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Book Reviews

Epidemiology and Biology of Multiple Myeloma

Edited by G.I. Obrams and M. Potter.
Berlin, Springer, 1991. 192 pp. ISBN 3-540-54061-X. DM60.00.

MYELOMATOSIS (MM) is a lymphoproliferative disorder for which there are very few aetiological clues. Because there has been a substantial increase in the number of reported cases of MM in the past 30 years, particularly among the American black population, the National Cancer Institute of America (NCI) held a workshop in March 1990 to discuss epidemiological factors that may influence the development of MM. Furthermore, because the malignant plasma cell that characterises MM is unlikely to be the 'stem cell' of the disease, discussion also focussed on putative precursor cells and the possibility that there may be a premalignant condition. The texts that provided the basis for these discussions are contained in this volume. Topics include occupational and immunological factors, the possibility that MM may progress from a premalignant condition, such as monoclonal gammopathy of unknown significance, hypotheses regarding aetiology and pathogenesis from malignant precursors in the B-cell lineage and the role of growth factors, particularly interleukin 6.

Since the function of a workshop is to provide a forum for discussion of ongoing and future studies, written texts provide only an introduction for these discussions and are usually short and succinct. The contents of this volume are no exception, particularly as the text is printed in camera-ready format and authors appear to have been confined to brevity. Whilst the discussions at the workshop may well have been informative, stimulating and in-depth, this is not reflected in the texts. For example, in the section on epidemiology, the conclusions remain that there is no primary clue to prevention of MM, that black people may have to be considered separately and that further studies with larger sample numbers are required, whether it be to study the effect of chemicals or the contribution of allergy. Even review presentations such as MacLennon and Chan's "Origin of the bone marrow plasma cell", has not been afforded adequate page length to permit the authors to display their undoubted knowledge of the subject. This is not the fault of the contributors; however, the reader is left with the notion that very little is known about MM and that investigators should return to their laboratories and clinics. Whilst such conclusions may be expected from the participants at a workshop, they do not cater for the requirements of non-participants. The general reader is likely to find the texts limited because of the confines of the camera-ready format and would be advised to consult the numerous review articles published elsewhere, some of which are written by the contributors. Similarly, investigators into MM are likely to be familiar with the contents and would probably refer to original referred articles. The book, therefore, has limited appeal. Perhaps investigators who require financial support would find some of the many unanswered questions regarding MM of use in applications to funding organisations.

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Oral Contraceptives and Breast Cancer—Institute of Medicine, 1991

By M. Henderson, L. Dorflinger, *et al.*
Washington, National Academy Press, 1991. 200 pp. ISBN 0-309-04493-6. £21.50.

THIS BOOK gives the views of a committee set up by the USA Institute of Medicine to advise the federal government on policy options, directions for future research and the recommendations which should be given to practising physicians regarding oral contraceptive use as it relates to breast cancer.

Given that some 9% of women are likely to die of breast cancer and that the majority of younger women in Britain and the United States have used oral contraceptives, the subject of this book is of immense importance. The evidence is clear and consistent that oral contraceptives have had no substantial effect, either way, on breast cancer mortality for those who used the pill in the 1960s and 1970s, usually at a mature age. The controversial issue is whether oral contraceptives are safe for younger women before a first pregnancy. The increase in breast cancer risk observed in some studies among young pill users may foretell an epidemic of breast cancer as the women who grew up with the pill from adolescence reach middle age, but there are inconsistencies between the studies. None of them, of course, are randomized controlled trials but the design of the most recent case–control studies is sophisticated.

By the time the consequences of long-term use of the pill from an early age do become clear, the information will no longer be directly relevant to the choices faced by young women. The oral contraceptives on offer have changed and will continue to do so, rendering the epidemiological evidence always a little out of date. The big hope, therefore, lies in increasing biological understanding to the point where it becomes possible to predict the effects of different pill formulations and design oral contraceptives that would, in addition to their other desirable effects, protect against breast cancer.

The best part of this book lies in its appendices. Three excellent and complimentary reviews of the epidemiological evidence are included. The first, by Kathleen Malone, gives a very readable account of the evolution of this field of research, explaining the methodological problems and controversies that have arisen.

The second, by David Thomas, presents a review of the

evidence on combined oral contraceptives in which he focuses on one factor at a time, factors such as duration of use or use near the menopause, and provides tables which juxtapose the results from all the known case–control and cohort studies which address the importance of that factor. The third, by David Skegg, addresses the broader issue of how the possible excess risk of breast cancer resulting from pill use should be viewed in the context of other risks and benefits.

There are also informative appendices describing the evolving formulations of oral contraceptives and the limitations of animal models for elucidating the action of sex steroid hormones on humans.

The first half of the book is more disappointing. It attempts an overview not only of the epidemiology and public health issues but also of biological research. The Committee have had difficulty in structuring the presentation, perhaps because they were aiming at a wide audience. The style of writing is at times a bit annoyingly unscientific or banal: "About a dozen factors are at the core of what is—and is not—known". "It is always easier to record a case of disease than the fact that a disease did not occur".

A very large number of factors that may play a part in mediating the response of breast tissue to steroid hormones are mentioned, but I did not feel that the section on biology improved my general understanding of the subject or that I was left wiser about which lines of enquiry in so exciting a field should have the greatest priority. The book raises many questions but does not seem to provide a guiding light.

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News

Tumour Markers: A Personal Appraisal

A comprehensive review of the use of tumour markers in clinical practice and of recent research relating to the field was presented at the venue on 'Tumour Markers: Current Applications and Impact on Therapy' (Nice, 16–19 November 1991 *J Tumor Marker Oncol*, 1991, **6**, 1–143.), jointly organised by the Mediterranean Society of Tumour Marker Oncology (MESTMO) and the International Academy of Tumour Marker Oncology (IATMO). This conference recalled unsolved issues, but also highlighted new dilemmas.

Characterisation of tumour markers

Any progress in the study of proteins can impinge directly upon that of tumour markers. For instance, 'outlaw' oestrogen receptors (ER) with mutations have recently been identified in breast cancer. These could activate gene transcription and stimulate tumour growth in the absence of oestrogen (dominant positive) or prevent normal receptor activation by oestrogen and possibly inhibit cell growth (dominant negative) (W.L. McGuire, San Antonio). Since sequence differences influence 3D-conformations, some of these receptors may not be adequately assayed by classic radioligands nor by monoclonal antibodies that are raised against defined peptide sequences of the full-length normal receptor. Moreover, such observations could account for the different ligand affinities observed in earlier studies.

Standardisation and quality assurance

The notion that each antibody measures a different species as regards 3D-structure intensifies the existing challenge arising from varied assay methods and from markers from different companies with different units and cut-off levels. Diversity implies the need for standardisation vs. a chosen reference especially when government authorities plan to set proficiency tests for laboratories. A consensus was also reached on the need for participation in external quality assessment schemes as being the only way to evaluate a laboratory's performance over time and in relation to other institutions (M.K. Schwartz, New York).

One or more tumour markers?

Mutated oestrogen receptors in breast cancer may help to explain absence of correlation between receptor positivity and response to hormone treatment. An explanation has also been sought in the presence of independent factors implicated in cell growth. In about 65% of ovarian cancers, epidermal growth factor receptor (EGFR) overexpression is associated with a poor prognosis (R.C. Bast, Durham N.C.) but EGFR levels are liable to be inversely related to ER and thus constitute redundant information. Of the new markers under active study (HER-2/neu (*c-erb* B2) oncogene expression, Ki 67 antigen, PS 2, heat shock proteins, transforming growth factors, topoisomerase. . .), so far, only an aspartyl protease of lysosomes, cathepsin D, has proved to be an independent prognostic variable suitable for routine assay in breast cancer management (H. Rochefort, Montpellier).

The simultaneous measurement of osteocalcin for the presence of bone metastases in prostate cancer was recommended to improve the prognostic value of the proteolytic glycoprotein prostate-specific antigen (PSA), a more sensitive marker than orthophosphoric monoester phosphohydrolase prostatic acid phosphatase (PAP) (E.H. Cooper, Leeds) but, as the number of markers is increased, so does the difficulty in data analysis. Presently, the proportional hazard multivariate regression analysis of Cox is the norm. It establishes a hierarchy of importance in a series of variables chosen to explain a single end-point that is usually disease-free interval or survival. Using this method, the prognostic significance of the following criteria: primary

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