Fertility in a male with trisomy 21

In 1989, we reported¹ 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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Clinical consequences of deletion 1p35

We would like to make a correction to our paper¹ 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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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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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-Wiedemann 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

dental research. Three distinct themes, dental hard tissues, oral microbiology, and saliva, are covered. Four chapters relate to the molecular biology of the dental hard tissues. These include genetic control of the dentition, enamel proteins, and immunolocalisation strategies, enamel protein genes and their expression, and, lastly, dental mesenchyme and the expression of molecules therein. One chapter is devoted to the molecular genetics of oral bacteria and the microbial aetiology of dental caries and periodontal diseases. The remaining section deals with salivary composition, with separate chapters on salivary mucins, salivary proteins, and the proline rich salivary proteins. The chapters are contributed by distinguished researchers in each field. Some chapters appear somewhat subjective but this reflects the relative contribution of the author(s) to their subject of interest. The comprehensive list of references at the end of each chapter will provide a valuable source of further reading for those seeking to further their knowledge of the field. Although the editor acknowledges in the foreword that the content of the book will soon become dated because of the rapid advances in molecular biology both in general and in relation to dental research, this book is to be welcomed for bringing together in one volume current thinking regarding molecular biology as applied to the study of oral and dental structures and tissues.

M J ALDRED

Advanced Techniques in Chromosome Research. Ed Kenneth W Adolph. (Pp 462; £166.75.) New York: Marcel Dekker. 1991.

Over the last 20 years the purely descriptive field of cytogenetics, and the reductionist, analytical field of molecular biology have steadily approached each other until it is almost time for them to celebrate their wedding. Although it is not yet possible to construct a detailed model of chromosome organisation, the ways in which genes are organised in chromosomes and chromosomes in nuclei are beginning to be well understood, so that the present volume makes an appropriate appearance. However, the value of this book as a contribution to this important field is more debatable.

The title leads one to expect a series of detailed descriptions and evaluations of techniques at the leading edge of chromosome research, whereas what we find is a mixture of review articles (some quite excellent) and technical chapters, with the majority of the latter lacking sufficient detail to make them an adequate guide to implementing the techniques described. There is also a problem (presumably arising from the delay between submission of the manuscripts and publication) with material becoming outdated. Very few of the references cited by most of the authors are later than 1989, and in such a rapidly changing field, this is usually too long ago!

In a volume of such diverse character, I feel that the best way to give an idea of the value of the book is to run briefly through the chapters, with a brief description and comment on each. The book is divided into three sections, covering Molecular Techniques, Cytogenetic and Linkage Analysis, and Cellular Techniques respectively.

The first section begins with a review of 'Molecular diagnostics' (Summar and Phillips), which is detailed and well written, my

only criticism being that mentioned above, that there is no reference more recent than early 1989. This is followed by a chapter on 'Cloning and analysis of large DNA molecules' (Scherer and Tsui). This is primarily concerned with YAC technology and the analysis of YAC DNA by pulsed field gel electrophoresis (PFGE). There is thorough coverage of this important area, but, although protocols are given, they tend to lack the precise details necessary to translate them into successful laboratory procedures. The next chapter is a detailed report of a single piece of work involving the 'Molecular analysis of a single chromosome sub-band' (Yunis). While this is an excellent paradigm for the sort of work involved in molecular cytogenetics, it is not sufficiently universal for the reader to be able to apply it to similar problems in a different system. Chapter 4 describes a method for purifying DNA fragments by immobilised oligonucleotide probes as a stage in high efficiency cloning (Wada, Tsurui, and Suyama). Although the data are presented in great detail, again I feel that the protocols are not sufficiently detailed to be useful as laboratory guides without further amplification. Chapter 5 covers 'In situ hybridization of oligonucleotide probes' (Nanda, Schmid, and Epplen). This is an excellent chapter, reporting a new approach in good and adequate detail. Chapter 6, on the 'Analysis of flow-sorted chromosomes' (Shimizu and Minoshima) has useful protocols, but limited application owing to the use of a single fluorochrome and laser, with the limited resolution available with this system. Again, the most recent references are 1989. The last chapter in this section covers 'Pulsed-field gel electrophoresis', and I am grateful to John Maule for reading it and providing me with his comments. Although it provides a basic introduction to PFGE, the experimental procedures are not sufficiently detailed or accurate to allow a novice to carry them out. Some of the figures are of poor quality and the legends are, in some cases, inaccurate, while some of the information is out of date, and some of the cited references are inappropriate. Although the list of references is extensive, there is again nothing after 1989.

The second section begins with a chapter on the 'Analysis of chromosomal alterations in human solid tumors' (Meese and Trent). This is a useful review, though it omits to point out that classical analysis of complex translocations by banding is subject to error, and chromosome painting by fluorescent in situ hybridisation (FISH) often shows very different conclusions and detects translocations overlooked by classical analysis. Chapter 9 is a comprehensive review of the whole subject of 'Fragile sites on human chromosomes' by Sutherland, the doyen of the field, while chapter 10 is again a review, in this case of 'Immunocytogenetics', again by two of the leading exponents of the field, Haaf and Schmid. It is primarily a historical survey of the development of the subject, from the early 1970s up to 1989. The remaining three chapters in this section cover aspects of gene linkage studies. As D'Eustachio, the author of the first of these ('Molecular linkage genetics of the mouse') says, construction of linkage maps is not a new activity, and it is difficult to see what these chapters, however sound they may be (and I certainly have no criticism of this one), are doing in a book with the title this one bears. The second of the linkage chapters discusses 'Genome duplication and compar-

ative gene mapping' (Nadeau), an interesting and important subject. However, the data are so poorly presented, either because of careless proof reading or errors in composition, that the value is much reduced. The final chapter in this section, 'Human linkage analysis: strategies for locus ordering' (Weeks) presents an advanced mathematical and statistical approach to the topic, likely to be of value to dedicated constructors of maps.

The final section, on 'Cellular techniques', begins with the editor's own contribution, on the 'Arrangement of chromosomes in human mitotic cells'. This describes the construction of 3D images by computer graphics from electron micrographs of serial sections through mitotic cells. This seems to me an interesting piece of work, though less valuable than the work by Heslop-Harrison *et al* (1988) cited by the author, which applies a similar approach to analysing the organisation of individual chromosomes in cells. This is followed by a chapter entitled 'Production of transgenic animals' (Gordon). The first part of this chapter is a thorough review of this topic, but the remainder covers a series of subjects more akin to subfertility studies than basic science. These include micromanipulation fertilisation, pronucleus removal, and prenatal diagnosis by embryo biopsy. The next chapter is a review of 'Mutagen testing using mammalian cells' (Hsu and Elder) and is again a useful review without being in any way a technical guide. The penultimate chapter may be considered as an appendix to that by Meese and Trent in the second section, as it describes the 'Culture of solid lung tumors for cytogenetic analysis' (Siegfried *et al*). Again, while technical information is given, it is not in sufficient detail to permit a novice to perform the procedures. The last chapter discusses the use of 'Colchicine and colcemid to block microtubule assembly' (Sluder) and, again, while it is a first class research report, the methodology is not described in sufficient detail for it to make an adequate laboratory guide.

In summary, this volume may have a misleading title, as the majority of the contributors do not provide more than a review of the field covered by their titles, and few of those chapters which do provide practical details do so in sufficient detail for the book to be a useful manual. To whom, then, will it appeal, because, make no mistake, this is a good and worthwhile book? I find this a very difficult question to answer. It is not, because of the delay between writing and publication, a useful introduction to the field, yet it is the sort of book that departments of genetics and cell biology ought to have on their shelves.

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Therapy for Genetic Disease. Ed Theodore Friedmann. (Pp 127; £16.50.) Oxford: Oxford University Press. 1991. ISBN 0-19-261971-3 (pbk).

Though prenatal diagnosis has provided a valuable tool in helping families with genetic disease, most recognise that this can only ever be a partial solution. Selective abortion will never be entirely acceptable to everyone, and unless all fetuses are screened, affected children will still continue to be born with serious genetic disorders. Many have recognised this dilemma and have hoped that one day effective treatments will be found. This little book addresses this problem.