majority of readers will be looking at individual chapters or using this as a reference text, thus repetition is inevitable to ensure comprehensiveness in the individual chapters. The chapter by Petros and Peters on dose intensity to overcome drug resistance deals with resistance more by implication than by direct reference to resistance data, and avoids dealing with the controversies. The chapters on molecular mechanisms of anti-oestrogen resistance and tamoxifen metabolism from the groups Jordon and Osborne unfortunately lack the more recent data on non-isomerisable tamoxifen derivatives, which is an important component of the current interpretation of data from this field. This illustrates a more general point: throughout there are almost no references beyond 1992. The two chapters on progestins and anti-progestins have few data on resistance to these compounds, but they provide a useful summary of data from in vitro models.

Part 3, dealing with chemotherapeutic drugs, has substantial overlap throughout some of the chapters on multi-drug resistance and the importance of MDR1. The chapter by Goldstein is in itself quite exhaustive, taking this area from the molecular through to importance in clinical trials. It goes outside of the breast cancer area dealing substantially with areas where MDR1 involvement is apparently important. Non-MDR1-associated resistance include the importance of extra chromosomal DNA, which is somewhat speculative in contrast to the chapter on fluoropyrimidine chemotherapy which deals with quite well-known data. The chapter by Harris and Carmichael gives a comprehensive discussion specifically on topoisomerase inhibitors, as well as reflecting on the relevance of multidrug resistance mechanisms to them.

Weienthal provides a valuable discussion for those interested in in vitro tests to predict breast cancer sensitivity to these agents. This particular chapter is unusual in this book in that the tables are poorly annotated and reduced in value as a result of that.

The last two chapters on approaches to reversing multi-drug resistance could have been excluded since they are highly repetitive of other chapters in this section.

The three chapters on chemohormonal interactions deal with separate issues: (i) the relationship between cell kinetics and hormonal receptors and their utility for treatment selection; (ii) hormonal synchronisation before chemotherapy, reflecting that this has proven to be uniformly without benefit; (iii) an extensive laboratory-oriented discussion of the interactions of chemo- and hormonal therapy in cell culture. It would have been valuable either within the context of this last chapter or possibly by the inclusion of an extra chapter to have given a further discussion of the interaction of these drugs in vivo, particularly since the 'overview' analysis of 1992 of adjuvant treatments in breast cancer provided compelling indirect evidence on the additive effects of these two approaches in the adjuvant setting.

Overall I found it to be highly readable and valuable, and the wide interest of such a text was emphasised to me by the large number of people that picked up the book while I was carrying it with me over a period of some weeks. Many of them requested details in order that they could purchase it. I for one, will be guarding this book in my cabinet carefully since I am sure that it is one of those which will walk very easily.

M Dowsett

Non-Reproductive Actions of Sex Steroids

Edited by GR Bock and JA Goode, John Wiley & Sons: Chichester, 1995, 307 pp. £49.95, ISBN 0 471 95513 2.

CIBA FOUNDATION SYMPOSIUM 191: NON-REPRODUCTIVE ACTIONS OF SEX STEROIDS

The reports of the Ciba Foundation Symposium always make interesting reading, dealing as they do with topics at the leading edge of science or medicine, and bringing together leading investigators in the area. This meeting, held in August 1994, is no exception. It turns the spotlight away from the reproductive aspects of the sex steroids, which have justifiably attracted extensive exploration, and focuses it on the wider role that these hormones play in a variety of other physiological processes.

In the first paper, Miguel Beato reviews our knowledge of how steroid hormones modulate the expression of a variety of genes by binding to hormone-responsive elements of DNA or interacting with various transcription factors to influence signal transduction pathways. The interactions of hormone, receptor and the several other factors involved are complex, and an important mechanism may involve the hormone itself changing the chromatin structure. Similarly, the concept of anti-hormones occupying the receptor site, thereby preventing hormone action, may be only one of several possible mechanisms, and specific binding sites for anti-hormones may also exist.

Etienne-Emile Baulieu points out that non-genomic mechanisms of hormone action are also important. Effects of membrane interaction and changes in membrane structure have been noted, and the role of binding proteins in the intracellular machinery is still unclear. There are several examples of progesterins influencing biochemical activity at the membrane and also modulating calcium entry into cells.

Bruce McEwen discusses neural effects of steroids. Apart from their well-known role in reproduction, they also affect pain perception, cognitive function and mood. Oestradiol induces choline acetyltransferase activity in the forebrain and reduces synapse density. The mechanism is unclear; only a few classical oestrogen receptors exist in pyramidal cells, although the oestrogen receptor may perhaps be atypical. Interestingly, hormone replacement therapy (HRT) has been reported to ameliorate the symptoms of Alzheimer's disease.

Michael Schumacher discusses the role of sex steroids in nerve repair. Progesterone is actively synthesised and metabolised in brain tissue, and the hormone or its metabolites may accelerate the repair of myelin sheaths after injury.

There is a lesser incidence of coronary heart disease in women than in men. It is likely that oestradiol is a major factor, the mechanism, in part, involving lipoprotein changes. Francis Bayard's paper points out that direct effects on the blood vessel wall should not be ruled out. The enzymes that synthesise and metabolise oestrogens are present on the vascular wall, and their effects on cytokines, growth factors and the cholesterol molecules are probably involved in the pathogenesis of atherosclerosis. Following this theme, Marie Foegh presents data on transplant atherosclerosis, which is a major clinical problem. Oestradiol profoundly influences the immune system and it is notable that women are more susceptible to autoimmune diseases than men are. Oestrogens enhance the differentiation and maturation of lymphocytes and diminish suppressor T-cell function. In transplant patients, HRT is an unfavourable factor. However, in an animal model, oestradiol inhibited myointimal hyperplasia and prevented entry of macrophages, which is probably the initiating factor. Thus, oestradiol has complex effects on the vascular system, still not well defined or understood.

Madge Vickers reports that coronary heart disease is the most common cause of death in post-menopausal women and that some protection is given by HRT. She describes a proposed epidemiological study of users of HRT in the UK and elsewhere in Europe, which would address many of the unanswered questions, including the effect of HRT on vascular disease. The problems with such a trial are considerable (e.g., changing fashions in dose, type of steroid, route of administration) but if the trial were postponed, no answer would ever be forthcoming.

Torbjorn Backstrom considers the effects of oestrogen on mood. Progestogens may increase depression, and progesterone and some of its metabolites can cause anaesthesia. Indeed, this observation has been used in clinical practice. Oestrogens can alter sensory perception, locomotory activity
and balance, and may also cause memory improvement in some patients.

Osteoporosis is a major problem in post-menopausal women. Stavros Manolagas explains that bone marrow cells possess classical oestrogen receptors; both androgens and oestrogens suppress interleukin 6 (IL-6) and, after oestrogen is reduced, the increase in IL-6 causes an increase in osteoclast production. Conversely, IL-6 suppression decreases bone loss.

Women suffer disproportionally from autoimmune diseases, and Howard Fox explains that androgens and oestrogens are probably the major determinants of this phenomenon. In rats, androgen was necessary to maintain low levels of autoantibodies, and treatment with androgens prevents diabetes. The sex hormones act by altering gene expression; oestrogen treatment positively regulated the gamma-interferon promoter.

Many breast tumours are hormone responsive in the sense that they are dependent on oestrogen for their growth and development. Oestrogen deprivation is still the keystone of treatment. However, sooner or later tumour cells lose their hormone dependence and escape therapeutic control. Kate Horwitz suggests that this is because the cells have altered responsiveness through changes in the regulatory mechanisms; this may be due to activation of inhibitors by oestrogen metabolites. Progesterone receptors exist in two functionally different (inhibitory and activatory) forms that interact. In discussion, it was accepted that translation of experimental data to in vivo models is difficult but all these experiments offered an insight into specific aspects of oestrogen action in breast cancer.

Several oestrogen-induced proteins occur in oestrogen receptor-positive cancers. Henri Rochefort explains that some had prognostic significance, particularly pS2 and cathepsin D, a lysosomal protease. Oestrogen also modulates transcription of various genes, and the oestrogen receptor and various transcription factors interact.

Prostate cancer is common in older men, and testosterone is closely involved in the development and growth of these tumours. Using prostate cancer cell lines in vitro, Luigi Castagnetta had examined the role of oestriadiol and showed that some cell lines are inhibited in their growth by oestradiol, whereas others are stimulated. This hormone may act synergistically with testosterone. The mechanism by which androgens act does not seem to involve an androgen receptor. Oestrogen receptors were clearly shown to be present in prostate cancer cells and so the mechanism presumably involves activation of oestrogen receptor and transforming growth factor beta, as growth can be blocked by antibodies to this growth factor.

What emerges from this meeting is that oestrogens and androgens have multiple effects on a variety of tissues, not just those classically recognised and defined as ‘target tissues’. The brain, cardiovascular system, muscle, bone, the immune system and many other tissues are apparently influenced, albeit subtly in some cases, by sex steroids. Equally striking is the emerging concept that hormones may exert their effects not only by direct interaction with receptor proteins, which then activate the appropriate biosynthetic events, but also by modulating a large variety of intra- and extracellular control mechanisms which, in turn, can control the signalling mechanisms. We are only just starting to discover the extent and complexity of this aspect of hormone action.

VHT James

Novel Approaches in Anticancer Drug Design

WJ Zeller, MD D’Incalci and DR Newell (eds.) Karger, Basle: 1995, 195 pp. $143.50

Symposia, however well organised, are usually a mix of up-to-date presentations describing novel and interesting results and, at the other end of the scale, fairly boring accounts of work already completed and out of date. This volume is an account of the proceedings of that part of a joint symposium between the German Cancer Centre and the EORTC devoted to new approaches in drug design and, as expected, is a curate’s egg mix of interesting new data and material from the ark. The first seven chapters make an interesting read and deal with the design of new drugs using computational chemistry and molecular modelling based on a knowledge of, for example, the crystal structure of receptors. The chapter by CW v d Leith and his colleagues sums up the state of the art of this approach. Twelve years ago the expectations of computer-supported drug design were enormously high but ‘the fall was deep when it was recognised that computational methods alone cannot predict reliable new lead structures’. This is true, of course, but with the introduction of combinatorial chemistry, for example, and user-friendly computer programs to study receptor–drug interactions at the atomic level one can predict that this will be an important future approach. Indeed, drugs are already in the clinic that have been uncovered by these methods and, should they prove to be superior to analogues discovered by screening or biochemical approaches, then one would expect programs dedicated to discovering agents acting on abnormal pathways in cancer such as the work described on the active site of protein kinase C or CCR methytransferase to expand rapidly. Apart from some interesting findings with suramin, the middle of the book is disappointing in that it deals with rather mundane approaches involving cisplatin and other conventional anti-cancer agents and attempts to improve their selectivity by the design of analogues, the use of combinations or attempts to overcome resistance. The Cancer Chemotherapy Annual deals with these approaches each year and this volume adds nothing that is either new or exciting.

The book perks up towards the end with some interesting presentations on the bisphosphonates, bioreductives, steroid carriers of BCNU and new agents for BNCT (boron neutron capture therapy), an old approach but one which is now being reapplied clinically on the basis of sound scientific data.

T Connors

Cancer of the Breast (4th edn)

Edited by WL Donegan and JS Spratt
WB Saunders Company: 1995, 860 pp. £115, ISBN 0-7216-4694-8

This is a comprehensive text that is clear and well written by the contributors. Many of the chapters are written by the editors and draw on their experience as well as being well referenced.

The book is well organised and begins with an entertaining historical account of breast cancer, tracing the origins of treatment to the earliest records available.

The subsequent chapters then describe the basic sciences of anatomy, physiology and pathology of breast and serve as a useful source of reference. The often confusing area of benign breast disorders and the overlap with pathology is then tackled and clarified in chapters 6 and 7, with a helpful description of abnormalities of normal breast development and involution (ANDI).

The text then describes the epidemiology and aetiology of breast cancer in a clear and concise way. Chapter 10 describes the diagnosis of breast cancer and draws on the author’s (Donegan) own experience. The section is well illustrated with line drawings demonstrating clear examination and surgical techniques. The following chapter (11) similarly gives an account of imaging, again combining experience with referenced data. The author (Moskowitz) writes authoritatively, describing the development of imaging techniques and screening. This section also describes ultrasound needle localisation techniques as well as other