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PRACTICE

CLINICAL UPDATES

# Giardiasis

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*Giardia* is a leading but treatable cause of infectious gastroenteritis worldwide, with a reported prevalence of 2-7% in high income countries and 2-30% in low income countries.[1] Giardiasis is included in the World Health Organization Neglected Diseases Initiative owing to its burden and association with poverty.[2] Its incidence in the United Kingdom is underestimated because of the lack of diagnostic sensitivity of traditional faecal microscopy[3] and the mistaken belief that it is mostly acquired abroad, so often only people reporting foreign travel are tested. This update discusses the epidemiology, clinical presentation, diagnosis, and management of giardiasis specifically in high income countries.

## What is *Giardia*?

*Giardia lamblia* (synonyms *G duodenalis* and *G intestinalis*) is a flagellated protozoan. *Giardia* is transmitted through the ingestion of the infective cyst stage shed in human or animal faeces and might be present in faecally contaminated water, food, or fomites. *G lamblia* comprises eight genetic "assemblages" (named A to H), of which only A and B cause disease in humans but which can also infect pets, livestock, and wild animals and show potential for zoonotic transmission.[4]Figure 1⇓ depicts the life cycle and transmission of *Giardia*. The actively multiplying trophozoite form of the organism hatches from the cyst and attaches to the small intestine (fig 2a⇓),[5] where it induces epithelial inflammation, villous flattening, and diarrhoea due to malabsorption.[6-8] In the large intestine, the trophozoites differentiate forming new cysts (fig 2b⇓), which are shed in the faeces and contaminate the environment. Cysts present in faeces can remain viable in a variety of environments, particularly water and at lower temperatures: viability can range from 28 to 84 days in lake or river water[9] but is reduced in soil[10] or cattle slurry.[11]

## Who gets giardiasis?

Box 1 summarises the risk factors for acquisition of *Giardia* in high income countries. Travel to low income settings is a common risk factor, with the highest risk areas being South Asia and South East Asia, North Africa, the Caribbean, and South America.[25 26]*Giardia* is the most common intestinal pathogen in travellers returning to countries such as the UK with gastrointestinal disorders.[25-27] However, a case-control study in north west England in 2013 found that 75% of cases were acquired in the UK.[12] Between 3000 and 4000 cases are reported annually in England and Wales.[28] However, detection of cases increased fourfold after the introduction of an enzyme linked immunosorbent assay for the detection of parasite antigens in stools,[3] and another study estimated there were 50 000 community cases of giardiasis between April 2008 and August 2009.[29]The highest incidence of giardiasis is in under 5s and adults aged 25-44 years[3-30]: most studies report giardiasis being more common in males,[3-21] and it is more often reported in late summer and early autumn in temperate regions such as the UK and United States.[13 30]

The source of many infections is unknown but is likely to be person-to-person transmission through exposure to human faeces, including sexual transmission.[22] In a recent prevalence survey in northwest England, 30% of households in which a family member had a diagnosis of *Giardia* had a second person with a stool sample positive for *Giardia*.[31] Outbreaks have been reported in daycare centres and custodial institutions,[20 32]favoured by overcrowding and poor hygienic conditions.

## When to consider *Giardia*?

*Giardia* infections can be asymptomatic (estimated in 5-15% of infected people),[33] but typical symptoms include diarrhoea,

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**What you need to know**

- The number of patients detected with *Giardia* will increase as routine testing of stool samples using highly sensitive diagnostic tests becomes more widespread
- Most patients with *Giardia* in the UK acquire their infection in the UK and not from overseas travel
- Tinidazole and metronidazole are equally effective as first line treatments, although tinidazole has a simpler regimen and fewer side effects
- Second line agents used in cases of treatment failure are unlicensed for giardiasis in the UK but are routinely used in many countries
- Asymptomatic carriage of *Giardia* is common among household contacts, and testing of contacts is indicated in treatment failure and in household clusters

**Sources and selection criteria**

We searched PubMed and Medline from 1980 to 2016 for authoritative reviews and research articles on *Giardia* and giardiasis, which were added to clinical experience, national guidelines, and personal reference collections. We also searched the Cochrane database and reference lists in review articles. Searching was limited to publications in English.

**Box 1: Risk factors for *Giardia* acquisition in high income countries**

- Foreign travel, particularly in low income settings[12-16]
- Toileting young children and changing nappies[12-15]
- Drinking contaminated water or swallowing contaminated water while using swimming pools or other recreational fresh waters[12-19]
- Attending childcare settings[20]
- Eating fresh products raw[18 21]
- Sexual transmission[22]
- Dog ownership (*Giardia* assemblage A)[12]
- Some immunodeficiency disorders: X linked agammaglobulinaemia, common variable immunodeficiency[23 24]

flatulence, abdominal pain, and bloating.[33] In the early stage of disease, diarrhoea is often explosive, especially in the morning, and the stool is difficult to flush away. Blood in the stool is unusual[34] and would suggest the presence of another pathogen. Patients sometimes mention "eggy burps" of uncertain cause. Later, the diarrhoea becomes more intermittent, with periods of normal bowel function interspersed with the diarrhoea. Weight loss due to malabsorption occurs in more than 80% of patients, with a typical loss of 5 kg in adults over four or more weeks[35]; chronic infection in children might result in failure to thrive.[36] Intestinal lactase deficiency occurs in up to 40% of patients with giardiasis and might persist for several weeks after parasite eradication.[8] This manifests as diarrhoea that is worse after consumption of food or drugs containing lactose. Rarer symptoms include vomiting and fever.[33] Patients often present with diarrhoea but without typical symptoms of giardiasis and the condition is diagnosed unexpectedly by microbiological examination of a stool specimen. Examination is usually unremarkable apart from features of weight loss, but patients with prolonged symptoms might have features of malabsorption, including pallor due to anaemia. Diagnosis is often delayed, sometimes for months, owing to the insidious onset and relapsing clinical course.

## Giardia and irritable bowel syndrome

The symptoms of giardiasis can resemble irritable bowel syndrome (IBS).[37] An Italian study of 137 patients investigated in secondary care for IBS or dyspepsia found *Giardia* in 6.5% of patients.[38] However, this finding was not replicated in a larger study[39] and guidance from the UK National Institute for Health and Care Excellence recommends that faecal testing for ova and parasites is not routinely required to confirm the diagnosis of IBS in people who meet the diagnostic criteria for IBS.[40 41] Clinicians should be alert to the possibility of both diagnoses. If there is any doubt, or where there is a relevant exposure history for giardiasis (box 1) consider parasitological examination of a stool sample.

## How should suspected giardiasis be investigated?

Giardiasis is usually diagnosed by laboratory analysis of stool samples (table 1⇓), either by traditional microscopy (ova, cysts, and parasites (OCP) examination) for visualisation of cysts (or more rarely, trophozoites) or by stool antigen detection assays.[3-43] The sensitivity of antigen detection assays is superior to microscopy for the diagnosis of giardiasis, but sensitivity between different formats varies (table 1⇓). Highly sensitive molecular methods (polymerase chain reaction, PCR) that contain parasitology panels are increasingly being used but are not universally available in UK laboratories.[44 45] Not all laboratories routinely test stool samples for the microorganism, so specifically request examination of samples for *Giardia* and document travel or other risk factor history. Owing to variable shedding, three stool specimens (ideally taken two or three days apart) might need to be examined when traditional microscopy is used. If the result is negative, three more specimens should be submitted at weekly intervals,[51] with a minimum of six negative results required for microscopic exclusion of infection.[52] There is evidence of improved detection of *Giardia* in single stool samples using PCR over microscopy of several stool samples or antigen detection assays.[46 47] At present PCR is only offered as a first line test in a few UK hospital laboratories, and clinicians are advised to discover what tests are available in their local laboratory. In secondary care when giardiasis is highly suspected but stool results are negative, diagnosis can be made through duodenal aspiration and biopsy, which have been shown to detect infection in the absence of cysts on stool microscopy.[39 48] Serological tests for circulating IgG and IgM antibodies to *Giardia* are not appropriate for clinical diagnosis.

## What treatments are available for giardiasis?

Unlike many causes of infectious gastroenteritis, giardiasis is treatable (table 2⇓). Many drugs have been evaluated in reviews and several meta-analyses,[53-59] including a Cochrane Review in 2012 that examined 19 trials for the effectiveness of the four agents most commonly used to treat giardiasis—metronidazole, tinidazole, albendazole, and nitazoxanide.[54] Trials included in these reviews are of variable quality and heterogeneous in their location and types and ages of patients included. Some trials have been conducted in low income settings where there is a high prevalence of *Giardia* infections, and where the resulting partial immunity might alter the clinical picture and observed response to treatment compared with that observed in non-endemic countries or in non-immune people. In most analyses, the 5 nitroimidazoles metronidazole and tinidazole have similar efficacies, with parasitological cure rates and symptom relief in more than 90% of patients.

### Symptomatic patients

The British National Formulary[60] currently recommends a five day course of metronidazole as preferred treatment in the UK. Most specialists prescribe a single dose of tinidazole, which is licensed for this indication, has similar efficacy to a multiple dose metronidazole regimen, and is better tolerated.[57] Repeat either course if unsuccessful, together with exclusion of reinfection (from a household or sexual contact) or lactose intolerance. Advise patients to avoid milk and milk products for at least two weeks (some clinicians advise up to six weeks) to evaluate whether persisting symptoms truly represent treatment failure rather than temporary lactose intolerance. Giardiasis is associated with prolonged symptoms that can have a detrimental impact on quality of life.[61 62] Second line agents such as albendazole or nitazoxanide are routinely available in some countries but are not licensed for the treatment of giardiasis in the UK. Specialist advice is recommended if second line agents are required. Albendazole has similar efficacy to metronidazole and is better tolerated.[55 59] Nitazoxanide is more difficult to obtain and more expensive in the UK, and paromomycin is the only second line agent that can be used in pregnancy. Mepacrine (quinacrine) is effective but has numerous side effects and is reserved for management of refractory cases by specialists.

Confirmation of treatment failure is best provided by PCR, which offers improved detection in single stool samples over microscopy.[63 64] Treatment success is indicated by complete resolution of symptoms or lack of detection of *Giardia* DNA by PCR one week after treatment.

Treatment failure might be due to host factors or to true drug resistance, which is well recognised and increasingly common, particularly in travellers returning from South Asia and South East Asia.[16-65] However, tinidazole or metronidazole should still be used as first line treatment for travellers returning from these areas despite cross resistance between these drugs.[65] Patients with treatment failure should be discussed with or referred to a specialist, who should exclude underlying problems such as coeliac disease, inherited disaccharidase deficiency, and immunodeficiency disorders, particularly of total and IgA antibody production.[23-61] Combination treatment with the above agents may be used under specialist care.

A variety of combination treatments are effective, although the evidence is based on observational studies and individual clinician preference.[56-69] Combinations of albendazole and a 5 nitroimidazole, or nitazoxanide with a second agent, are the usual next steps in the treatment ladder. Paromomycin and mepacrine have specific niches, as already discussed.

### Asymptomatic patients

Asymptomatic carriage of *Giardia* is common in contacts of cases, and household clusters do occur. In a recent study in north west England, routine testing of all household contacts of 91 primary *Giardia* cases found a contact positive for *Giardia* in 27 households (30%): of the 212 contacts, 41 (19%) were positive, most of whom were asymptomatic.[31] In the absence of research as to whether treatment of asymptomatic carriage is effective in curtailing transmission, management is based on expert opinion.[53] Asymptomatic carriage is generally not treated, but treatment is rational in failed treatment of a case or in household clusters. In these situations a pragmatic alternative may be to offer blind treatment to all household contacts based on their preference. Wider availability of sensitive PCR diagnostic tests may allow a more targeted approach to contact treatment in future.

## Can *Giardia* infection be prevented?

Individual cases require investigation, usually by environmental health officers, to prevent onward spread and identify likely exposures. In many high income countries, including the UK, surveillance is underpinned by statutory notification of *Giardia* diagnoses by hospital laboratories to the local public health system.[70-72] Prevention of secondary transmission is mainly through antiparasitic treatment of cases and advice on the prevention of person-to-person spread through stringent personal hygiene (box 2). Exclusion on the basis of the absence of diarrhoea for 48 hours applies to children in nurseries, food handlers, and those caring for vulnerable adults.[73] Microbiological evidence of stool clearance is not usually required, but this might be considered in outbreak situations.

*Giardia* cysts are more resistant to chlorine disinfection than most bacteria, and outbreaks have been reported linked to contaminated mains drinking water, swimming pools, and paddling pools.[17 19] Adherence to guidelines for swimming pool management[74] reduces the risk of giardiasis to a minimum. Outbreaks due to drinking water are uncommon in the UK[75] because of the full treatment of public water supplies (filtration and disinfection), but they are a risk where treatment is inadequate. Travellers should check that water disinfection filters or systems they use are certified to remove *Giardia*.

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**Box 2: Advice on *Giardia* for patients and carers**

*General*

- Wash your hands carefully with soap and hot water and dry them thoroughly each time you go to the toilet or before preparing food
- Do not share towels
- Remain off work until free of diarrhoea for 48 hours if you work with food or in social care or healthcare and have direct contact with patients or clients

*Young children with Giardia*

- Ensure scrupulous hygiene when changing nappies
- Supervise children's hand washing
- Keep young children away from playgroups, childminders, or nursery until free of diarrhoea for 48 hours

*Household contacts of a Giardia case*

Testing is not advised unless the original patient remains unwell despite treatment or if someone else becomes unwell

**How patients were involved in the creation of the article**

No patients were involved in the creation of this review.

**Questions for ongoing and future research**

- What behavioural or immunological factors could explain the excess of giardiasis in males?
- What is the extent of zoonotic transmission risk for *Giardia*?
- Do different *Giardia lamblia* genetic assemblages differ in transmission and clinical outcome of disease?
- Is previous exposure to *Giardia* protective against successive infections in travellers?
- What is the relation between *Giardia* and irritable bowel syndrome or other post-infectious gastrointestinal disorders?
- Why are some infections refractory to treatment?
- How common is drug resistance and what is the molecular basis of resistance?
- What is the most effective and safe treatment for refractory infections?
- Is treatment of asymptomatic excretors effective in curtailing transmission, and, if so, when should it be offered?
- Is there a role for prebiotics or probiotics in prevention or management of infection?

**Education into practice**

Do you request specific *Giardia* testing in patients presenting with relapsing diarrhoea, negative results on bacterial stool culture, and no history of overseas travel?

**Additional educational resources**

*Information for healthcare professionals*

- Public Health England (www.gov.uk/guidance/giardia)—for surveillance information and epidemiological trends of giardiasis
- US Centers for Disease Control and Prevention (www.cdc.gov/parasites/giardia/audience-health-professionals.html)—for epidemiological information and links to veterinary and environmental aspects of *Giardia*

*Information for patients*

- US Centers for Disease Control and Prevention (www.cdc.gov/parasites/giardia/)—provides answers to frequently asked questions about *Giardia*
- New Zealand Ministry of Health (www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/food-and-water-borne-diseases/giardia)—has general information about giardiasis
- Patient website (http://patient.info/health/giardia)—has an information leaflet with preventive advice
- National Travel Health Network and Centre (NaTHNaC) (http://travelhealthpro.org.uk/travellers-diarrhoea/)—provides pre-travel advice, as well as links to country specific advice
- Fit for Travel (www.fitfortravel.nhs.uk/advice/disease-prevention-advice/travellers-diarrhoea.aspx)—provides similar pre-travel advice on hygiene and disease prevention

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# Tables

**Table 1| Comparison of diagnostic tests for Giardia42434445464748495051**

| Specimen type by patient group | Usual test (target) | Relative diagnostic performance for *Giardia* | | Comments |
|---|---|---|---|---|
| | | Sensitivity (%) | Specificity (%) | |
| Any patient with community acquired or unexplained diarrhoea | | | | |
| Most preserved or unpreserved stool | Ova, cysts, and parasites (OCP) examination by microscopy of unconcentrated and concentrated preparations from which permanent stained smears can be made (cysts; trophozoites may be seen, although some preservatives may affect their morphology) | 31* | 100* | May not detect low level, chronic infection. Provides differential diagnosis of many (but not all) parasites. Smaller parasites will be missed (eg, *Cryptosporidium*; microsporidia). Labour intensive; high level of skill required; cheap. Most useful where burden of illness and intensity of infection is high |
| Formalin or SAF preserved† or unpreserved stool | Enzyme immunoassay (cyst antigens) | 85-100 | ≥95 | Only provides diagnosis of specific parasites included in assay; often in combination with *Cryptosporidium* and sometimes *Entamoeba histolytica*. Useful for high throughput testing; kit cost maybe offset by use of low skilled staff |
| Formalin or SAF preserved† or unpreserved stool | Immunochromatographic lateral flow (cyst antigens) | 95.8-100 | 97.1-100 | Only provides diagnosis of specific parasites included in assay. Useful where there is low capacity for complex testing; expensive |
| Formalin or SAF preserved† or unpreserved stool | Immunofluorescent microscopy (cysts) | 94-100 | 100 | Only provides diagnosis of specific parasites included in assay. Useful where other highly sensitive and specific tests are not available, for confirmation of equivocal results, and where the burden and intensity of infection is low. Labour intensive; moderate level of skill required; fluorescent microscope needed; expensive. |
| Unpreserved stool or only those in specified preservatives† | Nucleic acid amplification based (PCR) | 90-100 | 75-100 | Only provides diagnosis of specific parasites included in assay. Useful for high throughput testing. Kit cost maybe offset by decreased staff time. Improves diagnosis where burden of illness and intensity of infection is low. Rapidly becomes negative after successful treatment. Sensitivity and specificity can vary according to sample processing, amplification approach, and molecular marker chosen |
| Patients where *Giardia* is suspected but not detected in stool | | | | |
| Duodenal or jejunal biopsy or aspirate collected through intubation or string test (Entero-test) | Microscopy (trophozoites) or nucleic acid amplification based (DNA), flattening of villi (histology) | Will probably be supplanted in most cases by sensitive PCR stool assays, but occasionally useful in areas where this and antigen assays are not available | | |

SAF=sodium acetate-acetic acid formalin solution.

*Using PCR as reference test.[50]

†Other preservatives may interfere with assay performance. Refer to kit insert.

Table 2| **Current treatment options for Giardia in UK***

| Drug | Use in pregnancy | Use in children | Licensed in UK |
|---|---|---|---|
| Metronidazole | Avoid first trimester if possible | Yes | Yes |
| Tinidazole | Avoid first trimester if possible | Yes | Yes |
| Albendazole | No | Yes | No |
| Nitazoxanide | No | Yes | No |
| Paromomycin | Yes | Yes | No |
| Mepacrine (quinacrine) | No | No | No |

*Many are unlicensed in the UK (see text for indications for these in secondary care practice).

# Figures

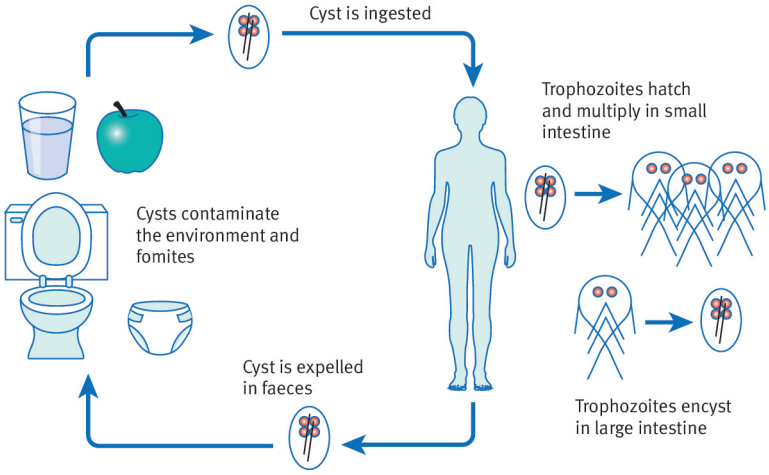


**Fig 1** Life cycle and transmission of *Giardia*

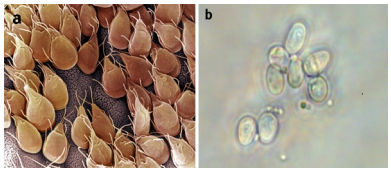


**Fig 2** (a) Trophozoites under electron microscopy. (b) Giardia cysts on microscopy