Cryptosporidium and diarrhoea

Fifteen years ago the only organisms known to cause gastroenteritis in man were enteropathogenic bacteria. Since then a number of different viruses, detected by electron microscopy of diarrhoeal stools, have been implicated as important causal agents. Nevertheless no known pathogen can be detected in many episodes of gastroenteritis, suggesting that further gastrointestinal pathogens await our detection.

Recently a new pathogen has been described in association with gastroenteritis of children and adults, and this organism, *Cryptosporidium*, is a coccidian parasite related to *Toxoplasma*.

History

Cryptosporidia have been known to be pathogenic to animals since 1907,¹ but the first human case was not reported until 1976.² Since then there have been an increasing number of papers describing human cryptosporidiosis. Initially these described chronic, life threatening diarrhoea occurring in immunocompromised patients, but more recently there have been descriptions of self limiting gastroenteritis in seemingly immunocompetent adults and children.

Detection of *Cryptosporidium*

The main reason for the increasing number of reports on *Cryptosporidium* is the development of easy and rapid techniques for identifying oocysts in stool samples. Various techniques have been described and most are successful in experienced hands. A modified Ziehl-Neelsen technique using hot or cold carbol-fuchsin to stain oocysts is most commonly employed,³ although others have argued the merits of sugar flotation, Giemsa,³ safranin/methylene blue,⁴ and carbol phenol auramine staining.⁵

When intestinal biopsy material is available, *Cryptosporidium* schizonts may just be visible by light microscopy adhering to the intestinal mucosa, but the characteristic morphology is readily identifiable with the electron microscope.^{6 7}

Acute gastroenteritis

In seemingly normal children *Cryptosporidium* may cause mild gastroenteritis lasting up to two weeks, with four to six watery, mucoid, offensive stools a day.⁸ Abdominal pain may be prominent in older children; indeed, failure to recognise cryptosporidial

enterocolitis in a 24 year old woman resulted in a hemicolectomy for presumed Crohn's disease.⁹ Vomiting, nausea, headache, and fever are frequent.^{7 10} Transient asymptomatic carriage may occur, but is seemingly rare.^{7 10}

Cryptosporidium is responsible for up to 7% of episodes of acute gastroenteritis in Western children.^{7 8 10} Cryptosporidiosis has also been described in children with gastroenteritis in Liberia¹¹ and Bangladesh.¹² In Rwanda a significant association was found between cryptosporidium in the stools and measles-related diarrhoea.¹³

Prolonged diarrhoea and failure to thrive

Casemore and Jackson reported a 1 year old child with recurrent diarrhoea and failure to thrive in whose stools cryptosporidial oocysts were detected.¹⁴ Isaacs and colleagues⁷ have described two children with chronic diarrhoea and failure to thrive. Both had a small intestinal enteropathy; one had cryptosporidial oocysts in stool specimens obtained two months apart and the other had cryptosporidial schizonts attached to the jejunal mucosa. Recovery occurred spontaneously after several months, coincident with stools becoming negative for oocysts.

Chronic, bloody diarrhoea

It is possible that *Cryptosporidium* occasionally causes colitis but the position is unclear. A 3½ year old girl has been described with a histologically indeterminate colitis associated with cryptosporidial oocysts in the stool, but also moderately raised antibody titres to Yersinia: sulphasalazine was started and symptoms resolved after three months.⁷ Cogswell and Richardson isolated cryptosporidial oocysts from a 9 year old girl with recurrent episodes of bloody diarrhoea with mucus, symptoms having begun five years previously after exposure to calves.¹⁵

Immunocompromised patients

A syndrome of chronic, profuse watery diarrhoea has been described in association with cryptosporidial infestation of the small and large intestines, and occasionally other epithelial surfaces such as lung, pancreas, bile ducts, and gall-bladder.^{16 17} The mortality of this syndrome is high: in adults it has been described mostly in patients with the acquired immune deficiency syndrome (AIDS),¹⁸ while chil-

dren have had hypogammaglobulinaemia,¹⁶ severe combined immune deficiency,¹⁷ or have been receiving immunosuppressive treatment for malignancy^{19 20} or renal transplant.²¹

Mode of transmission

Cryptosporidiosis is transmitted by the faecal-oral route. Animals and birds are susceptible to infection, and humans have been infected by calves,²² cats,²⁰ and probably dogs,¹⁹ although the great majority of infections cannot be shown to be transmitted either from animals or from water.⁸ It has been suggested that contaminated milk might be one source of infection.⁸ Cases spread readily within families, however, and hospital and veterinary staff have been infected by patients and animals.

Mechanism of diarrhoea

Cryptosporidium does not penetrate the intestinal mucosa but attaches to the microvillous surface of the enterocytes, where it may be seen in different stages of its life cycle.⁶ Intestinal biopsy specimens from infected calves, lambs, and goats²⁴ have shown extensive mucosal changes and similar changes have been noted in biopsies from children with acute² or chronic diarrhoea.⁷ The presumed mechanism of diarrhoea is malabsorption secondary to mucosal damage.

Treatment

There is at present no specific treatment for cryptosporidiosis, many different drugs having been tried without any effect. Limited success has been reported in the United States, however, using the macrolide antibiotic, spiramycin, to treat affected AIDS patients.²³ If a patient on immunosuppressive treatment develops life threatening diarrhoea secondary to cryptosporidiosis, immunosuppressive drugs should, where possible, be stopped until the organism is cleared.

It is hoped that the recent achievement of Current and Haynes²⁵ in culturing *Cryptosporidium* through its complete life cycle in cell culture will permit the discovery of effective treatments against the organism.

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