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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 null hypothesis (as expressed by binomial expectation) is not that there should be exact equality because the sex ratio (proportion male) of cases is not exactly 0·5.

(2) Since the sex ratios of spina bifidas in general exceed those of anencephalics,[2 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,[4-6] though the point has been disputed.[1] Account has been taken of such a possibility by disaggregating the data into sib pairs of anencephalics, sib pairs of spina bifidas, and pairs comprising one of each.[7] In that paper, data were pooled from a number 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]).

Defects	MM	MF	FF
2 anencephalics	9	35	48
2 spina bifidas	38	73	57
1 anencephalic + 1 spina bifida	15	75	62
Σ	62	183	167

(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 of lesion and sex of case. If both these premises were true, there should be concordance for sex within sibships. So the present data suggest that at least one of these premises is false.

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BOOK REVIEWS

All titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the UK and for members of the British Forces Overseas, but overseas customers should add 15% to the value of the order for postage and packing. Payment can be made by cheque in sterling drawn on a UK bank, or by credit card (Mastercard, Visa, or American Express) stating card number, expiry date, and full name.

Fetal Tissue Transplants in Medicine. Ed Robert G Edwards. (Pp 352; £60.00.) London: Cambridge University Press. 1992.

I came to this book as a clinical neurologist interested in the potential for fetal grafting in treating brain diseases. Geneticists, embryologists, and ethicists quite probably have different agendas. Among those tempted by the title, there is something for everyone but, perhaps with the exception of the distinguished editor, few will find all the chapters either relevant or wholly comprehensible. The book therefore strikes me as a bit of a reverend's oocyte, to be dipped into in the library but not necessarily bought and read in its entirety. Nevertheless, it is a valuable source of useful material in an embryonic, but rapidly expanding, field.

Of the 13 chapters, the ones I personally found useful were those on 'Organogenesis and CNS development', 'The procurement of human fetal tissues for clinical transplantation', 'The biology of fetal brain tissue grafts', 'Cell grafting and gene therapy in metabolic diseases', and 'Law and ethics of transplanting fetal tissue'. In the last of these, most of the Reverend Polkinghorne's recommendations sound pretty sensible to me, but not all. For example, will the impermissibility of a tissue bank expressing a preference or need for material from a specific trimester eventually seem as dubious as Thomas Aquinas's pronouncement that ensoulment takes place at 40 days in a male, and at 90 days in a female fetus?

Areas outside my specific field of competence or interest were grafts of haemopoietic and immunogenic tissue, gonads, and corneas. However, the chapter on clinical results of transplanting human fetal pancreas was depressingly familiar and familiarly depressing. Thus, from over 100 human fetal nigral 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 vast and inconclusive series, fewer data 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.

NIALL QUINN

Molecular Basis of Inherited Disease. 2nd edition. K E Davies, A P Read. (Pp 95; £8.95.) Oxford: IRL Press. 1992.

Human molecular genetics is one of the most rapidly developing fields within the biological sciences and this coupled with its 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 role and the second edition is an admirable successor. A second edition was essential to include new developments over the past four years, for example, interphase 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, as are two glossaries for technical and medical terms.

The present emphasis is rightly on the mapping and cloning of genes for the single gene disorders and I suspect that future editions will want to place more emphasis on approaches to the analysis of multifactorial disorders, to gene therapy, and to transgenic studies for elucidation of pathophysiology. Minor criticisms are the use of unusual sym-