

Protozoal gastrointestinal infections

Dinesh Aggarwal
Alastair McGregor

Abstract

Protozoal gastrointestinal infections predominantly affect people in lower income countries, with poor sanitation a significant contributing factor. In the developed world, outbreaks mainly affect identifiable high-risk groups and returning travellers. These infections carry a significant morbidity and mortality worldwide. The definitive diagnosis for these infections has traditionally relied upon stool microscopy, but this technique has a poor sensitivity in many infections, and newer technologies such as polymerase chain reaction and enzyme-linked immunoassay-based tests are becoming available. Identification of infection is particularly important in patients with HIV or those otherwise immunosuppressed, as they often suffer severe disease.

Keywords *Amoeba*; *Balantidium*; *Blastocystis*; *Cryptosporidium*; *Cyclospora*; *Cystoisospora*; diarrhoea; *Dientamoeba*; *Giardia*; *Microsporidium*; MRCP; protozoa; treatment

Introduction

Protozoa are single-celled eukaryotic organisms, some of which cause disease in man. Protozoa are a diverse group and, although the term is in common usage in medicine, its use as a formal taxon is discouraged because protozoa are not monophyletic (i.e. do not all share the same evolutionary ancestor). The current classification is outlined in Figure 1.

In general, protozoal infections are linked to poor sanitation, with lower income countries most affected. Outbreaks in the developed world are limited to specific risk groups such as children at nurseries, men who have sex with men (MSM) and prisoners. Mortality associated with protozoal infections is generally low. Infection with *Entamoeba histolytica*, however, can be serious and causes an estimated 100,000 deaths annually, making it the third most common parasitic cause of death.

Flagellates

Flagellates are organisms characterized by the possession of whip-like organelles (flagella), used as a means of motion.

Dinesh Aggarwal MB BS MA (Cantab) MRCP is a second-year Core Medical Trainee in the North West London Deanery, Northwick Park Hospital, London, UK. Competing interests: none declared.

Alastair McGregor MB BS MRCP MSc FRCPath DTMH is a Consultant in Infectious Diseases and Microbiology at London Northwest NHS Trust and an Honorary Senior Clinical Lecturer at Imperial College, London, UK. Competing interests: none declared.

Key points

- The application of molecular phylogenetic techniques has led to the reclassification of several gastrointestinal protozoa
- Infections with these organisms remain a global health issue, with the highest prevalence a consequence of poor sanitation in low-income countries. In more wealthy countries, protozoal infections are often seen in returning travellers, water contamination-related outbreaks, childcare centres and immunocompromised individuals
- Diagnostic techniques are evolving, with microscopic examination now supplanted by rapid antigen enzyme-linked immunoassay and polymerase chain reaction-based tests in some areas
- Treatment options have not substantially evolved in the last 10 years

Giardia lamblia

Giardia lamblia, also known as *Giardia intestinalis*, is often encountered as a cause of traveller's diarrhoea but can also cause outbreaks in MSM and children attending nurseries.

Pathology and pathogenesis: in its trophozoite form, *Giardia* adheres to the apical surface of the duodenal epithelium, where, through processes not entirely understood, its presence results in loss of epithelial tight junction integrity, reduction in glucose and sodium absorption and eventual shortening of the brush border and decreased mucosal surface area. Barrier dysfunction, increased anion secretion and malabsorption contribute to the typical symptoms of infection. Outside the human host, *Giardia* can encyst and prolong its survival in the environment.

Course of disease: infection with *Giardia* can be asymptomatic. The classic symptoms, watery diarrhoea, flatulence and abdominal cramping, are associated with malabsorption. Symptoms start shortly after infection and are usually acute and self-limiting. Longer term manifestations can take the form of exacerbations of irritable bowel syndrome, and prolonged post-infectious symptoms are well recognized.

Diagnosis and investigation: direct microscopic observation of cysts and trophozoites, the traditional gold standard, has a sensitivity of only about 66.4%. Assays using the polymerase chain reaction (PCR) or enzyme-linked immunoassay (ELISA) are more reliable, claiming sensitivities approaching 100%.¹ Duodenal biopsy and aspiration have been used, but their role in the PCR era is unclear. Ultimately, given the poor performance of stool microscopy, the diagnosis is often made on clinical grounds, and treatment given empirically.

Management: nitroimidazole drugs remain first line for treatment of giardiasis. The failure rate with nitroimidazoles appears

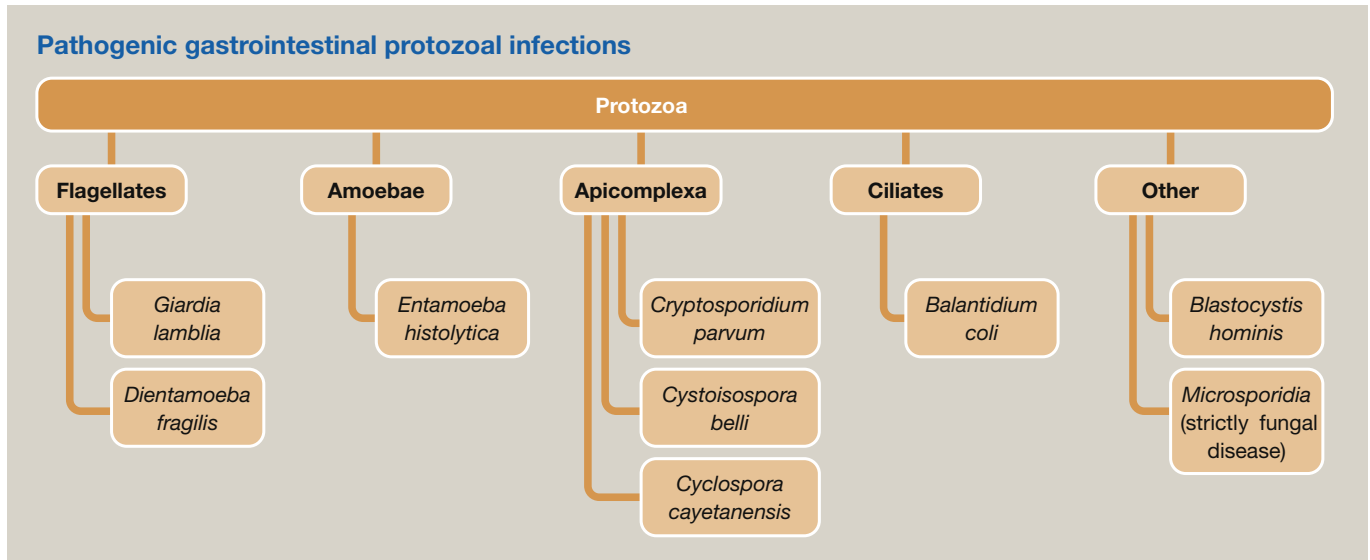


Figure 1

to be increasing (and may be as high as 40%). Second-line treatments include albendazole, paromomycin, nitazoxanide and mepacrine.²

Dientamoeba fragilis

First reported as an amoeba, *Dientamoeba* was later found to express flagella in its cystic form. This organism was thought to be non-pathogenic, but there is mounting evidence that infection can be associated with symptoms. Sensitive diagnostic tools are not widely available, and the incidence of infection is unknown. Treatment with tetracyclines, nitroimidazoles or paromomycin has been shown to be effective.

Amoebae

Amoebae are protozoa that can change shape and move by forming pseudopodia.

Entamoeba histolytica

There are approximately 500 million *Entamoeba histolytica* infections every year, 50 million of which are associated with symptomatic disease. In countries with poor sanitation, carriage rates of *E. histolytica* can reach 40%. Understanding of the epidemiology of amoebiasis has been complicated by the lack, until recently, of a specific test – using microscopy, the cysts of *E. histolytica* cannot be distinguished from *Entamoeba dispar*, which is far more common and is not pathogenic.³

Pathology and pathogenesis: *Entamoeba histolytica* and *Entamoeba moshkovskii* are known to cause disease, but there are numerous (and more common) species that are non-pathogenic. Cysts of *E. histolytica* can survive in the environment for months. When ingested, they excyst and become motile trophozoites. These bind to the mucosal surface of the colon and can activate inflammatory and apoptotic pathways, causing inflammation.

Course of disease: asymptomatic carriage of *E. histolytica* has a mean half-life of 12.9 months.⁴ Symptoms, when present, range from mild diarrhoeal illness to severe colitis. Translocation across the bowel wall can lead to extraintestinal amoebiasis, most commonly in the form of liver abscess.

Diagnosis and investigations: trophozoites rapidly encyst as the temperature falls, and therefore examination of fresh stool for motile trophozoites containing phagocytosed erythrocytes is required to distinguish *E. histolytica* from *E. dispar* using microscopy. Antigen-based ELISA test kits are available, providing a sensitivity and specificity of 71–100% and 93–100%, respectively. PCR performs even better but is not widely available. Serology is useful for the diagnosis of amoebic liver abscess, but the sensitivity in colitis is low³ and it is more applicable to returning travellers than in endemic countries.

Management: nitroimidazoles have excellent activity against *E. histolytica* and remain first line. They may not kill encysted organisms in the gut lumen, so follow-up treatment with agents such as paromomycin and diloxanide, as cysticides, may prevent recrudescence of infection.

Apicomplexa

Encompassing *Cryptosporidium*, *Cyclospora* and *Cystoisospora*, these spore-forming pathogens are particularly prevalent in HIV-positive individuals, in whom they can cause severe disease. Coccidia were previously included in this class but have now been reclassified as fungi.

Cryptosporidium

In the developed world, infection with *Cryptosporidium* is usually acquired from contaminated water. The organism can colonize water treatment facilities or community swimming pools. Worldwide, *Cryptosporidium* is the second most common cause, after rotavirus, of diarrhoeal disease and related mortality in

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