LETTERS TO THE EDITOR

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

We read with interest the series of reports in the journal on the ATR-X syndrome. 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. Cole et al suggested that our family may have the ATR-X syndrome. We studied the three living affected males in the family. 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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4 Donnan D, Clayton-Smith J, Gibbons RJ, Higgs DR. The non-deletion \( \alpha \) thalassaemia/mental retardation syndrome: further support for \( X \) linkage. \( J \) Med Genet 1991;28:742-5.

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 Medical Association Overseas, but overseas customers should add 15% to the value of the order for postage and packing. Payment may 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.


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 caring, 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, castration, and origami. Professor Wolpert’s belief that embryonic development can be described by a series of relatively simple mechanisms, and that there is an underlying theme throughout, provides 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 fulfills its intended purpose (triphanatically). 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


An academic paediatrician who recently reviewed advances in genetics commented that the subject has become much too important to be left to geneticists. His realisation of the only way later generations of obstetricians and gynaecologists should congratulate themselves on being far-sighted 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 breadth 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 medical 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, that a single 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
areas of epidemiology of congenital abnormalities and routine screening, DNA analysis, cytogenetic and biochemical disorders, special techniques (two sections, including a review of immunology and the application of economics and ethical issues, and service provision. In the latter section there is a detailed description of the financial and operational basis of the system in the Netherlands (H Galjaard). Here, perhaps, an opportunity was lost to appraise this critically and speculate in the light of the radical changes now threatening our working practice in Britain. In particular there are detailed discussions of heterozygote screening for cystic fibrosis, cardiac ultrasound scanning, and the karyotyping of chionic villi; there are also thoughtful essays on psychological, economic, and ethical aspects of prenatal diagnosis (the latter contains a memorable rebuttal of George Steiner's airing on television of the argument that prenatal diagnosis would have deprived us of Beethoven, in the author's words, Steiner's 'ode to joy'). Finally, there are several reviews which draw attention to new techniques such as preimplantation diagnosis and magnetic resonance imaging.

Given the list of distinguished authors, sustained excellence in content was assured, but for me an additional bonus was the sheer elegance of the book which could be read from cover to cover. The editors are to be congratulated on this count, also for getting the book published so promptly and for providing us with edited transcripts of the discussions which followed papers. Many interesting points emerge from these discussions, for example, a scientist wonders how couples can be made anxious by a negative test result, the psychologist argues that the process of prenatal testing causes anxiety in women who do not realise they are at risk (presumably we are dealing with low risk here), and later on in the book a professor claims that in his region it takes four or five weeks to get an amniocentesis result and he spends 20 to 25% of his time on the telephone to patients justifying the delay! Now, if you are itching to discover what these people are or where they work, then you'll just have to read the book. At £50 it is perhaps only painfully affordable to an obstetrician; perhaps your local bookshop might be persuaded to purchase an extra copy for those who work in the laboratory. The contents of this book certainly qualify as essential, extremely pleasurable reading for everyone whose clinical work is in the field of antenatal diagnosis.

JOHN TOLMIE


A curious title for a book chosen for review in Journal of Medical Genetics? In content, only 23 pages out of the 294 of text touch on topics of clinical relevance (the haemoglobinopathies and thalassemia) and, apart from malaria in this context, there is barely a mention of any other genetic or otherwise. No justification is necessary, for the book is fascinating as well as informative, and will leave the clinician whose primary concern with DNA is diagnostic very aware of the much wider range of uses to which modern techniques can be put. The sheer physical difficulties of the colonisation of the Pacific islands, of surviving and making a landfall in primitive canoes after hundreds or thousands of miles of ocean, challenge the imagination. The technical advances of genetics in recent decades, that are used in this book to trace colonisation routes, are parallel if different types of achievement.

Increasing knowledge in the last couple of centuries of the islands and their peoples stimulated enquiries in many disciplines — biology, ethnology, oceanography, oral history — and, in the opening chapter, Bellwood summarily reviews the evidence other than genetic: anthropometry, dentition, fossil remains, linguistics, archaeology. Here the only criticism is one of regret at the omission of any mention of the classic work of early investigators, for example, Te Rangi Hiroa; other than to Cook's exploratory and Wilson's missionary voyages at the end of the 18th century and the maverick Heyerdal in 1952, the earliest reference is 1962, by which time the general outlines of the colonisation of the Pacific had become clear. But this chapter is by way of an hors d'oeuvre to the main work of appraisal of genetic data. Each of the next four chapters is devoted to a particular set of polymorphisms.

Kirk, with his characteristic thoroughness, reviews the data on red cell antigens, serum protein, and enzyme systems of the blood. These groups he deals with in parallel with the widely used polymorphic systems, but also shows the utility of the very rare antigens unique to this region. For the proteins he deals comprehensively with 24 polymorphic systems, draws attention to others for which there are few or no data, and incorporates previously unpublished results.

In chapter 5 the B, C, and I and II antigen distributions in Pacific populations are reviewed in detail for the serologically defined HLA-A, B, C, and DR antigens. Restriction fragment length polymorphisms in class I genes have not yet been explored in Oceania, but those of class II, the RFLPs associated with DR and DQ, are given detailed treatment since they show an unexpected heterogeneity among Pacific populations. The linkage disequilibrium among the several loci not only show many haplotypes that are unique in Oceania but give an extra dimension to the definition of population affinities, added to the ones described by gene frequencies alone. The principal surprise is that the molecular data show greater diversity among groups than serological studies predict, but that such a small segment of the human genome provides such an accurate summary of the history of the colonisation of the Pacific.

The complement components (chapter 4) are less informative, since several are less polymorphic, with fewer available alleles or more extreme frequencies, though again there are alleles unique to the Pacific. There are few data on the major histocompatibility complex (chapter 5), but then chapter 6 on mitochondrial DNA and chapter 7 on nuclear DNA of the globin gene region clearly show the potential for DNA markers in population studies. They show once again the extreme position of the highlanders of Papua/New Guinea, characterised by low frequencies of single gene deletions, and the striking difference between highland and coastal New Guinea populations. In Melanesia the distribution of high frequencies of α deletions as well as α is typical. It shows a clear relationship to malarial endemcity, the two commonest — α deletions being either rare or absent outside Oceania. In Polynesia no haemoglobinopathies and no β thalassaemia had been reported, but the DNA analysis of the globin gene clusters shows clear evidence of ancestry from south-east Asia (high frequencies of the Ia region and the 

Book reviews


Many doctors and their colleagues shudder at the thought of genetic statistics and this introduction to the subject should both reassure and educate them. It was designed for those who come across genetic risks, either in a clinical situation or in a laboratory setting. The text is simple, clear, and accurate. Risks for a dominant disease are compared with the subjects of reduced penetrance, variable expression, and gonadal mosaicism; those for autosomal recessive diseases together with consanguinity; those for X linked diseases with discussion of different mutation rates in the two sexes and gonadal mosaicism. Empirical risks are given when theoretical risks are uncertain.

The book is clearly written and goes through with figures and lucid calculations, and once the reader has understood the basic argument, a further question is asked to test his/her understanding. Are there any couple already have two healthy children? How do the risks change if the couple are first cousins instead of second cousins? The