BOOK REVIEWS

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Tetrahydrobiopterin - Basic Biochemistry and Role in Human Disease. Seymour Kaufman. (Pp 420; £37 hardback.) Baltimore: The Johns Hopkins University Press. 1997. ISBN 0-8018-5344-3.

This is a well written and authoritative book. The author, Seymour Kaufman, and his research collaborators at the USA National Institutes of Health have contributed much to the subject; 17% of the 1300 or so references cited bear his name. I would specifically recommend it to readers of this Journal who have a particular interest in inherited metabolic disease. Its content serves to emphasise how our understanding of the biochemical, and clinical, phenotypic expression of mutant genes is highly dependent on our knowing, in precise mechanistic detail, how the gene product functions normally.

During the 1950s there began a major biochemical research effort aimed at discovering how molecular oxygen was used during enzymic hydroxylation of the ring structure of aromatic amino acids. Much of the stimulus for this activity derived from the knowledge that this reaction constituted the first step in synthesis of the "biogenic amine" neurotransmitter substances, and also that a defect in the hydroxylation of phenylalanine occurred in the recessively inherited neurological disease, phenylketonuria. This book describes in considerable detail the ensuing 40 years of scientific endeavour which has led to our contemporary knowledge of the structural and functional aspects of aromatic amino acid hydroxylation, including the unique cofactor requirement for these reactions in the form of reduced biopterin. This work, in turn, provides the scientific basis for our understanding of the inherited hyperphenylalaninaemias and, in particular, those rare variant forms owing to defects in the biosynthesis and recycling of tetrahydrobiopterin.

Approximately one quarter of the content is devoted to pathological aspects of the biochemistry described, although one might be tempted to criticise the title of the book as misleading for there is little here specifically related to biopterins. Nevertheless, the author provides a particularly comprehensive review of the many facets of the neurochemical pathology of the hyperphenylalaninaemias. This serves to remind the reader how much more work needs to be done in this area, not least because the clinical management of these conditions is, as yet, far from ideal.

Dr Kaufman then leads the reader on into exciting pastures new. Novel mechanisms in cellular metabolism are often later found to have a much wider functional role than the specific type of reaction where they first come to light. In this respect, the discovery of biopterin cofactors is no exception and of particular importance is the relatively recent recognition of their role in nitric oxide synthase activity. Among the topics of contemporary interest in biochemical physiology and pathology, few could be considered as important as that of nitric oxide and the extraordinary properties it possesses as a modulator of cellular activity in processes as diverse as vascular tonicity, central and peripheral neurotransmission, and cell mediated immunity. Undoubtedly the mechanisms which regulate the biosynthesis of such a highly reactive molecule will be of paramount importance in the control of its biological activity. This is an area of basic research very much in its infancy, and one in which the role of biopterins is yet to be fully explored.

It is perhaps in this respect that Dr Kaufman's treatise is most timely and welcome. On a firm foundation of current biochemical knowledge in a very specific area, he focuses the reader's mind on the work which remains to be done. Those who engage in this will be drawn from many different specialist fields in bioscientific research, including those which encompass the field of human genetics.

It is unfortunate, in these days of often inadequate budgets, that the price of this book will be a disincentive for its inclusion on the shelves of most departmental libraries. However, I would commend this book for consideration to those who advise on the acquisition of new material for their Institutional Libraries; in these it would be available for the wider readership it deserves.

A F HEELEY

Genome Structure and Function: From Chromosome Characterization to Gene Technology. Nato ASI Series (High Technology) volume 31. Editor Claudio Nicolini. (£99, US$170.) Dordrecht, The Netherlands: Kluwer Academic Publishers. 1997. ISBN 0792345657.

Rapidly moving fields in science spawn review style books that often struggle to be relevant much beyond their publication date. This view of the world of chromosomes and chromatin reported in the proceedings of the NATO Advanced Study Institute on Genome Structure and Function (held in June 1996), however, can still hold its own. The book achieves this by combining a series of in depth reviews interspersed with specialist chapters containing applications of chromosome and genome research, the topics covered ranging from oncology to biophysics.

The book opens with a chapter from the Editor, Claudio Nicolini, reviewing the biophysical methods used in unravelling the layers of successive folding the genome undergoes in order to be packaged into a functional chromosome. Subsequent excellent chapters then concentrate on padding out the detail of what these techniques have found with chapters discussing loop/domain models of chromosome structure (Razin), chromatin models (Belmont), and models of how the nucleosome functions in chromatin (Bradbury). From here we progress to chapters which concentrate on gene function and regulation within chromatin (Wolffe), steroid hormone regulation (Beato), and histone acetylation (Turner). This is the area of the book which suffers most from the passage of time and those wishing to be absolutely up to date would do well to follow up this very rapidly expanding area of research in more current journal based reviews. The applications of current gene technology and a hint of tomorrow's genome is discussed in chapters on the fields of cancer (Cavenee and Georgiev), sequence analysis (Cantor), and in the increasingly important field of plant biotechnology. I found Cantor's chapter on DNA sequencing beyond the genome project particularly interesting. He has some interesting thoughts on how we will identify new genes or perform diagnostics, evolutionary studies, and expression screens when the completed human sequence is available. Will we be using DNA as an additive, rather like an invisible bar code, to tag medicines or samples for which we will subsequently have the ability to screen for authenticity. Is the future really based in chips with everything?

The order of topics in the book is progressive with an overall trend of moving down the hierarchy of structure from chromosome to sequence and then to applications of this technology. They carry the reader along, but by no means preclude one from dipping into a favourite area as each chapter stands alone on its own merit. It is refreshing to have a book on chromosome and chromatin analysis, with a broader view of the field. One only has to note the increasing interest in the field owing to new molecular insights in the field of epigenetics and genome partitioning to appreciate the resurgence of this area of research. As such, the broader feel to this makes it an excellent text for more advanced students of the field who want to widen their horizons.

As to the style of the book, it has to be said that there is little cross referencing between chapters and the index is adequate rather than extensive. The references for each chapter again range from good to excellent, but are more than adequate launching points into other publications. I was initially somewhat worried when the opening chapter launched in at the very deep end with detailed experimental procedures and its emphasis on technical aspects of chromatin and chromosome analysis. However, subsequent chapters achieve a good balance between technical and review styles. The book more than lives up to its promise. Within its rather ordinary cover lie interesting tales of how today's genome is gradually becoming understood as multiple layers of interlocking functional environments. What is more, it throws in some hints about what tomorrow's human genome sequence might have in store for us. Somehow, I think that the completed sequence will just be the beginning, a start for integrative functional studies addressing whole genome function.

MARK C HIRST

Culture, Kinship and Genes. Editors Angus Clarke, Evelyn Parsons. (£45.00.) UK: Macmillan. 1997. ISBN 0-312-17499-3.

Genetic counselling "consists largely of talking", says Angus Clarke in the introduction to this volume. Through it, a person, couple, or family at risk of developing or

transmitting a hereditary condition seek information about their risk and explore its implications with a trained professional. However, this apparently simple procedure in fact involves complex cultural processes, because information about genetic risk is itself shaped by scientific discourse and is neither transmitted nor received in a cultural vacuum. Cultural assumptions, of which the participants may be unconscious or only partially aware, can significantly influence the counselling process, sometimes by assisting and sometimes by hampering it. This book, the outcome of a conference which gathered together health professionals, psychologists, social anthropologists, and sociologists, is an exploratory investigation of the role of cultural factors in genetic counselling.

Clinical investigation of biological inheritance necessarily entails knowledge of systems of categorising and defining relatives and understandings of conception and modes of inheritance. Traditionally the preserve of social anthropologists, it is a clinician, Bernadette Modell, who, in the first chapter, sets out a model of kinship patterns in different populations and discusses its implications for understandings of the causality of genetic disease, management of illness, and genetic counselling. Chapters by Aamra Darr, a medical sociologist, and Nadeem Qureshi, a general practitioner, then draw out some positive implications of marriage within the family for the genetic counselling of British Pakistanis.

In Britain, the question of cultural difference most frequently arises when clinicians are of white, middle class backgrounds and their clients are from "ethnic minorities"; the existence of cultural difference is implicitly linked to the classification of groups on the basis of either biological or cultural features or some combination of the two. Helen Macbeth's chapter usefully dismantles the idea of the ethnic (or, indeed, racial) group as a genetically discrete entity, showing that gene frequencies are clinal, and underlines the fact that biological factors are dependent variables because human reproduction occurs within a social context. Similarly, Ursula Sharma's chapter emphasises that although ethnic groups are frequently defined (by the media, race relations, service providers, and ethnic group activists, etc) in terms of an inherited or "fixed" culture, such reifications do not withstand empirical scrutiny.

Assuming that a Muslim woman will never consider termination of pregnancy, or assuming, like four of the five Asian GPs interviewed in Josephine Green and Merry France-Dawson's study of women's experience of antenatal screening in the West Midlands, that women of African descent can cope without medical intervention may have serious clinical implications. Gulshan Karbani, Susie Godsil, and Robert Mueller argue that stereotypical images of white, Asian, or black people, images which black or Asian people may themselves share, may reflect unconscious "fantasies" about "black" or "primitive" cultures and "white" or "civilised" ones which inhibit realistic thinking in the counselling process.

To focus on one particular cultural feature in the context of genetic counselling, particularly if it represents a value or practice very different from one's own, can blind us to other factors. For example, Sue Proctor and Iain Smith argue in their discussion of birth outcome among Bradford Pakistanis that the focus on consanguineous marriage as the "cause" of congenital defects may inhibit scientific understanding of the other socioeconomic factors involved in influencing birth outcome. It is vital to increase awareness of cultural difference, but too much can be made of it as well as too little. As Marilyn Strathern argues in her critique of the concept of culture, the part played by culture in relation to other socioeconomic factors cannot be assumed but must be established through empirical research.

It is not just in relation to "others", particularly "ethnic" groups, that cultural differences can affect the counselling process, but in relation to people from one's "own" culture. Drawing on ethnographic data collected in south Wales, Charlie Davison explains how "lay" understandings of inheritance may mean that clients give the results of genetic tests more meaning than clinicians intend. Martin Richards's discussion of how "lay" models of understandings of inheritance are linked to ideas about kinship and of how these understandings vary for different genetic conditions raises issues at the heart of the genetic counselling process. Even for clinical geneticists themselves, a "lay" model of inheritance may have more power than a scientific model outside the clinical situation or when the clinician is also a client.

A book such as this inevitably risks becoming a series of loosely connected essays and Angus Clarke's introduction makes no grand claims to an integrated perspective on cultural factors in genetics. Even so, the first three sections of this book could be described as explorations of the uses and abuses of culture in genetic counselling. The chapters mostly deal with British situations, but the volume includes two papers from Africa. Trefor Jenkins and Jennifer Kromberg, both professors of genetics in South Africa, give a preliminary account of changing perceptions of genetic disorder among black South Africans, and Olu Akinyanju, a professor of medicine in Lagos, tells a riveting story of introducing counselling for sickle cell disease in Nigeria.

The fourth section of the book considers some of the social and political issues raised by recent advances in genetics, issues which include fears of genetic discrimination and fears that genetic knowledge will be used to account for behaviour which has social as well as genetic causes. These chapters are important in promoting awareness of the wider context in which genetic counselling takes place and also point to the need for research into the range of public understandings of scientific knowledge. The volume will be of interest to clinicians and also to students and lecturers in both the social and medical sciences, including those who are exploring the links between the culture of science and the science of culture.

ALISON SHAW

Hereditary Kidney Diseases. Contributions to Nephrology Series volume 122. Editors A Sessa, F Conte, M Meroni, G Battini. (Pp xii+218; US$199.25.) Basel: Karger. 1997. ISBN 3-8055-6551-8.

Dr Sessa and his colleagues have organised a series of excellent meetings focusing on various aspects of nephrology during the last few years, and each paper and poster presented has been published subsequently in the beautifully produced Contributions to Nephrology series. Together they form an excellent library. The most recent volume relates to a meeting held in Autumn 1996 which included sections on polycystic kidney disease, tuberous sclerosis (TS), von Hippel-Lindau disease (VHL), Alport's syndrome, primary hyperoxaluria, cystinuria, and Anderson-Fabry disease. The speakers and authors of the papers are all acknowledged experts in their various fields, with a predominance of nephrologists, so that the clinical aspects are particularly well covered. The paper by Torres on the renal manifestations of TS is particularly useful as it emphasises the frequency and importance of clinically significant and sometimes life threatening renal complications, something which a geneticist may not fully appreciate. A practical approach to screening is included. The surgical management of renal carcinomas in patients with VHL was the subject of much debate in the meeting and this is reflected in the papers. Dr Neumann and his colleagues in Freiburg adopt a very conservative approach with nephron sparing surgery so as to postpone the need for dialysis for as long as possible. They may wait until tumours are 5 cm or even 7 cm in diameter, while other centres would operate on tumours of 3 cm diameter. It is possible that the range of VHL mutations found in the German population is associated with less aggressive renal carcinomas than those found elsewhere. I would recommend this slim volume for geneticists with an interest in hereditary kidney diseases who would appreciate well written and referenced, up to date papers on the specific conditions included.

FRANCES FLINTER