LETTER TO THE EDITOR

Marfan syndrome

In the May issue of the Journal, Gray and Davies¹ present a nice short overview of the clinical features, natural history, and molecular genetic aspects of Marfan syndrome. For the clinical diagnosis of Marfan syndrome, they refer to the so-called "Berlin Nosology",² a set of criteria established in 1986 by a group of experts at the ISHG Meeting in Berlin. With these criteria Marfan syndrome is diagnosed in the absence of an unequivocally affected first degree relative if involvement of the skeleton and at least two other systems is found, with at least one of those systems showing a major manifestation. In the presence of one or more unequivocally affected first degree relatives, involvement of only two organ systems and preferably, although not necessarily, a major manifestation of the disorder is required.

In a reply in the December issue of the Journal, Galasko³ rightly points to the danger of mistakenly diagnosing Marfan syndrome in unaffected relatives of Marfan patients if the Berlin criteria are strictly applied. It was widely realised that, in particular with the advent of molecular testing, weaknesses in the Berlin Nosology existed. Therefore, recently, a revised version of the diagnostic criteria for Marfan syndrome has been put forward.⁴ These new criteria (which may be called the "Ghent Nosology", in analogy to the "Berlin Nosology") are still based on a combination of major and minor clinical manifestations in different organ systems. The major differences from the Berlin Nosology are: (1) skeletal involvement as a major criterion if at least four of eight typical skeletal manifestations are present; (2) more stringent requirements for diagnosis in relatives of an unequivocally affected subject (a major criterion in the family history and one major criterion in an organ system and involvement of a second organ system, the major criteria being dilatation/dissection of the ascending aorta, ectopia lentis, dural ectasia, and the skeleton); (3) potential contribution of molecular analysis to the diagnosis (presence of a causal FBN1 mutation or disease associated FBN1 haplotype).

In addition, initial criteria for diagnosis of the conditions partially overlapping Marfan syndrome are presented. It is hoped that these new and more stringent criteria can serve as an international standard for clinicians who are confronted with the problems of diagnosing this variable and pleiotropic syndrome.

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1 Gray JR, Davies SJ. Marfan syndrome. *J Med Genet* 1996;33:403-8.

2 Galasko G. Marfan syndrome. *J Med Genet* 1996;33:1051-4.

- 3 Beighton P, De Paepe A, Danks D, *et al.* International Nosology of Heritable Disorders of Connective Tissue, Berlin, 1986. *Am J Med Genet* 1988;27:139-40.
- 4 De Paepe A, Devereux RB, Dietz HC, Hennekam RCM, Pyeritz RE. Revised diagnostic criteria for the Marfan syndrome. *Am J Med Genet* 1996;62:417-26.

BOOK REVIEWS

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Emery and Rimoin's Principles and Practice of Medical Genetics. 3rd edition. Editors D L Rimoin, J M Connor, R E Pyeritz. Senior advisory editor A E H Emery. (£295.00, 2 volumes.) Edinburgh: Churchill Livingstone. 1996. ISBN 0-443-04851-7.

The title of this work is correct, this is a state of the art study of the principles and practice of medical genetics. However, the title underplays the breadth, quality, and usefulness of the book that the three distinguished editors, David Rimoin, John Connor, and Reed Pyeritz, have produced.

It is seven years since this work was last published and now it is in its third edition. While it is again published in two volumes the amount of new information included has led to an increase in both its size and usefulness. Despite this, the style and layout of the book is clear, making it easy to read, scan, or to find information about a particular question. The reference lists at the end of each chapter and the index printed in both volumes are comprehensive. The editors have written chapters and assembled contributions from 234 authors. The editors have clearly kept the focus of the book on clinical relevance and also enforced a clear style, kept repetition to a minimum, and avoided any major deficiencies.

The book is arranged by clinical approach, genetic methodology, and body system and not by specific diseases. There are 142 chapters arranged in three sections: Basic Principles, Clinical Applications, and Future Considerations. The Clinical Applications section is subdivided into "General Principles", from clinical genetic methodologies to ethical and legal issues, and "Approaches to Clinical Problems", containing seven particularly useful chapters, and 19 system specific sections each usually with multiple chapters covering specific topics. Some of the chapters are relatively short reflecting a tight focus, but all are written by experts in their field. There are few books with such an impressive list of contributors.

If you have long, lonely winter nights you can try and find faults in this work. You will

have to be patient, for while there are a few, for example, Cockayne syndrome does not lead to a strong cancer predisposition as stated on page 431, they are infrequent.

In many ways this book is a testament to medical genetics as it has evolved from a mathematically based science to a broadly applicable and useful part of established medical care. This clinically useful, comprehensive, clearly written, authoritative book is an essential work for any department involved in clinical practice or training in medical genetics.

C G WOODS

London Dysmorphology Database and London Neurogenetics Database with Photo Library. Windows versions. R M Winter, M Baraitser. (£395.00 for each of three components, £750.00 for any two, £1100 for all three, +VAT.) Oxford: OUP, Oxford Medical Databases. 1996.

All the medical specialities have their own touchstones, to which they turn to gain reassurance and a sense of belonging. Cardiologists have angiography and balloon technology, orthopaedic surgeons have rows of gleaming metalwork, and psychiatrists have comfortable leather chairs. In clinical genetics, one turns again and again to the excellent London Dysmorphology and Neurogenetics databases by Robin Winter and Michael Baraitser.

The databases have always described the known and less well known genetic syndromes in succinct and perceptive summaries, along with a list of the features of the syndromes, and the important references. Individual case reports, which are thought to represent distinct clinical entities, are also included. They are an unparalleled resource to turn to for a quick resumé of the many conditions that may not be in the forefront of our memory. The search facility lets us check our differential diagnoses using a cluster of dysmorphic or malformation handles, to make sure we haven't overlooked any diagnosis. The authors quite correctly make the point that the databases are not meant to substitute for the diagnostic process, simply to aid it. However, it is often useful to have the databases on a laptop at an outreach clinic. One can miraculously produce knowledge about a rare condition, with a discreet consultation with your trusty laptop!

The previous edition introduced on CD-ROM photographs of many of the conditions, to try and answer the often difficult task of translating written summaries of facial dysmorphology into a characteristic picture. The number of photographs was limited, access to photographs could be slow, and installation could be somewhat tricky (speaking from personal difficulty, solved eventually by several phone calls to Oxford University Press). Until now the databases have been supplied as a DOS based system, with no concessions to Windows point and clickers, or to the die-hard band of Macintosh users.

The latest Windows version of the databases is a great improvement, and is more than a simple DOS to Windows conversion. For the technical minded, the system ran extremely well under Windows 95 on a Pentium 133 MHz processor, with 16 MB RAM, a 1.6 GB hard disk, an 8x CD-ROM drive, and a super VGA screen. This is a considerably higher specification than the requirements suggested by the system manual. In

principle, I would suggest running the databases on the best PC system you can get.

The screens are much clearer, and it is much easier to switch between syndromes, references, and selected items. The photographs appear as a thumbnail on one side of the screen, and can be enlarged simply by clicking with the mouse, provided that the photo library CD-ROM is in the CD-ROM drive. The printing options are more straightforward and allow previewing what you want to print, rather than realising with horror than you have accidentally printed the entire details of a selection of 150 syndromes. The facility of adding your own unclassified cases to the databases, which was available in previous DOS versions, has been removed. There are good help screens, which are now more useful than a manual that is relatively unchanged from former editions. My one minor gripe is that when searching for a specific indexed feature, for example "hypertelorism", the programme tells you that "hypertelorism" is present, but not whether it is listed under "face", "cranium", or any other group of features.

However, the improvements are not just in presentation and ease of use. The number of photographs has increased greatly, and new case descriptions of malformation syndromes have been added. The relative merits of lumping or splitting closely related syndromes are as hot a topic as ever. There are more entries on chromosomal disomy, which are very useful, although not strictly the domain of a dysmorphology database. The transition of several syndromes from a cluster of clinical features to a molecular genetic abnormality is well covered, with good summaries of molecular genetic events in

craniosynostosis syndromes and many others. Recent review articles on clinical or molecular genetic advances in syndromes are all cited. The depth of the databases emphasises the continuing need for accurate classification of syndromes, even in the age of molecular genetic diagnosis.

I would wholeheartedly recommend this software package as an essential tool for every clinical genetic service. The breadth of experience and insight of the authors can be brought into every genetic clinic. The presentation is a great improvement over previous editions, and the updated abstracts, references, and photographs provide enormous help in the ever difficult problem of the diagnosis of rare syndromes.

ANDREW GREEN

Molecular Biology of Cancer. F Macdonald, C H J Ford. (£19.95, US\$ 39.95 pb.) UK: BIOS Scientific Publishers. 1996. ISBN 1-85996-225-4.

The first edition of this book was called *Oncogenes and Tumour Suppressor Genes* and the preface to this sequel points out the major advances in knowledge in this field necessitating a change in title in this version as well as many other major changes. The aims in the preface are clear and the authors have achieved their goal, aiming the text at students and practitioners of medicine without specialist knowledge of genetics and similarly at postgraduate scientists with an interest in the subject. With this stated audience in mind, the content and layout are easy to follow but sufficiently comprehensive to give a broad outline as well as some depth.

The illustrations are plentiful, simple, and useful and references are comprehensive.

The first chapter sets down some general principles and the next three consider the three broad classes of cancer related genes: the oncogenes, tumour suppressor genes, and the control and repair genes. The next seven chapters approach cancer genes in a systems orientated way. These chapters include information about sporadic carcinogenesis, molecular mechanisms, molecular and cytogenetic prognostic indices, as well as relevant descriptions of hereditary cancer predisposition syndromes which enable molecular genetic investigations to be set in context. Areas of controversy and uncertainty are covered where relevant without unhelpful diversions.

Cancer is an area in which gene therapy may potentially be useful and the current status, challenges, and future possibilities are covered in the next chapter. All the detailed methodology is collected together in the final section to facilitate the even flow of the book, and again the illustrations and explanations are pitched at just the right level.

This is a useful text for those embarking, for example, on research into the molecular biology of cancer or becoming involved in diagnostic testing either in the laboratory or the clinic. Although there is no intention of giving comprehensive information about clinical conditions and diagnoses, there is sufficient information to set in context genetic testing in cancer, which is likely to prove useful to oncologists, geneticists in training, and other clinicians interested to increase their understanding of this ever widening subject.

DIANA M ECCLES