

resent a parent testing him or her "when you were too young to remember". Controlled surveys are unrealistic but we could discover the views of 8 to 20 year olds. Has anyone asked them?

A CAROLINE BERRY
Division of Medical & Molecular Genetics, Guy's
Hospital, 7th & 8th Floors Guy's Tower, St Thomas
Street, London SE1 9RT, UK

This letter was shown to Drs Michie and Marteau, who reply as follows.

Dr Berry raises several important questions concerning predictive genetic testing in children: the age at which a child's opinion about his/her own testing should be sought, whether a proxy should give an opinion in the case of a young child, and the extent to which a child should have a say in the decision about whether and when to be tested.

In the absence of data to inform these questions directly, research concerning children's informed consent in other areas can shed some light.¹ The general trend over the last decade has been one of discovering greater competencies in young children than previously attributed² and of giving more responsibility to children for decisions about, for example, their medical treatment and participation in research.^{3,4}

Views about whether parents should be allowed to make such decisions for their children vary and, again, we lack the evidence of the impact on children and family life of parents either being allowed to make this decision or of not being allowed to make this decision. Our recently reported single case study suggested that the latter can lead to anger both within the family and with health professionals.⁵ Dr Berry argues that teenagers may resent having been tested as a child. Our case study found resentment of not having been tested as a child. As Dr Berry states, we need more information about what children and teenagers think about these issues.

We are currently conducting a multicentred trial to investigate the psychological impact of predictive test results on children and their parents. Much more research is needed if we are to have an informed debate on these important issues.

SUSAN MICHIE
THERESA MARTEAU
Psychology & Genetics Research Group, UMDS,
Ground Floor, Old Medical School Building, Guy's
Campus, London SE1 9RT, UK

- 1 Michie S, Marteau TM. Predictive genetic testing in children: the need for psychological research. *Br J Health Psychol* 1996;1:3-14.
- 2 Karmilof-Smith A. *Beyond modularity: a developmental perspective on cognitive science*. London: MIT Press, 1995. Children Act. London: HMSO, 1989.
- 3 British Paediatric Association. *Guidelines for the ethical conduct of medical research involving children*. London: British Paediatric Association, 1992.
- 4 Michie S, McDonald V, Bobrow M, McKeown C, Marteau T. Parents' responses to predictive genetic testing in their children: report of a single case study. *J Med Genet* 1996;33: 313-18.

BOOK REVIEWS

If you wish to order or require further information regarding the titles reviewed here, please write to or telephone the BMJ Bookshop, PO Box 295, London WC1H 9JR. Tel 0171 383 6244. Fax 0171 383 6662. Books are supplied post free in the UK and for BFPO addresses. Overseas customers should add 15% 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 price and availability are occasionally subject to revision by the Publishers.)

Genetics of Criminal and Antisocial Behaviour. Ciba Foundation Symposium. (Pp 283; £50.00.) UK: John Wiley. 1996. ISBN 0-471-95719-4.

As possession of the Y chromosome provides the clearest evidence for a genotype with a predisposition to antisocial behaviour, a possible subtitle for this could be "Adam and evil". The proceedings, however, mainly concentrate on an evaluation of non-Y linked genetic factors. As several contributors point out, an inclination to aggression is integral to our survival mechanism and thereby provides pitfalls for its simple genetical analysis. Criminality is not a biological characteristic, it is a social construct; labelling particular constellations of behaviours as "disorders" can therefore be unhelpful. Several other important reservations are addressed in this volume. For example, many would agree with Cairns (p55) that "there is a special folly in recent attempts to identify the 'gene' for aggressive behaviours, whether by the methods of molecular genetics or by pedigree analysis". I think we all recognise that behaviours are plastic and genetically rather intractable by virtue of their distance from the primary levels of gene function. In spite of these and other considerations, there are compelling reasons for investigating the role of genetic factors in antisocial behaviour. Many current experimental approaches are covered including animal studies, evaluation of specific candidate loci, linkage mapping, and familial correlations. The proceedings conclude with highly readable chapters providing both evolutionary and anthropological insights and a consideration of behavioural genetics in context of individual responsibility.

For my money, there is too much emphasis on previously reported attempts to assign the relative contribution of genes and environment through the interpretation of adoption and twin studies. Much of the text is also devoted to the discussions, which follow each chapter and each section; these could be extensively edited without significant loss. So, for those with a pressing schedule, it would be worth concentrating on the clear introduction and concise conclusions by Rutter. The contributions by Goldman and Brunner with a major emphasis on the contributions of molecular approaches are also highly recommended.

The chapter by Maxson provides a balanced account of the practical advantages and theoretical problems to be encountered in mouse models for human aggression. A very positive approach to their role is also taken by Cairns, who discusses aggression

from a developmental perspective. One of the mainstays of animal studies has been linkage mapping, either of discrete traits or via surveys for quantitative trait loci (QTL). This approach has been notable recently through the identification of loci implicated in the aetiology of stress (Flint *et al. Science* 1995;269:1432-5). Another major contribution from animal studies is through "gene knock-out". The example discussed in this context is that of the 5-HT1Db serotonin receptor. Perhaps surprisingly, mice lacking this gene show normal gross behaviours, although males show a twofold increase in frequency of attacks on intruders. While judgement should be suspended as to the consequences of equivalent aberrations in human behaviour, two more dramatic examples of neurotransmission defects resulting in aggression in "knock-out" mice have been reported recently for the monoamine oxidase, MAOA, and neuronal nitric oxide synthase, NOS1, genes.

It is instructive to note that the most direct and controversial implication of a gene defect in human aggressive behaviour also involves the MAOA locus (see chapter by Brunner). In contrast, attempts to confirm the role of many candidate genes identified through allelic association have, in general, been unsuccessful. As noted by several contributors, marker associations have often proved to be fragile and unreplicable.

In conclusion, the symposium underscores how difficult it is to separate cultural, sociological, and emotional influences from hard science in behavioural studies. We can now hope that the rapid advances in molecular biology will increasingly enable the roles of specific candidate genes (such as MAOA) with small total impact, but with well established psychopharmacological function, to be teased out. Evidence for the roles of both genes and environment and even for their interaction has been generally accepted for more than a decade. What emerges from the symposium is a fairly resounding confirmation of these general conclusions. The next 10 years should see some of the contributing factors hung on more specific pegs. So, although already dated, these proceedings are worth studying by those involved in the field and particularly by the advanced guard of molecular biologists moving into this challenging area.

IAN CRAIG

Color Atlas of Genetics. Eberhard Parsarge. (Pp 420; DM 48.00.) Stuttgart: Thieme. 1995. ISBN 3-13-100361.

This excellent pocket sized text book encompasses, very successfully, the fundamentals of genetics, functional aspects of genetics, and information about genomic organisation. It is aimed towards students of medical sciences and biology but would also be a very useful reference book for physicians who are beginning genetic research and who wish to read a basic but comprehensive text book.

The book has been written so that each page of text has opposite a full page of explanatory diagrams. These are all in colour and have been well thought out so that they complement the text. This means the book is easy to read and the information is very accessible. Instead of being put off by pages of turgid text full of jargon the reader feels encouraged to read on or at least to look at all the pictures!

The book is divided into three sections. In 200 pages and 100 illustrations the first section covers the fundamentals of genetics including cell structure, molecular genetics, prokaryotic and eukaryotic cells, mitochondria and the mitochondrial genome, linkage analysis and inheritance, chromosomes, and gene expression. The second section addresses the more medical aspects of genetics with some excellent summaries of diseases in which the disease is described in text and a series of diagrams illustrates the clinical picture (with a photograph) and the molecular basis of the condition. For example, the pages covering neurofibromatosis 1 and 2 have a page of text describing the main features of each condition. The accompanying diagrams show a list of facts about NF1, three clinical photographs and three diagrams of the NF1 gene, the NF1 gene product, and a regional map of the NF2 region. The NF2 gene is not described, presumably because this was identified too recently to be included in the book. The third section of the book describes genomic organisation in prokaryotes and eukaryotes. There are comparative chromosome maps of human, mouse, cat, and cow, and human chromosome disease maps along with a list of diseases and map locations in alphabetical order.

This whole book has around 400 pages and will fit into a pocket. In that restricted space the whole of genetics is covered in remarkable detail and in a very readable format. It was originally written in German and there are occasional words which have not been translated, but this does not detract from the quality of this book. This is not just another book about genetics but is an excellent addition to the available texts.

DOROTHY TRUMP

Color Atlas of Congenital Malformation Syndromes. Michael Baraitser, Robin M Winter. (Pp 233; £65.00.) UK: Mosby-Wolfe. 1996. ISBN 0-7234-2073-4.

Baraitser and Winter have translated some of their extensive experience in diagnostic dysmorphology into this excellent book. It is written in an atlas type format, with over 400 malformation syndromes being described. Each entry contains a succinct description of the syndrome, including a few key references,

and concentrating on areas of clinical and genetic relevance. Although these "thumb nail" descriptions are useful, the real strength of this book lies in the 900 illustrative colour photographs which accompany them. Clinicians grappling with the problems of making a diagnosis in dysmorphic children will find these photographs invaluable. They will also be helped by the problem oriented approach of the book; syndromes are grouped into chapters based on their principal mode of presentation.

Who should buy this book? In their introductory chapter, Baraitser and Winter state that the aim of the book is to improve the ability of the reader to make "gestalt" diagnoses. The high quality of the book is such that the simplest answer to this question is, perhaps, anyone who wants to improve this skill. It will certainly be a useful addition to the bookshelves of most clinical geneticists and many paediatricians.

EVAN REID

NOTICE

Human gene mutation database

The *Human gene mutation database (HGMD)* (supported by SmithKline Beecham) is now available on the worldwide web at <http://www.cf.ac.uk/uwcm/mg/hgmd0.html>.

HGMD represents an initial attempt to collate the majority of known (published) human germline gene mutations. HGMD thus comprises single base pair substitutions and short (<20 bp) deletions in human nuclear genes causing inherited disease. Somatic gene mutations and mitochondrial genome mutations are not included. Each mutation is entered only once to avoid confusion between recurrent and identical by descent lesions.

Data acquisition has been accomplished by a combination of manual and computerised search procedures. In excess of 250 journals are scanned on a weekly/monthly basis for articles describing germline mutations. Coverage is limited to original published reports although some data are taken from "Muta-

tion Updates" and review articles. Mutations reported in abstract form are not generally included. All entries comprise the disease state as specified in the original article, the gene name, symbol (as used by the *Genome database*) and chromosomal location, and a reference to the first published report of the mutation.

HGMD currently (June 1996) contains >5400 different single base pair substitutions from >400 gene loci, each represented by the nucleotide and ensuing amino acid change plus the number of the affected codon. Single base pair substitutions outside coding regions (that is, in promoter regions, splice sites, introns, or untranslated regions), complex substitutions involving the replacement of more than one base at a specific site, and silent mutations within the coding region which do not alter the encoded amino acid are not yet included. (Hypertext links to 18 WWW based Locus Specific Mutation Databases are however provided and serve to augment coverage of these loci.) Mutations inferred from amino acid sequencing have also been excluded since, in the absence of direct DNA analysis, some ambiguity may exist as to the DNA sequence change involved.

HGMD currently also contains over 1100 different microdeletions derived from some 220 gene loci, each represented by the deleted bases ± 10 flanking bases and their location in the respective gene sequence. Deletions over 20 bp in size and complex rearrangements involving the insertion as well as deletion of bases are not included.

Originally established for the study of mutational mechanisms in human genes,¹ HGMD has now acquired a much broader utility. For the categories of mutation covered, HGMD represents the most comprehensive available reference source to the spectrum of mutations underlying human genetic disease and provides information of importance to researchers in human molecular genetics, physicians, and genetic counselors. DAVID N COOPER and MICHAEL KRAWCZAK *Institute of Medical Genetics, University of Wales College of Medicine, Heath Park, Cardiff CF4 4XN, UK.*

¹ Cooper DN, Krawczak M. *Human gene mutation*. Oxford: Bios Scientific Publishers, 1993.