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BOOK REVIEWS

Genetic Biochemical Disorders.

By PHILIP F. BENSON and ANTHONY H. FENSOM. Oxford: Oxford University Press. 1985. 692 pages. £55. ISBN 0 19 261193 3.

More than 3000 genetic phenotypes showing Mendelian inheritance have been catalogued in man. Little is known of the biochemical basis of many of these conditions, particularly those that are inherited in a dominant manner. However, in about a third of the recessively (autosomal or *X*-linked) inherited conditions the nature of the primary gene product has now been identified. Recognition of these defects at the biochemical level not only provides precise methods of diagnosis (and carrier detection) but also allows suitable methods of treatment to be implemented. However, as the authors rightly point out, many of these disorders are individually very rare and may therefore escape detection. As a consequence there may be a serious delay in establishing treatment or failure to intervene in subsequent cases in affected families. It is therefore felt that there is a need for a book summarizing aspects of these diseases.

Basically this book is well laid out and easy to follow. There are fifteen chapters each dealing with a specific group of biochemical disorders. A comprehensive list of references covering nearly 200 pages is collected at the end of the book preceding a full index. Apart from disorders of blood coagulation – the haemoglobinopathies and thalassaemias which are considered outside the scope of this volume – most of the remaining 200 or so metabolic disorders known in man are discussed. I could think of only a few omissions but perhaps α-1-antitrypsin deficiency, Tangier disease, Cerebrotendinious Xanthomatosis and Zellweger syndrome might have been mentioned. With regard to the last disorder and perhaps the previous one this is particularly unfortunate (especially when space was found for Hyperpipecolic aciduria) in view of the exciting new developments in peroxisomal disorders.

Where sufficient information is at hand, each disorder presented is subdivided into: clinical features; pathology; molecular defect; diagnosis; genetic counselling and prenatal diagnosis; and animal models. I found this a very convenient arrangement even though at times there was some repetition. After a brief introduction to patterns of inheritance and prenatal diagnosis, the first three chapters deal with the lysosomal storage diseases (mucopolysaccharidoses, oligosaccharidoses and sphingolipidoses). No doubt reflecting the authors' particular interests, these section are well illustrated with clinical photographs, although it is unfortunate that these do not feature much elsewhere in the book. The question of expression of the *X*-linked disorder, Hunter's disease, in females is open to debate but the two girls mentioned probably had the autosomal multiple sulphatase deficiency. Two other girls have however since been shown to have Hunter's disease, but in each there was an *X*-chromosome defect. Under the glycoprotein disorders I wonder whether 'urinary oligosaccharides are (really) more than 100 times normal'. Certainly the concentration may be. Another statement leading to misinterpretation is the fall in serum hexosaminidase A activity (deficient in Tay-Sachs disease) during pregnancy. This is not strictly true but the increased appearance of another (heat-stable) component may give this impression. In this sphingolipidosis section, *X*-linked ichthyosis is included perhaps for convenience, but surely this would be better placed in the chapter dealing with steroid disorders.

Disorders of amino acid metabolism are well covered, and it is of course in this section that dietary management first comes to the fore. However, as the authors point out, it is often important to establish the precise diagnosis in certain variants in order that specific therapies can be tailored to individual needs. But in discussing Garrod's classical studies on darkening urine in Alkaptonuria I would be surprised if the term diaper was used, but perhaps this was for the benefit of North Americans. At times we may forget the relative incidences of different disorders, for example in the urea cycle defects some are certainly more common than others and this could have been emphasized.

The organic acidaemias and related disorders were once felt to be very rare but with recent developments in gas chromatography and mass spectrometry it is

now thought that as a group they may be as frequent as the amino acid disorders. Prompt intervention is particularly important in this complex group of diseases. However, I found the figures dealing with branched-chain metabolism rather difficult to follow and felt the section dealing with the dicarboxylic acidurias in general poorly covered. Disorders of purine and pyrimidine metabolism were well presented, but on the glycogen storage diseases, histopathological features of biopsy samples which may provide initial diagnoses could have been presented more fully. Also, I would not agree that diagnosis of Type III glycogenosis should be confirmed by enzyme assay of fibroblasts or leucocytes. In some patients the deficiency may not be expressed in these cells; liver as well as muscle should be used. The problem of different classifications of defects affecting the phosphorylase system is highlighted, although confusions are perpetuated here with the *X*-linked phosphorylase b kinase deficiencies in man and mouse. It is the liver enzyme in man but the muscle enzyme in mouse. On the subject of animals I was intrigued to learn that the level of blood catalase activity in normal ducks is similar to that in Japanese homozygotes for acatalasaemia. Although no specific reference supports this statement it does none the less illustrate the extent to which the authors must have researched this volume. I would not however accept that the hair changes in Menkes' patients are similar to those in copper-deficient sheep and chickens (wool and feathers).

Despite a variety of minor typographical errors, including the apparent omission of Fig. 8.8 (p. 353) and purine nucleoside phosphorylase from the index, my overall impression was that this is a very useful book which probably achieves its aims. Although it is not cheap I am sure it would be referred to regularly by all engaged in the diagnosis, study and management of inherited metabolic disease, and I would recommend it as such. As a final comment and to assist in such referral I would have preferred the use of McKusick numbers throughout.

GUY T. N. BESLEY
Biochemical Genetics Unit
Department of Pathology
Royal Hospital for Sick Children
Edinburgh EH9 1LF

Gene Manipulation in Fungi. Edited by J. W. BENNETT and LINDA L. LASURE. Orlando: Academic Press. 558 pages. Cloth £65, Paper £35. ISBN 0 12 088640 5.

This book is the outcome of a meeting held in South Bend, Indiana. In one way its subject matter is more wide ranging than its title would suggest – 'gene manipulation' here is a very broad church including conventional genetic analysis, biochemical genetics and computer simulations as well as developments in cloning, transformation and sequencing that have become synonymous with manipulation in its narrow sense. On the other hand, 'fungi' in the title refers mostly to the analysis of the well-characterized ascomycetes Saccharomyces, Aspergillus and Neurospora, although there is one chapter on Mucor, another on fungal human pathogens, and sections of others are devoted to Podospora and Uromyces.

The book consists of twenty-one chapters and two appendices and is divided into four main parts. Part I, curiously entitled 'Historical Perspectives: Mutants to Models', contains only one article on historical developments. Other chapters are devoted to molecular taxonomy, mitochondrial genomes and computer simulation studies. The rapid progress made in developing *Saccharomyces cerevisiae* as a system for wide-ranging genetic analysis justifies the decision to devote Part II entirely to this species. The development of efficient transformation procedures and directed mutagenesis are two outstanding attributes which have greatly facilitated genetic analysis in yeast. Our understanding of the mating type system, the structure of yeast centromeres and the development of methods for studying heterologous gene expression are just three examples of recent progress. This section, however, is disappointing in that there is too much overlap between chapters 5 and 6. Part III – 'Molds' has 7 chapters on Aspergillus and Neurospora and is particularly interesting and useful. I was impressed by the amount of previously unpublished information contained in this section, which conveys to the reader the accurate impression that these reviews are up to date and authoritative. The efforts which are being made to obtain an efficient transformation system and the analysis of the regulation of gene expression are just two aspects of gene manipulation which are fully discussed. Part IV is concerned with applications to particular problems such as fungal pathogenicity to plants and humans, industrial fermentations, and morphogenesis and dimorphism in Mucor. This section illustrates very clearly the great potential of some of the experimental systems. For example, in the process of infecting a leaf the rust fungus *Uromyces appendiculatus* differentiates an appressorium when the germ tube reaches a stoma. This differentiation step occurs at 'stomata' of polystyrene replicas of the leaf surface. The prospect of being able to analyse experimentally how an external, tactile stimulus at the hyphal tip is transmitted to the nucleus where differential gene action ensues is an exciting one. The impact of genetic manipulation on systems like this one makes fungal morphogenesis a progressive area of research at the present time.

Taken as a whole this is a stimulating and commendable book. It is an excellent reference source, some of the chapters having extensive bibliographies. For example, the chapter on 'Fungal Mitochondrial Genomes' has 217 references, while that on 'Primary Metabolism and Industrial Fermentations' cites 353 sources. I was glad to see that this book is published in a