Possible Linkage between Xg and the Locus for a Gene causing Mental Retardation with or without Hydrocephalus

K. FRIED* and RUTH SANGER

From the University Department of Human Genetics, Western General Hospital, Edinburgh and the MRC Blood Group Unit, The Lister Institute, London

Summary. The Xg groups of a kindred in which an X-borne gene evidently caused mental retardation with or without hydrocephalus suggest that the locus for this gene may be linked to Xg.

Hereditary hydrocephalus (Bickers and Adams, 1949) is now known, at least in some families, to be an X-borne condition (Edwards, 1961).

A few families with the X-borne type of hydrocephalus have been tested for the Xg blood groups but with no hint of linkage between their two loci (Edwards, 1968; Jabbour, 1968).

In a kindred recently reported by Fried (1972) a single X-borne gene has apparently caused mental retardation sometimes with and sometimes without hydrocephalus. The Xg groups of the family (Fig. 1) pose a difficult exercise in scoring for linkage.

The deceased maternal grandparents, I.1 and I.2, of the propositus could have had one of three arrangements of Xg genotypes.

1. Xg\(^a\)Xg\(^a\) × Xg. From the groups of the family this is the most likely guess and the linkage information would then be: Generation II, no score Generation III, 9 non-recombinants:1 recombinant

for which the lod scores for the various recombination fractions would be:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>lod score</th>
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<tbody>
<tr>
<td>0.00</td>
<td>0.05</td>
</tr>
<tr>
<td>0.1</td>
<td>0.15</td>
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<tr>
<td>0.2</td>
<td>0.25</td>
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<tr>
<td>0.3</td>
<td>0.35</td>
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<tr>
<td>0.4</td>
<td>0.45</td>
</tr>
<tr>
<td>0.6</td>
<td>0.614</td>
</tr>
<tr>
<td>0.8</td>
<td>0.323</td>
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2. Xg\(^a\)Xg × Xg\(^a\). This we calculate to be about 15 times less likely than arrangement 1, but cannot be disregarded. The linkage information would now become:

Generation II, z\(_1\) 6:0
Generation III, 1 non-recombinants: 8 recombinants

and the evidence, though notably conflicting between the two generations, would, in the sum, be strongly against linkage.

3. Xg\(^a\)Xg × Xg. This is the least likely arrangement, for the probability of finding all eight daughters and sons in generation II to be Xg(a+) would be only 1 in 256. However, the score (excluding II.2 who may or may not be a carrier) would be:

Generation II, z\(_1\) 6:1
Generation III, 9 non-recombinants: 1 recombinant

and again very suggestive of linkage.

Professor G. R. Fraser and Professor J. H. Edwards kindly gave a great deal of thought to presenting all the possible arrangements in this family to the assessment of the computer: the outcome (Fig. 2) was in favour of linkage between the disease locus and Xg with a maximum likelihood of 20.2 at a recombination fraction of 0.11.

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* Present address: Department of Human Genetics, Tel Aviv University, Tel Aviv, Israel.
Fig. 1. The Xg groups of the family.

Fig. 2. Relative probabilities of linkage for various values of the recombination fraction between the locus for this form of mental retardation and Xg. (With acknowledgment to Professor G. R. Fraser and Professor J. H. Edwards.)

REFERENCES

Fried, K. (1972). X-linked mental retardation and/or hydrocephalus. Clinical Genetics, 3, 258–263.