ENDOCRINE ASPECTS OF BREAST CANCER

Proceedings of a Conference held at the University of Glasgow, 8th to 10th July 1957

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EDITOR'S PREFACE

I AM indebted to many colleagues who have contributed to the preparation of the Proceedings of the Conference for publication. The discussion and summaries following the various sections of the book have been written by Professor C. F. W. Illingworth, C.B.E., Professor G. F. Marrian, F.R.S., Dr John A. Loraine and Dr P. R. Peacock. Professor Symington helped in many ways, in particular with the editing of the discussion and in the writing of the summary of the Pathology Section. I am grateful to Professor Illingworth for his advice and encouragement throughout and to Professor Marrian for his guidance on chemical nomenclature.

Dr Ian Carr, Dr J. K. Grant, Dr V. J. O'Donnell, and Dr Beryl Davies read galley proofs and Mr A. P. M. Forrest, Miss Hamilton and Miss A. W. Allan undertook the difficult task of recording the discussions at the time of the Conference. To Miss A. W. Allan I express my most sincere thanks for all the painstaking secretarial work inherent in editing this volume and for her help with the index.

Finally, it is a pleasure to record my appreciation of the cooperation of all contributors and in particular of our publishers. Mr Macmillan and Mr Parker have been very helpful and it is largely due to them that the official report of the Conference is published at this relatively early date.

A. R. CURRIE.

January 1958.

FOREWORD

STUDIES of cancer of the breast have passed through many phases. There was the phase of histopathological inquiries when the microscopic characters were determined and the relation to duct hyperplasia and similar lesions was studied. Then came the phase of clinical investigations into the spread and distribution of metastases and the scope of operative treatment. Then the focus of interest switched to cancer of the breast in the mouse, and during the past few decades this field has yielded a rich harvest, particularly in relation to genetic factors and transmissible agents. Now our attention has been turned to hormonal influences, and once again the human cancer patient occupies the centre of the stage.

At the present time research work on the endocrine aspects of breast cancer is proceeding apace in many different centres throughout the world, at the hands of clinicians—endocrinologists and surgeons—in departments of biochemistry and in special research institutes. It therefore seemed to us that it might be useful to call a conference to review these recent developments, to exchange information on work in progress and to discuss ideas for the future.

The Conference took place, under the auspices of the University of Glasgow, in the Western Infirmary and the Royal Infirmary during the period 8th to 10th July 1957. This volume provides a permanent record of the proceedings. The papers have been printed in the form in which they were presented. For the discussions, in place of a verbatim report we have substituted brief epitomes when necessary, and to each section's debate we have added a critical commentary in order to knit the various discussions together and to present for the reader some idea of the pattern which emerged from our debates.

It is my pleasant duty, on behalf of the Organizing Committee, to thank all those who contributed to the success of the Conference. Through the good offices of the Vice-Chancellor, Sir Hector Hetherington, we were fortunate in obtaining support and a considerable grant of money from a friend of the University who

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prefers to remain anonymous, and we also acknowledge with gratitude the generous help we have received from the Boards of Management of the two teaching hospitals. For all the preparation and the detailed organization we express our particular indebtedness to the two Honorary Secretaries, Dr Alastair Currie and Mr A. P. M. Forrest. In addition, Dr Currie has undertaken the task of editing this volume. This he has done with characteristic zeal, discretion, and assiduity. That the volume is now ready, within six months of the Conference, is in itself a notable tribute to the efficiency with which he and the publishers have addressed themselves to their task.

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January 1958.

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PART ONE

CLINICAL

ADRENALECTOMY IN CANCER OF THE BREAST

SIR STANFORD CADE
Westminster Hospital, London

IN the past four and a half years 170 patients with disseminated breast cancer, including two males, have been submitted to adrenalectomy and gonadectomy. The cases have been analysed with the object of ascertaining the value of the procedure and the length of survival. Histological evidence is available in each case. Previous treatment consisted in surgery to the primary growth, radiotherapy in patients deemed unsuitable for surgery, and the administration of hormones, either oestrogens or androgens, when dissemination of the disease had occurred. At first the operation was undertaken only in the late stages of the disease, but with increased experience it was offered to patients at earlier stages of dissemination.

In no given case can hormone dependence or independence be predicted with accuracy, but it has been observed that aggravation of the patient's condition locally or generally by androgens or oestrogens seems to indicate hormone dependence, and conversely improvement following administration of prednisone is also a sign of hormone dependence. In the later series of cases, hormones were used mainly as a preliminary to adrenalectomy, and only if hormones were well tolerated and improvement achieved was treatment continued for any length of time. The lack of response to hormones is not an indication that the tumour is hormone-independent.

CLINICAL RESULTS

The effect of adrenalectomy is assessed by subjective and objective improvement. In about 40 % of patients no effect on the disease is obtained; there is no subjective improvement, the lesions do not regress, fresh metastases occur and the course of the disease is unaltered. These patients are hormone-independent, although a few of them improved after subsequent hypophysectomy. In 60 % of patients both subjective and objective improvement follows adrenalectomy. The length of improvement varied from 3 months to nearly 4 years. The degree of improvement varied from regression and disappearance of lesions to a state of quiescence when no increase in size or number of metastases occurred. It was noted that if regression occurred it affected all types of metastases, skeletal and

visceral, as well as the local disease in the breast and local recurrences. This apparent law of ' all or nothing ' becomes evident only when a sufficiently large number of cases are observed. The postulate that skeletal metastases are more likely to respond than visceral metastases has not been noted in this series of patients. It has also been observed that neither the age of the patient nor the histological variety of the breast cancer can be correlated with the response to treatment. Both premenopausal and postmenopausal women have responded favourably and failure to respond was also distributed in both these groups. All histological types—scirrhous, medullary and adenocarcinoma—provided both successes and failures, and the statement that only the adenocarcinoma is hormone-dependent has not been substantiated.

In patients whose tumours are hormone-dependent, improvement is immediate, sometimes within a few days of adrenalectomy, and often, when a two-stage operation is done, after the removal of the first adrenal. The degree of improvement has been classified as ' excellent ' and ' good.' The group ' excellent ' includes the most dramatic clinical improvement with a return to a near normal life of patients previously bedridden, requiring pain-relieving drugs, cachectic and with a short expectation of life. By ' good ' is meant a degree of improvement with considerable but not complete relief of symptoms and partial regression of lesions without further development of new detectable metastases.

Subjective improvement

The most important subjective improvement is relief of pain from skeletal metastases. In the ' excellent ' group relief is immediate and complete. No pain-relieving drugs are necessary. There follows an improvement in general health, increase in weight (which may be due to cortisone), a sense of well-being, capacity for work and a return to normal life. Although subjective improvement cannot be measured or assessed accurately, it is of great clinical importance and, in fact, is what is valued most by the patient.

Objective improvement

This is easier to record with accuracy. Skeletal metastases undergo obvious and recordable changes: osteolytic lesions recalcify; sclerosing lesions become more localized and sclerosis is increased; pathological fractures unite. The appearance of some lesions is that of callus and in some patients the structure of the bone returns to normal.

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