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Book Reviews

The Biology & Clinical Applications of Interleukin-2

Edited by R.C. Rees. Oxford, IRL Press, 1990, 181 pp., £22.50. ISBN 019 963137 9.

THE CYTOKINE interleukin-2 (IL-2) has a controversial but potentially exciting therapeutic potential. In recent years advances in the biology of this cytokine and its receptor proteins, and the availability of large quantities of recombinant cytokine, has facilitated both experimental and clinical studies particularly relating to malignant disease. A timely meeting at the University of Sheffield discussed the biology of clinical application of IL-2 and the salient features of this meeting are described in this concise and useful book edited by R.C. Rees of the University of Sheffield Medical School. Chapters submitted by presenters at this meeting cover the structure of IL-2 and its receptor complex. The generation of lymphokine activated killer (LAK) activity and regulation of T cells is then discussed along with an interesting theoretical chapter on the range of IL-2 action, the constraints that the architecture of the immune system put upon this range, and the implications for therapeutic administration of exogenous cytokine. Target cell recognition by natural killer cells and cytotoxic T lymphocyte (CTL) is extensively covered by Kärre. Discussion of the clinical application is confined to malignant disease, starting with preclinical data in animal models of renal cell carcinoma from Wiltrout, and studies in B16 melanoma and mouse sarcoma from Herberman. The clinical chapters include detailed description of the production of effector cells, including LAK, adherent LAK, tumour infiltrating lymphocytes (TIL), CTL, and helper T cells from cancer patients' peripheral blood, lymph node and tumour. Then results from a series of clinical trials of IL-2 alone, or in combination with other agents, particularly cytokines, are described. In all, over 5000 cancer patients have been treated with IL-2 over the past 6 years, and the chapters in this book provide a useful guide to many of the important trials. There are chapters from the groups of Rosenberg and West, two of the major contributors to the development of this therapeutic approach.

Although this field is rapidly moving, the contents of this book appear to be relevant to those interested in the clinical use of IL-2 in 1992. Some discussion of other therapeutic applications of this cytokine, for instance, as adjuvant to vaccination and in immune deficiency, would have widened the scope of this book. However, I think this book provides a useful guide to this interesting area of experimental cancer therapy, particularly for those clinicians and scientists who are not familiar with the field.

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Manual of Quantitative Pathology in Cancer Diagnosis and Prognosis

Edited by J. P. A. Baak. Springer, Heidelberg, 1991. 616 pp., DM 350.00. ISBN 3540512 756.

THIS USEFUL volume brings together a large amount of up-to-date information on the use of quantitative methods in histopathology. There are some 41 contributors to the work with the major input from the editor, Jan Baak.

Histopathological diagnosis can reasonably be described as both an art and a science and it is not surprising that even experts may differ over the classification of individual tumours. Histological grading of tumours causes even greater dissent among histopathologists and, naturally, they have increasingly been tempted to use quantitative methodology rather than subjective impressions to resolve their differences. Quantitation in microscopy contains many pitfalls for the unwary and this manual provides at least some guidance through the various minefields.

In the majority of the chapters the authors have resisted the temptation to "hard sell" the various methodologies described. I particularly liked chapter 3 on "Diagnosis—Error Sources" which draws our attention to the ways in which we can provide the clinicians with information which may lead them to give the patient inappropriate treatment. Chapter 5 takes the reader into the area of prognostic factors and proposes that quantitation has an important role in this respect.

The second section of the book consists of a series of authoritative accounts of the techniques and equipment which are now available for quantitation including, in many cases, how one should set out to assess the equipment before you buy it and the potential sources of error in the various types of equipment. Techniques dealt with include basic morphometry, image cytometry, digital image processing, laser microscopy, flow cytometers and 3-dimensional reconstruction.

The third part of the book deals with the application of the various techniques and it is interesting here to compare the conclusions at the end of image cytometric DNA analysis (chapter 15), which are very positive, with flow cytometry (chapter 17) where the final remarks are that a lot more study is required before firm conclusions can be drawn. The problem, of course, is that image cytometric DNA analysis is very much slower than flow cytometry. Chapter 18 consists of a detailed analysis of the use of both image and flow cytometry in various tissues and tumours. As with all the earlier parts of the book this chapter is very well referenced and there is an abundance of basic data here which can be used as a base for further research studies. However, the problem here is that much of the data seems to have been included because it exists and not because it is particularly important or significant. Thus, in the differentiation of glial tumours from secondary carcinoma in the brain, an epithelial marker of the cytokeratin variety is likely to be more useful than a quantitation method, yet this is not mentioned.

I am rather sceptical about the practical use of artificial intelligence systems for assistance with histopathological diagnosis in view of the time required to prepare them and consequent costs, but the case is well set out in chapter 19. There is no doubt that setting up an expert system would be a superb educative experience. Perhaps histopathologists should have

gone down the road of analysing the degree of certainty and uncertainty of their diagnostic opinions. Chapter 20 on "Reasoning with Uncertainties" looked initially very interesting but I became completely lost in the jargon and equations.

The final chapters on neurocomputing, translation and voice recognition are irrelevant to the declared aims of this book and should have been omitted. The numerous addenda are impressive and potentially very useful, dealing with glossaries, equipment suppliers, journals, societies and manufacturers.

Overall a very useful book for anyone contemplating embarking on the use of quantitative techniques in tumour pathology, provided that one remains aware that there may be other simpler methods of solving particular problems.

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Incidental Carcinoma of the Prostate

Edited by J.E. Altwein, P. Faul and W. Schneider. Heidelberg, Springer, 1991. 272 pp., DM 118.00. ISBN 0 387 53225 0.

NON-UROLOGISTS may find it strange that this title should attract sufficient interest to fill a book. Why all the fuss about this stage of this particular cancer? The answer has been sharpened in the past year or two by an increasing clamour for screening of men to detect early and asymptomatic-cancer of the prostate. There is nothing wrong with this yearning for early diagnosis but what is wrong is the implication that having found an early focus of cancer then there is a treatment which will therefore improve survival statistics. This is the central question that has yet to be answered. Moreover we do not have very good tests for early cancer and that three which are under close study—digital rectal examination (DRE), prostate specific antigen (PSA) and transrectal ultrasound (TRUS)—are not as specific as some would imply. Undoubtedly PSA and TRUS techniques have improved but they are still not all that good for mass screening.

As for the management of focal or early disease, this is fraught with debate with a choice between watch and see, irradiate or radical surgery. All have their firm supporters.

Surely there is some evidence to help guide us through these questions. This book examines the present position on these vexing questions. The chapter on prophylactic ultrasound screening is typical of the muddled thinking on this subject: the authors say that it is obvious that early diagnosis of prostate cancer by population screening is warranted; the next sentence admits that TRUS is no good because of its low predictive value. They then suggest that DRE, PSA and TRUS can give the answer. Pilot studies have already been done using these three measurements and while undoubtedly the three combined do produce a better detection rate, there is no suggestion that this can be translated into a population screening study.

The chapter by Guinan from Chicago concludes that screening for stage T1 carcinoma of the prostate with TRUS is appealing but due to ethical and economic considerations it should not be carried out but confined to high-risk groups provided that prognostic tests are developed to identify the biologically active cancers.

Thus we start to get a picture of an important subject, hitherto much neglected (especially by grant-giving bodies) that is now pushing into the public eye. Prostate cancer may not be so eye catching as breast cancer but fully deserving of further study. Sooner or later the weight of male public opinion will want better answers about incidental prostate cancer. For now, urologists should be careful with their statements and not hold out hopes that quite clearly cannot be met. Urologists know that this is a vexing question and they will welcome this book as a summary of the present position on this subject. They must be careful not to offer expectations about the benefit of screening for these early cancers before there are much better data and much better methods for studying the prostate and more reliable predictors of malignant potential.

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News

Report of the Italian Pediatric Cancer Research Group on the Neuroblastoma Research Programme

In the past few years cancer and other pathologies have been studied deeply in their molecular and genetical aspects. Today the clinician cannot give up trying to understand the biological and molecular mechanisms underlying cancer. Besides, the biologist cannot exclude the potential therapeutical aspect of his study. Thus, several therapeutic protocols include biological studies on specimens of primary tumour and metastasis. In 1989 the Italian Pediatric Hematology and Oncology Association (AIEOP) founded an Operative Task Force (Director, Prof. Guido Paolucci, University of Bologna) to which the Italian Pediatric Cancer Research Group (IPCRG) belongs. The IPCRG (including the universities of Bologna, Modena, Napoli, Roma, Padova and Torino, G. Gaslini Children's Hospital and the National Cancer Institutes of Genova and Milano) has developed research programmes on neuroblastoma, rhabdomyosarcoma and Wilms' and brain tumours. For example: in association with the clinicians involved in the Neuroblastoma Therapeutic Program, the IPCRG studied MYCN gene amplification, loss of 1p heterozygosity, multidrug resistance gene (*mdr1*) expression, and expression of the cell-cycle dependent genes. The success of the cooperative study depends on the possibility to analyse a large series of specimens in a short time. For this reason the (IPCRG) has also constituted a National Tissue Bank. To date IPCRG has analysed more than 200 neuroblastoma specimens. We report here some results of IPCRG research on neuroblastoma (references available from G.P.T.): (1) MYCN oncogene amplification was found to be an age-dependent factor. (2) In Italian cases of advanced neuroblastoma MYCN amplification has a significantly lower frequency (20.6%) compared with the USA (53.2%) and Japan (55.2%) (Table 1). (3) There is an inverse correlation between MYCN amplification and vanillylmandelic acid urinary level as also reported by Nakagawara and colleagues from Kyushu University, Japan. (4) There is an