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 disproportionately 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 cornerstone 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 p52 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 oestradiol 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, Basel: 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 O-D-methyltransferase 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, bioreductive, 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
less commonly used imaging techniques. The gross pathology section is again a useful reference account and is well placed in the text, preceding an excellent account of the molecular and genetic aspects of breast cancer. Chapter 14, describing the genetic basis for the emergence and progression of breast cancer, leads from an historical account to pathology and then to an easy to understand yet comprehensive review of the relevant features of molecular biology, while keeping this particularly difficult subject within a clinically relevant sphere.

The next chapters (15 and 16) on growth rates and hormone and growth factor receptors provide a good explanation of growth rates and equations used but become very lengthy with a description of the author's own laboratory protocol for oestrogen and progesterone receptor analysis. However, this does serve to emphasise the value of stringent laboratory technique and quality control if such results are to have clinical relevance.

Chapter 18 describes surgical management from an American perspective but nevertheless is useful for British surgeons. This section clearly demonstrates a transatlantic difference in practice, with American surgeons not relying on fine needle aspiration cytology but preferring to perform core cut biopsies or open incisional biopsies under local anaesthetic in the out-patient department. When mastectomy is planned, the merits of immediate and delayed reconstruction are discussed but subcutaneous mastectomy in high-risk women, e.g. with lobular carcinoma in situ (LCIS), is thought to be an inadequate procedure. Each procedure is described in detail in a step by step fashion with the author's own preferences and is well complemented by clear illustrations.

The next chapters on endocrine and chemotherapy are succinct but may emphasise data that may already have been superseded in this country with the more recent overviews of breast cancer treatment and the new aromatase inhibitors. Specifically the chapter on endocrine treatment clearly describes the principles of treatment. It also describes the different clinical groups that benefit from adjuvant tamoxifen as well as the possible benefits of chemoendocrine therapy in post-menopausal women with stage II breast cancer. In contrast to practice in the UK oophrectomy is discussed at length and the author suggests that ovarian ablation should be re-examined as an adjuvant for premenopausal oestrogen receptor-positive tumours.

The chapter on screening, co-written by Donegan, gives a very balanced overview of the background and goals of screening in general. It also describes in detail screening in the USA and other centres such as Sweden and the UK. The chapter also tackles the important issue of interval cancers. The concluding guidelines for screening—1–2 yearly mammography over 40 years of age and yearly over 50—are not in agreement with UK screening and the fact that screening 40- to 50-year-old women has not been proven to be of benefit.

The chapter on reconstructive surgery demonstrates the range of techniques available with photographs of their optimal outcomes rather than being a comprehensive account of this field.

The chapters on the specialist treatment of secondary breast cancer and pain are particularly useful for the clinician caring for patients with metastatic disease and describes the range of treatment modalities available, with the section on orthopaedic problems being particularly useful as it clearly describes both the pathology and treatment.

The rarer conditions of the breast, cancer in pregnancy, male breast cancer and sarcoma are dealt with by one of the editors (Donegan) in an elegant and authoritative way with useful advice on situations in which experience may take the place of scientific data and clinical trials.

The later chapters on the psychosocial aspects and community resources are specific to the USA but the fundamentals of patients' needs are explored—even if the machinery of delivery and facilities are different from those in the UK. Quality of life is not specifically addressed but is covered in these chapters.

The final chapter on statistics is useful in describing the rudiments of data analysis and clinical trials, which all clinicians involved in breast cancer should appreciate to help with the interpretation of the expanding data on breast cancer.

Overall this is a comprehensive text that describes not only breast cancer but also basic sciences, genetics and benign breast conditions. Although it could not really be used as a surgical atlas or pure oncology text, it nevertheless has many virtues to recommend it.

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