BOOK REVIEWS

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Methods in Molecular Medicine: Molecular Diagnosis of Genetic Diseases. Editor R Elles. (pp 356; $69.50 pb). Totowa, NJ: Humana Press. 1996. ISBN 0-896-03346-5.

With his contribution to the series Methods in Molecular Medicine, Rob Elles has filled a gap. The 356 page book he has edited is the first which provides a fairly complete overview on the current state of the art in clinical molecular genetics. This book promotes the possibility of making a first step towards standardisation and validation of clinical molecular genetic tests. Both uniformity and quality of the diagnostic service would increase if every laboratory took this book as a guide. A wealth of information and experience is described by Elles. The first chapter is called Overview of Molecular Genetics and is followed by chapters provided by experts in the field, with stepwise worked out protocols for a few of the most frequent genetic disorders. Each of these chapters is either disease based, like Roger Mountford's, which covers the Duchenne and Becker muscular dystrophy protocols in an excellent way, or covering a set of disorders which have a similar type of genetic defect, like the unstable trinucleotide repeats presented by Wallace. The haemogloginopathies are covered by Old, cystic fibrosis by Schwarz and Malone, 21-hydroxylase by Ramsden and Sinnott, familial adenomatous polyposis by Frayling and Rowan, and Prader-Willi/Angelman by Harvey and Crolla.

General topics vital for running a DNA diagnostic laboratory are described in the chapters written by Read on risk analysis, by Kerzin-Storrar on genetic counselling and molecular testing, and Stenhouse and Middleton-Price on quality assurance.

Special diagnostic techniques are described in specific chapters on SSCP analysis and protocols for automated genotyping and fluorescent sequencing. There are two topics addressed in this book, preimplantation diagnosis by single cell PCR and FISH and non-invasive prenatal diagnosis using fetal cells in maternal blood, which are far from routine yet, but because the techniques improve almost daily they rightfully have a place here. Two less often used techniques in the clinical molecular genetics laboratory are pulsed field electrophoresis and microtitre array diagonal gel electrophoresis. Pulsed field gel electrophoresis is a very powerful technique to detect deletion or duplication carriers in DMD and BMD unambiguously, as is again shown in the chapter by Cockburn and Seller.

The only key diagnostic method which is not discussed in this book is denaturing gradient gel electrophoresis (DGGE). DGGE has been and still is a major mutation detection technique used in many diagnostic laboratories. This technique is a very powerful one; however, it needs special primers (often with a GC clamp) and often the specific electrophoresis conditions are very critical. These are the reasons why some laboratories switched to SSCP.

During the last 10 years many diagnostic tests have been developed within research laboratories and some of these laboratories have slowly moved into the field of clinical diagnostics. Other laboratories transferred the techniques to clinical laboratories. Most tests have become routine now and are being applied by clinical molecular genetic laboratories. These new types of clinical laboratories not only deal with individual patients but mostly with families. In the first chapter Elles discusses the ins and outs of running a clinical molecular genetic laboratory as a service to medical specialists/clinical geneticists. His view is based on the UK situation where these laboratories on average serve a region of 1-4 million people and are associated with genetic counselling clinics. Tests for the most frequently occurring genetic disorders are operational in these laboratories. Samples for more rare genetic disorders are sent to specialist laboratories at a national or even at an international level. The quality of the tests performed is best ensured if the diagnostic laboratory has a regular throughput of samples, has good internal and external quality control, and is closely associated with a research laboratory. This allows the odd interesting case to be followed up more adequately and ensures that the diagnostic laboratory is constantly kept up to date with the most recent new techniques and information about the disorder. Pedigree information is often necessary and genetic archives are being built within the genetic centres. Unique disciplines and requirements have to be issued to laboratories performing molecular genetic tests.

As Elles states, the field of molecular genetic testing has not yet stabilised and new techniques for known genes and for new genes to be analysed appear almost daily. The demand for testing disease genes has urged many laboratories to go into diagnostics.

E BAKKER

Genetic Intervention on Human Subjects. Working Party of the Catholic Bishops' Joint Committee on Bioethical Issues. (Pp 80; £6.75.) 1996. ISBN 0-9520923-1-X.

This short book is the fruit of a four year process of collaboration by a Working Party comprising a paediatrician, a general practitioner, an anatomist, a lawyer, and three medical ethicists, under the auspices of The Catholic Bishops' Joint Committee on Bioethical Issues. It is the Catholic perspective on the moral problems raised by gene therapy and other genetic interventions. After a useful lay person's guide to genetics, the book examines what it is to be human, and the way in which people are fulfilled as human beings. It emphasises the Christian view that humans are both spiritual and bodily beings and that life is a gift from God and it is from this that people acquire value and need to be respected, the starting point for considering any proposed intervention. The book then looks at the purpose of medicine, and the responsibilities people have to maintain their own health and to ensure the genetic health of their children. Somatic and germline gene therapy and non-therapeutic genetic interventions are considered in the light of all this, but very briefly.

It is all to the point and very clearly written. However, it achieves this apparently by making every point either black or white, while many of us consider some of the points to be shades of grey. For instance, it states that conception by in vitro fertilisation is not appropriate to a human person. "The child conceived through a production process geared at meeting the wishes of the parents, comes into being as a product, and thus in a symbolically subordinate relation to the parents, even if the parents accept that the child is a person equal in dignity to themselves. In contrast, where the child is received by the parents as an outcome of marital self-giving, he or she embodies an interpersonal act of love, not a wish to produce what the parents want". Many would not think it so straightforward. The book emphasises the basic worth of the disabled and suggests that genetic counsellors should have training in advocacy on behalf of the disabled. In fact the authors would even argue that all genetic counsellors should be required to work for a time with the disabled and their families outside the realm of genetics. More than one third of the book (which totals only 80 pages) is taken up with appendices detailing extracts from Vatican documents on disability and clinical genetics, various notes, and an extensive bibliography. It is essentially a parochial document, but no doubt it will be useful to the Roman Catholic constituency.

MARY J SELLER

Genomic Imprinting: Causes and Consequences. Editors R Ohlsson, K Hall, M Ritzen. (Pp 374; £45.00, $80.00.) Cambridge: Cambridge University Press. 1995. ISBN 0-521-47243-1.

This book comprises 24 papers from the participants of the 1994 Nobel Symposium on Genomic Imprinting. The breadth covered by the contributions is wide and most of the distinguished contributors review their topic well, making the whole volume a fully referenced and authoritative source for those who wish to understand the key issues in genomic imprinting research as of 1994. In a subject where there still remain more questions than answers, being three years old does not make the book seriously outdated. For those not familiar with the imprinting publications, but who seriously wish to get to grips with the subject, this could provide an excellent start. This is particularly so for clinical geneticists who are less likely to have encountered the basic molecular biological research questions. Examples would be epigenetic effects, how they are maintained despite DNA replication during cell division, and how they influence gene expression and cellular determination during development. These are the topics of Alan Wolffe's chapter "Epigenetic inheritance: the chromatin connection", and "Chromobox genes and the molecular mechanisms of cellular determination" by Prim Singh and Tharappel James.