the proband did not have any cardiac anomaly, mental deficiency, or deafness.

Another point we want to make is that although our common abnormalities were similar to the cases of Glanz and Fraser, especially malformations of the toes, others, such as spina bifida, vitiligo, hypoplastic spleen, and scoliosis, were not noted.

**Nejat Akar and Sevgi Gözdəşoğlu**

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**References**


This letter was shown to Drs Glanz and Fraser who reply as follows:

We thank Drs Akar and Gözdəşoğlu for drawing attention to their paper and apologise for its omission from our review. We included café-au-lait spots as hyperpigmentation.

**Philtrum length and intercommissural distance in newborn infants**

**Sir,**

In their very useful paper, Sivan *et al* have provided normal values for philtrum length and intercommissural distance in newborn infants. I am glad to know that their standards correspond well with those I previously found in healthy Hungarian neonates. However, since gestational age cannot always be determined and intrauterine growth retardation is characteristic of many congenital syndromes and malformations, the consideration of gestational age alone may be misleading in a significant proportion of pathological infants.

Therefore, I would recommend that gestational age and birth weight should be taken into account. This has been our policy in determining standards for several measurable minor malformations and variants so far.

**K Méesès**

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**Genetic heterogeneity in Duchenne muscular dystrophy**

**Sir,**

From the results of linkage studies using two restriction fragment length polymorphisms, Dr O'Brien and colleagues question our earlier suggestion that Duchenne muscular dystrophy (DMD) may exhibit genetic heterogeneity. We would disagree with the interpretation of their results for several reasons.

Firstly, our suggestion was that a subgroup of DMD may possibly exist in which affected boys have severe (which we stressed) mental handicap usually requiring institutional care. Such boys in fact represent only a very small proportion of all affected boys. Over the years we have collected information on 302 affected boys (of whom 182 have been personally examined), but fewer than 20 have been classified as severely mentally handicapped.

In Dr O'Brien's study it is not clear in how many kindreds the affected boys were severely mentally handicapped, and in several kindreds data from mentally handicapped boys and boys with normal IQ were combined, which would not seem justified.

Secondly, as was discussed in our paper, there is already some convincing biochemical evidence of heterogeneity in DMD, though it is not clear if this is related to the observed clinical differences.

Thirdly, as the authors themselves point out, linkage studies cannot exclude heterogeneity resulting from different mutations at the same or closely linked loci. From what we know already about the fine structure of disease loci, if genetic heterogeneity in DMD does exist it would seem quite reasonable that it could be within a single locus.

For these various reasons we feel that the case against heterogeneity in DMD is therefore still 'non-proven'. The situation is likely to remain unclear until such time as the molecular defect(s) has been characterised.

**Alan E H Emery**

*The Medical School, Teviot Place, Edinburgh.*

**References**

1. O'Brien T, Harper PS, Davies KE, Murray JM, Sarfarazi M, Williamson R. Absence of genetic heterogeneity in Duchenne muscular dystrophy shown by...
Correspondence


Duchenne muscular dystrophy

Sir,

Lane et al1 claim that almost 90% of mothers of one boy with Duchenne muscular dystrophy, and no affected relatives, are carriers.

The probability of a mother of one affected boy being a carrier of muscular dystrophy is the commonest, and most disturbing, problem at the presentation of this disease. Its resolution is made more urgent by the use of DNA probes at neighbouring loci, which, by nature, cannot diagnose carriers but can make predictions on the children of known carriers.

A priori the gametes in man are so different that an equality of mutation rate is not to be expected, so we should expect that the proportion of mothers who are carriers, which must be between a half and one, would be nearer to one or the other. Bayes, from the precision with which he spoke of the equality of his two billiard balls, would hardly have argued for the equality in mutation which would give two-thirds of mothers as an 'expectation'.

The bulk of published data show a recurrence risk to further boys of about 25%, and an inferred proportion of mothers who are carriers of 50%. Estimates based on the overlapping distributions of creatine kinase are usually substantially more than this, a difference now explicable by the predisposition to stillbirth and neonatal death of boys found in some families,1 and plausibly related to weakness of respiratory muscles.

The simplest estimate of recurrence risk is made by dividing the affected sons by the total sons born after the proband. This can be elaborated by methods which weight the informative families, and Cheeseman et al2 derived an elegant solution, based on large sample approximations, for the estimation of these weights. This approximation makes no full allowance for the equality, in information provided on heterozygosity, by women with two or many affected sons, since the total number of affected sons enters the calculation. This approximation can now be bypassed by small computers to give the exact likelihood distributions. If $h$ is the proportion of mothers who are carriers, and $g = 1 - h$ then, for a sibship with a affected out of s sons, all born after the proband, the likelihood is proportional to $(h/2 + g)$ when $a = 0$ and to $(h/2)^a$ when $a > 0$.

The figure gives the likelihoods. The three sets of curves give those for Virginia (V), Duke (D), and combined (C). The curves to the left are the exact likelihoods, those on the right from Cheeseman's approximation.

There is a wide distribution of plausible results from 0.6 to 0.9 on the exact solution, and no justification for unduly depressing prognoses while awaiting more exact diagnostic methods.

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References
