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Fertility in a male with trisomy 21

In 1989, we reported[1] the first fully documented case of an apparently non-mosaic male with Down's syndrome fathering a pregnancy. This pregnancy subsequently miscarried about nine weeks after a CVS procedure.

The same couple returned to the Genetics Centre early in 1991 in the first trimester of pregnancy. A chorion villus sample was again obtained (Mr D Maxwell) and this showed a normal karyotype. DNA samples from the CVS were analysed with the highly polymorphic probes *D7S21*[2] and *D17S30*,[3] the results confirming that paternal alleles for both markers in the CVS were also present in the putative father. This second pregnancy proceeded to term, and a normal boy has now been born to this couple.

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1 Sheridan R, Llerena J Jr, Matkins S, Debenham P, Cawood A, Bobrow M. Fertility in a male with trisomy 21. *J Med Genet* 1989;**26**:294–8.
2 Wong Z, Wilson V, Patel I, Povey S, Jeffreys AJ. Characterization of a panel of highly variable minisatellites cloned from human DNA. *Ann Hum Genet* 1987;**51**:269–88.
3 Horn GT, Richards B, Klinger KW. Amplification of a highly polymorphic VNTR segment by the polymerase chain reaction. *Nucleic Acids Res* 1989;**17**:2140.

Clinical consequences of deletion 1p35

We would like to make a correction to our paper[1] previously published in the journal. Upon analysis of another blood specimen at higher resolution, we found a balanced translocation. The corrected karyotype is 46,XY,t(1;11)(p34.3;q25).

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1 Wenger SL, Steele MW, Becker DJ. Clinical consequences of deletion 1p35. *J Med Genet* 1988;**25**:263.

Maxillonasal dysplasia (Binder's syndrome) and chondrodysplasia punctata

In a recent letter to the editor, Sheffield *et al*[1] discussed the true relationship between maxillonasal dysplasia (Binder's 'syndrome') and chondrodysplasia punctata. The authors noted that the number of patients diagnosed as chondrodysplasia punctata had been underestimated because punctate epiphyses disappear with age, and they suggested looking at old radiographs that had been performed in infancy.

We have another suggestion. If the patient is a male, it would be advisable to examine the hands of his maternal relatives, especially uncles and nephews, to look for brachytelephalangy. Moreover, if the disease seems to be inherited in an X linked recessive manner, an analysis of Xp could be indicated as the gene CDPX 1 has been mapped to Xp22–32. In one familial case, Petit *et al*[2] found an interstitial deletion in Xp22.3.

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1 Sheffield LJ, Halliday JL, Jensen F. Maxillonasal dysplasia (Binder' syndrome) and chondrodysplasia punctata. *J Med Genet* 1991; **28**:503–4.
2 Petit C, Melki J, Levilliers J, Serville F, Weissenbach J, Maroteaux P. An interstitial deletion in Xp22.3 in a family with X-linked recessive chondrodysplasia punctata and short stature. *Hum Genet* 1990;**85**:247–50.

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.

Congenital Chromosome Aberrations and Tumour Predisposition. Gyorgy Fekete. (Pp 162; £13.00.) Budapest: Akademiai Kiado. 1990.

In this book, the Hungarian author reviews some of the clinical and scientific publications, published up to 1989, concerning the association between genetic factors and malignant disease, with particular emphasis on congenital chromosome aberrations and tumour development.

In the first chapter the nature and frequency of congenital chromosome aberrations associated with cancer predisposition and associated clinical symptoms are described. The relationship between induced chromosome aberrations, chromosome instability, oncogenes, fragile sites, and malignant disease is discussed in chapter two. Chapter three is very short and deals with the topic of genetic counselling for cancer patients and their families. An attempt is made to give advice concerning screening for malignancy and the author only very briefly covers the subject of risk assessment. The final chapter describes a number of culture and banding techniques for the preparation of chromosomes from various tissues. The classification of structural chromosome aberrations and the nomenclature (ISCN 1985) used to describe them is included.

Much work has been done over the past few years in this fast developing field and a review of this subject is timely. Unfortunately, much of the data presented here are out of date and in places the experimental data derive mainly from the author's own laboratory. There is a wealth of world publications available concerning congenital chromosome aberrations and cancer predisposition and a number of important recent developments have not been included in this volume. For instance, the association between Beckwith-Wiedmann syndrome and Wilms' tumour and the suggestion of two possible loci for Wilms' tumour on chromosome arm 11p (Mannens *et al. Hum Genet* 1988;**8**:41–8) are not mentioned. Also, many of the incidence figures quoted for particular disorders relate only to Hungary and therefore may not have much relevance for a wider readership. It must be mentioned, however, that there may be problems in obtaining some current journals in eastern Europe which may have contributed to this lack of up to date references.

A number of serious scientific inaccuracies are also present in this book. The author states incorrectly that carriers of constitutional 13q14 deletions usually develop unilateral retinoblastoma rather than bilateral tumours. When describing the t(9;22) observed in chronic myeloid leukaemia (CML) the author states that the breakpoint on 9q34 is located close to the c-abl oncogene. However, it is known that the breakpoints on 9q34 are scattered and can be located both 5′ of the first c-abl exon as well as located within the c-abl oncogene (Heim and Mitelman. *Cancer cytogenetics*. New York: Liss, 1987). It is also stated that in CML the c-abl oncogene is associated with the immunoglobulin heavy chain locus. This statement is incorrect as the t(9;22) translocation involved in CML places c-abl next to the breakpoint cluster region on chromosome 22 (Shtivelman *et al. Nature* 1985; **315**:550–4) and not in association with the immunoglobulin heavy chain locus.

The translation into English is poor and consequently the book is difficult to read in places. Also, the quality of many of the figures, including those reproduced from other publications together with ones from the author's own laboratory, is very poor. For example, in a figure showing deletions of chromosome 13 involved in retinoblastoma it is very difficult to see the GTG banding pattern on the chromosomes. Similarly, the poor reproduction of figures on pages 52 and 53, depicting induced chromosome aberrations, makes their interpretation difficult. Finally, the representation of Q, G, and R bands reproduced from the Paris Conference (1971) has been altered by the addition of extra and incorrectly positioned light G bands on the long arms of chromosomes 13,14,15, and 16.

The book is primarily aimed at paediatricians, oncologists, and medical geneticists. However, as it is sadly out of date, it will only be useful as a general introduction to the topic. If greater detail is required by the reader then it will be necessary to read more up to date publications.

ERIKA L D MITCHELL

Aspects of Oral Molecular Biology. Frontiers of Oral Physiology, volume 8. Ed DB Ferguson. (Pp 144; £67.40.) Basel: Karger. 1991.

This book presents an overview of molecular biology in relation to fundamental oral and

This edition also shows how much wider the impact of molecular approaches has become; while haemoglobin disorders are still used prominently as examples, the advances in numerous mendelian and non-mendelian disorders are well covered and illustrate the convergence between medical genetics and the various specialities using molecular techniques. The potential and actual ethical problems are covered with both sensitivity and common sense; the applications to our understanding of cancers and the possibilities of gene therapy are fully explored.

Much of the original influence of the book was because the author was not only a scientist but a practising clinician, enabling him to act in a remarkable way as a bridge, not only for molecular concepts and techniques to become applied to clinical problems, but also for other clinicians to cross and to see for themselves the extraordinary possibilities for their own fields of work. The need for a bridge of this kind remains very great; one senses the author's frustration at what the past decade has not achieved, as well as what it has. In particular, the need for society as a whole to be scientifically and genetically literate has become imperative if the 'New Genetics', having firmly become part of clinical practice, is to be fully accepted by society for the ways in which it influences patients and families with many important and common disorders.

PETER S HARPER

London Neurogenetics Database. M Baraitser, R M Winter. (£395·00 plus optional annual updates. Available on 5·25" or 3·5" discs. For IBM microcomputers.) Oxford: Oxford University Press. 1991.

Those familiar with the *Dysmorphology database* built up by the same authors will understand both the aims and workings of the *Neurogenetics database*, which was compiled in order that clinicians involved with neurological disorders and syndromes would have ready access to reports of similar patients in medical publications. The authors also intended that the *Neurogenetics database* would be comprehensive and quick to use. These aims have been admirably achieved.

The Database is amazingly easy to install and it is easy to use AS LONG AS YOU READ THE MANUAL FIRST. This is small, compact, and clear. Some uses of keys are unexpected, and some have different uses at different levels, so a little study beforehand is essential. The manual explains the different ways in which you can search for syndromes, or search for references if you so wish, or add in your own patient data. This latter feature is very useful for those of us who frequently see undiagnosable patients.

The *Database* is concerned with syndromes rather than common conditions, and complicated varieties of, for example, spinal muscular atrophy or spastic paraplegia are easier to find than the more common uncomplicated forms. Nearly 2000 syndromes with 8000 references are included, and many of these belong to just single patients. It is remarkably comprehensive to include such isolated cases, and saves the user much time and effort in searching through published reports. However, such conditions may in fact never be seen again in another patient.

Firstly, the user has to learn how to select a few conditions out of the 2000, and the art here is of choosing relatively uncommon features to lead into the syndrome search. Classified features are listed in the lucid and brief manual that accompanies the *Database*. For example, it is more useful to choose 'cystic changes' than 'dementia', although choosing both features on separate lines (which means add) is just as good. There are 229 syndromes which manifest dementia, and 100 with 'sparse hair'! Having found syndromes that you wish to learn about, you can ask for clinical features, abstract, and references. The abstracts (which are dated) are the high spots of the *Database*. They are composed by the authors and express their opinions as to the significance of the syndromes, how they relate to other conditions, and generally are wise and experienced assessments. For those disorders in which DNA techniques help carrier detection or prenatal diagnosis, the latest information is provided. If you wish to keep a record of these valuable comments and the appropriate references, you just have to request 'Print'; it does not matter what printer you have so long as it is connected to your computer.

The authors should be congratulated on what must surely be a very altruistic service, namely reading and assessing the body of neurological publications on behalf of the rest of us, and I do not envy them their "regular review of over 1000 journals". I am sure that many others, like me, will find it most rewarding to search through the *Database* for an unusual combination of signs, will thereby learn about many disorders other than the one being searched for, and will, in passing, be familiarised with neurological publications. At the same time it is reassuring to know that the features of an undiagnosed patient are not already listed as a reported syndrome.

How often the *Database* is used will depend upon how often patients with rare syndromes are seen. Therefore, clinicians who deal with neurological syndromes will find the *Database* more useful than those who predominantly deal with common disorders, which is why paediatricians will find it more valuable than adult neurologists. Clinical geneticists will find it a helpful adjunct to the *Dysmorphology database*. One *Database* for each centre should be sufficient, particularly in view of the expense (£150) of the yearly updates.

SARAH BUNDEY

NOTICES

Ehlers–Danlos Support Group

The Ehlers–Danlos Support Group has produced an information booklet on Ehlers–Danlos syndrome. This has 20 pages and 15 sections covering various aspects of the syndrome. The authors of the booklet are Professor P Beighton, Professor A C Bird, Professor R Grahame, Mr A P Barabas, Dr H A Bird, Dr F M Pope, and Mr I P Hunter. The first copy of the booklet is free with subsequent copies costing £1.00 plus postage. They can be obtained from The Ehlers–Danlos Support Group (Mrs V A Burrows), 2 High Garth, Richmond, North Yorkshire DL10 4DG. Tel 0344 57695.

European School of Medical Genetics

The Fifth Course of the European School of Medical Genetics will be held on 5 to 12 December 1992 in Sestri Levante (Genoa), Italy. Directors: Victor A McKusick, Baltimore, and Giovanni Romeo, Genoa. Enquiries to: Istituto G Gaslini, Lab di Genetica Moleculare, L.go Gerolamo Gaslini, 5, 16148 Genova-Quarto, Italy. Tel: (010) 5636-370/400.

Notice to contributors (general guidance)

The readership of *Journal of Medical Genetics* is world wide and covers a broad range of workers, including clinical geneticists, scientists in the different fields of medical genetics, clinicians in other specialities, and basic research workers in a variety of disciplines. It publishes original research on all areas of medical genetics, along with reviews, annotations, and editorials on important and topical subjects. It also acts as a forum for discussion, debate, and information exchange through its Letters to the Editor columns, conference reports, and notices. The editor is always grateful for suggestions or criticisms from readers and authors.

ORIGINAL PAPERS

These may be on any aspect of medical and human genetics and may involve clinical or laboratory based and theoretical genetic studies. Guidance on length can be obtained from studying the Journal. Shorter articles may be most appropriately submitted as *case or family reports*, not exceeding 1000 words, with no more than three figures, one table, and 10 references. *Short reports* should not exceed 500 words, with a single illustration. Contributions may also be submitted as *Hypotheses*, *Technical Reports*, *or Short Communications*. Accelerated publication of papers of particular importance will be considered.

REVIEWS

Short or longer reviews on all aspects of medical genetics are welcome, but should be discussed first with the Reviews Editor. Contributions on historical topics, or which could form part of specific series, are particularly acceptable.

ANNOTATIONS AND EDITORIALS

These are written or commissioned by the editors, but suggestions are welcome regarding possible topics and authors.

LETTERS

These are welcome on any relevant topic and will be published rapidly. Those relating to or responding to previously published items in the Journal will be shown to those authors, where appropriate. Although a paper submitted as an original report may sometimes be published in shortened form as a letter, it is preferable for initial submissions to be as a short report, unless directly related to a previous journal article.

CONFERENCE REPORTS

Reports from small to medium sized meetings, especially international workshops on specific topics, will be appreciated. Authors intending to submit conference reports should liaise with the Reviews Editor to avoid duplication.

SPECIAL ISSUES AND SUPPLEMENTS

These are published at intervals on topics of particular relevance. Enquiries are welcome from those organising workshops or symposia who may have material suitable for such an issue.

BOOK REVIEWS

The Journal aims to review as wide a range of relevant books as possible. Authors or others wishing to check if a book has been received may check with the Journal office. Computer programs and databases, official reports, and other material relevant to the field may all be appropriate for review. Enquiries about such items are welcome.

OBITUARIES

The Journal would like to be informed rapidly of the death of any senior or important person in the field of medical or human genetics, regardless of geographical location. In general, a brief notice would be published rapidly, with a longer obituary as appropriate. Since such deaths often occur many years after retirement, it will be appreciated if readers will contact the Reviews Editor so that appropriate arrangements can be made.

NOTICES

Notice of forthcoming meetings in different countries should be sent as far ahead as possible. Extensive descriptions should be placed as advertisements.

'CALLS FOR PATIENTS'

The Journal receives an increasing number of requests to publish notices of proposed studies involving patients or families with rare genetic disorders. In general such notices are appropriate only for major international collaborations; the proposer should ensure that such a notice does not conflict with existing studies or proposals.

ILLUSTRATIONS

High quality black and white photographs are preferred for most illustrations, particularly of patients. Colour illustrations can be accepted; however, authors are asked to pay part of the cost, so their desirability should be discussed in advance of submission. All identifiable photographs of patients must be accompanied by written permission for use.

Specific instructions to authors

Papers, which should be in triplicate and in the Vancouver style (*BMJ* 1988;**296**:401–5), should be sent to the Editor, *Journal of Medical Genetics*, BMA House, Tavistock Square, London WC1H 9JR and not to individual editors, with the exception of papers from the USA, which can be submitted to the North American Editor, Dr P M Conneally, Department of Medical Genetics, James Whitcomb Riley Hospital for Children RR129, Indiana University Medical Center, Indianapolis, Indiana 46223, USA. Submission of a paper will be held to imply that it contains original work which has not been previously published. It is the responsibility of the submitting author to ensure that all co-authors are agreeable for their names to appear on the manuscript. A FAX number should be provided. Permission to republish must be obtained from the Editor.

Where a patient(s) with a structural chromosome abnormality is described, the availability of a cell line(s) should be stated in the text together with its identifying number, cell bank, and, where appropriate, contact person.

All contributions should be accompanied by an abstract (preferably structured) giving the main results and conclusions. Typescripts should be at least double spaced with wide margins. One page proof will be sent to the author submitting the paper and alterations on the proof, apart from printer's errors, are not permitted. Reprints may be ordered when the proof is returned.

Figures should be kept to a minimum and should be numbered consecutively in Arabic numerals. Legends should be typed on a separate sheet.

Tables should not be included in the body of the text, but should be typed on separate pages and numbered with Arabic numerals. A legend should be provided.

References should conform precisely to the style current in this journal. Authors are responsible for the accuracy and completeness of their references as these will not be checked by the Editorial office.

NOTES ON NOMENCLATURE

Authors should refer to the following publications.

(1) Chromosomes: *ISCN 1985. An international system for human cytogenetic nomenclature*. Basel: Karger, 1985.

(2) Genes: Shows TB, *et al.* In: Human Gene Mapping 5 and 7. *Cytogenet Cell Genet* 1979;**25**:96–116, 1984;**37**:340–3.

(3) Loci: Conventional nomenclature should be used, with lower case lettering as appropriate (for example, Race RR, Sanger R. *Blood groups in man.* 6th ed. Oxford, London: Blackwell, 1975; and Giblett ER. *Genetic markers in human blood.* Oxford, London: Blackwell, 1969).

(4) Blood coagulation: International Committee of Haemostasis and Thrombosis (Graham JB, *et al*). A genetic nomenclature for human blood coagulation. *Thromb Haemostas* 1973;**30**:2–11.

(5) Enzymes: *Enzyme nomenclature: recommendations of the nomenclature committee of the International Union of Biochemistry.* New York: Academic Press, 1984.