The combinations of the sexes of familial cases of neural tube defect

Mariman and Hamel\(^1\) report that in families where two offspring are affected with neural tube defects (NTD) there are more same sex affected pairs than opposite sex affected pairs. A number of points arise:

1. The sex ratio (as expressed by binomial expectation) is not that should be exact equality because the sex ratio (proportion male) of cases is not exactly 0.5.

2. Since the sex ratios of spina bifida in general exceed those of anencephalics,\(^3\) one would expect concordance for sex in affected NTD sib pairs if the defects, to some extent 'breed true'. There is evidence for such a suggestion,\(^4,5\) though the point has been disputed.\(^6\) Account has been taken of such a possibility by disaggregating the data into sib pairs of anencephalics, sib pairs of spina bifida, and pairs comprising one of each.\(^7\) In that paper, data were pooled from a variety of sources, and the table here reproduces those pooled data. None of these three individual distributions, nor (more important) their components treated separately, nor their overall total, shows a significant departure from binomial expectation.

The combinations of the sexes of cases of neural tube defect in sibships in which exactly two are affected (by the nature of the defects) (reproduced from James\(^7\)).

<table>
<thead>
<tr>
<th>Defects</th>
<th>MM</th>
<th>MF</th>
<th>PF</th>
</tr>
</thead>
<tbody>
<tr>
<td>anencephalics</td>
<td>9</td>
<td>35</td>
<td>48</td>
</tr>
<tr>
<td>spina bifida</td>
<td>38</td>
<td>73</td>
<td>57</td>
</tr>
<tr>
<td>anencephalics +</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>spina bifida</td>
<td>15</td>
<td>75</td>
<td>62</td>
</tr>
<tr>
<td>Σ</td>
<td>62</td>
<td>183</td>
<td>167</td>
</tr>
</tbody>
</table>

(3) It is well established that in samples in which anencephaly is relatively common, the sex ratio of cases is lower than in samples in which it is rare.\(^2\) This suggests two causes, one (presumably environmental) being responsible for mainly female cases, and the other (possibly genetic) for cases of both sexes. Such a notion is strengthened by the observations\(^8\) that (i) vitamin therapy resulted in a greater reduction of incidence in Northern Ireland (previously a high risk area) than in south-east England (previously a low risk area), and (ii) there was an excess of males among the recurrences which occurred to the supplemented mothers.

However, since the sex ratio of cases born to anencephalic prone women does not differ appreciably from that of those born to other women,\(^9\) it was inferred that the typical case is the result of both causes acting simultaneously on the same woman, rather than separately on different women. It remains to be seen whether this form of reasoning will prove useful in the search for causes.

Mariman and Hamel\(^1\) speculate that (i) there is concordance within multiple case sibships for location of lesion, and (ii) there is an association between location and sex of case. If both these premises were true, there should be concordance for sex in sibling sibships. So the present data suggest that at least one of these premises is false.

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BOOK REVIEWS

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Human molecular genetics is one of the most rapidly developing fields within the biological sciences and this edition will be of widespread importance for clinical practice means that many scientists and clinicians need an introduction to this subject. The first edition of Molecular Basis of Inherited Disease was very successful in this respect and the second edition is an admirable successor. A second edition was essential to include new developments over the past four years, for example, interactive FISH, mutational screening approaches, unstable length mutations, genomic imprinting, and gene therapy.

Four sections cover the types of genetic markers, methods for locating genes (for single gene disorders), gene cloning strategies, and the molecular pathology of a variety of the commoner single gene disorders. A basic knowledge of DNA and the basic principles of genetics is assumed (as would be covered in school biology) but otherwise techniques and concepts are clearly explained with concise text and bicolour diagrams. References to original work and for further reading are included.

Areas outside my specific field of competence or interest were grafts of haemopoietic and immunogenic tissues, gonads, and corneas. However, the chapter on clinical results of transplanting human fetal pancreas was depressingly familiar and familiarly depressing. Thus, from fetal cell grafts in parkinsonians, there is conclusive evidence of success in only four; some others may well have been successful, but definite proof is lacking. Similarly, despite 1582 human fetal pancreatic grafts for diabetes up to June 1990 and "numerous claims of graft functions", in only four patients has graft survival been shown, and in none of these is there conclusive evidence of graft functioning. Excellent basic and preclinical work in this field so often seems to fall at the last hurdle with clinicians who can operate with great skill but inadequately understand the disease they are experimenting upon, and hence lack the means to show whether the procedure itself has been effective. I have heard one such pioneer claim that because of information overload from his varied and incoherently worded paper should be collected from each subject. On the contrary, rather like Aesop's tortoise, I tend to feel that the opposite approach (meticulous controlled monitoring of a few carefully studied subjects) has more to offer. If this message is beginning to trickle through, then perhaps the recent temporary moratorium on NIH funding for human fetal grafts in the USA may actually have been no bad thing.

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