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LETTERS TO THE EDITOR

X linked α thalassaemia/mental retardation (ATR-X) syndrome

We read with interest the series of reports in the journal on the ATR-X syndrome.[1–4] The facial features are similar to affected subjects with another X linked MR syndrome in a Canadian family described by us a few years ago.[5] Cole *et al*[2] suggested that our family may have the ATR-X syndrome. We studied the three living affected males in the family again. All showed normal haematological indices, no detectable haemoglobin H on electrophoresis, and no cells containing haemoglobin H inclusions using 1% brilliant cresyl blue preparations of peripheral blood smears.

In addition, our patients appear to be less severely retarded than the British families described. The possibilities are that these two disorders may (1) be the result of different mutations, (2) be allelic, or (3) represent an X chromosome contiguous gene syndrome with different sized deletions. In respect to the last hypothesis, high resolution chromosome analysis in our laboratories (Winnipeg and Calgary) and in Houston (courtesy of David H Ledbetter) showed no deletions. Identification of the gene locus and molecular studies will ultimately resolve the issue.

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1 Gibbons RJ, Wilkie AOM, Weatherall DJ, Higgs DR. A newly defined X linked mental retardation syndrome associated with α thalassaemia. *J Med Genet* 1991;**28**:729–33.
2 Cole TRP, May A, Hughes HE. α thalassaemia/mental retardation syndrome (non-deletion type): report of a family supporting X linked inheritance. *J Med Genet* 1991;**28**:734–7.
3 Wilkie AOM, Gibbons RJ, Higgs DR, Pembrey ME. X linked α thalassaemia/mental retardation: spectrum of clinical features in three related males. *J Med Genet* 1991;**28**:738–41.
4 Donnai D, Clayton-Smith J, Gibbons RJ, Higgs DR. The non-deletion α thalassaemia/mental retardation syndrome: further support for X linkage. *J Med Genet* 1991;**28**:742–5.
5 Chudley AE, Lowry RB, Hoar DI. Mental retardation, distinct facial changes, short stature, obesity, and hypogonadism: a new X linked mental retardation syndrome. *Am J Med Genet* 1988;**31**:741–51.

49,XXXXY syndrome: behavioural and developmental profiles

I read with great interest the recent paper by Lomelino and Reiss,[1] reporting behavioural, psychological, and cognitive profiles of two cases of 49,XXXXY and one of 48,XXXXY/49,XXXXY mosaicism.

In 1964[2] I reported two cases of severely mentally handicapped patients with XXXXY syndrome, who suffered from similar developmental profiles. Case 1 improved very little in cognition, behaviour, and language development since 1964 and died from bronchopneumonia at the age of 23 years.

Case 2 is now 44 years of age and intellectually he has improved slightly since 1964. Assessed on the Merrill Palmer Scale, his MA is 5·11 years but he still cannot read or write. His verbal comprehension and expression has shown some improvement. Results of testing on the Reynell Development Language Scales were: raw scores 42, equivalent age 3·03 years. The main characteristics which make him difficult to understand are the very low volume of his voice (he mostly speaks only in a whisper) and his shyness.

However, there are increasing problems with his behaviour. He suffers from temper tantrums, kleptomania, and self-injury, particularly to his hands. He constantly picks a chronic hypostatic ulcer[3] on his leg. He is often untruthful and mischievous. The patient has been caught setting fire on many occasions and therefore requires constant supervision.

Sometimes he becomes verbally abusive, swearing and threatening violence, and will resort to throwing things.

Physically he is prone to falls and sustained a fracture of the neck of the right femur and fracture of the left patella, which is adding to his frustrations.

J JANCAR
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1 Lomelino CA, Reiss AL. 49,XXXXY syndrome: behavioural and developmental profiles. *J Med Genet* 1991;**28**:609–12.
2 Jancar J. Mentally defective males with XXXXY chromosomes. In: *Proc Int Copenhagen Conf on SS Ment Retard.* Copenhagen: Øster, 1964; 179–95.
3 Jancar J. Hypostatic ulceration and male sex chromosomal anomalies. *BMJ* 1978;**2**:434.

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.

The Triumph of the Embryo. Lewis Wolpert. (£14.95.) Oxford: Oxford University Press. 1991.

This book is intended as an introduction to developmental biology for non-specialist readers. The majority of the book is devoted to the mechanisms of embryonic development, but cancer, ageing, and evolution are also covered from a developmental perspective. The reader is taken through the stages of embryonic development by careful discussion of important experiments and well chosen analogies, for example, gastrulation and origami. Professor Wolpert's belief that embryonic development can be described by a series of relatively simple mechanisms, and his sheer enthusiasm for the subject, provide the basis for a clear and comprehensible account of complex processes, such as limb formation and central nervous system development.

This is an excellent book. It is informative and readable and fulfils its intended purpose (triumphantly). I would recommend it to lay readers wanting a clear and comprehensible account of embryonic development and to any health professional who wanted a gentle introduction to the subject.

E R MAHER

Antenatal Diagnosis of Fetal Abnormalities. Ed J O Drife, D Donnai. (Pp 400; £60.00, DM190.) Berlin: Springer-Verlag. 1991.

An academic paediatrician who recently reviewed advances in genetics commented that the subject had become much too important to be left to geneticists. His realisation only came lately; thus obstetricians should congratulate themselves on being farsighted enough to have established (with perhaps more than a little prompting from a few pioneering geneticists) a multidisciplinary subspeciality which, paradoxically for a subspeciality, has grown to touch upon the lives of nearly everyone in the general population. This, of course, means that workers in the field carry a very heavy burden of responsibility, so it is timely that the Royal College of Obstetricians and Gynaecologists should, in its 23rd study group meeting, examine the state of antenatal diagnosis.

This book contains papers presented at the meeting and edited transcripts of the resulting discussions. Its title is brief but do not be misled into anticipating that its contents will merely be another account of the latest clinical and laboratory techniques, although there are certainly many expert and critical expositions of these. One only has to run through the list of the meeting's participants, noting a philosopher, an economist, a psychologist, a civil servant, and several epidemiologists, to realise that a wide brief is being addressed. The broad sweep of the contribution is reflected in a list of 19 conclusions and recommendations at the end of the book. As well as statements on clinical procedures and laboratory tests, such as ultrasound examination, fetal blood sampling, and maternal serum screening, there are more general statements supporting the organisation of regional genetic centres and fetal medicine centres, calling for improved professional and lay education in genetics and recommending that ethicists should be involved in the introduction of new techniques. Two other recommendations are, firstly, each district general hospital should have a consultant obstetrician with a special interest in and responsibility for the various aspects of prenatal diagnosis and, secondly, that appropriate support, obstetric follow up, and genetic counselling should be available to women who undergo termination of pregnancy for fetal abnormality. I thought there might be a statement on the relative merits of amniocentesis and chorionic villus sampling, given that there is discussion of this at several points in the text, but perhaps the study group did not wish to prejudge the then unpublished MRC trial comparing these procedures.

The book's 25 chapters, which embrace almost the whole subject, are arranged in seven sections and comprise reviews in the

subtitled 'Promises kept and pending'. The promises kept are mainly so far on the technical side and are truly impressive. Clinical applications come more into the pending category.

Probably the chapter with the greatest long term significance is that on fluorescence in situ hybridisation (FISH) (Jeanne Lawrence). It starts with a lot of technical information optimising the conditions for efficient signal detection. Numerous technical parameters are fairly easy to test with fluorescence detection but in fact, for the most part, the studies end up confirming the knowledge acquired in the days when radioactive probes were used. The best examples given in this chapter concern hybridisation of probes to interphase nuclei. One beautiful example concerns probes from different regions of the dystrophin gene. Two probes just over a Megabase apart are shown as two distinct clearly spaced dots in the nucleus of a male. The corresponding hybridisation to nuclei from a female shows two such pairs of dots. The corresponding experiment using probes only 375 kb apart shows a closer spaced pair of dots in the male and two pairs in the female. These examples must surely point the way to solving the perennial problem of carrier diagnosis in the female relatives of boys with Duchenne muscular dystrophy associated with deletions of the dystrophin gene. Many other potential applications will arise as this technology becomes more widespread.

Each chapter opens with a clear introduction and a list of major points to be covered, but many of the gems are well hidden in the chapters.

S MALCOLM

Hereditary Tumors. Ed M L Brandi, R White. (Pp 230; $82.50.) New York: Raven Press. 1991.

This book is the proceedings of a conference on hereditary tumours held in Florence, Italy on 22 to 24 April 1991. The book is notable for the speed of publication and the number of distinguished contributors. It therefore provides an up to date and authoritative account of a number of aspects of this important subject. Although the range of topics covered is wide (including articles on molecular genetics, genomic imprinting, and clinical aspects), it is not comprehensive. The multiple endocrine neoplasia syndromes are covered in most detail (five contributions) but there are contributions on the molecular genetics of neurofibromatosis type 1, Beckwith–Wiedemann syndrome, familial melanoma, lung cancer, genomic imprinting, and tumour suppressor genes (general aspects and specific articles on Wilms's tumour, retinoblastoma, and p53 genes).

Although most of the material contained in this book can be found separately in recent review articles, this book presents a convenient collection of up to date articles on selected aspects of hereditary tumours. One price of rapid publication using camera ready manuscripts is a lack of conformity in the presentation of individual articles.

EAMONN MAHER

DNA Fingerprinting: Approaches and Applications. Ed T Burke, G Dolf, A J Jeffreys, R Wolff. (Pp 400; SFr 168.) Berlin: Birkhauser. 1991.

This book is a collection of papers presented at the First International Symposium on DNA Fingerprinting held in October 1990. It contains a wealth both of technical information and fascinating reading, detailing a wide range of applications ranging from parasitology to population genetics and with comprehensive reference lists. Who would have thought that sequences useful for disentangling family relationships in humans would be closely related to sequences which can perform the same function in rice plants? Another chapter which caught my interest was a contribution to the problem of altruism in animals – the demonstration that bee eaters who help at the nest of other birds invariably help their relatives but do not in general contribute by paternity to the offspring.

Is this book useful to those whose main interest is in medical genetics? On the whole the emphasis is on true fingerprinting, that is, the generation of complex highly individual patterns which are the product of multiple loci. The human applications of these are in forensics and law rather than medicine. The establishment of true biological relationships between individuals is often of importance in genetic counselling but probably most laboratories would find it easier to use a series of locus specific probes rather than a core probe. The finding of an additional band in the fingerprint of one of a pair of monozygotic twins with Proteus syndrome is interesting but does not advance understanding of the condition. On the whole it reinforces the depressing conclusion previously reached that although a pair of MZ twins, one of whom has a clearly inherited disease, should be a valuable resource it is very hard to think of anything useful to do with them.

If you are an aficionado of DNA fingerprinting or if you dabble in forensic problems or in extracting results from minute and degraded samples then this is definitely the book for you. However, if you would really prefer a locus specific probe or a dinucleotide repeat to solve your problem, perhaps you should just persuade your library to buy a copy.

S POVEY

NOTICES

Latin American Directory of Research Centres in Human Genome. R Cruz Coke. 1991

Copies of this directory are available from the Department of Biochemistry, University of Chile School of Medicine, Independencia 1027, Casilla 70086, Santiago, Chile 7. Fax: 56–2–376320.

Standing Committee on Human Cytogenetic Nomenclature 1991–96

Elections for the Standing Committee on Human Cytogenetic Nomenclature were held at the 8th International Congress of Human Genetics in Washington, DC, on 10 October 1991. The following members were elected for the period 1991–96: Felix Mitelman, Sweden (Chairman), Jose Carlos Cabral de Almeida, Brazil, H John Evans, UK, Patricia N Howard-Peebles, USA, John M Opitz, USA, Avirachan T Tharapel, USA, Walther Vogel, Germany. Issues regarding human cytogenetic nomenclature can be addressed to any member of the committee.

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.