**Giardiasis**

Corrado Minetti1, Rachel M Chalmers2, Nick J Beeching3, Chris Probert4, Kenneth Lamden5

1Postdoctoral research assistant, Vector Biology Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK

**2Consultant Clinical Scientist and Head of Unit,** Cryptosporidium Reference Unit, Public Health Wales Microbiology ABM Singleton Hospital, Swansea SA2 8QA, UK

3Senior Lecturer in Infectious Diseases, Clinical Sciences Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK

4Professor of Gastroenterology, Institute of Translational Medicine, University of Liverpool, Crown Street, Liverpool L69 3BX, UK

5General Practitioner, Wingate Medical Centre, 79 Bigdale Drive, Kirkby L33 6YJ, UK

Correspondence to: Kenneth Lamden – kenneth.lamden@sky.com

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**Introduction**

*Giardia* is a leading but treatable cause of infectious gastroenteritis worldwide, with a reported prevalence of 2 to 7% and 20 to 30% in high and low income countries respectively1. Giardiasis is included in the World Health Organization Neglected Diseases Initiative due to its burden and association with poverty2. Its incidence in the United Kingdom is underestimated because of the lack of diagnostic sensitivity of traditional faecal microscopy3 and the mistaken belief that it is mostly acquired abroad, so often only people reporting foreign travel are tested. This clinically-focused review discusses the epidemiology, clinical presentation, diagnosis and management of giardiasis specifically in high income countries.

**What is *Giardia*?**

*Giardia lamblia* (syn. *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 that may be present in faecally contaminated water, food or fomites. *Giardia lamblia* comprises eight genetic “assemblages” (named A to H), of which only A and B cause human disease but can also infect pets, livestock and wild animals showing potential for zoonotic transmission4. The life cycle and transmission of *Giardia* is depicted in **Figure 1**.The actively multiplying trophozoite form of the organism hatches from the cyst and attaches to the small intestine5 (**Figure 2**), where it induces epithelial inflammation, villous flattening and diarrhoea due to malabsorption6-8. In the large intestine, the trophozoites differentiate forming new cysts (**Figure 3**) that are shed in the faeces contaminating the environment. Cysts can remain viable in a variety of environments, particularly in water and at lower temperatures: viability can range from 28 up to 84 days in lake or river water9 but it is reduced in soil10 or cattle slurry11.

**Who gets giardiasis?**

The risk factors for *Giardia* acquisition in high income countries are summarized in **Box 1.** Travel to resource-poor settings is a common risk factor with the highest risk areas being South and Southeast Asia, North Africa, the Caribbean and South America25,26. *Giardia* is the most common intestinal pathogen in travellers returning to countries such as the UK with gastrointestinal complaints25,26,27. However, a case-control study in Northwest England in 2013 revealed that 75% of cases were acquired in the UK12. Between 3000-4000 cases are reported annually in England and Wales28. However, detection of cases increased four-fold following the introduction of an enzyme linked-immunosorbent assay for the detection of parasite antigens in stools3, and another study estimated there were 50,000 community cases of giardiasis between April 2008 and August 200929. The highest incidence rates of giardiasis are found in children under five years and in adults aged 25 to 44 years3,12,13,18,21,30: most studies report giardiasis being more common in males3,12,21 and it is more frequently reported in late summer and early autumn in temperate regions such as the UK and the United States13,30.

The source of many infections is unknown but is likely to be person-to-person transmission through exposure to human faeces, including sexual transmission22. In a recent prevalence survey in Northwest England, 30% of households of a diagnosed case had a second person with a *Giardia*-positive stool sample31. Outbreaks have been reported in day-care centres and custodial institutions20,32, favoured by overcrowding and poor hygienic conditions.

**When to consider *Giardia*?**

*Giardia* infections can be asymptomatic (estimated 5-15% of infected people)33 but typical symptoms of giardiasis include diarrhoea, flatulence, abdominal pain and bloating33. In the early stage of disease diarrhoea is often explosive especially in the morning, and difficult to flush away. Blood in the stool is very unusual34 and would suggest the presence of another pathogen. Patients sometimes complain of “eggy burping”, of uncertain aetiology. Later, the diarrhoea becomes more intermittent, with periods of normal bowel function interspersed with diarrhoea. Weight loss due to malabsorption occurs in more than 80% of patients, with typical loss of 5 kg in adults over 4 or more weeks35; chronic infection in children may cause failure to thrive36. Intestinal lactase deficiency occurs in up to 40% of patients with giardiasis and may persist for several weeks after parasite eradication8. This manifests as diarrhoea that is worse after consumption of food or medication containing lactose. Rarer symptoms include vomiting and fever33. Cases often present with diarrhoea but without typical symptoms of giardiasis and are diagnosed unexpectedly by microbiological examination of a stool specimen. Examination is usually unremarkable apart from features of weight loss, but patients with very prolonged symptoms will have features of malabsorption including pallor due to anaemia. Diagnosis is often delayed, sometimes for months, due to the insidious onset and relapsing clinical course.

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 patients38. However this finding was not replicated in a larger study39 and NICE Guidance recommends that for people who meet the diagnostic criteria for IBS, faecal testing for ova and parasites is not routinely required to confirm the diagnosis of IBS40,41. Clinicians should be alert to the possibility of both diagnoses and if there is any doubt, or there is a relevant exposure history for giardiasis (refer to **Box 1**) then parasitological examination of a stool sample should be considered.

**How to investigate suspected giardiasis?**

Giardiasis is usually diagnosed by laboratory analysis of stool samples (**Table 1**), either by traditional microscopy (“ova, cysts and parasites examination”, OCP) for visualisation of cysts (or more rarely, trophozoites) or stool antigen detection assays3,42,43. The sensitivity of antigen detection assays is superior to microscopy for the diagnosis of giardiasis but there is variability in sensitivity between different formats (**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 laboratories44,45. General practitioners are advised to specifically request examination of samples for *Giardia* and document travel or other risk factor history as not all laboratories routinely test stool samples for *Giardia.* Due to variable shedding, three stool specimens (ideally taken 2-3 days apart) may need to be examined when traditional microscopy is used. If negative, three more specimens should be submitted at weekly intervals51 with a minimum of six negatives required for microscopic exclusion of infection52. There is evidence of improved detection of *Giardia* in single stool samples using PCR over microscopy of several stool samples and/or antigen detection assays46,47. Following successful treatment the DNA of the parasite is rapidly cleared within one week from the stool53,54. PCR is only offered as a first-line test in a few UK hospital laboratories at present, and clinicians are advised to discover what tests are available in their local laboratory. In secondary care when giardiasis is highly suspected but stools are negative, diagnosis can be made via duodenal aspiration and biopsy, which has been shown to detect infection in the absence of cysts on stool microscopy39,48. 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. Treatment options for giardiasis are summarised in **Table 2**. Many drugs have been evaluated in reviews and several meta-analyses55–61 including a Cochrane Review in 2012 which examined 19 trials for the effectiveness of the four agents most commonly used for the treatment of giardiasis – metronidazole, tinidazole, albendazole and nitazoxanide56. Trials included in these reviews are of variable quality and are heterogeneous in their location and the 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 may alter the clinical picture and observed response to treatment compared to that observed in non-endemic countries or in non-immune individuals. In most analyses, the 5-nitroimidazoles metronidazole and tinidazole have similar efficacies to each other with parasitological cure rates and symptom relief in over 90% of patients. Although the British National Formulary62 currently recommends a five day course of metronidazole as first line treatment in the UK, most specialists prefer to prescribe a single dose of tinidazole, which has similar efficacy to a multiple dose metronidazole regimen and is better tolerated59. Second line agents such as albendazole or nitazoxanide are routinely available in some countries, but are not licenced for the treatment of giardiasis in the UK and would not normally be prescribed in primary care. Albendazole has similar efficacy to metronidazole and is better tolerated57,61. 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.

Treatment for giardiasis is usually successful in primary care but the treatment pathway (**Figure 4**) needs to take account of the possibility of re-infection if the original source is not eliminated, for example asymptomatic infection in a household or sexual contact, or if there is a relapsing infection due to treatment failure. First line treatment should be with tinidazole or metronidazole followed by a repeat course of either of these if unsuccessful, together with exclusion of re-infection or lactose intolerance. Advise patients to avoid milk and milk products for at least 2 weeks (some clinicians advise up to 6 weeks) to evaluate whether persisting symptoms truly represent treatment failure rather than temporary lactose intolerance. Confirmation of treatment failure is best provided by PCR, which offers improved detection in single stool samples over microscopy53,54. Treatment success is indicated by lack of detection of *Giardia* DNA by PCR one week after treatment.

Treatment failure may be due to host factors and/or true drug resistance, which is well recognised and increasingly common, particularly in travellers returning from South and Southeast Asia16,54,63. However, tinidazole or metronidazole should still be used as first line therapy for travellers returning from these areas despite there being cross-resistance between these drugs63. 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 production23,24,64. A variety of combination therapies are effective, although the evidence is based on observational studies and individual clinician preference54,58–60,65–68. Combinations of albendazole and a 5-nitroimidazole, or nitazoxanide with a second agent, are the usual next steps in the therapeutic ladder (**Figure 4**). Paromomycin and mepacrine have specific niches as already discussed.

Asymptomatic carriage of *Giardia* is common in contacts of cases and household clusters do occur. In a recent study in Northwest England, routine testing of all household contacts of 91 primary *Giardia* cases found a *Giardia* positive contact in 27 households (30%): of the 212 contacts, 41 (19%) were positive most of whom were asymptomatic31. In the absence of research as to whether treatment of asymptomatic carriage is effective in curtailing transmission, management is based on expert opinion55. Asymptomatic carriage is generally not treated but treatment is rational in failed treatment of a case or in household clusters (**Figure 4**). 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.

**What is the prognosis of giardiasis following treatment?**

Giardiasis is associated with prolonged symptoms that can have a detrimental impact on quality of life64. A longitudinal study with follow-up six years following a large waterborne outbreak of giardiasis in Norway showed a statistically significant higher prevalence of IBS (46%) in those exposed compared to controls (14%) (RR 3.4, 95% CI: 2.9-3.8)69. Furthermore, three years after the outbreak the prevalence of perceived food intolerance was 63.9%, compared to the control group (47.6%) (OR 2.0, 95 % CI: 1.6 to 2.4) and chronic fatigue syndrome was more common following giardiasis than in controls69. The mechanism of these symptoms is unclear. However there is evidence for increased visceral sensitivity70 and abnormalities in cholecystokinin and serotonin in patients with post-*Giardia* IBS71.

**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 system72–74. Registered medical practitioners should notify cases suspected to have been contracted as food poisoning to their Health Protection Team72–74. Prevention of secondary transmission is mainly through anti-parasitic treatment of cases and advice on the prevention of person-to-person spread (**Box 2**) through stringent personal hygiene (wash hands carefully and do not share towels). Exclusion based on the absence of diarrhoea for 48 hours applies to children in nurseries, food handlers and those caring for vulnerable adults75. Microbiological evidence of stool clearance is not usually required but this may 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 pools17,19. Adherence to guidelines for swimming pool management76 will reduce the risk of giardiasis to a minimum. Drinking water outbreaks are uncommon in the UK77 because of the full treatment of public water supplies (filtration and disinfection), but are a risk where treatment is inadequate. Travellers using water disinfection filters or systems should check that they are certified to remove *Giardia*.

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**Table 1** Comparison of diagnostic tests for *Giardia*42–51*.*

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| **Patient group** | **Specimen type** | **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 (e.g. *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 the 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 | Immunochromatographiclateral flow(cyst antigens) | 95.8-100% | 97.1-100% | Only provides diagnosis of specific parasites included in the assay. Useful where there is low capacity for complex testing; expensive. |
| Formalin or SAF preserved\* or unpreserved stool | ImmunofluorescentMicroscopy(cysts) | 94-100% | 100% | Only provides diagnosis of specific parasites included in the 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(polymerase chain reaction, PCR) | 13-100% | 75-100% | Only provides diagnosis of specific parasites included in the 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) orNucleic 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 |

\*other preservatives may interfere with assay performance. Refer to kit insert. \*\*using PCR as reference test50. SAF= Sodium acetate-acetic acid-formalin solution.

**Table 2** Current treatment options for *Giardia*in the UK. Many are unlicensed in the UK, see text for indications for these in secondary care practice.

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| **Drug** | **Adult Dose** | **Use in Pregnancy** | **Use in Children** | **Licensed** **in UK** |
| Metronidazole | 2 g daily x 3 days OR400 mg tds x 5 days OR400 mg bd x 7-10 days | Avoid first trimester if possible | Yes | Yes |
| Tinidazole | 2 g once only | Avoid first trimester if possible | Yes | Yes |
| Albendazole | 400 mg daily x 5 days | No | Yes | No |
| Nitazoxanide | 500 mg bd x 3 days | No | Yes | No |
| Paromomycin | 500 mg tds x 5-7 days | Yes | Yes | No |
| Mepacrine (quinacrine) | 100 mg tds x 5-7 days | No | No | No |

**BOXES**

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| **Methods**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.  |

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| **Box 1: Risk factors for *Giardia* acquisition in high income countries** * Foreign travel, particularly in low income settings12–16
* Toileting young children and changing nappies12,14,15
* Drinking contaminated water or swallowing contaminated water while using swimming pools or other recreational fresh waters12–15,17–19
* Attending child care settings20
* Eating fresh products raw18,21
* Sexual transmission22
* Dog ownership (*Giardia* assemblage A)12
* Some immunodeficiency disorders: X-linked agammaglobulinaemia, common variable immunodeficiency23,24
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| **Box 2: Advices for patients with *Giardia***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 48 hours after diarrhoea stops if you work with food, or in work in social / health care and have direct contact with patients / clients

Advice regarding young children with *Giardia** Ensure scrupulous hygiene when changing their nappies
* Supervise their handwashing
* Keep young children away from playgroup*s,* childminders, or nursery until free of diarrhoea for 48 hours

Advice for household contacts of a *Giardia* caseTesting is not advised unless the original case remains unwell despite treatment or if a second person becomes unwell  |

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| **Questions for ongoing and future research*** What behavioural or immunological factors could explain the male excess of giardiasis?
* What is the extent of zoonotic transmission risk for *Giardia*?
* Do different *G. 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 relationship 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?
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| **What you need to know*** The number of detected *Giardia* cases will increase significantly as routine testing of stool samples using highly sensitive diagnostic tests becomes more widespread
* The majority of *Giardia* cases in the UK acquire their infection in the UK and not from overseas travel
* Tinidazole and metronidazole are equally effective as first line treatments but 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 amongst household contacts and testing of contacts is indicated in treatment failure and in household clusters
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| **Education into practice*** Request specific *Giardia* testing in patients presenting with relapsing diarrhoea, negative bacterial stool culture and no history of overseas travel - particularly if there are other cases in the household
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| **Additional educational resources***Resources/ Information for healthcare professionals** Public Health England <https://www.gov.uk/guidance/giardia>: For surveillance information and epidemiological trends of giardiasis
* USA Centers for Disease Control and Prevention <http://www.cdc.gov/parasites/giardia/audience-health-professionals.html>: For epidemiological information and links to veterinary and environmental aspects of *Giardia*

*Resources / Information for patients** USA Centers for Disease Control and Prevention <http://www.cdc.gov/parasites/giardia/>: Provides answers to frequently asked questions about *Giardia*
* New Zealand Ministry of Health <http://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](http://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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| **How patients were involved in the creation of the article**No patients were involved in the creation of this review. |