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to women normally resident in Oxfordshire[7] and (2) spina bifida births and terminations of pregnancy in 1973 to 1987 among women booking for their antenatal care at the John Radcliffe Maternity Hospital, Oxford. Information on the site of the lesion was available from hospital records and necropsy reports on 184 cases of spina bifida in the earlier series and 103 in the later series. The sex ratio was 0·67 (49/73) in cases of spina bifida confined to the lumbar or sacral region and 0·54 (58/107) in those with higher lesions, but this difference was not statistically significant ($p = 0·18$, one tail test).

The table summarises the results from the four published studies on the subject, our own data, and two other studies[8,9] of spina bifida where information on fetal sex and spinal location was not included in the original publication but has been provided to us by the authors. Using standard methods to combine the results from all seven studies yielded an overall statistically significant increase in sex ratio among those with low lesions (Mantel-Haenszel, $p < 0·01$). Because there is considerable heterogeneity between the studies in both the overall sex ratio and in the proportion of low lesions, it is not possible to estimate reliably the magnitude of the effect. The between study differences in proportion of low lesions are probably related to the accuracy with which the site of the lesion was determined. If *x* ray or necropsy examination were used the lesion may be found to be more extensive than on clinical examination. The between study differences in sex ratio are likely to be the result of chance.

Following the original observation of sex differences in the spinal location, explanations have been suggested which relate to the fact that the neural tube is formed by neural folding in a craniocaudal direction followed by canalisation in the sacrum. If female fetuses are less developed at a specific gestational age because on average they are conceived later in the cycle, they may be more susceptible to higher lesions from a gestation specific insult.[10] In the curly tail mouse, female embryos are growth retarded at the time of neurulation[1] and this may, by changing the rate of neural tissue growth, affect neural folding and canalisation in different ways.[5,11]

Whatever the explanation, information on the site of the lesion now needs to be included in epidemiological studies of spina bifida which are aimed at elucidating the aetiology of this disorder.

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*Sex ratio (male/female) according to spina bifida location in seven studies.**

Study	Low lesions	High lesions
London[1,2]	3·00 (15/5)	0·42 (10/24)
Madrid[3]	1·26 (110/87)	0·67 (2/3)
Glasgow[4]	1·67 (10/6)	0·21 (5/24)
Vancouver[5]	0·76 (95/125)	0·86 (37/43)
Cambridge[8]†	0·94 (32/34)	0·55 (18/33)
Grand Rapids[9]‡	0·96 (76/79)	0·66 (21/32)
Present study	0·67 (49/73)	0·54 (58/107)

* A 'high' lesion is defined as one including the thoracic, cervical, or occipital region; a 'low' lesion is below this.
† When the sensory, rather than cutaneous, level is used they are 1·53 (23/15) for below L3 and 0·57 (27/47) for higher lesions. Five were unclassifiable because of widely asymmetrical levels (G M Hunt, personal communication).
‡ H V Toriello, personal communication.

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.

Molecular Genetic Medicine. Volume 2. Ed T Friedman. (Pp 233; $55.00.) New York: Academic Press. 1992.

In my (favourable) review of the first volume of this new book series (*J Med Genet* 1992;29:519), I made a plea for more articles about the practical applications of molecular genetic medicine. I was pleased to find that volume 2 adequately answers this need.

There is a great art (which means that a little luck is needed) to choosing appropriate topics for a review series such as this. For instance, the article on the fragile X syndrome (Brown and Jenkins) would have been a damp squib had it appeared in volume 1. Fortunately, the unstable CGG mutation was described just in time: it provides a dramatic finale to a good review of the events leading up to its discovery. Naturally, one would look elsewhere to find out the latest news on genotype/phenotype correlation, but attempts by series such as this to describe the up to the minute situation can easily backfire. This is illustrated by the less successful article 'The impact of molecular biology on the diagnosis and treatment of hemoglobin disorders' (Berg and Schechter). The first half is a standard summary of globin mutations, which can be found elsewhere. The second half launches into locus control regions, globin switching, transcriptional factors, and—confusion. The story will have changed by next year, and those who need to be bang up to date will be better served by following the original publications.

Three of the other five articles will be of particular interest to the geneticist. I was surprised to learn from 'The molecular genetics of Down syndrome' (Holtzman and Epstein) that expression levels of some chromosome 21 genes in this condition are greater than normal by more than the predicted factor of 1·5. Such deregulation of expression dosage may be important in the pathogenesis of the condition. 'Mammalian X chromosome inactivation' (Gartler *et al*) is a scholarly review that summarises basic biological knowledge of the process. The candidate gene for the X inactivation centre (XIST) is not described in detail, a sensible decision as its significance is still unclear. However, of all the articles, I found 'Molecular analysis of mutation in the human gene for HPRT' (Lambert *et al*) the most interesting, probably because of my previous ignorance of the subject. The existence of both positive and negative HPRT selection systems, together with PCR/sequencing technology, make possible the rapid characterisation and comparison of HPRT mutations in both the germline and the soma, currently a unique situation, with important lessons for mutation detection of other genes, oncology, and gerontology. In fact the mutational spectrum in different contexts is generally remarkably uniform, 10 to 15% being gross deletions. A notable exception is that neonatal cord blood T cell mutants comprise 85% deletions: speculatively, this may be related to the massive recombinase mediated somatic gene rearrangements that take place during thymic differentiation of T lymphocytes.

The final two articles 'Hepatitis B virus biology and pathogenesis' (Chisari) and 'Regulatory genes of human immunodeficiency viruses' (Wong-Staal and Haseltine) are no doubt good too. I have to admit that virology became too complicated for me some time ago, and I did not read them in detail.

ANDREW WILKIE

Genome Analysis: Genes and Phenotypes. Volume 3. Ed Kay E Davies, Shirley M Tilghman. (Pp 174; $40.00.) New York: Cold Spring Harbor Laboratory Press. 1992.

Genes and Phenotypes presents a rather forbidding title to what is, in fact, a very user