Two year study of cryptosporidium infection

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SUMMARY During a two year period 48 children admitted to hospitals in the Blackburn district were found to have cryptosporidium in stool samples. Cryptosporidium accounted for 6% of the 742 cases of childhood gastroenteritis, being as common as campylobacter. Altogether, 89% of children with cryptosporidiosis had diarrhoea, which was usually offensive and watery, and 80% vomited, the mean duration of both symptoms being six days. A substantial proportion were moderately ill with dehydration and persistent vomiting. Over half of all cases were aged 2 years or more and 37% were over 5 years. Most of the ill children were over 2 years, in contrast with other cases of gastroenteritis. Eight children were less than the 3rd centile for weight and three of these were investigated for failure to thrive. Only 6% of cases occurred in Asian children, but Asians accounted for 32% of all admissions with gastroenteritis and 59% of admissions with shigella. This unexpected ethnic difference may be due to limited contact with animals among Asians or to differences in diet.

Cryptosporidium is a protozoal coccidian parasite first identified in 1907 in the mouse and known for many years to be a cause of diarrhoea in calves. The first report of its association with gastroenteritis in man came 11 years ago,¹ and it is known to be a cause of severe intractable diarrhoea in immuno-compromised patients.² In the last few years numerous epidemiological reports have shown cryptosporidium to be present in between 0.9%³ and 7.2%⁴ of faecal samples submitted to laboratories in the United Kingdom. Few reports, however, have detailed the clinical features in children admitted to hospital. An annotation stated that gastroenteritis due to cryptosporidium is mild, lasting up to two weeks, with four to five watery mucoid offensive stools a day, and often associated with vomiting, headache, and fever and abdominal pain in older children.⁵ Of 27 cases who presented to a children's hospital, however, 52% were severe enough to require admission and 33% were dehydrated.⁶

This study attempted to ascertain the incidence, clinical features, and importance of cryptosporidium infection in children admitted to a district general hospital.

Patients and methods

The study group comprised all 48 children who were found to have cryptosporidium in faecal specimens during the two years 1 April 1984–31 March 1986.

All children had been admitted to the paediatric wards of Park Lee Hospital, Blackburn Royal Infirmary, or Queen's Park Hospital, Blackburn, most of them with symptoms of gastroenteritis, prolonged diarrhoea, or failure to thrive. All faecal samples submitted to the district microbiology laboratory during the two years were examined for cryptosporidium oocysts. Smears of faeces on glass slides were stained by the safranin-methylene blue technique⁷ and examined by light microscopy. Concentration methods were not used. Oocysts of cryptosporidium were identified as spherical orange/pink bodies 4–6 µm in diameter, with evidence of more deeply staining internal structure.

Clinical details were ascertained retrospectively from the hospital case notes when cryptosporidium was identified. The total number of children with gastroenteritis was obtained from the district medical records department and numbers of other enteric pathogens from laboratory and ward record books and the district diagnostic index.

In a survey of 58 consecutive cases of cryptosporidium infection of any age identified by our laboratory on routine examination of stools submitted from April 1984–March 1985 details were requested of animal contact and consumption of raw unpasteurised milk. The parents of 73 consecutive admissions with gastroenteritis to the children's infectious disease ward were also asked whether the family drank raw or pasteurised milk.

Statistical results were obtained using the χ^2 test.

Results

A total of 48 patients were identified, with ages between 11 days and 15 years. The boy:girl ratio was 1.6:1. Two patients, aged 11 days and 5 years, had no gastrointestinal symptoms and were analysed separately. The age distribution of the 46 remaining patients was compared with that of the 696 children with other causes of gastroenteritis admitted over the two years. Twenty five (54%) of those with cryptosporidium were aged more than 2 years compared with only 199 (21%) of those with other causes of gastroenteritis ($p<0.001$), and 18 (37%) were over 5 years. Only nine (20%) were less than 1 year of age compared with 429 (61%) of those with other causes of gastroenteritis admitted to our children's infectious disease ward ($p<0.001$). The duration of admission to hospital was one to 14 days, with a mean of 4.2 days. Eight patients (17%) stayed in hospital for seven days or more as a result of prolonged symptoms. In contrast, the mean duration of admission in 1985 of patients with non-bacterial gastroenteritis was three days, and only 5.5% of these stayed in hospital for seven days or longer. The mean duration of admission for salmonella was 4.2 days, for shigella 6.0 days, and for campylobacter 4.7 days.

Clinical features (Table 1). A total of 41 patients (89%) had acute diarrhoea, the duration of which ranged from two days to three weeks, with a mean of six days. In 27 of these patients (66%) the diarrhoea lasted more than five days and in eight (20%) more than 10 days. There was no significant difference in duration of diarrhoea at different ages. In most patients the diarrhoea was described as

watery and often as very offensive. In two children, aged 2 and 3 years, respectively, there was a small amount of blood in the motions.

Altogether, 37 patients (80%) vomited for a duration of one to 15 days, with a mean of nearly six days. In 15 (40%) of these patients the vomiting lasted more than five days and in seven (19%) more than 10 days. Two patients vomited without any diarrhoea. One child with severe vomiting was constipated. Eleven (24%) were dehydrated (5% or greater). Of these, 10 were aged over 2 years and six over 5 years. Intravenous fluids were needed in 12 patients, all of whom were aged over 12 months. Ten of 25 children (40%) aged over 2 years were dehydrated and needed intravenous fluids compared with only two of 21 children (9%) aged under 2 years ($p<0.01$).

Fourteen children (30%) aged more than 1 year had definite abdominal pain, which lasted from one to 10 days. Eight children had fever, which was usually mild and lasted less than three days. Eight children had coughs that persisted for five to 14 days.

Failure to thrive

Eight children, aged 3 months to 5 years, presented with gastrointestinal symptoms and weight below the third centile. Cryptosporidium was found in stool specimens in all of these patients, including the three below who were investigated for failure to thrive.

Case 1. A 5 month old girl had chronic diarrhoea for 11 weeks with failure to thrive. She had a low one hour blood xylose concentration of 0.45 mmol/l but normal faecal fats and jejunal biopsy. Cryptosporidia were not seen on light microscopy of the biopsy specimen. She spontaneously recovered in the next month with a return to normal weight gain.

Case 2. A 16 month old girl had diarrhoea for six days and vomiting for 11 days. Weight was well below the third centile. The one hour blood xylose concentration was 0.3 mmol/l, improving to 1.33 mmol/l three weeks later, with resolution of her symptoms. Her weight slowly returned to the 10th centile over the next three months.

Case 3. A 16 month old boy presented with vomiting and an 800 g weight loss over one month without diarrhoea. The one hour blood xylose concentration was 0.7 mmol/l and light microscopy of jejunal biopsy specimen yielded normal results. He returned to normal weight gain in the next seven weeks without treatment.

In none of these three cases did investigation

Table 1 Acute clinical features related to age distribution in 46 children with cryptosporidiosis. Values are No of patients

	Age group (years)			Total No
	<1	1-≤2	>2	
Diarrhoea:				
Total	7	11	23	41
Duration >10 days	3	1	4	8
Vomiting:				
Total	6	10	21	37
Duration >10 days	2	2	3	7
Dehydration (5% or more)	0	1	10*	11
Intravenous fluid replacement	0	2	10*	12
Abdominal pain	0	4	10	14
Fever	1	1	6	8
Cough	1	0	7	8

* $p<0.01$.

reveal any other cause for the failure to thrive and no other pathogens were identified.

Neonatal infection. A 31 year old primigravida developed severe diarrhoea two days before the rapid delivery at home of a girl with birth weight of 1380 g and gestational age of 31 weeks. Cryptosporidium oocysts were found in the mother's stools and her diarrhoea continued for seven days post partum. The mother visited her baby regularly after the first two days. The baby required ventilation for hyaline membrane disease for three days but thereafter did well and at no stage had diarrhoea or vomiting. Cryptosporidium oocysts were identified in her stool three weeks after birth but were no longer present 11 days later. No oocysts were identified in the mother's expressed breast milk, in nasopharyngeal aspirate from the baby, or in any other babies or staff on the unit. No other faecal pathogens were found in the mother or child.

Other pathogens. In association with the finding of cryptosporidium one child had a triple infection with giardia and campylobacter, having just returned from Pakistan. Three other children had dual infections, one with campylobacter, one with *Shigella sonnei*, and one with rotavirus. Two children had concurrent measles infection.

Seasonal incidence. The Figure shows the incidence by month of diagnosis. There was an early autumn and a smaller spring peak.

Figure Seasonal incidence of cryptosporidium over two years by month of diagnosis.

Table 2 Comparison of cases of cryptosporidium gastroenteritis with cases with other causes of gastroenteritis, with reference in particular to the Asian population

	Total No of cases	% Total	No of Asians in each group	Asians as % of the total in each group
Total	742	100	238	32
Rotavirus	162	22	42	26
Enteropathogenic <i>Escherichia coli</i>	47	6.3	12	26
Cryptosporidium	46	6.2	3*	6
Campylobacter	46	6.2	18	39
Shigella	34	4.6	20†	59
Giardia	27	3.6	12	44
Salmonella	23	3.1	8	35
Unspecified/other virus	357	48	123	34

* $p < 0.001$; ** $p = 0.001$.

Comparison with other causes of gastroenteritis.

Table 2 shows the incidence of other major causes of gastroenteritis in the 742 children admitted to the district hospitals in the two years. The two children with cryptosporidium who had no bowel symptoms were excluded.

A significantly high percentage (59%) of children with shigella were of Asian origin ($p = 0.01$), while only 6% of children with cryptosporidium were of Asian origin. Asians comprised about 22% of the child population, 28% of admissions to the children's infectious disease ward, and 32% of all admissions with gastroenteritis. The incidence of cryptosporidiosis in this ethnic group was unduly low compared with all Asian admissions with gastroenteritis ($p < 0.001$).

The survey of 58 consecutive patients with cryptosporidiosis revealed that 31 of 54 responders (57%) regularly drank unpasteurised milk. This compared with 24 of 73 (33%) consecutive admissions of children with gastroenteritis ($p = 0.01$). In addition, it was found that 32 of 53 (58%) of the patients with cryptosporidiosis had regular contact with pets or domestic animals. A study is in progress to ascertain the importance of this finding.

Discussion

This study confirms recent reports that have shown cryptosporidium to be a common cause of gastroenteritis. In our district it was as common as *Escherichia coli* and campylobacter and more common than giardia, shigella, and salmonella, findings that are similar to those from another hospital.⁸ The age incidence in our cases admitted to hospital (37% over 5 years and only 20% under 1 year) contrasts

markedly with that of children admitted with non-specific or viral gastroenteritis, who are usually infants. In our hospital 59% of all cases of gastroenteritis were in children less than 1 year. Laboratory surveys, however, show a greater proportion of cases of cryptosporidium in younger children.⁹ The reason for the difference seems to be that cryptosporidiosis in the older child is more often unusually severe, necessitating admission to hospital. In the older children in our study admission to hospital was precipitated in most cases by severe and prolonged vomiting in addition to diarrhoea. A quarter of all our cases were sufficiently dehydrated to require intravenous fluids. Nearly all these children were aged over 2 years, and no infants under 12 months required intravenous fluids. In a smaller survey of 27 patients with cryptosporidiosis nine were dehydrated, and although there were few children aged over 5 years, only two of those dehydrated were aged less than 1 year.⁶

We feel certain that the older children in our study had more severe illness, but some admissions of older children could have been delayed because general practitioners do not expect dehydration in the older child. We do not know why the illness seems to be severer in older children. None of the children in our study showed any clinical evidence of immune deficiency.

Outside hospital, many cases are mild and even asymptomatic. In an outbreak in a day nursery in north west England the rate of attack was seven of 13 children aged less than 3 years and 14 of 70 in the nursery overall. (Riordan T. Personal communication.) None of the 14 required admission. Similarly, during a period of two months, 25 of 53 children at a day care centre in the United States had diarrhoea: cryptosporidium was found in 65% of symptomatic and 11% of asymptomatic children.¹⁰ Asymptomatic excretion of oocysts is, however, generally rare in this country,⁹ although it is common in India.¹¹ The mean incubation period after contact is six days,¹² and the shedding of oocysts generally stops within two weeks of the stopping of diarrhoea, though it may continue for longer in 15% of cases.¹³

The diarrhoea is typically very foul smelling and watery, such that our ward sister could suspect a case with some accuracy. Abdominal pain was quite common in the older children but fever only occurred in a small proportion. Headache was seldom prominent. Eight (24%) of our patients, nearly all of them aged over 2 years, had cough. Cryptosporidium is commonly found in the respiratory tract of fowls, and a recent report from Papua New Guinea described finding cryptosporidium in respiratory secretions from a child with acute diarrhoea and cough.¹⁴ Respiratory symptoms are

known to be common in other cases of gastroenteritis.

To document the full range of disease due to cryptosporidium infection, it would be ideal to search for oocysts in the stools of all children with diarrhoea and vomiting. This may not always be possible, however, in every district general hospital, and we recommend that a search for oocysts be made when a child aged over 1 year presents with prolonged watery offensive diarrhoea, severe or prolonged vomiting, and abdominal pains. The symptoms seem to be less specific in infants, but there may be failure to thrive with prolonged diarrhoea or vomiting. Failure to thrive has been reported previously,¹⁵ with the cryptosporidial schizonts adhering to the intestinal mucosa on electron microscopy.¹⁶ No abnormalities were seen on light microscopy in our two patients (cases 1 and 3) who underwent jejunal biopsy examination and had abnormal xylose absorption. Both recovered in a few weeks without treatment, but failure to thrive for several months has been reported¹⁶ and it may now be advisable to look for cryptosporidium oocysts in the stools before more extensive investigation of a child with failure to thrive and chronic diarrhoea or vomiting.

The relative rarity of cryptosporidiosis in our Asian patients who were admitted to hospital was striking and unexpected and might be a valuable clue in assessing the importance of possible sources of infection. Asians, who are mainly Pakistani Moslems, make up about 22% of the child population and contribute an excess proportion of all cases of gastroenteritis, except for cryptosporidium. Cryptosporidium infection is common in developing countries, being particularly prevalent in children with diarrhoea in Liberia (7.9%),¹⁷ Ghana (12.9%),¹⁸ and India (13.1%),¹¹ although apparently it is often asymptomatic in infants under 6 months in southern India. Cryptosporidium is known to be zoonotic, causing diarrhoea in a wide range of domestic animals, and close contact with animals is normal in many developing countries. In Blackburn few Asians have any contact with animals and our Asian families do not keep pets.

In contrast, 32 of 55 (58%) patients with cryptosporidium in Blackburn had regular contact with pets or domestic animals. Some reports of cryptosporidiosis in country areas suggest animals as a source of infection,¹⁹ although this association has not been confirmed in urban areas⁹ where case to case spread seems to be more usual. Contact with pets, however, is extremely common—72% of the patients in the study from Bristol⁹ and 58% in our survey—so it is difficult to obtain clear evidence of their importance as a reservoir of infection. The

striking difference in incidence of cryptosporidiosis between Asians and non-Asians may indicate the importance of animals, and further work is needed to clarify this.

Dietary differences might account for the ethnic variation in incidence of cryptosporidiosis. A significantly greater proportion of our cases drank unpasteurised milk compared with children admitted to the ward without cryptosporidiosis, a result that contrasts with another study, which failed to confirm that raw milk is a source of infection. The Northwest and Yorkshire regions have the highest incidence of consumption of unpasteurised milk in the country.²⁰ We do not know the proportion of Asians who drink raw milk. Sausages¹⁹ and tripe (Nichols G. Personal communication.) have both been implicated as possible sources of infection, tripe as a food for pets who may then infect their owners. Neither tripe nor sausages are eaten by our Asian population. A further possibility is of spread among day nurseries, but most cases seemed to be sporadic. Muck spreading and infected water¹⁹ seem unlikely to be important factors in our patients, who mostly live in towns.

Finally, the association of preterm labour with an acute attack of cryptosporidiosis has not previously been reported. It is interesting that the baby remained asymptomatic despite her mother's quite severe illness, and the evidence points to cryptosporidiosis being less pathogenic in young infants than in older children. The mode of transfer of cryptosporidium from mother to child was not ascertained with certainty, but further spread in the special care nursery was probably prevented by the strict infection control procedures that normally operate there.

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