Book Reviews

Molecular Genetics for the Clinician

D.J.H. Brock, Cambridge University Press, 1993, 289 pp. £35.00. Hardback. £15.95 Paperback

Clinicians can no longer afford to be unaware of the advances made in molecular biology and the impact these are making on their subject. Indeed, this is the case for every aspect of medicine and surgery. One of the problems with molecular genetics is that for many clinicians its importance and relevance to clinical medicine has grown so fast that what one learnt at medical school is now inadequate for an understanding of the subject today. Therefore a clearer understanding and appreciation of the subject must be obtained at a later date. Unfortunately, by this stage one's knowledge of biochemistry, cell biology and genetics is also in need of a little updating, so any book that brings these subjects together between its covers, as well as demonstrating their application to Medicine, is welcome.

Apart from the obvious potential therapeutic values of gene therapy and genetically engineered enzyme replacement, molecular biology is contributing a vast resource to clinical diagnostics. Applications vary from the elucidation of genetic disorders affecting the foetus, to the detection of *M. tuberculosis* DNA in sputum by the Polymerase Chain Reaction (PCR). However, to appreciate the value of molecular biology in these applications it is important to understand the techniques fully and also be aware of their limitations. Before incorporating molecular genetic techniques into professional practice, clinicians will want to feel informed about basic molecular biology, and comfortable with its language and 'jargon'. So where does the clinician look? He or she could certainly do worse than start with Professor Brock's user-friendly introduction, which also includes much basic molecular biology. There is no shortage of books on the matter. Most are large and aim to be comprehensive, though this is often difficult to achieve with the science advancing so rapidly. Many are pure molecular biology or cell biology textbooks, while others cover mainly medical genetics. Many books, however with some exceptions, suffer from size and so will probably not leave the bookshelf. Professor Brock's book is conveniently small in size and only 289 pages long, a blessing for its target readership of busy people and medical students (who always like a short book). This book however is not short on information and comprehensively covers the field, from classical Mendelian genetics to gene therapy. It is as up to date as can be expected with the most recent references being from 1992. Areas of impending interest are also highlighted, an example being the increasing recognition that repeat sequences are not just 'junk DNA', but have the ability to cause inherited diseases. This is illustrated by a discussion of the Fragile-X-Syndrome. No doubt in the second edition Huntington's Disease will provide an equally good example for the trinucleotide repeat problem. Gene tracking is clearly described with relevant examples and Lod score (second nature to geneticists, merely an abbreviation to non geneticists) are lucidly explained. Professor Brock does not shy away from describing methodology which includes useful descriptions of the omnipresent PCR reaction, DNA sequencing, Pulse Field Gel Electrophoresis, and a very inviting diagram of Subtractive Hybridization (not quite as easy as it looks). Cytogenetics, mapping techniques, including Fluorescent *in situ* Hybridization (FISH), and imprinting are well covered. Thankfully a description of numerous chromosomal abnormalities with their resultant clinical phenotypes is avoided. There are also up to date accounts of cancer genetics and the genetics of multifactorial disorders. The last chapter is dedicated to current and future developments which involves a brief introduction to the controversial and

vastly expensive Human Genome Mapping Project, and the use or possible abuse of gene therapy. There is also a section discussing the avoidance of genetic disease including a consideration of the ethical issues raised by the investigation of genetic disease at both pre- and post-conception stages.

The book is well indexed and interesting suggestions are made for further reading. It would have been nice to have seen a few more colour plates, but with the radiographic nature of many molecular biology techniques, the subject lends itself well to black and white illustrations which are liberally used. The only serious criticism that I have is that I found the front cover rather uninspiring. This is unfortunate because beyond the cover, the content is enjoyable to read and will help clinicians to come to grips with the molecular genetic advances occurring in their speciality.

A.P. Cahn

Ovarian Cancer

S.C. Rubin & G.P. Sutton, New York: Marcel Dekker, 1993, 498 pp. £67.00

Yet another book about ovarian cancer, but does it represent a useful contribution? Yes, I believe it does, and one which will be of value both to oncologists in training and to specialists in this field. The editors have produced a well-structured work covering the basic science, histopathology and clinical management of ovarian cancer. There is a clear editorial policy to take the reader back to square one in each area. The basic science section includes excellent reviews on cancer genetics, oncogenes and mechanisms of chemotherapy resistance in the treatment of ovarian cancer. These are easy to read and a handy source of references.

Histopathology occupies a significant portion of the book, which is justified by the complexity of the subject. Further details are covered in the clinical chapters on germ cell tumours, stromal tumours and in an excellent review of tumours of low malignant potential, otherwise known as 'borderline tumours'.

There is some needless repetition, such as the presence of two chapters on cancer genetics and two covering intra-peritoneal chemotherapy, which, given recent waning of enthusiasm for this approach, seems excessive. There are also, perhaps inevitably, some gaps. Controversial issues, such as the importance of dose intensity in this disease, are discussed, including the potential for dose escalation using haemopoietic growth factors. However, there is no mention of peripheral blood stem cells as an alternative to bone marrow transplantation, and the importance of carboplatin dosing according to renal function fails to receive adequate attention. The role of the tumour marker CA-125, while mentioned frequently with regard to surgical management, is seemingly ignored in relation to chemotherapy. This is surprising, given the evidence that the rate of marker fall in response to chemotherapy yields prognostic information, in addition to the potential use of CA-125 as a surrogate marker of response and a sensitive early indicator of recurrent disease.

I liked the use of 'case histories' in the chapter on quality of life considerations, which was thought-provoking and well argued. For a disease in which much of the treatment is necessarily palliative in intent, it is certainly right that we be encouraged to think in this way. Major surgical controversies, such as the potential value of second-look laparotomy and cytoreductive surgery, are well covered, indeed each has a chapter to itself. It is acknowledged that such procedures

are of questionable benefit unless associated with a survival advantage and the dearth of randomised clinical trials is noted. The recent presentation concerning just such a study at this year's ASCO meeting suggests that secondary debulking surgery may indeed prolong survival.

Overall this is an enjoyable book that is easy to read, well laid out and does aim to provide a comprehensive look at all aspects of this disease. Although it is impossible to cover all the controversial aspects of such a subject to everyone's satisfaction, it does not attempt to be didactic and tries to be as up-to-date as possible. I would warmly recommend it to libraries and to anyone with a particular interest in ovarian cancer management.

I. Judson

Photodynamic Therapy: Basic Principles and Clinical Applications

Edited by B.W. Henderson & T.J. Dougherty, New York: Marcel Dekker, 1992, 480 pp. \$155.00

This multi-author book covers the spectrum from molecular to clinical studies in the developing subject of photodynamic therapy (PDT), also known as photochemotherapy. For a modality to which the adjective 'novel' is invariably applied, PDT has been intensively investigated over a period of years, with a considerable expansion in the 1980s. There are indications that the subject is maturing, in that national or international formal trials, as opposed to relatively small series on a disparate range of tumour sites, are under way (chapter by S.L. Marcus). Additionally, since the publication of this book, the widely-used sensitiser Photofrin has received full marketing approval in Canada, the first approval for clinical use of a photosensitiser in any country. The hope is that this recognition will release the regulatory 'log-jams' of applications worldwide.

Even its most ardent proponents recognise that Photofrin is not ideal, and the book contains a number of articles dealing with potential second-generation sensitisers, such as the phthalocyanines (chapters of J. Moan, E. Ben-Hur, B. Paquette) and the chlorins and their derivatives (A.R. Morgan). The choice of classes of novel compounds has usually been as a result of their photophysical properties, but it is of interest in this book that the properties of drugs (and the possibility of their manipulation) in relation to 'targeting' pharmacokinetic carriers such as lipoproteins (G. Jori) or antibodies (T. Hasan) are now being considered. Porphyrins and their relatives are a chemist's delight in that the possi-

bilities for structural modification are legion; these become particularly relevant when related to the properties of cells, and in particular those that may distinguish some malignant cells, at least, from their normal counterparts. A.R. Oseroff advocates the use of cationic sensitisers on the imperfectly understood grounds of, for example, possible differences in cell and mitochondrial membrane potentials. Curiously, one conclusion of the immediate preceding chapter was that 'positively-charged phthalocyanines are taken up poorly by cells, as is generally true with positively charged molecules'. The two authors may be talking about different things, but the effect is confusing. A major omission from the book in the light of recent interest is detailed discussion of the manipulation of the endogenous haem pathway by adding aminolaevulinic acid (ALA) exogenously to produce excess intracellular protoporphyrin IX, which is an efficient photosensitiser. The biologically short-lived ALA is now being applied to patients investigatively and results are awaited with keen interest.

The (bio)chemistry of PDT cannot be divorced from its physics, in that the biological/clinical effect is the outcome of the quantitative interactions of the two. Understanding of this becomes more important as the developments of fibre-optic delivery systems (W.M. Star) enable access to deep-seated sites with sometimes critical surrounding or adjacent organs. Endoscopic and fibre-optic methods measuring photosensitiser fluorescence and tissue optical characteristics *in situ* in patients offer approaches to a true 'photodynamic dosimetry' (D. Braichotte).

The responses of cells and tissues to photodynamic insult may be measured at a number of levels, and the article by C.J. Gomer indicates that PDT has begun to dip its toe in the waters of molecular biology, in a brief review of stress responses and their transcriptional regulation. It is in the response of normal tissues that further hopes are raised for PDT, in the claims of excellent healing, i.e. re-epithelialisation without scarring. This hope rests on a thin experimental database, with much of the work being done and reported here by S.G. Bown.

This book can be recommended as a good, largely up-to-date, overview of an intrinsically complex (and scientifically interesting) modality with applications considerably wider than cancer, as some chapters describe. The hundred or so pages of clinical reports provide the expectation that the next few years will reveal the actual utility of PDT both as a sole modality and in combination with current therapies (the latter a somewhat neglected area).

J.V. Moore