

a linkage study using two cloned DNA sequences. *J Med Genet* 1983;20:249-51.

<sup>2</sup> Emery AEH, Skinner R, Holloway S. A study of possible heterogeneity in Duchenne muscular dystrophy. *Clin Genet* 1979;15:444-9.

### Duchenne muscular dystrophy

SIR,

Lane *et al*<sup>1</sup> 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,<sup>1</sup> 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 al*<sup>2</sup> 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

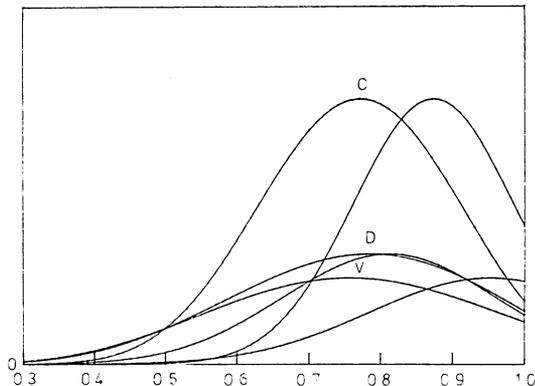


FIGURE Likelihoods plotted against proportion of carriers.

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  $(h/2)^s$  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

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