Dientamoeba fragilis: an emerging role in intestinal disease

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First described in 1918 by Jepps and Dobell, *Dientamoeba fragilis* is a binucleated, unflagellated protozoan related to the trichomonads,[1] readily identified in stool specimens by means of routine iron-hematoxylin stains. First observed in 7 patients, of whom 6 had diarrhea or dysentery, the parasite was dubiously classified as a nonpathogen based on its source of nutrition: its voracious appetite is for the commensal bacteria of the gut rather than the tissues of its host.[1] For decades, the organism was thrown into the grab-bag of human commensal protozoa with the likes of *Entamoeba coli* and *Endolimax nana*. Questions about the nonpathogenicity of this protozoan have emerged, however, and there can now be little doubt of its role in gastrointestinal disease.[1–3]

Only recently has the evidence supporting *D. fragilis* as a cause of diarrhea, abdominal pain, cramping and a plethora of vague abdominal complaints come to light. The organism has been isolated from patients with clinical disease in countries around the world, including an Australian study reporting that all of 60 patients with confirmed *D. fragilis* infection were symptomatic.[3] Moreover, treatment with drugs known to have parasiticidal activity in vitro has led to prompt and dramatic clinical improvement in the majority of reported cases.[1,2] In some cases, patients with prior misdiagnoses of irritable bowel syndrome (IBS) or chronic diarrhea have been found to be infected with the parasite and cured with antiparasitic agents.[1] Such observations indicate a need not only for appropriate investigation but also treatment of patients who have symptoms of irritable bowel syndrome before a reputedly incurable condition is diagnosed. As a result of these and other observations, many countries have finally recognized *D. fragilis* as a true gastrointestinal pathogen.[1]

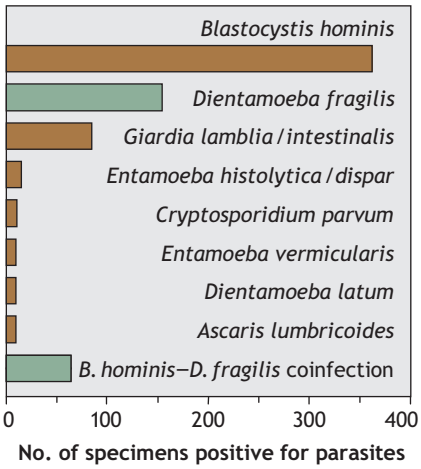

Fig. 1: Nonrepeat occurrence of the 8 most common intestinal parasites diagnosed via stool examination at Cadham Provincial Laboratory, Winnipeg, Man., over a 1-year period.

The prevalence of *D. fragilis* would surprise most clinicians. A review of stool-examination reports at the Cadham Provincial Laboratory in Winnipeg, which handles 80%–90% of stool examinations for parasites done in Manitoba, revealed that the incidence of this parasite was second only to *Blastocystis hominis* and far in excess of more commonly incriminated parasites such as *Giardia lamblia/intestinalis*, *Entamoeba histolytica/dispar* and *Cryptosporidium parvum*. Coinfection with *B. hominis* and *D. fragilis* was also common (Fig. 1).

To examine the epidemiology of *D. fragilis* infection in Manitoba, we reviewed the examination results for all fecal specimens submitted over a 12-month period (Feb. 2005 through Jan. 2006) to the Cadham Provincial Laboratory for ova and parasites: a total of 11 100 specimens from 6363 patients (mean 1.74 specimens per patient). The parasite was found predominantly in specimens from young adults: 50% of people found to have dientamoebiasis in Manitoba were younger than 24 (mean 28.7) years. This contrasts with a median age of 41 years for all patients submitting samples (mean 40.8 yr), which suggests that sample bias does not account for the observation of differences in the incidence of this parasite in younger people.

Specimens from patients 11–15 years of age had relatively high rates of positive reports (boys 10.3%, girls 9.6%). Those from young men aged 16–20 years had the highest rate: 11.5% (95% confidence interval [CI] 4%–19%). The positivity rate of specimens from young women aged 16–20 years, on the other hand, was much lower (1.1%, 95% CI 0.3%–1.9%; $p < 0.01$), in contrast with reports from other countries[1,2] where a female predilection has been suggested. Furthermore, 45.9% of positive results applied to specimens from female patients, who furnished 58.3% of the specimens submitted ($p = 0.03$). Adults over 20 years of age had the lowest incidence rates (0.6–2.0%); the rates in children under 10 were intermediate (1.3%–5.7%). Incidence rates showed no seasonal variation over a 5-year period (data not shown), which contrasts sharply with the summer–fall seasonality of pathogens traditionally associated with contaminated water (e.g., *G. lamblia/intestinalis*, *C. parvum*).

The mode of transmission of *D. fragilis* remains a mystery, perhaps because its acknowledgement as a pathogen is so recent. The organism has never been found to have a cyst stage, deemed necessary for efficient feco-oral transmission.[1–3] Moreover, direct transmission via trophozoite forms was deemed unlikely when, in keeping with a longstanding practice among early parasitologists of self-experimentation, Dobell swallowed a culture containing millions of trophozoites.[1] Not only did he remain asymptomatic, but for 10 years he examined his own stool specimens and never observed the parasite.

Because of its morphological, biological and genetic similarities to protozoan parasites of nonhuman animals that are known to use the eggs of parasitic worms as vectors, it was speculated

Table 1: Treatments that have exterminated *Dientamoeba fragilis**

Agent	Dose, mg†	Duration, d
Iodoquinol	650	20
Doxycycline, twice a day	100	10
Metronidazole	500	10
Paromomycin, mg/kg body wt	8-12	7
Secnidazole, single dose	2000	1

Note: wt = weight.
*Adapted from references 1, 2 and 5-9.
†Administered by mouth: 3 times per day, unless otherwise indicated.

that *D. fragilis* may also be transmitted that way.[1] Early studies pointed toward the pinworm, *Enterobius vermicularis*, as a potential vector: coinfection with *D. fragilis* and *E. vermicularis* initially appeared to be far more common than expected; amoeboid bodies resembling *D. fragilis* have been described in the eggs of *E. vermicularis*; and the parasitologist Ockert (again, in the tradition of self-experimentation) successfully infected himself and 2 other adult volunteers by ingesting *E. vermicularis* eggs taken from a child coinfected with *D. fragilis*.[1]

Despite these observations, many have questioned a role for pinworms in transmission, frequently citing the paucity of well-controlled epidemiological experiments.[1] In one study, Stark and colleagues[3] performed appropriate pinworm testing in conjunction with microscopic stool examination and found no association between infection with *Enterobius* and *Dientamoeba*. The authors acknowledged, however, that spontaneous remission of pinworm infection could have occurred while *Dientamoeba* infection persisted. Similarly, our study did not identify any coinfections with *Enterobius* and *Dientamoeba*, but appropriate testing (sticky tape or paddle) for *Enterobius* eggs was not performed consistently. Lastly, PCR of nucleic acid extract of *Enterobius* eggs did not identify *Dientameoba* DNA in coinfected individuals.[4] As it stands, although the mode of transmission remains unknown, it seems fair to query the role of *Enterobius* in the transmission of *Dientamoeba*.

Several drugs are thought to have paraciticidal activity against *D. fragilis*. Unfortunately, in vitro testing is inaccurate and cannot reliably predict treatment outcomes because *Dientamoeba* requires xenic media (media containing bacteria for the parasite to feed on). Furthermore, no large-scale randomized control trials have been done. Many agents have, however, led to the eradication of *D. fragilis* from stools and resolution of symptoms as documented in case reports (Table 1).[1,2,5–9] The most commonly employed and best studied treatments currently are iodoquinol and doxycycline.[1,8] This regimen was studied in a small case series of 21 people with IBS-like symptoms and concomitant infection with *D. fragilis* who were treated with iodoquinol and doxycycline: the symptoms resolved in 14 of the patients (67%), in whom the organism was eradicated. In a more recent study of secnidazole treatment,[9] a single dose eradicated the parasite in 34 of 35 patients (97%, 95% CI 92%–100%) and resolved clinical symptoms in 27 cases (77%, 95% CI 63%–91%).

Intestinal parasites, particularly those found in temperate climates, are often forgotten as causes of disease. Increasing evidence of pathogenicity in common parasites previously deemed as nonpathogenic, including *D. fragilis,* should prompt clinicians to consider eradicating *D. fragilis* when it is found in all patients with gastrointestinal complaints. Furthermore, people who have symptoms of IBS should be evaluated for the presence of this and other parasites. Where required, treatment should be provided before a diagnosis of IBS is given.

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