

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and may accentuate fluid loss by targeting crypt secretion either directly or via cryptosporidial toxins (Quarino, unpublished observations, 1992).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.**

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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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years of age because of learning difficulties gave a verbal intelligence quotient (IQ) of 73 and performance IQ of 86 on the Weschler intelligence scale for children (3rd edition).

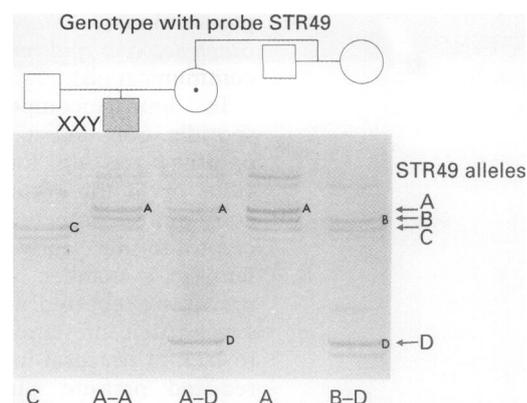
As the patient's presentation was typical for Duchenne muscular dystrophy, it was likely that both his X chromosomes carried an Xp21 mutation or that X inactivation was non-random. Had this not been so then any muscle disease occurring would have presented with a much milder course as in manifesting female carriers of Xp21 mutations. The most likely mechanism causing homozygosity of an Xp21 mutation would be a non-dysjunctional error at the second maternal meiosis involving the X chromosome carrying an Xp21 mutation. This was confirmed by analysis with the STR49 CA repeat polymorphism within intron 49 of the dystrophin gene. This demonstrated that the mother was heterozygous for alleles A and D, but the patient was homozygous for the maternal allele A (figure). DNA analysis revealed no deletion at the Xp21 locus (for exons 1, 3, 6, 8, 13, 19, 43, 44, 45, 47, 48, 50–53, and 60), indicating the presence of a non-deletion mutation in the dystrophin gene.

The family study showed that the patient's X chromosome came originally from his maternal grandfather implying that either he was affected or that there had been a new mutation at the time of conception in the patient or his mother. The maternal grandfather on examination had excellent muscle bulk and no weakness. His serum creatine kinase activity was within normal limits therefore he did not have muscular dystrophy. The maternal serum creatine kinase measured on two separate occasions was well above the normal female range. Although she was clinically asymptomatic, this gave a high probability that she was a carrier of the Xp21 mutation.

### Discussion

This is the first report of the occurrence of Duchenne muscular dystrophy in conjunction with Klinefelter's genotype 47XXY. Suthers *et al* reported a case of Becker muscular dystrophy and Klinefelter's syndrome,<sup>1</sup> diagnosed at the age of 18 years. Pedigree analysis with two DNA markers within the muscular dystrophy locus showed that this latter patient had received both a maternal and a paternal X chromosome indicating a non-dysjunction error during paternal meiosis. In our patient both X chromosomes were maternal in origin arising by non-dysjunction at the second meiotic division during gametogenesis, giving rise to two copies of the same X chromosome. Klinefelter's syndrome is quite a common sex chromosomal aneuploidy with an incidence of one in 1000.<sup>2</sup> The mechanism is a non-dysjunctional error in meiosis and is maternal in some 60% and paternal in 40% of XXY individuals.<sup>2</sup>

Our patient had inherited two identical copies of the same maternal X chromosome, with the Xp21 non-deletion mutation making



Genotype with probe STR49 (from intron 49 of the dystrophin gene). Each of the four alleles (designated A, B, C, D) identified by probe STR49 produces a series of bands. The uppermost band in each group identifies the particular allele/alleles present in each individual.

him homozygous and resulting in the severe Duchenne phenotype. About one third of patients with Duchenne muscular dystrophy have non-deletion Xp21 mutations.<sup>3</sup> The gene involved in Xp21 muscular dystrophies is the largest human gene as yet identified and shows a high rate of mutation. Approximately one third of patients with Duchenne muscular dystrophy are estimated to be due to new mutations.<sup>3</sup>

Learning difficulties are common in both Klinefelter's syndrome<sup>2</sup> and Duchenne muscular dystrophy<sup>4</sup> and therefore it is not surprising that this occurred in our patient. Specific learning difficulties particularly in respect to literacy are found in 70% of boys with Duchenne muscular dystrophy of normal intelligence,<sup>4</sup> and similar learning disabilities are also found in patients with Klinefelter's syndrome. The verbal to performance discrepancy found in our patient is indicative of specific learning difficulties. However, they are not particularly more severe than would be expected to be found in either Duchenne dystrophy or Klinefelter's syndrome alone, suggesting that the cognitive deficits occurring in both disorders are not manifesting in an additive manner in our patient.

The frequency of additional chromosomal abnormalities in boys with Xp21 muscular dystrophy is unknown as karyotyping is not routinely performed in all affected males. The identification of a numerical or structural abnormality involving the X chromosomes in boys with muscular dystrophy may have implications for counselling other family members and karyotyping should be considered in boys presenting with additional or unusual features.

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