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Giardia and Giardiasis

THE PARASITE *Giardia*,[1] and the infections and diseases it causes, attracted little interest for the first 110 years after its description by Lambl in Prague in 1859. It was widely believed that *Giardia* was a commensal parasite of doubtful pathogenicity. It is now recognized that *Giardia lamblia* frequently causes a mild, self-limiting disease in man and is, more rarely, responsible for serious illness. It is now the most commonly isolated intestinal pathogenic protozoon worldwide; in countries such as the USA and the UK where worm infections are rare, it is the most commonly isolated of all intestinal pathogenic parasites. In addition, *G. lamblia* has been found to be responsible for several recent waterborne diarrhea outbreaks in the USA and USSR, and a combination of these circumstances has created a wave of interest and research in this previously neglected parasite. Recent reviews of the subject include Jakubowski and Hoff (1979), Knight (1978), Meyer and Jarroll (1980), Meyer and Radulescu (1980), Raizman (1976), WHO Scientific Working Group (1980), and Wolfe (1978, 1979*a*, 1979*b*).

Description of Pathogen and Disease

Although the clinical picture of giardiasis is well described, several aspects of its pathology, immunology, and epidemiology remain uncertain, and some of the information in this chapter is therefore preliminary and tentative.

Identification

Giardiasis is an infection of the small intestine of man by the flagellate protozoon *Giardia lamblia*. The bile duct and gall bladder may also be infected. Symptoms may be absent, but when present may include frequent diarrhea with greasy, foul-smelling stools, usually without blood. There may be fatigue, abdominal cramps, flatulence, anorexia, and in some cases fever and vomiting. During the infection, damage to the intestinal epithelium, detectable histologically, may take place; bacterial colonization of the small intestine may be a predisposing condition for this damage or may be consequent upon it. The damage leads to malabsorption of carbohydrates, fats, fat-soluble vitamins, and vitamin B_{12}. Malabsorption and bile duct inflammation are the most serious complications of giardiasis, since the malnutrition consequent on malabsorption increases susceptibility to other diseases. The disease is diagnosed by identifying the cysts or trophozoites of *G. lamblia* in the stools, or by recognition of the trophozoites in duodenal or jejunal aspirates or biopsies. *G. lamblia* is morphologically indistinguishable from other *Giardia* species common in many mammals. In cases of malabsorption, serology can aid the diagnosis.

Occurrence

The disease is cosmopolitan, associated with poor sanitation and inadequate protection of drinking water sources. Prevalence of *Giardia* infection worldwide is estimated to be about 7 percent. It is about 3 times more common in children than in adults. Local prevalence in children may exceed 50 percent. In Europe and the USA, there is a considerable variation from place to place in the likelihood of contracting the disease, and this appears to be related to the safety of the drinking water. Intrafamilial infection is well recognized.

Infectious agent

The taxonomy and nomenclature of *Giardia* are in a confused and fluid state. Two genus names are used

1. See the subsection "Infectious Agent," below, for a note on taxonomic nomenclature.

interchangeably: *Giardia* (giardiasis) is most commonly used in North America and Western Europe, whereas *Lamblia* (lambliasis) is favored in Eastern Europe and the USSR. Resolution of this issue is simply a question of agreement about the historical precedence of the rival names—the nature of the organism being described is not in doubt. It is probable that *Giardia* will become adopted worldwide, and *Giardia* is used in this book.

The definition of species within the genus *Giardia* is far more complex. In the first half of this century it was believed that *Giardia* species were highly host specific, and therefore specific names were allocated on this basis. It is now known, that some *Giardia* species infect several different animals. The morphology of the trophozoites provides the other main avenue for species definition. Three primary species have been suggested on the grounds of trophozoite morphology: *G. agilis* in frogs and tadpoles, *G. muris* in rodents and birds, and *G. duodenalis* in mammals including man. The matter remains unresolved, and research is in progress on improved species definition.

The species or subspecies that infects man is called *G. lamblia* in this book, although it is also referred to in the literature as *G. intestinalis*, *G. enterica*, or, in Eastern Europe, *Lamblia intestinalis*.

G. lamblia is a flagellated protozoon. The trophozoite, found in the small intestine or in diarrheic stools, is pear or kite shaped, 9–21 micrometers long by 6–12 micrometers broad, with an anterior sucking disc on the flattened ventral surface (figure 21-1). There are four pairs of flagella, and the organism is binucleate. The cysts are ovoid, 14–16 micrometers long and 6–12 micrometers broad, and are quadrinucleate.

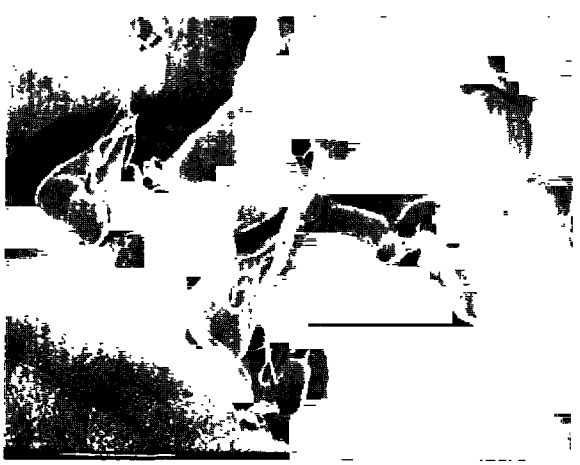

Figure 21-1. *Trophozoites of* Giardia lamblia, *on and over the surface of the small intestine of a patient with giardiasis, under scanning electronmicroscopy.* Scale bar = 10 micrometers. (Photo: R. L. Owen, Cell Biology Section, Veterans Administration Medical Center, San Francisco, USA. Reproduced by permission of the Royal Society of Tropical Medicine and Hygiene)

Reservoirs

The reservoir of *G. lamblia* is man, but there is some evidence that man may acquire infections from other animals. Many mammalian species harbor their own *Giardia* species whose relationship to *G. lamblia* has not yet been properly elucidated. Beavers have been incriminated as a reservoir of infection for hikers drinking stream water that is contaminated by wild animal feces. *G. lamblia* from man has been transmitted to the rat, gerbil, guinea pig, beaver, dog, cat, racoon, bighorn, mouflon, and pronghorn (Davies and Hibler 1979; Meyer and Radulescu 1980). *Giardia* cysts from beavers and deer have caused infection in human volunteers (Davies and Hibler 1979).

Transmission

Up to 900 million cysts may be passed in the stools during 1 day. The cystic infective stage is quadrinucleate and relatively thick walled, and earlier thin-walled "precysts" and the trophozoites rapidly die and are not important in transmission. The median infective dose for man is between 25 and 100 cysts (Rendtorff 1954, 1979; Rendtorff and Holt 1954*b*). On being ingested, the cyst resists stomach acid and hatches in the small intestine, where the two trophozoites that emerge multiply by longitudinal binary fission in the crypts of the duodenum, jejunum, and ileum and attach themselves to the mucosa by means of the sucking disc. Infection of the lining of the bile duct and gall bladder has been reported, although there is no evidence for invasion of other sites. The trophozoites transform into cysts in the ileum, and the cysts are passed in the stool.

Unlike the acute amebic dysentery case, the patient with marked symptoms of intestinal giardiasis is a potent source of infective cysts. This may be a reason why outbreaks of giardiasis are more common than those of amebiasis.

Transmission of *Giardia* is by fecal contamination of hands, food, and water supplies. Water supply contamination has been definitely incriminated in several outbreaks. Although houseflies and other insects have not been shown to be efficient distributors of cysts, it is likely that flyborne transmission of the

organism may play a part in areas of high prevalence. Fecal contamination of the hands probably plays an even more important part in the transmission of *Giardia* than of *Ent. histolytica.* Although transmission of *Ent. histolytica* occurs only sporadically in the UK, *Giardia* is regularly transmitted, and in this country the water supply can probably be ruled out as a possible source.

Prepatent and incubation periods

In man the prepatent period has been recorded as 6–36 days, averaging 9 days in one study (Rendtorff 1954), 13 days in another (Rendtorff and Holt 1954*b*), and 14 days (median) in a third (Jokipii and Jokipii 1977). The incubation period in natural outbreaks is generally between 1 and 3 weeks, and a study of thirty-five cases in Finland recorded a range of 3–42 days and a median of 8 days (Jokipii and Jokipii 1977).

Period of communicability

Infections in adults, demonstrable by the presence of cysts in the feces (and therefore communicable), have been experimentally observed to last up to 41 days. In children the course of the infection may be much longer and has been reported to last for several years (the possibility of self-reinfection cannot be excluded). In a report from Delhi, two-thirds of adults and children naturally infected had lost their infections within 3 months.

Resistance

The higher prevalence of the disease in children and the relatively short duration of an infection indicate that a protective immune response, possibly age-related, may be involved. Antibody to *Giardia* is detectable in the serum of patients with the intestinal malabsorption syndrome and a *Giardia* infection, but there is no evidence of protection in such cases. Resistance following infection is probably not long-lasting, and reinfection is common, even in adults.

Epidemiology

Giardiasis occurs throughout the world but is more prevalent in poor communities with inadequate sanitation. There is no simple correlation, however, between levels of sanitation or economic development and the prevalence of giardiasis. Considerable unexplained variations in prevalence exist, even within a small geographical area.

The pattern of infection is typically endemic. A poor community may have a substantial proportion of asymptomatic carriers continuously contaminating the environment with *Giardia* cysts, although the duration of carriage is typically shorter than for amebiasis (chapter 20). Recorded prevalences in various communities range from 1 to over 20 percent. Children between 1 and 5 years old have the highest infection rates.

Prevalences of *Giardia* excretion among healthy children 1–5 years old in Guatemala were 26 percent of rural children, 44 percent of poor urban children, and 15 percent of more wealthy urban children (Pierce and others 1962). A longitudinal study of 45 children from birth to 3 years of age in a Guatemalan village showed that 93 percent had had one or more *Giardia* infections before their third birthday (Mata and others 1977).

Studies in the Gambia showed that age-specific prevalences of giardiasis rose from 1 percent in infants (under 1 year), to 24 percent in children 3–4 years old and fell steadily to 6 percent in those over 40 years old (Bray and Harris 1977). Giardiasis was more common than amebiasis in children under 5 years old, but less common in the whole community. In northern Nigeria the giardiasis prevalence rose from 1 percent in 0–3 month old babies to 51 percent in 2–3 year old children and fell to 18 percent in adults (Tomkins 1981).

Giardia excretion rates among healthy preschool children (0–6 years) were 4 percent in Sri Lanka, 22 percent in Iran, 14 percent in Bangladesh, and 21 percent in Venezuela. Except in Sri Lanka, giardiasis was more prevalent than amebiasis (van Zijl 1966). Giardiasis prevalences among Laotian refugees in Thailand were 23 percent in the under-5 age group and 7 percent in the total population (Temcharoen and others 1979). Corresponding figures for amebiasis were 3 percent and 2 percent. Mello and others (1978) found *G. lamblia* cysts under the fingernails of 1 out of 148 schoolchildren in Brazil.

Endemic giardiasis is found in temperate developed countries as well as in tropical developing countries. Prevalences are especially high among poor communities and disadvantaged ethnic groups. Prevalences among poor children (6 months to 16 years) in Glasgow (Scotland) were 13 percent of Scots, 10 percent of Asians, 1 percent of Africans, and 1 percent of Chinese (Goel and others 1977). Sole and Croll (1980) recorded a giardiasis prevalence of 5 percent among one racial group in Labrador (Canada), with no infections occurring in adults over 20 years old. Over a 1-year period 24 percent of Cherokee schoolchildren in the USA had giardiasis, and 14 percent had *Ent. histolytica* infection (Healy

1979). A survey in Tasmania (Australia) found that *G. lamblia* was the most commonly identified intestinal parasite of any kind (Goldsmid 1981). Giardiasis in developed countries is especially common in mental institutions (Jeffery 1960), in nurseries (Black and others 1977; Brown 1948), and among male homosexuals (Mildvan, Gelb and William 1977). Giardiasis is also associated with recent foreign travel to developing countries or to Leningrad (USSR).

In addition to the endemic picture of giardiasis described above, outbreaks also occur. The best documented of these are in developed countries, especially the USA and USSR, and most are believed to have been waterborne. In the USA, between 1965 and 1977 there were twenty-three waterborne outbreaks of giardiasis reported involving 7,009 cases (Craun 1979*a*; 1979*b*). *Giardia* cysts were isolated from the water in five of these outbreaks. The outbreaks occurred mainly in the mountainous areas of the Rocky Mountains, in the Northwest, and in New England. The incriminated waters were mostly surface waters either untreated (six outbreaks) or treated only by chlorination (ten outbreaks). *Giardia*-positive beavers were implicated as the source of infection in one outbreak in Washington State. Colorado has been the most affected state and has now made the filtration and chlorination of all surface water supplies mandatory. Endemic giardiasis in Colorado has been associated with the drinking of mountain stream water by hikers (Wright and others 1977). Waterborne giardiasis in the USA is reviewed at length in Jakubowski and Hoff (1979).

There is evidence for (Gupta and others 1972; Root 1921) and against (Rendtorff and Holt 1954*a*) the transmission of *Giardia* cysts from feces to food by flies and cockroaches. It a clear theoretical possibility. but of unknown epidemiological importance.

As with amebiasis (chapter 20), waterborne outbreaks occur, but endemic transmission is much more likely to be by person-to-person transfer especially in conditions of poverty, overcrowding, and inadequate water supply and sanitation. Person-to-person transmission has been strongly implicated in nurseries, schools, and other children's institutions in Czechoslovakia (Červa 1955), the USA (Black and others 1977), and elsewhere. Person-to-person transmission, and family clustering of infection, have also been suggested in community studies (for instance, Eyles, Jones and Smith 1953).

Control Measures

The gaps in knowledge about possible non-human reservoirs of *G. lamblia*, the survival of *Giardia* cysts in the environment, and the epidemiology of giardiasis in developing countries prohibit any definitive statements to be made on control.

Individual

A number of drugs are effective in treatment (for instance, metronidazole) but are not appropriate for mass chemotherapy or prophylaxis. There is no vaccine.

Individual protection is achieved by cleanliness and care in choice and preparation of drinking water and food. Suspected water should be boiled, and suspect fruit and vegetables should be washed and treated with warm water (55°C) or vinegar for 30 minutes.

Environmental

There is little direct evidence on the relative effectiveness of various environmental control approaches. In rural areas of Tennessee (USA), giardiasis prevalence was related to fecal pollution of the home, household cleanliness, personal cleanliness, and family size but not to water supply or sanitation facilities (Eyles, Jones and Smith 1953). Moving mental patients in California (USA) from old and unhygienic premises to a new and well-equipped building did not reduce *Giardia* transmission (Jeffery 1960). Improved water supplies, bored-hole latrines, refuse disposal, and preventive work by visiting nurses failed to reduce the prevalence of giardiasis in Egypt (Chandler 1954).

The comments on environmental control of amebiasis (chapter 20) apply to giardiasis. Improved personal and domestic cleanliness are probably crucial, and improved water supply and sanitation facilities may also be important.

Occurrence and Survival in the Environment

Tests for *G. lamblia* cysts in water and other samples are currently very inadequate. Cysts may be missed altogether at concentrations below 4,000 cysts per liter of water (a high concentration), and the cyst count may underestimate the true count by as much as 99 percent. When a cyst has been detected microscopically, there is no way of proving it to be a species capable of infecting man (other than by human volunteer studies), nor of showing it to be infective (other than by feeding it to laboratory animals). Even establishing viability (by eosin exclusion or excystation *in vitro*) is complex and controversial. There will be little progress in the

environmental study of *Giardia* until laboratory techniques are greatly improved.

The recent documentation of waterborne outbreaks of giardiasis in developed countries has stimulated an explosion of research interest in this disease and engineering approaches to control. Most of this interest is focused on *Giardia* cyst removal by water treatment processes and is therefore not relevant to this book. The state of the art, as in 1978, is comprehensively described by Jakubowski and Hoff (1979).

Pending more research, the best estimate of *Giardia* cyst survival in the environment is that it is similar to *Ent. histolytica* survival and may therefore be estimated from figure 20-2.

In water and water supplies

The inadequacy of laboratory techniques for isolating *Giardia* cysts from water has prevented progress in the study of *Giardia* in the environment. In five of the waterborne outbreaks of giardiasis recorded in the USA during 1965–77, *Giardia* cysts were found in raw water sources or tap water (Craun 1979*a*; Jakubowski and Ericksen 1979). Cysts were located with extreme difficulty, and, if the waterborne assumptions were correct, recorded cysts must have grossly underestimated the actual occurrence of cysts in the waters. In the case of the outbreak at Rome (New York, USA) in 1974, 1.1×10^6 liters of raw water were filtered over 10 days, and one cyst was identified microscopically in the residue. Two of ten samples of the residue induced giardiasis in beagle puppies that ingested them (Jakubowski and Ericksen 1979).

Bingham, Jarroll and Meyer (1979) studied *Giardia* cyst survival in unchlorinated tap water (pH 6.8) at various temperatures and evaluated cyst viability both by eosin-exclusion and by the ability to excyst *in vitro*. Judged by eosin staining (indicating dead cysts), 100 percent destruction took place in 24 days at 37°C, in 31 days at 21°C, and in over 77 days at 8°C. Judged by the failure to excyst, the equivalent times were 6 days, 25 days, and 77 days. Cysts were instantly rendered dead, by the criterion of failure to excyst, in boiling water.

It is widely believed that *Giardia* cysts are resistant to chlorination under conditions often found in water treatment plants. They are particularly resistant at low temperatures, and this fact has been linked to the occurrence of several waterborne outbreaks in the USA and the USSR in the winter months. Current concepts of *Giardia* disinfection come partly from early studies that adopted the very conservative criterion of eosin exclusion as the test of viability (for instance, Červa 1955; Thomas 1952), and partly from analogy with *Ent. histolytica* cysts (chapter 20). Both these approaches are unsatisfactory, and the recent development of *in vitro* excystation tests for viability will permit more informative research on *Giardia* chlorination to be conducted (Hoff 1979). The first reported study of the effect of disinfection on excystation confirmed that both chlorine and iodine compounds have considerably reduced cysticidal properties at 3°C compared with 20°C (Jarroll, Bingham and Meyer 1980).

Filtration experiments have indicated that *Giardia* cysts can be removed by coagulation plus granular medium filtration, or by diatomaceous earth filtration, but only with "conscientious, high quality filter plant operation" (Logsdon, Symons and Hoye 1979).

In feces and night soil

Cyst production by an infected individual is typically 10^5–10^7 per gram of stool but varies greatly. Some individuals excrete only small numbers of cysts intermittently, with 60 percent of stools negative.

In sewage

The probable concentration of *Giardia* cysts in sewage in the USA has been estimated theoretically as 9×10^3–2×10^5 per liter (Jakubowski and Ericksen 1979). These concentrations of cysts have not been confirmed, and the literature contains only the occasional, and mainly qualitative, report of *Giardia* cysts in sewage. Fox and Fitzgerald (1979) reported up to 530 *Giardia* cysts per liter of raw sewage in Chicago (USA). The cysts were more common in domestic than industrial sewage and occured more frequently during April–September.

Summary

There are only a few studies on *Giardia* cyst survival and all except the most recent use overconservative tests for viability. Workers have had to rely on observations of morphological changes, and the fact that eosin or neutral red will stain the contents of cysts which are (probably) dead (see Boeck 1921*a*, 1921*b*; Červa 1955). By analogy with *Ent. histolytica*, we might expect that stained cysts would certainly be dead, whereas some unstained cysts might also be dead.

No definitive statements on *Giardia* cyst survival can be made until a new generation of experiments, using *in vitro* excystation as the measure of viability, have been completed. In the meantime the literature suggests that *Giardia* cysts are somewhat similar to

Ent. histolytica cysts. They are rapidly killed by desiccation and freezing. They are resistant to a wide range of pH and osmotic pressure. Their survival in most moist environments is primarily temperature dependent and may be similar to *Ent. histolytica* (figure 20-2). The most recent data, using excystation techniques, on survival in water (6 days at 37°C, 25 days at 21°C and 77 days at 8°C) show a remarkably close agreement with figure 20-2 (Bingham, Jarroll and Meyer 1979).

Inactivation by Sewage Treatment Processes

Very little is known about the fate of *Giardia* cysts during sewage treatment. The cysts are similar in size to those of *Ent. histolytica* but are reported to be slightly denser (specific gravity 1.11; Rachmanow 1936).

The best assumption at present is that *Giardia* cysts respond to sewage treatment in the same manner as *Ent. histolytica* cysts (chapter 20). Studies on sedimentation, trickling filters, activated sludge, biodiscs, aerated lagoons, oxidation ditches, and waste stabilization ponds in India showed very similar removal rates for the two protozoa (Panicker and Krishnamoorthi 1978). All systems removed 52–93 percent of *Giardia* cysts (except waste stabilization ponds, which removed 100 percent).

Inactivation by Night Soil and Sludge Treatment Processes

This subject has not been investigated. Night soil and sludge treatment processes do not involve freezing, very rarely involve desiccation, and do not produce environments that are especially or particularly hostile to *Giardia* cysts. Therefore, cyst destruction may be expected to be a function of time and temperature. Pending research, the best assumption is that *Giardia* cysts behave as *Ent. histolytica* cysts, and their fate during any given process can be estimated from figure 20–2.

Most mesophilic and all thermophilic digestion and composting processes are likely to eliminate *Giardia* cysts. In Chicago (USA), despite the presence of *Giardia* cysts in raw sewage, none were found in anaerobically digested sludges (Fox and Fitzgerald 1979). Thermophilic composting may be expected to eliminate *Giardia* cysts with a wide margin of safety. Storage of night soil or sludge at tropical temperatures (>20°C) for 6 weeks or more should also eliminate *Giardia* cysts (figure 20-2).

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