Severe intrauterine growth retardation with increased mitomycin C sensitivity, or Nijmegen breakage syndrome?

We read with great interest the paper by Woods *et al*[1] entitled "Severe intrauterine growth retardation with increased mitomycin C sensitivity: a further chromosome breakage syndrome." We believe that this is an important paper. However, we do not agree that this patient has "a further chromosome breakage syndrome".

The reported infant had pre- and postnatal microcephaly and growth retardation, a distinctive facies, and developmental delay. He became pancytopenic at 16 months and died soon after. Increased spontaneous random chromosome breakage was seen in blood and fibroblast cultures. Mitomycin C induced chromosome damage was increased and comparable to that seen in Fanconi anaemia. The authors hypothesise that this entity of severe intrauterine growth retardation and increased mitomycin C sensitivity may be a distinct chromosome breakage syndrome.

We suspect that the patient of Woods *et al* most probably has the Nijmegen breakage syndrome (NBS).[2-4] The physical features, very well illustrated in the paper, as well as the chromosomal breaks, are very suggestive of this diagnosis. Unfortunately, a post-γ irradiation DNA synthesis test has not been performed on the child's cells, nor a serum α fetoprotein determination, to differentiate from ataxia telangiectasia (AT).

The hypospadias described in the patient of Woods *et al* has not been previously reported in NBS patients. However, we have followed up a boy of Yugoslavian origin affected with NBS who presented with hypospadias and thus suspect that the child reported by Woods *et al* and our patient are affected with a new clinical variant of NBS.

At the end of their paper the authors inform us that fibroblast cell line MI-C445 from their patient is available from the Murdoch Institute for additional studies. We suggest that a post-γ irradiation DNA synthesis test be performed on these cells to rule out or confirm the diagnosis of NBS.

In case this diagnosis is confirmed, the cells of their patient and ours should have complementation studies with cell lines of other patients diagnosed as NBS, to determine whether they represent a separate and new complementation group.

VAZKEN M DER KALOUSTIAN
ALISON M ELLIOTT
PATRICE EYDOUX
Divisions of Medical Genetics and Cytogenetics, Montreal Children's Hospital and McGill University, 2300 Tupper, Montreal, Quebec H3H 1P3, Canada.

1 Woods CG, Leversha M, Rogers JG. Severe intrauterine growth retardation with increased mitomycin C sensitivity: a further chromosomal breakage syndrome. *J Med Genet* 1995;32:301–5.
2 Weemaes CMR, Hustinx TWJ, Scheres JMJC, van Munster PJJ, Bakkeren JAJ, Taalman RDFM. A new chromosomal instability disorder: the Nijmegen breakage syndrome. *Acta Paediatr Scand* 1981;70:557–64.
3 Taalman RDFM, Jaspers NGJ, Scheres JMJC, de Wit J, Hustinx TWJ. Hypersensitivity to ionizing radiation, in vitro, in a new chromosomal breakage disorder, the Nijmegen breakage syndrome. *Mutat Res* 1983;112:23–32.
4 Barbi G, Scheres JMJC, Schindler D, *et al*. Chromosome instability and x-ray hypersensitivity in a microcephalic and growth-retarded child. *Am J Med Genet* 1991;40:44–50.

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.)

Prenatal Diagnosis: The Human Side. Editors L Abramsky, J Chapple. (Pp 211; £15.99.) London: Chapman and Hall. 1994.

This is the first book which devotes itself entirely to the psychosocial implications of prenatal diagnosis and screening. The multidisciplinary array of chapter authors participated in a conference at the Institute of Obstetrics and Gynaecology in London in 1992, which showed the increasing awareness among health care professionals of the emotional sequelae to antenatal testing for abnormality. The chapters, on the whole, complement one another rather than going over the same ground, and are enhanced by being approached from so many different perspectives (clinicians, genetic counsellors, midwives, ultrasonographers, research psychologists, parents). The only chapter which does not sit comfortably with the rest is the one on preimplantation diagnosis, as it mainly describes the procedure rather than focusing on acceptability and psychological aspects.

Jo Green and Lenore Abramsky's chapters clearly set out the case for improved pretest counselling, based both on research data (useful comprehensive list of references) and clinical experience, although they focus mostly on routine population screening tests rather than prenatal diagnosis for genetic indications. Christine Garrett and Lyn Charlton's excellent chapter on difficult decisions will be of particular interest to genetic counsellors (clinicians and coworkers) as they focus on those situations where the results of prenatal diagnosis are less than clear. Their discussion of decision making models is practically focused.

Although prenatal screening is provided routinely in ultrasound departments, the pressures and dilemmas this poses for radiographers has previously been given little attention, so the chapter by an ultrasonographer is an important contribution. Although the dilemmas outlined will no doubt be familiar to radiographers, it is also informative for the rest of us to appreciate the constraints placed on radiographers often because of historical protocol. The "human side" of prenatal diagnosis must include the emotional impact on staff as well as on parents, but the chapter devoted to this, "Caring for the carers", is too generic and staff concerns are in fact better dealt with in the chapter on late prenatal diagnosis (written by Lucy Turner, a midwife). It would also have been interesting to include the impact on laboratory staff.

Helen Statham, writing from her own personal point of view as a mother, as well as through her contacts with members of SAFTA, describes how each diagnosis of abnormality impacts on a family, even when the diagnosis and decision are "clear". The chapter I liked most of all was that written by Ray Hall, the father of a baby terminated after the diagnosis of spina bifida. As he states, so little is written about the father's perspective, and as genetic counsellors we so often feel at a loss as to know how to help fathers, that I avidly read his candid account and views on fathers' ways of coping.

Overall this volume is admirably comprehensive, with the omission of chapters on (1) support for couples who choose not to terminate, through the pregnancy and after, and (2) parents at high genetic risk, who may be facing a series of pregnancies and prenatal tests. The editors state in their introduction that the book is not intended to pass on a large body of information, but rather to draw attention to the extent of psychosocial sequelae stemming from prenatal screening and diagnosis. This is in fact overly modest, as I am sure that most people involved in providing prenatal diagnostic services will learn a great deal from this book as well as being stimulated to re-evaluate their practice.

LAUREN KERZIN-STORRAR

Friendly Fire: Explaining Autoimmune Disease. D Isenberg, J Morrow. (Pp 155; £17.99.) Oxford: Oxford University Press. 1995. ISBN 0-19-262220-X.

Together with single gene disorders and multifactorial diseases, such as cardiovascular disease and cancer, autoimmune diseases are currently the object of much investigative attention. As far as autoimmune disease is concerned I believe this to be because of two factors. The first is the intense contemporary intellectual ferment which is the study of immunology, while the second is the strong desire to exploit our emerging notions of self tolerance in some practical form. In the twilight years of the 20th century perhaps immunology expresses the ultimate search for self, the search for that which makes us different.

Autoimmune disease in its purest sense is the result of the immune system turning its considerable firepower on its own host tissues. In this book the authors attempt to explain the devastating impact of autoimmune disease on the unfortunate victim by invoking the concept of "Friendly Fire". The term was coined during the Gulf War to describe accidental attrition against one's own side (which operationally meant the anti-Iraqi coalition). The analogy is useful in that autoimmune diease is a relatively infrequent consequence of that most potent of defense mechanisms, the host immune system. However, the authors enjoy stretching their metaphor to the point where it becomes irritating. I fail to see how neutrophils can be seen as the equivalent of the SAS or Delta Force as claimed on p 20. The latter are not numerous and are reputed to be highly selective killers whereas neutrophil invasion of an inflamed tissue exhibits quite different characteristics. There are also problems with the Friendly

Fire metaphor itself. The victims in Kuwait and Southern and Northern Iraq were military personnel whereas autoimmune disease generally affects cells and tissues which are not part of the immune system. However, "Collateral Damage", while a more accurate description, would not have made such a racy book title.

Friendly Fire is written for the general reader and provides an engaging overview of the breadth of tissues and responses involved while giving an economical overview of the immune system itself. It is peppered with anecdotes relating to systemic lupus erythematosus (SLE) and HIV which are the major interests of the authors and are often entertaining. In this context it is a pity to see controversies within the research community dealt with as if there were unanimity. The authors present rheumatoid arthritis as a prototypical autoimmune disease although they will be aware of a strong current of opinion which refutes the evidence for this. On p 37 ankylosing spondylitis (AS) is described as "not a true autoimmune disease" yet it features in a figure on multiple cases of autoimmune diseases in a single family. To continue the military analogy, this seems to be a case of wanting their compo rations and eating them! Despite the fact that AS is strongly associated with HLA-B27 in populations and linked to the allele in affected sibs, there is no evidence for an autoimmune basis. The authors are guilty at times of overstatement, such as suggesting that the finding of abnormalities in T suppressor cell function in otherwise healthy relatives of SLE patients "is further confirmation that there are important genetic components of autoimmune conditions" (p 31). Indeed, this book includes the boldest declaration for the suppressor T cell in its purest form which I've seen in a long while.

Why should clinically orientated geneticists be interested in a book about autoimmune disease? Apart from the fact that around 5% of us will suffer from at least one autoimmune disease in our lifetime, the majority of these diseases have an inherited component. The development of almost every autoimmune condition is influenced by alleles at loci within the major histocompatibility complex or HLA system. However, we still have no clear understanding of the role of this gene system in the induction of such diseases other than a vague notion of thresholds being exceeded and balances upset. *Friendly Fire* ends with a chapter on potential therapies. These include several which have probably been mentioned for completeness rather than as serious candidates. However, the general reader will be interested to hear that there is real hope for the future as more immune system targets become identified and are experimentally manipulated. I was grateful to the authors for pointing out that it was Peter Parham who first elaborated the military metaphor. Perhaps he should be the one to arbitrate on whether macrophages represent heavy armour and whether cytokines count as chemical or biological warfare.

JERRY LANCHBURY

Secrets in the Genes. Editor Peter Turnpenny. (Pp 226; £12.95.) UK: British Agencies for Adoption & Fostering p/b. 1995.

As genetic knowledge increases and becomes more widely applied so it becomes more important for the adopted person to have information about his or her genetic parents and family history. Where this is unavailable he or she may feel particularly vulnerable when starting their own family and request "genetic testing" in general, a request difficult to discuss in a vacuum. Reasons for this anxiety will become clearer after reading this book.

It is multidisciplinary with contributions from clinicians, social workers, and a lawyer all involved in British Adoption Societies, together with clinical and laboratory geneticists and research psychologists. The only omission is perhaps an adopted person his or herself but a chapter of illustrative case studies and other case reports and quotes to some extent fill this gap.

The early sections outline medical aspects and stress the importance of obtaining adequate details of the birth parents' family history, although inevitably this may prove difficult. A number of chapters describe relevant genetic disorders with special emphasis on neurological, developmental, cardiac, and psychiatric disorders, and malignant disease. Inevitably repetition occurs as neurofibromatosis comes under several of these headings.

The middle section describes the "new genetics" and its clinical applications, including a chapter on the Human Genome Project. More detail is supplied than most readers will require but these chapters do make plain the rapidly changing backgrounds to which modern adoption practice has to adapt.

Throughout the book the exceedingly sensitive ethical issues weave and interweave. Confidentiality issues and the sometimes conflicting interests of the birth parents, the adopting parents, and, most importantly, of the child him or herself raise tensions often unresolvable.

Chapters on the genetics testing of children and on the psychological impact of genetic testing of any type illustrate how little factual information is available in these areas. There is a clear need for careful evaluation and scientific study so that guidelines for those involved in face to face encounter with both parents and children can be based on real information rather than anecdote.

Readers of this journal will know most of the genetics contained in this book but will benefit from reading it as their eyes will be opened to the impact of developments in genetics on adults adopted many years ago and on those currently concerned with the proceedings. It can be recommended as essential reading for all those professionally involved with the adoption process.

A CAROLINE BERRY

The Molecular Genetics of Cancer. Cold Spring Harbor Symposia on Quantitative Biology. Vol LIX. (Pp 739; $99.00.) New York: Cold Spring Harbor Laboratory Press. 1994.

This volume is the latest offering in a distinguished series of symposium proceedings emanating from the Cold Spring Harbor Laboratory Press. It presents a collection of well written papers/reviews from participants of the symposium of the same name held at Cold Spring Harbor Laboratory a year ago. The volume is organised around five subjects: control of cell cycle and cell growth, checkpoints and genome stability, apoptosis, genetic models, human cancer genes and their products, and genetic methods for diagnosis and cancer therapy.

Given that the papers presented in the final category were focused primarily on gene therapy, it is the penultimate category that would be of immediate relevance to medical geneticists. Two retrospectives review the genetic approaches deployed in the identification and cloning of the BRCA1 gene, which should prove a useful body of experience to geneticists contemplating a similar exercise on their favoured syndrome. Other papers discuss the characterisation of various cloned genes that were originally located by genetic approaches as well as discussing models of tumour development and progression.

The other chapters are much more heavily based on basic biological research into cell regulation. In this regard, they do not disappoint, providing handy reviews of the cutting edge in this burgeoning area of investigation and thereby offering a useful background into the processes that might be active in cancer. They may also supply a ready source of candidate genes for further investigation by medical geneticists wishing to characterise the aetiology of human cancer. A basic understanding of cell regulation is assumed in the reviews and less well prepared readers would be advised to have read the relevant chunks of the current edition of a decent undergraduate molecular biology text, say, *The molecular biology of the cell.*

In summary, the content of this volume is heavily biased toward the biology of cancer and although mostly not of direct relevance to medical geneticists, it is a useful reference text to consult when attempting to develop a fresh approach to genetic research in cancer and as such may be usefully acquired by medical libraries.

DAVID HUEN

Familial Adenomatous Polyposis and Other Polyposis Syndromes. Editors Phillips PAS, Spigelman AD, Thompson JPS. (Pp 234; £65.00.) London: Edward Arnold. 1995.

This is an extensive book about FAP and associated disorders by acknowledged experts in this field. The book inevitably has a surgical bias, but in some senses this makes it even more applicable to a clinical genetics readership. It contains strong chapters on introduction, history and registry, pathology, endoscopy, screening including CHRPE identification, and the various surgical options. The St Mark's experience with FAP is such that they of all people are probably best placed to offer surgical guidelines on the management of this condition. Inevitably there will be a slight bias in their ascertainment with more severely affected cases and families being referred. Nonetheless, their recommendations are broadly applicable, particularly to FAP itself.

There are, nonetheless, areas in which sometimes rather arbitrary guidelines are put forward for various aspects of screening in FAP and other polyposis conditions. For example, while the experience of St Mark's with screening of the upper GI tract for duodenal polyps and cancer is undeniable, they are yet to show a benefit for this form of screening, and in some senses this should be treated in the same way as screening in other cancer settings, such as that of the ovary with ovarian