does not occur outside the host; rather, excreted trophozoites disintegrate (figure 1).

_Giardia_ cysts are resistant to destruction in hypotonic solutions such as water. The length of their survival in water varies greatly, depending upon the temperature. For instance, at 8°C _Giardia_ cysts survive for more than two months, while at 21°C and 37°C they survive about one month, and four days, respectively (14).
Boiling immediately makes cysts incapable of excystation; the process of freezing and thawing renders more than 99 percent of cysts incapable of excysting (14).

Not all of the *Giardia* cysts in a freshly excreted specimen are capable of excysting. Experiments in which samples from a single batch of purified cysts were exposed to the same excystation conditions daily suggested that a maturation period varying from three to seven days may be required (14). It is possible that cysts in various stages of maturity, as both bi- and quadrinucleate forms, are present in a single human stool specimen.

When an appropriate host ingests mature cysts, the excystation process is induced, presumably by acidic conditions during gastric passage (13). This process is completed in the duodenum with the emergence of trophozoites; infection is established if they survive, attach and multiply. The necessity for trophozoite emergence in the small intestine is discussed in detail elsewhere (14). Briefly, trophozoites cannot long survive the acidity of the stomach, and may require nutrients in the intestinal fluids to complete the excystation process.

**Distribution**

Organisms in the genus *Giardia*, having been reported as intestinal inhabitants of a variety of mammals, birds, reptiles, amphibians and bony fishes, must be considered among the most widely occurring of the intestinal protozoan parasites (4).

Human infections with this organism occur endemically worldwide and have been reported from the tropics (15) to the arctic (16). Summaries of the average
prevalences generally range from 1.1 to 12.5 per cent, although higher percentages were found in some localities (17). The prevalences were highest in the tropics and subtropics, presumably reflecting the low standards of hygiene in these areas.

In much of the world the prevalence of endemic *Giardia* infection has been found to be greatest among infants and children (18, 19), and this may be related 1) inversely to decreased hygienic standards in low socioeconomic groups and 2) to the fact that this group has not been previously infected and immunologically stimulated by these organisms. This infection is frequently encountered in institutions for children (15, 20–25).

While it is true that the age distribution of endemic giardiasis in United States citizens parallels that seen in the rest of the world (26), numerous reports of outbreaks of this disease among Americans, both at home and abroad (27–47), underline the fact that this infection can occur in any economic or age group.

**Clinical aspects**

*Role in disease.* In light of the numerous reports of studies involving both humans (17, 48–50) and animals (51), there would seem to be little doubt that *Giardia* organisms should be considered potential pathogens.

Symptomatic giardiasis may present with any of a variety of signs and symptoms, including epigastric pain, diarrhea or loose stools, abdominal cramps, malaise, weight loss, and steatorrhea. In more severe cases, malabsorption (52),

**FIGURE 3.** Ventral view of *G. muris* trophozoite isolated from small intestine. Note the prominent ventral adhesive disk (21,500×).
and celiac-like syndrome and retarded growth (49) may occur.

Asymptomatic giardiasis appears to occur more frequently, and may be epidemiologically more significant, than symptomatic giardiasis. Individuals with asymptomatic *Giardia* infections are much less likely to be detected or to seek treatment than those with symptomatic infection and, therefore, are more likely to serve as carriers or disseminators of the disease. The *Giardia* carrier may excrete cysts for months or years (15).

**Diagnostic considerations.** Routinely, a diagnosis of giardiasis is made by finding cysts or trophozoites in diarrheic specimens, or cysts in formed stools. Due to the great variation in the number of cysts in fecal samples (15, 53, 54), the recommended diagnostic procedure calls for the examination of at least three different stool samples collected over the period of a week (55).

Another complication encountered in diagnosing giardiasis by fecal examination is the occasional case in which no cysts are excreted in the stool; this occurs, for example, during prepatency in this disease (56). Alternative methods of diagnosis, which include the search for trophozoites obtained by intestinal aspiration, biopsies or Enterotest capsules (manufactured by Hedeco Company, Palo Alto, California), may be used when *Giardia* infection is suspected but when no diagnostic forms can be found in the stool (55).

Serodiagnostic and skin tests have been attempted, and a few investigators have reported the presence of serum antibodies to *Giardia* in patients with symptomatic giardiasis (52, 57). The lack of a consistent supply of *Giardia* antigen has hampered the further development of these immunologic methods of diagnosis. The fact that *Giardia* trophozoites can now be cultivated *in vitro* (58) should facilitate characterization of the immune response of the host to *Giardia* infection and the determination as to whether this response will permit the development of immunologic diagnostic tests.

It is clear that a method capable of diagnosing all *Giardia* infections is not presently available. The availability of such a method would be an important contribution, not only as a means of diagnosing symptomatic cases, but also for the detection of asymptomatic cases as well.

**Therapeutic considerations.** Some controversy exists regarding the drug of choice for treating giardiasis. Presently, in the US, quinacrine is the most widely prescribed such drug (59), although metronidazole and furazolidone are also prescribed.

Both quinacrine and metronidazole have been reported to cause adverse effects. The administration of quinacrine is frequently accompanied by dizziness, headache and vomiting; psychotic reactions and blue or yellow staining of the skin, although not frequent, are important adverse reactions (59, 60). The ingestion of metronidazole results frequently in nausea and headache, and occasionally in vomiting and diarrhea. In addition, since this drug is reported to be carcinogenic, teratogenic, and mutagenic in nonhuman test subjects (61–63), it is contraindicated for treatment of pregnant women (59); it does, however, provide an alternative treatment method for the relatively small percentage of nonpregnant patients who are not cured by quinacrine.

Furazolidone is the only anti-*Giardia* agent available in the United States in a suspension; it is thus particularly useful for treating young children (64). However, its efficiency at eradicating giardiasis—about 80 per cent—is not quite as great as that of quinacrine or metronidazole.

Tinidazole, a nitroimidazole related to metronidazole, is used widely in Europe and elsewhere (65).

It is generally accepted that prompt treatment of symptomatic giardiasis is
indicated. Additionally, treatment of asymptomatic giardiasis should be strongly considered to prevent the perpetuation of the carrier and disseminator states and possible later appearance of symptoms (25, 64).

The observation that none of the anti-Giardia drugs used in this country are capable of curing all of these infections (64) raises the possibility that drug-resistant strains of Giardia may exist and, as has been observed with other microorganisms, may be selected for by drug use. If this is shown to be the case with Giardia, it will further complicate the epidemiologic picture.

Immunologic considerations. Various reports (66–82) suggest that the host responds to Giardia infection either with a humoral or a cell-mediated response. Roberts-Thomson et al. (66), using G. muris, presented evidence suggesting that recovery from infection with this organism is accompanied by the acquisition of prolonged resistance to reinfection with these same parasites.

The involvement of a humoral response may be inferred from several reports. For example, symptomatic giardiasis may present with symptoms of steatorrhea and malabsorption. These severe symptoms are apparently more likely to occur in individuals with hypo- or agammaglobulinemia than in those with normal immune mechanisms (67–70).

The role of immunoglobulin A (IgA) in the host response to Giardia infection has been the subject of study of several groups of investigators (71–74). Although their method was later criticized by McClelland et al. (71), Zinneman et al. (72) noted lowered secretory IgA concentrations in patients with giardiasis. Another study revealed that a low percentage of laminal cells from the Giardia-infected jejunum contained IgA, and low levels of secretory IgA were observed until after the infection was eradicated, at which time these levels were elevated (73). One report suggested that the early immune response in the jejunal lamina may be restricted to immunoglobulin M production followed by IgA and immunoglobulin G responses (74).

Several workers have demonstrated serum antibodies to Giardia (52, 57, 75), including antibody capable of fixing complement (76). These workers encountered difficulties in obtaining antigen 1) in consistent supply and 2) free of contamination. The antigen used in all of these experiments consisted of either trophozoites, recovered from the host by duodenal aspiration, or cysts, partially purified from the host’s feces.

Giardia infections apparently do not result in increased serum immunoglobulin E levels (77, 78).

Early work demonstrating cell-mediated immunity to Giardia infection included a report of positive intradermal skin tests in patients with giardiasis (79). Again, doubt must be cast on these results since the antigen used was isolated from human feces and may have contained extraneous nonspecific antigens. A recent attempt to implicate cell-mediated reactions in another way (80) has suggested that G. muris infections in nude mice may be a factor in the short average life span—not more than 100 days—of these animals. This life span could be increased by giving anti-Giardia chemotherapy, and could be further increased in nude mice which received a thymus transplant but no anti-Giardia therapy. These and other observations on Giardia infections in thymus-deficient mice (81, 82) suggest that the immune response to giardiasis will prove to be very complex and may well involve humoral as well as cell-mediated factors.

The information presently available regarding the role of immunity in Giardia infection is fragmentary, the result of a nonsystematic approach to the problem, and is in a number of instances contradictory. Perhaps a clearer understanding of
the host-Giardia immune interaction awaits the development of an appropriate animal model. Understanding the nature of the immune response or its suppression may yield information regarding 1) Giardia colonization of the host intestine, 2) production of symptomatic or asymptomatic infection, and 3) formation of cysts, both viable and nonviable.

Transmission

Giardiasis is an infection which, similar to a number of other gastrointestinal infections, is acquired by the ingestion of cysts occurring in fecal material. The usual method of acquiring this infection, by the relatively direct transfer of Giardia cysts to the mouth via food, drink or by hand contact, helps explain the generally observed inverse correlation between the distribution of giardiasis and the level of sanitary practices.

The study of a number of recent cases of giardiasis, the acquisition of which could not be explained readily by traditional concepts, has led to the recognition that the infection may be transmitted 1) in drinking water and 2) during sexual contact; the observations which implicate these two modes of transmission follow.

That water can serve as the vehicle by which even small numbers of Giardia can be carried to, and subsequently establish infection in, humans was demonstrated experimentally by Rendtorff and Holt (83). Subsequently, outbreaks of giardiasis in which water was implicated as the vehicle of spread were reported from a number of locations including Leningrad, USSR (33–35, 84, 85), the Mediterranean (86), and the island of Madeira (31). In the United States, such outbreaks have been reported in New York State (36), New Hampshire (37), Colorado (38–42, 87), Utah (43), Oregon (44, 45) and Washington State (46). Most such outbreaks of waterborne giardiasis have occurred in areas where the water temperature was cool or cold.

In the past, relatively little attention was paid to the possibility that humans may be susceptible to infection by Giardia from lower animals, or that reservoir hosts for this organism might exist. Indeed, there was little reason for doing so: the infection pattern in its usual endemic form is readily explained by assuming that the organisms are spread from person to person (88).

The possibility that animal Giardia may infect humans received increasing attention with the recognition that humans were acquiring giardiasis from drinking water in areas where the chances of fecal pollution of the water was greater from animal than human sources (37, 46). The possibility was strengthened with the discovery that the watershed of one affected city’s water supply harbored beaver whose Giardia, morphologically indistinguishable from human and dog Giardia, were capable of infecting dogs (5). There have been subsequent reports that Giardia cysts, obtained from several animal species, were capable of initiating human infections, and that, conversely, Giardia from humans can infect lower animals (5, 47).

In summary, the available data suggest that at least some of the Giardia are not highly host specific, and that infected lower animals cannot be excluded as possible reservoirs of human giardiasis.

That Giardia infection may be transmitted by sexual activity, particularly among male homosexuals, has been recognized only within the past decade. Lynch (89) and Shookhoff (90) in 1972 proposed such a means of transmission to explain recurrent giardiasis in a young man who had never left the United States, and who was infected with both Dientamoeba fragilis and Giardia. Lynch pointed out that D. fragilis is an extremely delicate organism which exists only in the trophozoite form, never as a cyst. How D. fragilis trophozoites are transmitted from host to host has never been adequately explained.

Shookhoff (90) reported that such com-
bined infections are not unusual among male homosexuals. Mildvan et al. (91) studied two male homosexuals in whom simultaneous or sequential occurrence of amebiasis, shigellosis and giardiasis were noted. Hurwitz and Owen (92) studied three male patients all of whom participated in homosexual activity; among them, they harbored seven intestinal protozoa, including Giardia. Although not conclusive, the results of these and other studies of intestinal infections among homosexuals (93–97), of Giardia proctitis (98) and of Giardia of the vagina (99), support the view that this organism may be transmitted by sexual activity.

Although this form of the disease has been reported primarily among homosexuals, the possibility of its spread by sexual activity among heterosexuals should also be considered. An awareness of this mode of transmission of Giardia infection is important if the physician is to differentiate between failure of chemotherapy and prompt reinfection. It is of additional importance because transmission of Giardia in this manner signals the possibility that the patient may have acquired, by the same route, more serious infections, including amebiasis, syphilis, gonorrhea or hepatitis.

Prevention

Presently there is no oral medication that can be taken to prevent infection by ingested Giardia cysts. Several precautions are available, however.

Precautions with reference to food are the same as those advised in preventing any of a variety of infectious gastrointestinal diseases (100). These include eating only those foods which are cooked or which have been peeled.

More importantly, since drinking water is a significant source of Giardia infection, measures should be taken to treat suspected water to destroy any Giardia cysts. Such measures include heating the water to boiling, since it has been shown that boiling kills these cysts instantaneously (14).

Many household pets, including dogs and cats (101), harbor Giardia. Symptomatic infection may occur in cats and dogs (102), particularly in the bitch and her newborn offspring. In light of the fact that these animals may share not only living quarters but also intestinal parasites with their human hosts, it is prudent to have Giardia-infected pets treated and freed of these potential pathogens.

Summary

Recent developments have revised the concept of giardiasis as an endemic infection of the young that is acquired in warm climates, particularly where hygienic standards are low. We now know that it can occur in epidemic form, that humans of every age and socioeconomic level are susceptible, and that it can be acquired anywhere in the world.

The possible sources of Giardia infective for man must now be expanded to include reservoir hosts; a variety of animal species have been implicated. When giardiasis occurs in epidemic form, the vehicle of spread is usually drinking water, the source of which may be either community water supplies or untreated water in recreational areas.

Cold water once contaminated with Giardia cysts may remain a source of infection for several months. Bringing water to boiling immediately destroys Giardia cysts.

Giardia must now be included among those organisms which may be transmitted by sexual contact. Although evidence suggestive of disease spread in this fashion has been encountered thus far principally among male homosexuals, the possibility of its spread among heterosexuals should not be overlooked.

References

2. Intestinal parasites ranging far afield in the


46. US Department of Health, Education and Welfare: Giardiasis in apes and zoo attendants, Kansas City, Missouri. (CDC) Vet Public Health Notes, January 1979, pp 7-8


63. Is Flagyl dangerous? Medical Letter on Drugs and Therapeutics 17:53-54, 1975


76. Funkoff PH, Kaplan AP: The association of giardiasis with reduced intestinal secretory immunoglobulin A. Am J Dig Dis 17:793-797, 1972


79. Funkoff PH, Kaplan AP: The association of giardiasis with reduced intestinal secretory immunoglobulin A. Am J Dig Dis 17:793-797, 1972

80. Funkoff PH, Kaplan AP: The association of giardiasis with reduced intestinal secretory immunoglobulin A. Am J Dig Dis 17:793-797, 1972


