The possibility that the loss of mutant alleles is balanced by the transition of larger normal ones into the lower DM range, which are more frequently found in DM males, should also be considered.

Although our data are at variance with the recent report of Chakraborty *et al*[11] for normal subjects, it is still unknown whether the mechanisms responsible for segregation distortion are the same for DM alleles in the normal range compared to full scale expanded ones. The preferential transmission of larger alleles could be modulated by as yet unidentified *cis* and *trans* acting genetic elements, or could be a direct consequence of the CTG repeat number, affecting gamete or zygote viability. The recent observations that the expanded allele is preferentially transmitted in male meiosis in other conditions caused by dynamic expansions, such as dentatorubral-pallidoluysian atrophy and MJD,[14 15] are more suggestive of a direct consequence of the CTG repeat number in these conditions, at least for full scale expanded alleles.

In summary, results from the present study confirm that the issue of meiotic drive and segregation distortion is still controversial and may vary in different populations. Further studies will be important to shed more light on this fascinating question.

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1 Aslanidis C, Jansen G, Amemiya C, *et al.* Cloning of the essential myotonic dystrophy region and mapping of the putative defect. *Nature* 1992;**355**:548-51.
2 Brook D, McCurrach ME, Harley HG, *et al.* Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member. *Cell* 1992;**68**:799-808.
3 Buxton J, Shelbourne P, Davies J, *et al.* Detection of an unstable fragment of DNA specific to individuals with myotonic dystrophy. *Nature* 1992;**355**:547-8.
4 Fu YH, Pizzuri A, Fenwick RG Jr, *et al.* An unstable triplet repeat in a gene related to myotonic muscular dystrophy. *Science* 1992;**255**: 1256-8.
5 Harley HG, Brook JD, Rundle SA, *et al.* Expansion of an unstable DNA region and phenotypic variation in myotonic dystrophy. *Nature* 1992;**355**:545-6.
6 Mahavedan M, Tsilfidis C, Sabourin L, *et al.* Myotonic dystrophy mutation: an unstable CTG repeat in the 3' untranslated region of the gene. *Science* 1992;**255**:1253-5.
7 Harper PS. *Myotonic dystrophy*. 2nd ed. London: Saunders, 1989.
8 Imbert G, Kretz C, Johnson K, Mandel JL. Origin of the expansion mutation in myotonic dystrophy. *Nat Genet* 1993;**4**:72-6.
9 Carey N, Johnson K, Nokelainen P, *et al.* Meiotic drive at the myotonic dystrophy locus? *Nat Genet* 1994;**6**:117-18.
10 Gennarelli M, Dallpaiccola B, Baiget M, Martorell L, Novelli G. Meiotic drive at the myotonic dystrophy locus. *J Med Genet* 1994; **31**:980.
11 Chakraborty R, Stivers DN, Deka R, Yu ML, Shriver MD, Ferrell RE. Segregation distortion of the CTG repeat at the myotonic dystrophy locus. *Am J Hum Genet* 1996;**59**:109-18.
12 Passos-Bueno MR, Cerqueira A, Vainzof M, Marie SK, Zatz M. Myotonic dystrophy: genetic, clinical, and molecular analysis of patients from 41 Brazilian families. *J Med Genet* 1995;**32**:14-18.
13 Brunner HG, Bruggenwirth HT, Nillesen W, *et al.* Influence of sex of the transmitting parent as well as of parental allele size on the CTG expansion in myotonic dystrophy (DM). *Am J Hum Genet* 1993;**53**:1016-23.
14 Iughetti P, Marie SK, Otto PA, *et al.* Analysis of Machado-Joseph locus (MJD1) in Brazilian families confirms the occurrence of meiotic drive. *Am J Med Genet* (in press).
15 Ikeuchi T, Igarashi S, Takiyama Y, *et al.* Non-Mendelian transmission in dentatorubral-pallidoluysian atrophy and Machado-Joseph disease: the mutant allele is preferentially transmitted in male meiosis. *Am J Hum Genet* 1996;**58**:730-3.

BOOK REVIEWS

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Human Genetics—A Problem Based Approach. Bruce R Korf. (£19.50.) Oxford: Blackwell Science Ltd. 1996.

I have never been keen on problem based learning and I was quite sceptical when I started to read this book. The book covers most aspects of clinical genetics in 10 chapters. Each of these deals with a different aspect of genetics, such as X linked genetic transmission or mitochondrial inheritance, and is based around a clinical scenario. The chapter dealing with X linked genetic transmission, for example, goes through the features of Duchenne and Becker muscular dystrophy (DMD), dystrophin, and X chromosome inactivation by discussing a couple who attend a genetic clinic for counselling because the woman's half brother has DMD. This clinical scenario is taken in stages and the scientific basis for each aspect discussed. There is also a small section written by the mother of a child with DMD explaining what it is like to live with a child with DMD.

The book is clearly presented, very readable, and the numerous diagrams simple and explanatory. The conditions discussed in each chapter have been well chosen and the sections written by patients are excellent.

After reading the book I have warmed to this method of learning. The facts are more memorable because the clinical applications are clear and because they all relate back to the couple or person discussed. I am not sure who would benefit most from this book. It is probably too clinical for undergraduates but I would recommend it to clinical students or clinicians wanting to learn more about genetics in practice.

DOROTHY TRUMP

Molecular Mechanisms of Dementia. Editors Wilma Wasko, Rudolph E Tanzi. (Pp 312; $99.50.) New Jersey: Humana Press. 1997. ISBN 0-896-03371-6.

This book describes molecular processes associated with dementia and is directed at scientists interested in the field. The molecular slant will decrease its appeal for most geriatric psychiatrists and geriatricians.

The 18 chapters consider a wide variety of processes which may be involved in the pathology of Alzheimer's disease and other dementias, ranging from genes involved in early onset familial Alzheimer's disease and a review of possible biological roles of apo E to discussions of β-amyloid metabolism, tau, energy metabolism, apoptosis, free radicals, inflammatory mediators, zinc metabolism, and transgenic approaches. There are also chapters on vascular dementia, Pick disease, and prion diseases. The editors and the authors are well respected workers in the field.

After reading the book, I felt slightly overwhelmed by the many possible mechanisms which can account for aspects of Alzheimer's disease pathology, which are supported to various degrees by experimental data. I found the breadth of approaches stimulating and was impressed by the well balanced arguments and lack of dogma. In general, the chapters are well written and scientifically detailed. Referencing is comprehensive. Appropriate diagrams and tables are provided.

One of the possible hazards of producing a book in a field which is witnessing rapid progress is that it may become out of date. This book is impressively up to date and many of the authors have included data which were unpublished at the time of going to press. I will continue to find the book useful for a number of years because of its breadth and the chapters which concentrate on areas I am less familiar with. I recommend this book to those interested in the molecular mechanisms of dementia—I will be reading many sections again.

DAVID C RUBINSZTEIN

Genetic Selection through Reproduction Technology. State of the Art and Implications. Editors S Webb, B Durston, D Moore. Australia: Health Department of Western Australia. 1996. ISBN 0-3709-8379.

This collection of five papers comprises the proceedings of a day long seminar held in Western Australia in 1994, ostensibly for non-scientists. It describes the latest developments in reproductive technology together with the genetic techniques which are being applied to the field, with the aim of enabling the community at large to engage in the debate about the social and ethical implications. We have been grappling with the ramifications of mid-trimester prenatal diagnosis for many years; now there is the immediate possibility of preimplantation genetic testing and selection which raise additional issues. The papers are short or very short; together they occupy less than 30 pages. The first is a sound "no nonsense" explanation of exactly what scientists are trying to achieve by these techniques and what they are not attempting to do. It is a pity the author of the last paper

did not take this into account. He was the only one against the technology, which is a legitimate stance, but his opposition starts with the mistaken and oft repeated notions of "attempts to create designer babies" and "the genetic search for perfection". However, the paper is a wide ranging critique, elements of which enthusiasts should not ignore. A genetic counsellor explains the emotional wrangles and experiences that women undergo while availing themselves of our existing system of CVS, amniocentesis, and induced abortion, with the timely reminder that there are no right or wrong decisions, just alternative choices. Of the remaining two papers, one is concerned with fertilisation, male infertility, and ICSI, and the other, in three and a half pages, deals with some ethical implications of all the new developments

This little book is eminently readable and in its modest way makes a useful contribution to informing and updating those who wish to contribute to the debate on the appropriateness and destiny of this increasingly complex field.

MARY J SELLER

Targeting of Drugs 5. Strategies for Oligonucleotide and Gene Delivery in Therapy. Editors G Gregoriadis, B McCormack. ($150.00.) New York: Plenum Press. 1997. ISBN 0-306-45504-8.

This volume is a collection of selected proceedings from a NATO Advanced Studies Institute held in Greece during 1995 and it is a tribute to the adventurous nature of such meetings that each chapter still remains up to date in 1997. Indeed, it is becoming increasingly clear that the ability to deliver oligonucleotides and recombinant genes to specific tissues will be vital for such therapies to be most effective in inherited disease and cancer. This is emphasised in the opening chapter by Professor Charles Coutelle, whose comprehensive summary of gene therapy would itself be a good enough reason to purchase this book for someone just entering this field. As the editors come from a department which has developed liposome mediated drug delivery from its earliest days, several chapters naturally concentrate on the latest advances in non-viral carriers of nucleic acids. These discuss factors which influence the incorporation of DNA in anionic and pH sensitive liposomes, the efficient delivery of antisense oligonucleotides to cells by liposomes, and fascinating accounts of lessons learnt from recent clinical applications of the technology (cystic fibrosis and brain tumours). However, while there is a bias towards non-viral systems, chapters are also included on retroviruses, adenoviruses, and, at the interface of the two approaches, the development of synthetic virus-like particles. These describe attempts to target viruses carrying therapeutic cDNAs by engineering surface ligands involved in the initial stages of infection and stress that while binding of virus particles to cell surface receptors is relatively easy to manipulate, subsequent delivery of viral genomes to the cell is more problematical. A need to understand the basic science behind some of these "high tech" therapies is an underlying thread in the volume with much to stimulate the virologist, immunologist, and organic chemist. In terms of immune responses to gene delivery systems, the authors fall into two camps: those trying to evade the immune reponse in order to express a therapeutic gene in their target tissue and those exploiting the immune system by developing genetic vaccines or by encouraging specific immune destruction of tumour cells. For the chemist, the apparently infinite modifications to nucleotides now possible with oligonucleotide synthesisers is clearly opening many new possibilities for effective antisense therapy, including the ability to conjugate antibody fragments, polyamines, and other ligands for specific targeting. If this seems daunting for the geneticist, most chapters are well written and clearly presented although the rather small print may strain the eyes of some readers. For those new to gene therapy or antisense oligonucleotides, not least the interested clinician, this book provides a useful summary of these fields and an excellent source of further references. It will also be a most valuable addition to the bookshelf of researchers more familiar with the topics, both for those references you need for grant applications and for inspiration. Indeed, if the excellent science in this volume is not enough, one look at the photograph of sun drenched participants on the final page may be sufficient inspiration to attend the next Advanced Studies Institute at Cape Sounion!

MATT DUNCKLEY
GEORGE DICKSON

NOTICES

European Study Group on Molecular Diagnostics

In association with the Second European Meeting on Diagnostic PCR on 16-17 October 1997, the second meeting of the ESGMD will be held on 15 October 1997, 13.30-17.30, at the Kurhaus Hotel, The Hague, The Netherlands. For further information contact M Altwegg, fax +41(1)2528107.

National Symposium on Angelman Syndrome

The Belgian Angelman Foundation is organising a National Symposium on Angelman Syndrome, which will be held in Brussels on 29 November 1997. For further information contact Dr B Dan, 147 Avenue du Parc, 1190 Brussels, Belgium, fax +32 2 4773287.

Advanced European Bioethics Course: Ethics and Genetics

This course, offered by the International Program in Bioethics Education and Research, will take place on 20-22 November 1997 in Nijmegen, The Netherlands. For further information contact Dr B Gordijn, Catholic University Nijmegen, 232 Dept of Ethics, Philosophy and History of Medicine, PO Box 9101, 6500 HB Nijmegen, The Netherlands, tel: 0031-24-3615320, fax 0031-24-3540254, email b.gordijn@efg.kun.nl Internet site: http://www.azn.nl/fmw/news.hym

Therapeutic and Prophylactic Uses of Nucleic Acids

This symposium, presented by the University of California School of Medicine, San Francisco, will be held on 19-22 March 1998 at the Holiday Inn Golden Gateway, San Francisco, California, USA. For further information contact the Office of Continuing Medical Education, University of California, 1855 Folsom Street, MCB-630, Box 0742, San Francisco, CA 94143-0742, USA, tel (415) 476-4251, fax (415) 476-0318, email inquire@ocme.ucsf.edu