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Dominantly inherited cleft lip and palate

SIR,

Temple *et al* (*J Med Genet* 1989;**26**:386–9) reported two families with dominantly inherited cleft lip and palate. We have recently seen a similar situation in a family (figure) presenting with non-syndromic, unilateral cleft lip and palate in at least three and probably four successive generations.

All affected family members were personally examined and in none of them could associated clinical findings suggestive of Van Der Woude syndrome or another autosomal dominantly inherited syndrome associated with cleft lip and palate be found.

III.5 and his wife asked for genetic advice after his healthy sister (III.10) gave birth to her first child (IV.5) with a left sided cleft of the lip, hard and soft palates, and alveolus. No lip pits or fistulae were present and the child was otherwise normal. On thorough clinical and *x* ray examination, no minimal signs of cleft lip/palate were found in III.10. The child's father (III.9) had no clinical abnormalities and his family history was negative.

One brother (III.2), one sister (III.4), and a niece (IV.3) of the consultand were born with a right sided cleft of the lip and palate. His mother (II.2) also had a cleft lip and palate at birth. She underwent several surgical repairs, including closure of the lip in early childhood, closure of the palate at 50 years of age, and a Lefort I type osteotomy because of retrognathia of the maxilla and hypoplasia of the upper

cheek. No preoperative photographic data were available but clinical examination showed that the cleft had been right sided. According to all family members, the dead maternal grandmother (I.2) had also had a unilateral cleft lip and palate.

Except for II.2, whose parents were first cousins, consanguinity was excluded between the parents of all the other affected family members.

The linear pattern of inheritance in this family is suggestive of autosomal dominant rather than multifactorial inheritance and adds further evidence to the hypothesis, which has already been suggested in other family studies,[1] that a single major dominant gene is responsible for cleft lip and palate in some families.

If we accept an autosomal dominant transmission pattern in this family, subject III.10 is a nonpenetrant heterozygote. Under the assumption of autosomal dominant inheritance with reduced penetrance, III.5 and his wife were given a maximum risk for an affected child of 8·6%. A detailed report of this family study is in preparation.

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Are abortions more or less frequent once prenatal diagnosis is available?

SIR,

Harris *et al*[1] have recently stated that the application of DNA techniques to inherited diseases reduces the risks of fetuses being aborted, since the majority will be found to be healthy after testing; they report 18 abortions of fetuses at risk for Duchenne muscular dystrophy, and state that this number is a reduction from previous years. However, our early experience from the West Midlands was different from that in Manchester, and showed that if prenatal diagnosis is not available, women at risk tend either to refrain from pregnancy or to take the risk and complete the pregnancy.[2] Similar observations have been made in Ontario.[3] We thought it important to be certain of women's attitudes and behaviour before analysing any effect
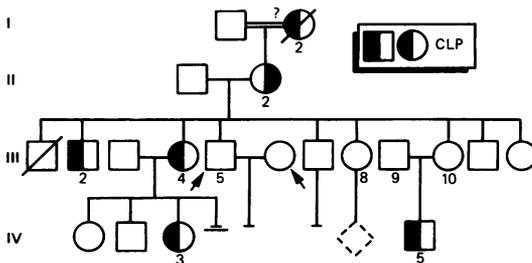

FIGURE *Pedigree of family with unilateral cleft lip and palate in four generations. ? represents a reportedly affected family member. I.1 and I.2 are consanguineous.*

TABLE 1 *Outcomes of pregnancies in women with a risk of 1 in 20 or worse for having a son with Duchenne muscular dystrophy (DMD): West Midlands data.*

	1976–1980*	1981–1985
Data from Register		
No of women with these risks aged 18–40	95	126
Outcomes of their pregnancies		
Total No	31	66
Late miscarriages	1	3
Terminations for social reasons	0	3
Terminations for male sex	3	14
Terminations for genetic risk (without fetal sexing)	0	2
Stillbirth	0	1
Liveborn healthy females	17	32
Liveborn healthy males	7	8
Liveborn affected males	3	3
Data from population		
Isolated cases of DMD born in this period		
Observed	37	26
Expected†	26	26
Familial cases of DMD born in this period		
Observed	9‡	4
Expected†	16	16

*The data from the Muscular Dystrophy Register were reported in 1982.[2]
†The numbers are those expected if the birth frequency is maintained at 1 per 4000 males, and if the percentage of familial cases is maintained at the 37% found in an earlier study from the West Midlands.[4]
‡In six of these families the second affected boy was already born when his brother was diagnosed.

of the introduction of DNA techniques, and we therefore examined the outcomes of pregnancies at risk in a second five year period. We were interested to observe rather different findings from those of the earlier series and have therefore presented them in the accompanying table.

The number of families on the Muscular Dystrophy Register had increased by the second period since there was a second ascertainment of families in 1979. Several points of comparison emerge between the two groups. First, the mean number of pregnancies per woman at risk has increased from 0·3 in five years to 0·5. This is presumably a result of more women being in favour of termination of pregnancy in the second five year period, for there were only three genetic abortions out of 31 pregnancies (9·6%) in the first period, compared to 16 out of 66 (24%) in the second. This increased number of abortions is not the result of more awareness of fetal sexing, since the women in the first series were given similar information. Probably one reason for the change is that termination of pregnancy for genetic reasons is becoming more socially acceptable. Chorionic villus sampling, which allows earlier fetal sexing and termination, was not available in the West Midlands until 1986.

In the second period only 4·5% of pregnancies resulted in a liveborn affected male, compared to 9·7% in the preceding period; this was at the expense of three times the number of genetic abortions. There were proportionally more liveborn and healthy children born as a result of the 31 pregnancies in the first group, but overall the mothers in this group had fewer healthy children (0·25 per mother) than those in the second group (0·32 children per mother) because more mothers in the first group refrained from becoming pregnant. In both groups there was a deficit of males, which was not explained by the terminations of pregnancy.

The population figures show that there has already been a fall in the number of familial cases of Duchenne muscular dystrophy, although the total number of patients may be incomplete for the second period as some of those born in 1984 and 1985 may not yet have come to our notice. This reduction in familial cases confirms previous findings that genetic counselling alone can reduce the birth frequency of Duchenne muscular dystrophy.[5]

The figures presented here will serve as a basis on which to assess the effect of offering prenatal diagnosis using DNA techniques from 1986 onwards. We predict that the number of pregnancies per woman may well increase further, and we hope that the number of familial cases of Duchenne muscular dystrophy will continue to fall. However, we do not know whether the overall number of genetic abortions for Duchenne muscular dystrophy will increase or decrease, since the current rate of abortions in the West Midlands appears to be lower than that in Manchester.

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