Journal of

MEDICAL GENETICS

Published by the BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, and printed in England by Latimer Trend & Company Ltd, Plymouth.

NOTICE TO SUBSCRIBERS
Journal of Medical Genetics is published monthly. The annual subscription rates are £163·00 (US $277·00). Orders should be sent to The Subscription Manager, Journal of Medical Genetics, BMA House, Tavistock Square, London WC1H 9JR. Orders can also be placed with any leading subscription agent or bookseller. (For the convenience of readers in the USA subscription orders with or without payment may be sent to British Medical Journal, Box 560B, Kennebunkport, Maine 04046, USA. All enquiries, however, must be addressed to the Publisher in London.) Subscriptions may be paid by Access, Visa, or American Express by quoting on the order the credit or charge card preferred together with the appropriate personal account number and the expiry date of the card. All enquiries regarding air mail rates and single copies already published should be addressed to the Publisher in London. Second class postage paid, Rahway N J Postmaster: send address changes to Journal of Medical Genetics, c/o Mercury Airfreight International Ltd Inc, 2323 Randolph Avenue, Avenel, NJ 07001, USA.

ISSN 0022–2593

corrected for by substituting $q^{2\prime}$ for q^2 and $r^{2\prime}$ for r^2 similarly in the formula above where:

$$q^{2\prime} = q^2 + F^p q(1-q) \text{ and } r^{2\prime} = r^2 + F^p r(1-r)$$

and F^p equals the coefficient of inbreeding of the population owing to prior inbreeding. The overall effect modelling for both of these effects reduces, to some extent, the power of this approach (fig 2).

Values for the long term background coefficient of inbreeding in populations in which complex consanguinity is common will need to be determined[12] before using such families in linkage studies.

R F MUELLER
Department of Clinical Genetics, Ashley Wing, St James's Hospital, Beckett Street, Leeds LS9 7TF, UK.

D T BISHOP
Imperial Cancer Research Fund Genetic Epidemiology Laboratory, Ashley Wing, St James's Hospital, Beckett Street, Leeds LS9 7TF, UK.

1 Duyk G, Gastier JM, Mueller RF. Traces of her workings. *Nature Genet* 1992;**2**:5–8.
2 Wong FL, Cantor RM, Rotter JI. Sample-size considerations and strategies for linkage analysis in autosomal recessive disorders. *Am J Hum Genet* 1986;**39**:25–37.
3 Smith CAB. The detection of linkage in humans. *J R Stat Soc [B]* 1953;**15**:153.
4 Lander ES, Botstein D. Homozygosity mapping: a way to map human recessive traits with the DNA of inbred children. *Science* 1987;**236**:1567–70.
5 Morton NE. Genetic epidemiology of hearing impairment. *Ann NY Acad Sci* 1991;**630**:16–31.
6 Heney D, Mueller R, Turner G, *et al.* Familial microcephaly with normal intelligence in a patient with acute lymphoblastic leukaemia. *Cancer* 1991;**69**:962–5.
7 Shaw NJ, Haigh D, Lealmann GT, Karbani G, Brocklebank JT, Dillon MJ. Autosomal recessive hypoparathyroidism with renal insufficiency and developmental delay. *Arch Dis Child* 1991;**66**:1191–4.
8 Ott J. Estimation of the recombination fraction in human pedigrees: efficient computation of the likelihood for human linkage studies. *Am J Hum Genet* 1974;**26**:773–5.
9 Morton N. Linkage and deafness. *Hereditary Deafness Newsletter* 1991;**6**:6.
10 Clarke A. Homozygosity mapping and Friedreich's ataxia. *Lancet* 1988;**i**:1168.
11 Morton N. *Outline of genetic epidemiology*. London: Karger, 1982.
12 Darr A, Modell B. The frequency of consanguineous marriage among British Pakistanis. *J Med Genet* 1988;**25**:186–90.

BOOK REVIEWS

If you wish to order or require further information regarding the titles reviewed here, please write to or telephone the BMJ Bookshop, PO Box 295, London WC1H 9JR. Tel 071 383 6244. Fax 071 383 6662. Books are supplied post free in the UK and for BFPO addresses. Overseas customers should add 15% 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. (The price and availability are occasionally subject to revision by the Publishers.)

HLA 1991, Proceedings of the XI International Histocompatibility Workshop and Conference. Volumes 1 and 2. Ed K Tsuji, M Aizawa, T Sasazuki. (Pp 1220; £175.00.) Oxford: Oxford Scientific Publications, Oxford University Press, 1992. ISBN 0 19 262217 X.

These proceedings are the eleventh from the International Histocompatibility Workshop (IHW) community in a history of almost 30 years; they are dedicated to the memories of the late Hilliard Festenstein and Flemming Kissmeyer-Nielsen. Anyone wishing to keep abreast of developments in definition of the human Mhc, its alleles, and clinically relevant products will find these volumes essential reading and reference. This review of such a significant publication is best restricted to highlighting the contents as a 'taster' to anyone contemplating the cost of £175.

Volume 1 contains the 11th IHW report and data analyses with an overview and WHO Nomenclature Committee report listing the newly accepted alleles, specificities, and genes as part of HLA. This IHW may be the last to have a complete serological component and the antigen society reports are the key reference for laboratories using serology to define HLA-A,B,Cw,DR, and DQ specificities. Although monoclonal antibodies to HLA specificities have not replaced the use of alloantisera for routine typing they were used in IHW studies to define new specificities and could detect sequence polymorphisms and specific epitopes such as the definition of HLA-DR103, to which alloantisera do not exist. The use of HLA transfectants for generation of monoclonal antibodies resulted in studies of eight HLA class I and 13 HLA class II specific monoclonals.

The most valuable aspect of the 'DNA component' report is the wide range of techniques documented for anyone to try. The 11th IHW protocols are inevitably already dated with the sequencing of many more HLA-DR and -DP alleles in the last 12 months.

A major objective of the IHW was the documentation of HLA alleles and specificities in different populations. This was achieved with some success and specific reports are included. The reference tables (155 pages) contain masses of data which are valuable to both researchers and routine histocompatibility testers.

Studies of HLA and disease associations now concentrate on defining specific susceptibility epitopes or seek functional relationships between specificities and infectious agents; the latter is best illustrated by HLA-B53 positivity in malaria patients reviewed in volume 2. Some 19 diseases were examined by serological and molecular techniques; these were those with established HLA associations (IDDM, RA, IMN, CD, etc) and new studies such as that of HIV. In the latter multicentre European study, 271 HIV positive persons showed no significant HLA association and the report concludes "the analysis does not provide much evidence that susceptibility to become infected with HIV or to develop AIDS is controlled by the HLA system". Some of the disease studies are more comprehensive than others with the RA study being insubstantial.

Unfortunately the studies of HLA and organ transplantation were rather restricted in this IHW and suffered from world wide organisational difficulties. This is disappointing given that recent studies continue to emphasise the imperative for HLA matching in marrow transplantation and the advantages of outcome in HLA matched solid organ transplants. The HLA community must not forget that much of the drive to elucidate this gene complex came from the need to apply the knowledge gained to clinical transplantation.

The technique of immunoprecipitation of metabolically labelled HLA molecules followed by isoelectric focusing is established in the definition of specificities and is a good bridge between alleles and antigens of HLA class I (HLA-A,B,Cw). It formed a small but useful part of this IHW.

The interaction of HLA molecules with the T cell receptor repertoire was studied with a number of approaches but one wonders if the HLA polymorphisms themselves really are the more functionally important partner? Notably, mixed lymphocyte culture assays and their associated complex data were not included in this IHW.

Other core IHW studies included C4, C2, and Bf complement genes which are encoded in the HLA-B/DR region, studies on human reproductive failure in 402 cases world wide of habitual aborter couples which showed no significant role for HLA genes, and studies of serum soluble HLA class I antigen.

Volume 2 of *HLA 1991* has 122 pages of invited overviews and 531 pages of papers presented at the IHW Conference. The overviews are essential reading for state of the art information on HLA and are varied from HLA genetics, antigen presentation, gene regulation, disease associations and clinical applications to evolutionary mechanisms. These areas and others are expanded in the themes of contributed papers; the section on molecular typing methodology is particularly thought provoking.

Volume 2 contains 33 pages of IHW participants names and addresses; this is most useful but inclusion of fax numbers would have been a great help in contacting this world wide community.

At first glance the two volumes of *HLA 1991* appear forbidding. Do not be put off! They are easy to 'get around' and follow a logical structure. The larger of the books, volume 1, contains the data needed for reference and will stay on the desk or in the laboratory while volume 2 can be carried home for digestion. The tradition of the IHWs is carried forward in these books and there are milestones such as population frequency data and methodology which will make them a continued reference. No HLA researcher or histocompatibility typer can be without them particularly since it is planned

that much of the data will be carried forward to the XII IHW to be held in Europe in 1996; as such, a personal rather than library copy would be advantageous.

PHILIP A DYER

Catalog of Prenatally Diagnosed Conditions. 2nd edition. David D Weaver. (Pp 415; $47.00.) Baltimore: Johns Hopkins University Press. 1992.

To avoid disappointment, read the title carefully. The book is essentially two cross referenced lists. The first list occupies 278 pages and is of conditions diagnosed prenatally and published. There are 601 of them and they are subdivided into chromosomal anomalies, congenital malformations, deformations, and disruptions, dermatological disorders, fetal infections, haematological disorders and haemoglobinopathies, inborn errors of metabolism, tumours and cysts, and 'other prenatal conditions'. Each entry lists the abnormal prenatal findings reported with that condition and relevant citations. Some entries also include brief notes and comments by the author. The reference section which follows contains 1848 references. The index (54 pages) includes the second list, that of abnormal findings. Thus, it is possible to look up the conditions in which a given prenatal finding, such as hydrops fetalis (71 entries), hydrocephalus (47 entries), or club foot (11 entries), has been reported.

While a catalogue approach to prenatal diagnosis is attractive, the method adopted seems excessively pedantic. It may be obvious that condition X could be diagnosed by method Y, but if that finding has not been published, it will not appear. On the other hand, much of the book is of mainly historical interest. For example, 43 separate prenatal findings are documented under 'spina bifida cystica', and the entry covers four sides, but there are only eight lines of discussion to clarify which of these many findings are likely to be the most useful in practice. The rigid layout results in entries based on single cases and findings of dubious importance occupying an inordinate amount of space. An authoritative and critical abstract for each condition would help to orientate the reader and give the book a more personal flavour.

There are inconsistencies in the terminology, for example, Down syndrome is listed under D, other trisomies under T, Klinefelter syndrome is under K, triple X under 'Chromosome XXX syndrome', XXYY syndrome under X, Turner syndrome under T, and 45,X/48,XXYY mosaicism under 4. This is a minor criticism, but it adds to the irritation produced by the book's inflexible approach and its air of encyclopaedic authority.

Although it may be useful as a survey of prenatal diagnosis publications up to 1991, this is not an ideal source of information when advising families about a pregnancy. It is doubtful whether the format is appropriate for a practical reference book in such a rapidly moving field.

N R DENNIS

Methodology for Genetic Studies of Twins and Families. Michael C Neale, Lon R Cardon. (Pp 496; £99.00.) London: Kluwer Academic Publishers. 1992.

This book deals with the analysis of twin and family data by model fitting, mainly using the computer package LISREL. This is a widely used package for structural equation modelling which has recently been taken up particularly by quantitative geneticists.

The first few chapters focus on basic genetics and statistics before moving on to explanations of model fitting. The first five chapters are fairly clear and although chapters 6 and 7 are difficult for non-mathematicians, the authors do say that the contents of these two chapters can be skipped. However, for those unfamiliar with LISREL, the assimilation of chapter 8 is crucial in order to understand the successive chapters and to comprehend the LISREL scripts. The remaining chapters deal with the application of LISREL to univariate and multivariate genetic analyses and become progressively more difficult, so that the last few chapters are hard to follow for those unfamiliar with LISREL.

The positive aspects of this book are that the beginning chapters start from scratch and allow for the reader having little previous experience in this field. The chapter on matrix algebra is particularly clear. Although on first glance this book looks very mathematical, if followed carefully and in order, the authors take the reader logically through each step. Thus with perseverance, most explanations can be followed by those with little mathematical expertise. In addition, the inclusion of real twin data to illustrate the different types of model is very helpful.

The main criticism of the book is that the title suggests more than the book actually gives. The book is primarily focused on the LISREL program and its applications. LISREL scripts are incorporated into each chapter. Thus it consists of a specific introduction to the uses and methods of LISREL in analysing data, rather than a general text on the analysis of twin data.

In conclusion this book is not suitable as general reading for those who want an introduction to analysing twin data. It is too specific, requires too much perseverance and motivation to work through, and may be offputting to a novice. However, it is likely to be useful and of great interest to those who are specifically planning to learn how to use LISREL. More experienced quantitative geneticists, who are non-LISREL users, will also find it useful as an overview.

ANITA THAPAR

NOTICE

International consortium on X linked myotubular myopathy. Call for information on patients and families

At a meeting of interested groups in March 1993 organised by the European Neuromuscular Centre, an international consortium has been formed to further the clinical, pathological, and molecular understanding of this rare disorder, and to form a resource of information and material available for research. The consortium would welcome information on any present or future patients and families, and will be happy to arrange for preservation of cell lines for molecular genetic studies and muscle for culture and special studies or biopsy material. Any clinician wishing to share such material or to obtain further information about the activities of the consortium should contact the coordinator: Dr Carina Wallgren-Pettersson, Department of Clinical Genetics, University of Helsinki, Haartmaninkatu 2B, SF-00290 Helsinki, Finland. Fax: 358-0-471-6089.

NOTICE

European Research Conferences

The following European Research Conferences will be held. 'Molecular Biology of Cellular Interactions: Adhesions Molecules'. Chairman: J A Williams (London), San Feliu de Guixols, Spain, 23–28 October 1993. 'Genetics and Structures of Animal Viruses'. Chairman: W Doerfler (Cologne), Mont Sainte-Odile (near Strasbourg), France, 22–27 October 1993. 'Inherited Disorders and their Genes in Different European Populations'. Chairman: A de la Chapelle (Helsinki), Obernai, France, 26–30 November 1993. For further details contact the Office of European Research Conferences, European Science Foundation, 1 quai Lezay-Marnésia, 67080 Strasbourg Cedex, France. Tel: (33) 88 76 71 35. Fax: (33) 88 36 69 87.

NOTICE

French Society of Human Genetics

The first annual meeting of the French Society of Human Genetics will be held on 15 December 1993 at Hôpital des Enfants Malades in Paris. The scientific programme includes three sessions on: Usefulness and Difficulties of Linkage Analysis in Human Genetics, Genomic Imprinting, and Unstable Expansion of Trinucleotide Repeats. We are soliciting submissions for oral presentations and posters. If you wish to present your research at this meeting, please send an abstract not later than 3 November 1993 to Professor Claude Stoll. For more information, contact Professor Claude Stoll, Institut de Puériculture, Service de Génétique Médicale, 23 rue de la Porte de l'Hôpital, 67091 Strasbourg Cedex, France. Tel: (33) 88.16.10.12. Fax (33) 88.16.13.30.