

the type of service covering their home district unless their paediatrician had a diabetes liaison service which covered them.

Time off school, diabetes related problems in school, school visits by the liaison service, teachers' knowledge of diabetes, and parental satisfaction with support and information in school were compared between children covered by paediatric and by adult services.

### Results

Adult services covered 226 (65%) children, paediatric services 103 (29%), and no service was identified for 22 (6%). There was no difference in mean age of children covered by adult and by paediatric services.

No significant differences were found between children with adult and paediatric services in the time lost from school, or in the proportions with diabetes related problems in school.

For only 171 (49%) children had there been a school visit by the liaison service. Children covered by paediatric services were 1.5 times (95% confidence interval 1.2 to 1.7,  $p=0.001$ ) more likely to get a school visit with 67 (65%) doing so compared with 104 (46%) of those covered by adult services. Parents whose children received a paediatric service were also more satisfied with information and support in school (table). Overall, 200 (57%) parents said teachers lacked know-ledge of diabetes, but this proportion did not differ between adult and paediatric services.

When parents were asked to comment about diabetes services, 292 (55%) of 531 comments concerned school. Of these, 198 (67%) related to teachers' lack of knowledge, 103 of which mentioned management of diet and of hypoglycaemia. Thirty comments concerned poor communication between teachers or uncaring attitudes, although 14 said the school was caring and understanding. Other comments concerned difficulties with school trips, mood changes, and deterioration in school work. Parents made 37 comments on improving school care, 31 suggesting school visits by professionals, and six suggesting an educational video for teachers.

Parental satisfaction with school support provided by adult and paediatric diabetes liaison services; number (%)

Satisfaction	Adult	Paediatric
Very satisfied	24 (13)	26 (29)
Satisfied on the whole	88 (46)	43 (47)
Somewhat dissatisfied	42 (22)	15 (17)
Very dissatisfied	36 (19)	7 (7)
Total*	190 (100)	91 (100)

\*48 'don't know'.

$\chi^2$  for trend=13.5, df=1,  $p=0.0002$ .

### Discussion

Children with diabetes spend considerable time at school; this time should be both tolerable and safe. The BDA recommends a school visit for every child, followed up at least yearly.<sup>6</sup> Disappointingly it appears that many paediatric nurses did not visit schools, although they were more likely to than adult nurses. Parents were more satisfied with paediatric nurses, but this did not improve their opinions of teachers' knowledge.

We therefore recommend that a trained paediatric diabetes nurse should talk to the class teacher, games teacher, dinner lady, playground supervisors, school doctor and nurse, before the child returns to school. Information must cover the main areas of concern, hypoglycaemia and diet. Information packs and telephone numbers should be supplied. The paediatric diabetes nurse should revisit the school at least yearly and liaise with the school health service.

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## Bovine colostrum immunoglobulin concentrate for cryptosporidiosis in AIDS

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### Abstract

**Lactobin-R is a commercial hyperimmune bovine colostrum with potent anticryptosporidial activity. It was administered to a 4 year old child with AIDS and severe diarrhoea associated with cryptosporidiosis.**

**There was significant clinical improvement in the diarrhoea and permanent elimination of the parasite from the gut as assessed through serial jejunal biopsy and stool specimens.**

(*Arch Dis Child* 1993; 69: 451-453)

Although the parasite cryptosporidium causes a self limiting diarrhoea illness in immunocompetent patients, it may be associated with life threatening diarrhoea in those with immunodeficiency.<sup>1</sup> Uniformly effective treatment is unavailable at present, and immunotherapies, such as hyperimmune bovine colostrum, have given mixed results.<sup>2-4</sup> We describe a 4 year old boy with AIDS whose cryptosporidiosis was successfully treated with a commercial hyperimmune bovine colostrum preparation.

### Case report

A 4 year old boy with vertically acquired HIV infection had a one month history of severe watery diarrhoea, vomiting, and failure to thrive. He was malnourished (weight of 13 kg, <3rd centile) with generalised lymphadenopathy and hepatosplenomegaly. Stool examination revealed cryptosporidia but no other pathogens. He was severely immunodeficient with a CD4 count of  $0.19 \times 10^9/l$ , but was negative for p24 antigen. He had specific iron, copper, and zinc deficiencies, and was hypoalbuminaemic (albumin concentration 30 g/l).

Two weeks of oral spiramycin, at a dose of 100 mg/kg/day, had no effect on the diarrhoea or weight loss. Cryptosporidial oocysts continued to be isolated from the stool. Total parenteral nutrition was instituted, but regaining to enteral feeds was impossible due to vomiting. Azithromycin was given intravenously for three weeks at a dose of 2.5 mg/kg twice daily, and oral loperamide and subcutaneous diamorphine were added. Although there was a clear reduction in stool volume, he remained intolerant of feeds, and oocysts persisted in his stools.

Lactobin-R (Biotest) was administered for two weeks in a dose of 50 g/day, made up to 500 ml in sterile water, and given via nasogastric tube and feeding pump over 12 hours. A specimen from a jejunal biopsy performed immediately before starting this treatment showed severe crypt hyperplastic partial villous atrophy and cryptosporidia, confirmed on electron microscopy, adherent not only to the epithelial surface but also to the crypts (figure A). No acid-alcohol fast bacilli were seen. Stool output did not decrease significantly during treatment. The patient, however, tolerated both the bovine colostrum and enteral feeds. Serial stool samples sent, after the commencement of Lactobin-R treatment, were negative for cryptosporidia. A repeat jejunal biopsy specimen after two weeks of treatment showed a marked improvement in villous architecture and absence of cryptosporidia (figure B). Six months after completion of treatment, stool samples had remained negative for cryptosporidia and were of normal volume and consistency. Unfortunately, the patient died of an encephalopathic illness soon after. No cryptosporidia were seen on post-mortem examination.

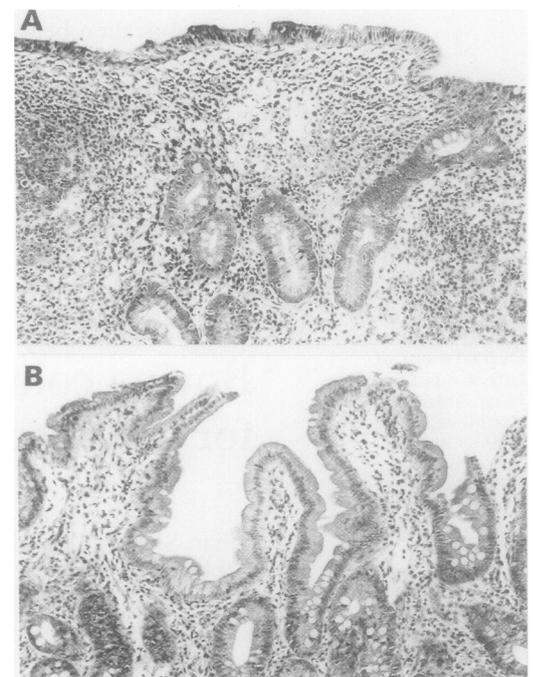
### Discussion

The increased severity of cryptosporidiosis

in patients with immunodeficiency and the lack of effective chemotherapeutic agents have encouraged attempts at immunological intervention. In the mouse model, it has been shown that the active anticryptosporidial component of bovine colostrum lies in the immunoglobulin fraction,<sup>5</sup> which presumably acts by interfering with parasite adherence to the gastrointestinal epithelium, although the exact mechanism is unknown.

We treated our patient with a new preparation consisting of an immunoglobulin concentrate, prepared from bovine colostrum (Lactobin-R). Despite the continuing severity of his immunodeficiency, the child's diarrhoea stopped and he was able to tolerate enteral feeds. His stools became permanently oocyst-free, and specimens from jejunal biopsies performed before and after treatment showed elimination of the infection and marked improvement in mucosal architecture.

Lactobin-R is the immunoglobulin fraction purified from the first colostrum of veterinary attested cattle. They are screened for foot and mouth disease, bovine viral diarrhoea, rotavirus, and mastitis. During production the colostrum is heated to 70°C and the pH reduced to 4.5 to inactivate herpes and sendai viruses. It is then lyophilised into 50 g sachets. Contamination with micro-organisms is at low levels. The preparation contains 87% IgG<sub>1</sub>, and small amounts of IgA and IgM. Anticryptosporidial titres of 50 g/500 ml solutions range from 1:2560 to 1:5120 in enzyme linked immunosorbent assay (ELISA) assays using cleaned cryptosporidial oocysts as the antigen. The same solution has significant titres against *Escherichia coli*, klebsiella,



Jejunal biopsy specimens before and after treatment (haematoxylin and eosin, magnification  $\times 40$ ). (A) Specimen shows crypt hyperplasia, partial villous atrophy, and cryptosporidia adherent to crypts and surface epithelium. (B) Specimen shows villous architecture much improved and no cryptosporidia seen.

pseudomonas, *Staphylococcus aureus*, and *Staphylococcus epidermidis* (J Nrunjun, personal communication).

In immunocompetent patients cryptosporidia only infect villous enterocytes and parasites are not found low down on the villus or in the crypts.<sup>1</sup> In our patient with compromised mucosal immunity there were cryptosporidia clearly adherent to crypt epithelium in a manner reminiscent of a patient previously reported with IgA deficiency.<sup>6</sup> We suggest that infestation of the crypts is related to lack of mucosal immunoglobulin; leads to reduced parasite elimination by secondary mucosal defences of mucus secretion and peristalsis; and may accentuate fluid loss by targeting crypt secretion either directly or via cryptosporidial toxins (Quarino, unpublished observations, 1992).

Oral hyperimmune bovine colostrum, obtained from cows immunised specifically with cryptosporidial antigens, has previously been used to treat cryptosporidiosis in immunodeficient patients. It transiently cleared parasites from one child with congenital hypogammaglobulinaemia and chronic cryptosporidiosis, but after three weeks there was biliary tract relapse.<sup>2</sup> In a pilot study of the use of hyperimmune bovine colostrum (immunofluorescence titres of 1:3200–1:25 600) in five patients with AIDS, one patient had marked reduction in oocyst excretion, one a moderate reduction, and the third no reduction, while neither of the control patients

showed any change.<sup>3</sup> Another group reported a further case of cryptosporidiosis in an AIDS patient responding to treatment with hyperimmune bovine colostrum. The illness recurred after three months but this may have been due to reinfection rather than relapse.<sup>4</sup>

This is the first reported case of a commercially available bovine immunoglobulin concentrate used successfully to treat chronic cryptosporidiosis in an immunodeficient individual resulting in permanent clearance of stools and mucosa. Further studies of Lactobin-R, including efficacy trials in immunodeficient populations such as those with AIDS, seem warranted.

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## Occurrence of Duchenne dystrophy in Klinefelter's syndrome

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### Abstract

**A boy with Duchenne muscular dystrophy and facial dysmorphism in conjunction with Klinefelter's genotype 47XXY is presented; this is an unusual situation with two genetic errors evolving over two generations. Karyotyping should be considered in boys with Duchenne muscular dystrophy who have unusual features.**

(*Arch Dis Child* 1993; 69: 453–454)

A case of Klinefelter's syndrome and Becker muscular dystrophy was reported in 1989.<sup>1</sup> We report a boy with Klinefelter's syndrome and Duchenne muscular dystrophy where two genetic errors were responsible. An Xp21 non-deletion dystrophin gene mutation in the mother was passed on in a double dose to the child because of maternal meiotic non-dysjunction; this has not been described before.

### Case report

A 3·5 year old boy presented with symptoms of proximal muscle weakness, speech delay, and a serum creatine kinase activity of 24750 U/l. Because of mild facial dysmorphism with hypertelorism and a prominent nose, a cytogenetic analysis was performed and revealed a 47XXY karyotype. There was no history of neuromuscular disease in the family, but his 57 year old maternal grandfather had been in a wheelchair from early adult life for apparently untreated Perthe's disease.

Examination revealed a boy with mild facial dysmorphism including hypertelorism and a prominent nose with height and weight on the 3rd and head circumference below the 3rd centile. He had bulky calves with pelvic girdle weakness. A percutaneous needle biopsy specimen from the quadriceps muscle showed a dystrophic process. On immunohistochemistry only a few fibres were positive for dystrophin 1 and 2. Psychometric assessment at 6

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