IRRITABLE BOWEL SYNDROME AND *DIENTAMOEBA FRAGILIS*

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Introduction

Diarrhoea-predominant irritable bowel syndrome (IBS) is a common disorder which is characterised by diarrhoea, cramping, sub-umbilical discomfort, symptom improvement on defecation and, at times, aggravation on defecation, flatulence, 'explosive' stools and systemic symptoms such as tiredness, nausea and occasional bloating. By definition, diarrhoea-predominant IBS is chronic, has no detectable organic cause and can fluctuate in severity. It can be exacerbated by certain foods, stress or miscellaneous factors and improved by various manoeuvres including restrictive dieting, medications, travel and other factors differing from person to person.

It is clear from experience in the literature that chronic infection with *Dientamoeba fragilis* (DF) can mimic many of the symptoms of diarrhoea-predominant IBS. This parasite was discovered in 1909 but, perhaps because due to the difficulties associated with detection, gastroenterologists and microbiologists have not worked together adequately to study it in greater detail. Hence, DF has remained a microbe of interest to microbiologists rather than a pathogen of gastroenterologists and perhaps one on which more clinical research should have been conducted. Most publications on this parasite originate from microbiologists with case reports coming from clinicians.

Dientamoeba fragilis

Dientamoeba fragilis is an intestinal protozoan originally seen by Wenyon in 1909 but was not recognised as a new species until its description by Jepps and Dobell in 1918. For some decades it was thought to be a harmless commensal, despite numerous published reports of illnesses associated with the infection Although its role as a pathogenic agent remains controversial, DF has been linked to chronic diarrhoea, abdominal pain, nausea, anorexia and excessive flatulence DF has also been implicated as a cause of colitis in adults. Allergic colitis with peripheral eosinophilia secondary to DF infection has also been described.

Much has been learnt about the epidemiology of DF since its original description. By 1924, only 33 DF cases were recorded world-wide. Over the past four decades its global incidence has been studied varying considerably from 1.5% to 52.5 per 100, generally being higher in immuno-compromised patients. The use of adequate culture techniques has increased detection of DF significantly with reported rates as high as 18% in Israel, 36% in Holland and 41.5% in Germany. Higher rates of infection are seen in crowded conditions with poor personal hygiene. Sampling and detection methods have an immense influence on the ability of a laboratory to detect DF. Identification is more probable when the faecal samples are examined in three rather than one sample and is not possible without the use of a fixative agent such as SAF (sodium acetate / acetic acid / formalin). There is also debate about whether the detection rate is higher in soft or fluid stool. When stool slides are suitably stained there is a five-fold increase in the rate of detection. Hence, methods used in the detection of DF are of crucial importance.

Transmission of DF still remains unclear although there has been fair substantiation of the hypothesis that *Enterobius vermicularis* (pinworm) is the vector responsible for person to person spread. *D. fragilis* mono-nucleated or bi-nucleated forms have been documented in the lumen of *E. vermicularis* found in the human appendix. Many authors have now reported a higher than anticipated co-incidence of DF and *E. vermicularis* infections. In fact, Ockert experimentally infected himself with pinworm eggs from a child and subsequently developed DF infection. Two other successful attempts at infecting humans with DF from pinworms were also described by Ockert. By contrast infection with DF by ingesting DF trophozoites has failed.

Clinical Presentation

Though the pathogenicity of DF continues to be questioned by some, the circumstantial evidence incriminating this organism as a pathogen is overwhelming. Onset of infection is accompanied by onset of colicky pain, loss of appetite, soft stools covered with mucus and irritation of the rectum. Numerous observations have shown that treatment which eliminates the organism results in clinical improvement. In the literature, abdominal pain, persistent diarrhoea, pruritus, abnormal stool with mucus, flatulence, fatigue or weakness, occasional eosinophilia, alternating diarrhoea and constipation, nausea or vomiting, weight loss, constipation, belching and tenesmus are found in decreasing order of frequency as symptoms in patients in whom only DF was identified Many of these symptoms mirror the symptoms of IBS.

Diagnosis

Clinical suspicion of DF in patients with diarrhoea-predominant IBS needs to be confirmed by the demonstration of the parasite in stools. Many commercial pathology laboratories in Australia rarely diagnose DF because stools are not promptly collected into the appropriate fixative and specifically stained specimens are not examined by those trained in DF recognition.

Trophozoites of DF degenerate rapidly and prompt fixation is necessary. SAF (sodium acetate / acetic acid / formalin) fixative is often used. Although many different staining methods have been employed to detect DF, the most commonly used stain today is probably iron haematoxylin. In our own experience with detection of more than 150 patients positive for DF in the last 12 months, *Giardia lamblia* was an uncommon pathogen by comparison - seen around 'one tenth' as commonly as DF. Hence, at least in clinical gastroenterological practice, DF is probably the most commonly detected parasite in Australia. Culture techniques are said to be the most sensitive method of detecting DF. However, few laboratories are capable of culturing DF at this stage.

Overall therefore, DF is infrequently sought for and is rarely detected using fresh, unfixed stool specimens.

Role of *D. fragilis* in diarrhoea-predominant IBS

At our Centre all patients with IBS-type symptoms are tested for the presence of DF. Complete data of long, post-treatment follow up has recently been reviewed for 21 consecutive patients who presented with at least two months through to lifelong history of IBS-like symptoms and were positive exclusively for DF. Three fixed and three unfixed stool specimens were used to diagnose these patients. DF was not found in any of the unfixed specimens examined routinely by an accredited pathology laboratory. When the same stools were delivered in SAF fixative to be stained and examined by a trained parasitologist DF was detected in all specimens. These stool-positive 'IBS-like' patients then underwent a combination therapy with iodoquinol and doxycycline and all became negative for DF (in our hands this combination has resulted in complete eradication of DF when re-tested using three stools in fixative). When re-interviewed at least four weeks after treatment, 16 of 21 patients reported global improvement post-treatment. In 16 patients with diarrhoea-predominant IBS-type symptoms, 14 reported the resumption of regular bowel habit with a reduction in frequency to 1-2 stools per day and improvement in associated symptoms. Those with minor symptoms or with constipation failed to improve post-treatment suggesting another cause for their symptoms. From our prospective study it is clear that the use of SAF fixative is crucial in the detection of DF. Also, diarrhoea-predominant IBS should not be diagnosed until appropriately fixed and stained stools are examined by a parasitologist experienced in DF detection. Such observations also point to the need for a larger placebo-controlled multi-centre trial in eradication of DF in patients with diarrhoea-predominant IBS. Until this is carried out however, since the therapy is of short duration, has an acceptable side effect profile, and DF can lead to colitis, those patients with ongoing chronic symptoms should probably seek diagnosis and treatment for DF.

For Medical Practitioners - Practical Tips
Diagnostic kits with fixative and appropriate instructions can be obtained by phoning HistoPATH on 02 - 9764 4300.

Combination therapy of doxycycline, 50 mg bd, together with iodoquinol, 630 mg tds, for 20 days can be obtained by prescription from a compounding pharmacy in Sydney. Contact Mr Graeme Skinner on 02 - 9416 2642.

Further information is available on an excellent web site: (http://bara.idx.com.au/dfragilis/info.htm)
(A list of references is available on request)

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"And you are an upright, honourable person who always tells the truth?" sneered the sarcastic lawyer to the witness.

"Yes," replied the witness. "And if I were not under oath, I'd return the compliment."