Giardiasis

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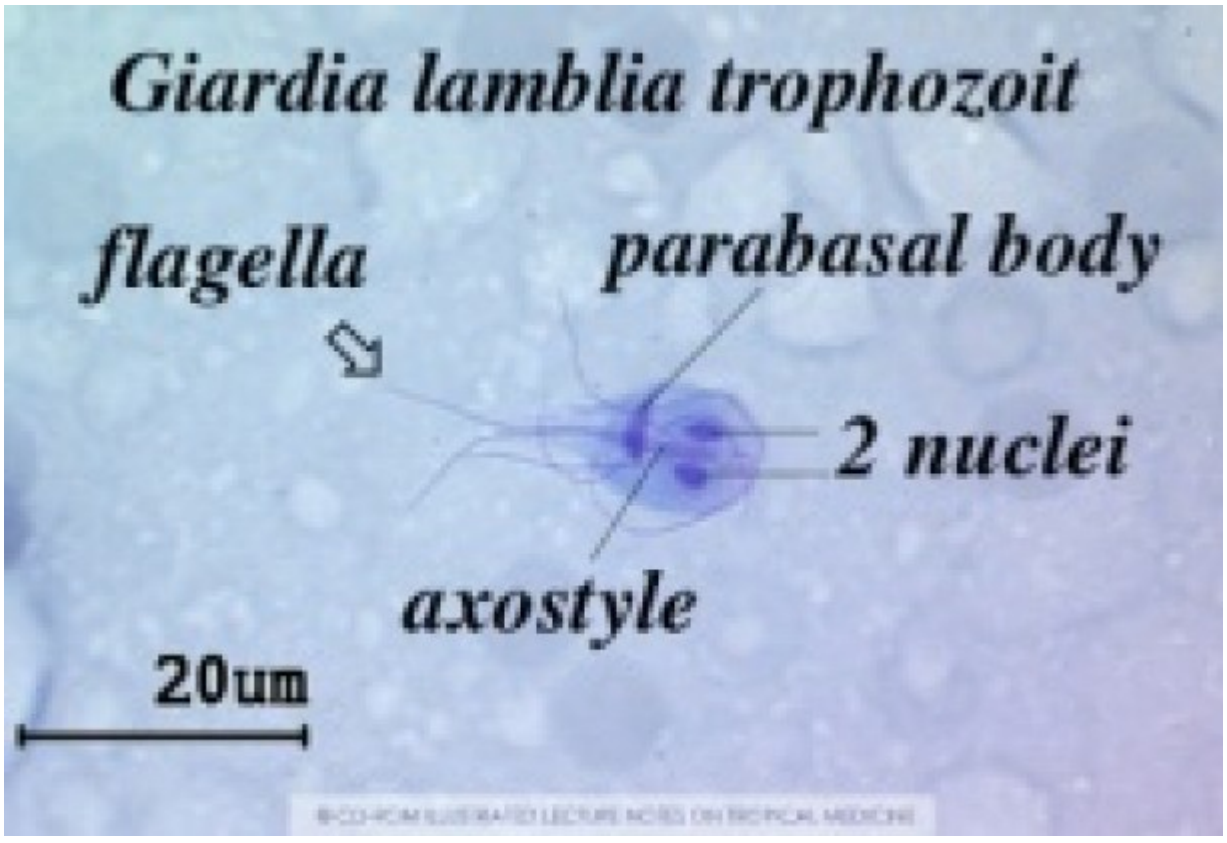
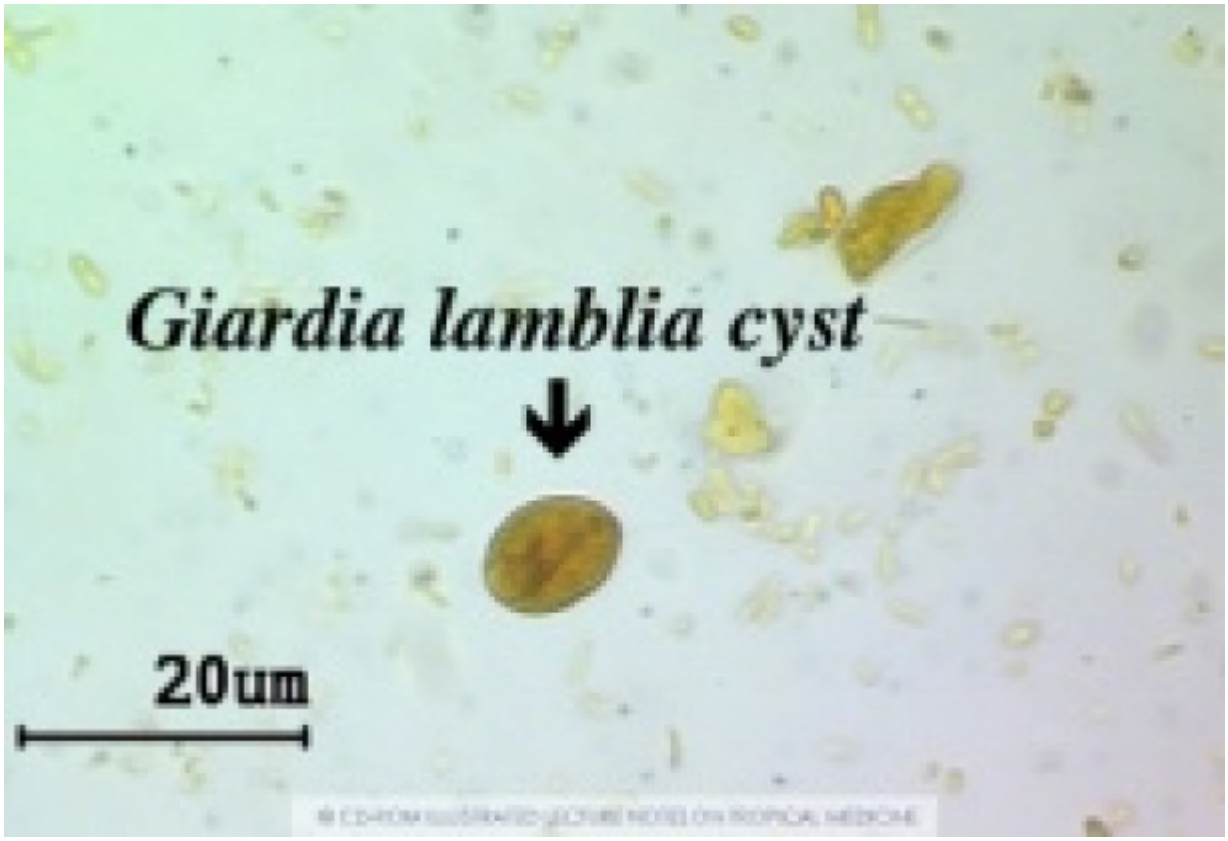
Summary

- *Giardia lamblia is* an unicellular flagellate
- Faeco-oral transmission via cysts
- Sometimes asymptomatic infection
- Sometimes diarrhoea, atypical abdominal discomfort, bloated abdomen
- First-line treatment with nitroimidazoles, by preference tinidazole

General



Giardia lamblia trophozoite in faeces. Copyright ITM



Giardia lamblia cyst. Copyright ITM

Giardia lamblia (*G. intestinalis, G. duodenalis*) is a unicellular parasite (flagellate) which causes intestinal infections. The infections are often asymptomatic and *Giardia* was for a long time thought to be non-pathogenic. Since 1981 it has been regarded as potentially pathogenic and as the cause of diarrhoea and various forms of abdominal discomfort. In developing countries the infection occurs often in children but its frequency diminishes as they grow older. *G. lamblia* may infect various animals, including dogs, cats and beavers.

The taxonomy of this intriguing species is still to be clarified. At present, seven distinct genetic groups based on protein and DNA polymorphisms can be distinguished in *Giardia*. Each group has its own host range, with group A and B able to infect humans.

Biological information

Giardia has no de-novo synthesis of lipids, which means that the parasite is dependent on

exogenous lipids and bile salts (hence its location in the duodenum).

Giardia lamblia is possibly a complex of different species. Chemotaxonomy via determination of antigens using monoclonal antibodies shows that there is significant antigenic variation. DNA-analysis is promising, but *Giardia* has a complex genome. Using iso-enzymatic analysis, 13 zymodemes are known at present.

Giardia contains two functionally equivalent and apparently identical nuclei. The two nuclei remain physically distinct during mitosis in the trophozoit. Both nuclei are diploid and transcriptionally active. The two daughters of a single nucleus segregate to different trophozoites. It is still not clear yet at present if *Giardia* is asexual (as traditionally assumed), parasexual (diplomixis : nuclear fusion of the 2 nuclei during encystations, accompanied by homologous recombination without meiosis) or sexual. Till present, *Giardia* has not been caught “in the act” however. If diplomixis occurs this would be unique to *Giardia*.

Life cycle of *Giardia*

Cysts are swallowed with water or food. In the duodenum excystation occurs which releases the trophozoite. This measures 12-18 µm. It attaches itself to the duodenal and jejunal intestinal villi by means of a kind of ventral sucking disk. The parasite reproduces only by asexual division. The trophozoites may multiply until the whole surface of the intestine is coated with parasites. Possibly this mechanical screening off the intestine contributes to malabsorption.

As trophozoites are carried to the more distal parts of the intestine, the parasite encapsulates. The cyst is resistant in the outside world but trophozoites perish. Cysts remain viable in a wet, cool outside environment. They are not very resistant to drying out. The cysts measure 10 x 7 µm. Transmission is via direct faeco-oral contact, food or via water. There is an animal reservoir and this is sometimes involved in human infection (giardiasis is known in Canada as “beaver fever”). In industrial countries dogs and cats are frequently found to be infected but almost always without symptoms.

Pathogenicity

In many cases infection is asymptomatic, but some patients develop symptoms. One hypothesis as to the pathogenicity is the mechanical covering of the intestinal epithelium (see above). This is not the only way in which the parasite gives rise to symptoms. *Giardia* is cytopathogenic on cell monolayers in vitro. Probably there is also in-vivo enterocytic damage with secondary disaccharidase (lactase) deficiency. Indeed, villous atrophy is found in patients. Another way in which *Giardia* may be

pathogenic, is the destruction of conjugated bile salts with secondary steatorrhoea. Yet another unanswered question is whether the immune response contributes to the pathogenesis. In vivo *Giardia* has frequent endosymbiotic bacteria up to 100 per trophozoite or so it was thought. This may possibly influence pathogenicity. The same question arises as regards any ectosymbionts. *Giardia* itself can be infected with an RNA virus of unknown clinical significance.

Clinical aspects

The disease is asymptomatic in approximately 80% of cases. The clinical spectrum ranges from silent carrier status to a malabsorption syndrome. The incubation time is 1 to 2 weeks. If symptomatic, an undifferentiated acute to subacute diarrhoea which lasts on average 1 to 6 weeks occurs. In some the diarrhoea is steatorrhoeic with malabsorption. This may be accompanied by mild fever, abdominal pain, ructus (“purple burps”), meteorism and anorexia, malaise and vomiting. The diarrhoea may be intermittent, chronic and recurrent, chiefly in patients with an IgA deficiency, hypogammaglobulinemia or agammaglobulinemia. This reflects the fact that secretory immunity in the intestinal lumen is more important for clearance than cell-mediated immunity within the intestinal lumen.

Diagnosis

Diagnosis is quite difficult due to the intermittent character of the presence of *Giardia* in the faeces. The diagnosis is mainly based on fresh or enriched faecal preparations. Sometimes several analyses of faecal specimens are needed. One specimen gives a detection rate of approximately 70% while 3 specimens increase this rate to approximately 85%. Generally cysts are found rarely trophozoites. Other techniques such as duodenal aspiration or the EnteroTest (the string test) are less practical. In rare cases infections have been recognised on jejunal biopsy material or mucus sampled during endoscopy. Recent techniques for detecting antigen in faeces have proved sensitive, specific and fast. PCR methods are increasingly available in high-resource settings. Microscopically a differentiation needs to be made with other flagellates such as the commensal *Chilomastix mesnilii, Enteromonas hominis, Trichomonas hominis* (= *Pentatrichomonas hominis*) and *Retortamonas intestinalis.*

The histological intestinal lesions are not very pronounced: flattening of the intestinal villi, lymphocytic infiltration of the mucosa, no ulceration. Radiology of the small intestine is non-specific. If giardiasis is suspected, but cannot be proven a trial of therapy can sometimes be used.

Treatment

Giardia is an anaerobic protozoon, which possibly explains its sensitivity to nitro-imidazoles (e.g. metronidazole). The drug of first choice are nitro-imidazoles, especially tinidazole (Fasigyn®), of which 2 gramss is to be taken in one dose (adult patient). This gives a cure rate of 90 to 95%. Metronidazole may also be used but produces more side effects. Ornidazole (Tiberal®) 500 mg b.i.d. is an alternative but is best given for 5 days. Alcohol should be avoided since there may be an antabuse effect. Other nitro-imidazoles are also sometimes used: secnidazole (Flagentyl®), nimorazole (Naxogyn®).

Refractory giardiasis possibly related to lower susceptibility/resistance to nitro-imidazoles is increasing. Mepacrine (quinacrine, atebrine) is an old drug (3 x 100 mg/day orally for 5 days) which gives good results if tinidazole fails. It also kills cysts, as opposed to metronidazole. It is a yellow product and may cause a jaundice-like skin discoloration, which the patient should be warned about beforehand. It may also cause haemolysis if there is severe G6PD deficiency. Albendazole has also proved effective in vitro but produces varying results in vivo. Nevertheless it is a good second choice. Paromomycin (Humatin®, Gabbroral®) is an aminoglycoside which has very low absorption when taken orally and is thus active in the intestinal lumen. However there is quite a high relapse rate (25%). Nitazoxanide is an expensive alternative (500 mg BD x 3 days for an adult).

Metronidazole is often available in tropical countries when tinidazole is unavailable. Selective toxicity is achieved because the drug is only reduced in an anaerobic environment (reduction is prevented by oxygen). Its action is limited to anaerobic protista (*Giardia, Entamoeba histolytica, Trichomonas vaginalis*: all three lack mitochondria) and anaerobic bacteria. Side effects of metronidazole include a metallic taste in the mouth, gastrointestinal disturbances: vomiting, nausea, cramps, headache, and a disulfiram (“antabuse”)-effect. Rarer are CNS toxicity, dizziness, drowsiness, lassitude, paraesthesia, pruritus and urticaria. In therapy-resistant giardiasis the questions should be considered as to whether (1) compliance is failing, (2) is there a possibility of counterfeit medication, a growing problem in many countries, (3) if there may be re-infection (e.g. via an asymptomatic cyst carrier), or (4) immunodeficiency, including IgA-deficiency, (5) possibly the presence of a duodenal diverticulum (mechanical reason for relapse, as the concentration of the therapeutic drug might be rather low) or (6) whether this is a genuine problem of resistance. There is in-vitro cross-resistance between the different nitro-imidazoles. If symptoms persist, (7) long-term lactase deficiency or (8) bacterial overgrowth in the small intestine with possible inactivation of nitro-imidazoles by Gram-negative bacteria should be considered.

Prevention

Prophylaxis is difficult both individually and in the community. Giardiasis is much more common than amoebiasis. The importance of giardiasis is underestimated according to some and it is thought to be one of the ten most important parasitic diseases in humans and may be responsible in poor countries of impairment in child growth. Nevertheless there is little connection between the prevalence and the pathology attributed to the infection. In general the treatment of asymptomatic infections in endemic regions is considered unnecessary.

Treatment of large amounts of drinking water (flocculation, sedimentation, filtration and chlorination) is important. Chlorine compounds work best in water with a low pH and a high temperature when the water contains little organic debris.

Alternatives for chlorine and hypochlorite compounds includes chlorine dioxide, ozonation and ultraviolet irradiation. Boiling of large amounts of drinking water is too costly.

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