may mediate local tumour invasion and up-regulation of receptors for peptide growth factors is found in tumours with a poor prognosis. Improvements in clinical management will undoubtedly ensue as the utility of molecular biological measurements as markers of behaviour become clear and as oncogenes, growth factors or their receptors are exploited as vehicles for treatment or imaging. In prostate cancer, steroid hormone receptors are important, although whether their effect is mediated through stromal cells via peptide growth factors or more directly remains unclear. Furthermore, as the editors of this book point out, *Urological Oncology* offers much for the clinical scientist, oncologist, radiologist or surgeon interested in tumour behaviour, imaging and treatment: they need to collaborate to achieve the best results. This point is well accepted in the management of Wilms' tumour and testis cancer and seems likely to be of increasing importance in invasive bladder cancer where multi-modality treatment may become the accepted method of management.

This book covers most adult urological tumours including cancers of the kidney, bladder, the prostate and testis. It is dedicated by the editors to the memory of Professor Julian Bloom whose interests in tumours of the brain and genito-urinary tract are well known. It is unusual for a festschrift because Professor Bloom not only contributed to the book, but apparently played a key role in its inspiration. It is also unusual since few contributors point out areas of their career or practice influenced by the dedicatee. It is not completely clear for whom this book is intended, although I feel that the urological trainee or general urologist would benefit most from the book which provides a set of short, up-to-date, albeit rather superficial reviews. The dedicated urological oncologist should be familiar with most of the original source articles. Most subjects are covered, but in many of the chapters the depth of review and the degree of healthy scepticism which was brought to bear is such as to leave the specialised reader dissatisfied. By contrast, some questions of interest to the more general reader are not covered. There is no chapter on the management of early prostate cancer, no section on recent changes in methods of urinary diversion, no section on penile cancer and nothing on the role of surgery in the management of residual abdominal masses after chemotherapy for testis cancer. To be fair, however, these latter subjects are well reviewed in other similar books.

Renal cancer is covered in most of its aspects, although some facets such as the usefulness of lymphadenectomy or renal sparing surgery are only sketchily reviewed. The chapter by Bloom and Oliver covering responses to non-surgical treatments of renal cancer is a good critical review of this area. The views of many of the authors in the section on bladder cancer have been well aired in other publications and unfortunately there are few new data here. The chapter by Lamm on comparison of BCG and intra-vesical chemotherapy brings together data which are not readily available elsewhere. He may be right in asserting that BCG has advantages over other agents, but his method of analysis of comparing the relative benefit of active agent (intra-vesical chemotherapy or BCG) against control and reaching the conclusion that BCG was better, leaves something to be desired—particularly when one randomised trial reported by Debruyne showed no benefit. The short chapter by Davies and Jones presenting their views as experimental biologists of bladder cancer was worth inclusion being unashamedly speculative and stimulating.

The section on prostate cancer included several chapters on second-line treatments. This field still offers a pessimistic prospect when treatments are reviewed objectively. The chapter on trans-spenoidal hypophysectomy included some rather alarming pictures of this procedure being performed; the suggestion that it was useful in patients with unresponsive bone pain was offered, but no data were included to demonstrate that it was any more effective than other available treatments for hormone un-responsive disease. The chapter on the aetiology of testis cancer was a useful review as was that on the use of surgery on thoracic metastases in testis cancer.

It seems to me that editors of specialised books covering developing fields such as uro-oncology have two options: either they ask authors to present in-depth, critical but balanced accounts of very carefully selected areas or they ask authors to write chapters providing a broad overview of the whole subject. On the whole, the latter policy appears to have been followed in this book which offers something of interest to the more general reader wanting short accounts of this rapidly changing area.

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*Eur J Cancer, Vol. 28A, No. 6/7, pp. 1283–1284, 1992.*
*Printed in Great Britain*
*0964–1947/92 $5.00 + 0.00*
*Pergamon Press Ltd*

## Photosensitising Compounds: Their Chemistry, Biology and Clinical use

By T.J. Dougherty. Oxford, Wiley, 1989. 241 pp. ISBN 0-471923087. £32.50.

THIS INTERESTING little book brings together the written account of papers presented at a CIBA Foundation Symposium held in London in 1989. It serves as an excellent introduction to the general topic of photodynamic therapy, the principles on which it is based, progress in the design and development of novel photosensitisers, biological studies in the laboratory and finally, accounts of some clinical trials. Photodynamic therapy is aimed at the production of highly cytotoxic chemical species by photoactivation of a suitable substrate. In cancer treatment, the technique usually involves administration of a photosensitising drug at various periods before stimulation by laser light of appropriate wavelength, transported directly into the tumour tissue by fibre optical methods.

The opening papers concentrate on the physical, chemical and photosensitising properties of these agents. Early studies, developing on compounds of the haematoporphyrin group, have led to a variety of new agents, particularly the metallocyanines. The cytotoxic effects induced by photodynamic treatments are believed to be due partly to the production of excited molecules of oxygen. Singlet oxygen ($^1O_2^*$) is formed from oxygen in the triplet ground state configuration, by energy transfer from triplet-excited sensitiser molecules. Singlet oxygen is very short-lived and highly reactive at, or near, the point of its formation. The early part of the book deals extensively, as would be expected, with the basic mechanisms of photo-excitation, triplet–triplet energy transfer, photostabilities and particularly mechanisms of tissue damage.

Critical requirements of successful photodynamic therapy include adequate means of light delivery and dosimetry. Several chapters address these points. The design of appropriate lasers, power and the wavelength of their outputs, the relation between wavelength of the laser light and tissue penetration, and techniques for measuring photodynamic dose are all covered in some depth. Ultimately, the success or failure of photodynamic therapy rests heavily on the ability to optimise drug and light dosage in the chosen treatment volume. This, in turn, must rest on sound knowledge of the pharmacokinetic behaviour of the photosensitisers. Much attention is paid by some authors to the study of drug transport and localisation, both in tissues and intra-cellularly, stability, and methods of drug delivery, particularly by carrier proteins. While inhomogeneity of distribution is an important factor, there is evidence that useful therapeutic differentials can be obtained in some situations, although there is no exclusivity of uptake in tumour cells. Tumour selectivity in treatment rests much more on the substantial degree of selectivity of light delivery that can be attained in some situations.

Several papers address the question of skin sensitivity to photodynamic treatments. Exposure of porphyrins to light of appropriate wavelength leads to the generation of a variety of complement activation products which can, in turn, induce several various types of response in experimental mice. Mechanisms of therapeutic strategies involving treatment of pathological disorders, including psoriasis with photosensitisers and light, are also discussed.

While photodynamic therapy of solid tumours is unlikely to have the widespread applicability of radiotherapy with high-energy beams of ionising radiation, evidence is accumulating that it will find a specialised place in the local treatment of some types of lesions. A survey of the use of photodynamic therapy with haematoporphyrin derivative has given encouraging results in the treatment of early stage lung cancer. Similarly, photodynamic therapy of some superficial bladder tumours that failed other primary treatments, have given encouraging results. Details of some ongoing studies of the response of brain tumours to photodynamic therapy are also reported with, as yet, few definitive results.

The future scope of photodynamic therapy generally remains admittedly uncertain, but still has promise. Increasing evidence that damage to tumour vasculature is an important feature of the effect, lends support to the view that photodynamic therapy may find an increasing role as an adjunct to other methods of attacking tumour vasculature. Further, indications that morbidity of photodynamic therapy is not exacerbated by previous exposure of the tissue to therapy with ionising radiation is another plus.

Overall, this book is a comprehensive introduction to the field of photodynamic therapy. It is informative to a degree in questions of detail without being too indigestible. The reports of the discussions are large enough to be useful, which is not always the case in publications of proceedings of conferences. The book is recommended reading to all participants in the field, as well as to educated outsiders.

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# News

## PET in Early Clinical Trials

The EORTC in collaboration with the UK Cancer Research Campaign has, over the past 10 years, developed a new initiative for the selection, preclinical toxicology and early clinical trials of new anticancer agents. The preclinical development is based on a simple subacute toxicology protocol which only uses rodents combined with pharmacokinetic studies. The system is so rapid and inexpensive that it has enabled 50 new chemicals to be assessed during the period the scheme has been in operation. There are already indications that some of these new chemicals, for example, 4-hydroxyandrostenedione, the anthrapyrazolones and temozolomide, may become established clinically.

A major problem in early clinical trials is that methods used to measure tumour response are insensitive and many potentially new classes of chemical may have been lost in the past because their small but important antitumour properties were not detected. Had they been, they would then have been studied further in the laboratory and more effective analogues would have been developed.

Position emission tomography (PET) provides the opportunity to measure the regional tissue content and kinetics of antitumour agents labelled with such radionuclides as carbon 11 and fluorine 18. With the availability of suitably labelled methionine, fluorodeoxyglucose, water and thymidine, PET scanning allows small changes in protein synthesis, glucose utilisation, perfusion and DNA synthesis induced in tumours by therapy to be monitored. It has already been shown in some investigations that PET scanning with these chemical tracers can accurately predict the sensitivity of some cancers to treatment.

At a meeting between EORTC clinical triallists and the EC Concerted Action group on PET on 14 November 1991 at the Cancer Research Campaign headquarters in London, the two groups reviewed their experience with phase I/II clinical trials and the use of PET in oncology. Various ways in which early clinical trials could be integrated with PET were discussed. Some chemicals at present on clinical trial can be labelled with positron emitters and used for tumour and normal tissue pharmacokinetic studies. Besides using PET to measure early response to treatment and changes in metabolic status induced by therapy, it may also be possible to use PET to measure the therapy resistant fraction of tumours, tumour hypoxia, the multidrug resistance status of tumours and their $O^6$-alkyltransferase content.

Further thought is to be given to formulating specific PET projects that could be carried out in parallel with current and future phase I/II trials. In addition, mechanisms for financing such initiatives need to be identified. To this end it was agreed that a workshop should be held in late 1992 to discuss further the use of PET in early clinical trials. Anybody interested in obtaining further details should contact Professor T.A. Connors, MRC Toxicology Unit, Woodmansterne Road, Carshalton, Surrey SM5 4EF, U.K.