BOOK REVIEWS


There is no doubt that if a neurologist or geneticist comes across an unusual combination of signs in a patient then he or she will look it up in Dr Baraitser’s book, or alternatively in the Neurogenetic Database that he has compiled. The Genetics of Neurological Disorders is a thoroughly comprehensive account of neurological syndromes and is an invaluable source of reference. Where else could one learn about epilepsy with yellow teeth, or epilepsy with infantile balding? The purpose of this second edition is “to update the clinical delineation of genetically determined neurological disorders” in order to help neurologists make an accurate clinical diagnosis before using DNA probes. A secondary aim is “to incorporate new information about DNA”.

Not only is Dr Baraitser’s survey of neurological publications extensive, it is also critical and accompanied by experienced advice on empirical recurrence risks, although the latter have not changed much between the two editions. Pedigrees and anecdotes are helpful, such as those given for spastic paraplegia on page 278. There are definitions of dentatorubropallidoluysian atrophy and of olivopontocerebellar atrophy on page 298 which are particularly useful to non-neurologists. The application of DNA findings to genetic counselling is well described, particularly in the section on predictive testing for Huntington’s chorea, and in carrier assessment in Duchenne muscular dystrophy. However, I was sorry not to read of the contribution made by DNA studies concerning our understanding of the origins or mechanisms of mutations, and the demonstration of gonadal mosaicism.

Any book in such a rapidly expanding subject will contain omissions, but in this edition there are some inconsistencies. For example, there is no account of dystrophin and its use in clinical diagnosis, yet the prion protein gene is mentioned. I think that the problem lies in the fact that a book of this size (508 pages of text and 207 pages of references) takes so long to revise; therefore, I recommend that a third edition should be divided into two volumes. It is an improvement to find photographs included in the text, although more would be welcome, particularly of neuroradiology, DNA blotting, or muscle pathology. It is also a relief to find pedigrees the right way up and labelled correctly. This book has a justifiably renowned international reputation as a work of reference and I can wholeheartedly commend this second edition to postgraduates working in the fields of neurology or genetics.

Sarah Bundey


POSSUM is a computer program which uses a microcomputer and videodisc to aid the diagnosis of dysmorphic syndromes and is produced by the Murdoch Institute at the Royal Children’s Hospital, Melbourne. The initial versions of POSSUM mainly consisted of the better known syndromes, but subsequent versions have sought to be comprehensive and the latest version (2.5), released in January 1990, contains 1698 syndromes (160 more than version 1.5) and 890 traits for describing syndromes (155 more terms than in version 2.0).

In a cursory glance through the syndrome lists in the accompanying manual, I could find only a few mistakes (I did notice that both cystinosis and Flannery syndrome were included twice). The manual is in the same attractive, readable, and easily accessible format as before. One new feature in version 2.5 is the inclusion of a specific field on the screen under the syndrome commentary indicating the chromosomal location of the gene, where this is known. There has been no alteration to the videodisc and version 2.5 is therefore used with the disc that was supplied with version 2.0.

POSSUM can be used in the same way as the London Dysmorphology Database in syndrome diagnosis. One or more traits can be chosen from the accompanying lists and a search made to include some or all of these traits. There is a further refinement in that each choice is weighted as either m (major trait), o (ordinary), or s (specific) and some factors can be excluded (for example, chromosomal abnormality) using the mode x. The search is much faster than the current London program.

The synopses accompanying the syndromes are brief and less thorough than in the London database and only a few selected references are included, compared to the extensive referencing which makes the London system invaluable.

The POSSUM system includes chromosomal anomalies which may occasionally prove useful. I am aware of a recent case where the diagnosis suggested by POSSUM included a chromosome anomaly which was subsequently detected on reviewing the karyotype with that specific chromosomal region in mind.

POSSUM can be used without the videodisc system but this really negates its greatest asset, which is its teaching potential. The pictures produced are of variable quality and the value of some is severely impaired by having the eyes blacked out. It is to be hoped that in future it may be possible to obtain consent from more patients or their parents for full facial photographs to be shown. There are numerous slides available for all of the common syndromes, including displaying the appearance at different ages. For Rett’s syndrome there is even a moving video of the hand wringing movements. There is also a visual demonstration of what is meant by many of the traits, useful for easy demonstration of midface hypoplasia, triangular facies, etc. One question mark relates to the accuracy of some of the diagnoses shown in the pictures and there are some cases where there would be room to quibble, but the Melbourne group are to be congratulated on having the courage to display their findings and diagnoses to public scrutiny in such a difficult and subjective field.

It is because of this teaching potential in particular that I believe that the POSSUM system does have a place in genetics departments. It is complementary to the London Dysmorphology
Database and as the numbers of recognisable syndromes increase, the educational value of POSSUM will increase further, as textbooks find it increasingly difficult to keep pace with the published data.

ALAN FRYER


These are two very different texts, with quite different objectives. The first, by Mange and Mange (M+M) is a brave attempt to make a personal statement about how human genetics (or anything else) should be taught. Although entitled Human Genetics, the book is clearly oriented towards medical topics. The second book, by Gelehrter and Collins (G+C) is a presentation of the principles of genetics as relevant to medicine. G+C do not attempt to cover all of medical genetics, but define the areas they feel should be understood, and select suitable diseases as examples.

M+M is a long book (522 pages, excluding appendices, bibliography, and index), but the layout and the illustrations are clear. Little biological background is assumed, and the first 100 pages are devoted to the phenomena of inheritance, chromosomes, gametogenesis, and development. The second part of the book is a clear exposition of clinical cytogenetics. A brief third part covers segregation and probability, recombination, and confusing areas such as penetration and ascertainment effects. The largest section of 180 pages covers 'Genes, metabolism and disease'. Topics include gene structure, function, and organisation; the basis of mutation; recombinant DNA technology; and a selection of clinical disorders. The chapter on inborn errors integrates clinical and molecular discussions of phenylketonuria, albinism, Tay-Sachs disease, familial hypercholesterolaemia, Lesch-Nyhan syndrome, and pharmacogenetics. There are chapters on blood groups, immunogenetics, and cancer.

The fifth part of M+M covers population genetics, with discussions of inbreeding, evolution, heritability, and behavioural genetics. The discussion of the Hardy-Weinberg equilibrium uses a clumsy notation, in a largely vain attempt to make it less frightening to the non-mathematical. Otherwise, this section of the book is highly successful. The final two chapters then cover, and confront, the history of genetics and its future. Ethical and historical aspects of genetics, particularly eugenics are outlined, and the point is made that eugenacists existed and thrived, not just in Nazi Germany but also in the USA and other states. Finally, the techniques used in prenatal diagnosis, genetic screening (of pregnancies and the newborn for disease, and of populations for healthy heterozygotes) and possible gene therapies are described.

This volume provides a thorough treatment of all these areas, and sets out to provide an insight into the historical basis of discoveries and the techniques used. It intends to educate in genetics, rather than merely to provide information. The authors largely succeed, and the book is commendably up to date. Faults that I found were that points are laboured, although clear, and there is duplication of information in text and diagrams. The chapters read like a seminar, and some students might fail to persevere with the book. There is also an occasionally odd choice of illustrative disorders, and the discussion of a single disease entity may be split between several different parts of the volume. While Bayesian calculations are explained well, I was disappointed that linkage analysis with lod scores is only mentioned in passing.

The text by G+C is much shorter (297 smaller pages, including references), and is less ambitious in its goals. Chapter 1 discusses the role of genetics in medicine and disease. Chapter 2 outlines DNA structure and chromosome behaviour in cell division. Chapter 3 presents Mendelian inheritance. Chapter 4 covers population aspects of genetics, but at a much simpler level than in M+M, giving little insight into evolutionary mechanisms. The threshold model of polygenic inheritance as applied to some multifactorial disorders, however, is presented more fully than in M+M. Recombinant DNA technology and gene organisation in eukaryotes is covered very clearly in chapter 5. In contrast to M+M, little space is devoted to setting experiments in their historical context, or even to citing experiments at all in support of the stated facts. Instead, results are presented rather baldly: 'this is how it is'. This approach is all too common in medical education, although this book is a very fine example of the form; the writing is clear and concise, and the text and illustrations are usefully complementary.

Chapter 6 examines the nature of gene mutations, by studying particularly the β globin mutations in thalassaemia. Chapter 7 looks at inborn errors, and discusses α1-antitrypsin deficiency, familial hypercholesterolaemia, the urea cycle, collagen abnormalities, and G6PD deficiency. These chapters are clear and authoritative. Chapter 8 provides a brief outline of clinical cytogenetics, with perhaps less discussion of clinically important aspects of abnormal karyotypes than is appropriate for future medical practitioners. Chapter 9 covers gene mapping and linkage. Somatic cell hybrid mapping is described, the lod score method of linkage analysis is outlined, and the routes to the Huntington's disease and cystic fibrosis genes are discussed clearly.

Cancer genetics is outlined in chapter 10, and clinical genetics in chapter 11. Prenatal diagnostic techniques are presented, and Bayesian conditional probability calculations and genetic screening (of the newborn and of populations) are covered. Finally, in chapter 12, the human genome mapping project and the prospects for gene therapy both receive a mention.

Both books can be recommended to medical students. Of the two, M+M would be of more value to the interested student, G+C to the one who wanted to learn just enough. The strengths of G+C are the clarity and brevity of exposition of the molecular genetics, and the clinical importance of the disorders chosen for examination. The strengths of M+M are the thorough discussion of each point, the greater incorporation of historical background and experimental detail into the text, the inclusion of social and ethical aspects, and a fuller consideration of evolutionary genetics. M+M discus linkage disequilibrium, genetic imprinting, heritability, and pulsed field gel electrophoresis; G+C discuss