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General Editors: A. Canonico, O. Estevez, R. Chacon and S. Barg

Volume VIII

Gynecological Cancer

Editor: N. Thatcher

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Proceedings of the 12th International Cancer Congress, Buenos Aires, 1978

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GYNECOLOGICAL CANCER

Editor:

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XII - ABSTRACTS

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Foreword

This book contains papers from the main meetings of the Scientific Programme presented during the 12th International Cancer Congress, which took place in Buenos Aires, Argentina, from 5 to 11 October 1978, and was sponsored by the International Union against Cancer (UICC).

This organisation, with headquarters in Geneva, gathers together from more than a hundred countries 250 medical associations which fight against Cancer and organizes every four years an International Congress which gives maximum coverage to oncological activity throughout the world.

The 11th Congress was held in Florence in 1974, where the General Assembly unanimously decided that Argentina would be the site of the 12th Congress. Argentina was chosen not only because of the beauty of its landscapes and the cordiality of its inhabitants, but also because of the high scientific level of its researchers and practitioners in the field of oncology.

From this Assembly a distinguished International Committee was appointed which undertook the preparation and execution of the Scientific Programme of the Congress.

The Programme was designed to be profitable for those professionals who wished to have a general view of the problem of Cancer, as well as those who were specifically orientated to an oncological subspeciality. It was also conceived as trying to cover the different subjects related to this discipline, emphasizing those with an actual and future gravitation on cancerology.

The scientific activity began every morning with a Special Lecture (5 in all), summarizing some of the subjects of prevailing interest in Oncology, such as Environmental Cancer, Immunology, Sub-clinical Cancer, Modern Cancer Therapy Concepts and Viral Oncogenesis. Within the 26 Symposia, new acquisitions in the technological area were incorporated; such acquisitions had not been exposed in previous Congresses.

15 Multidisciplinary Panels were held studying the more frequent sites in Cancer, with an approach to the problem that included biological and clinical aspects, and concentrating on the following areas: aetiology, epidemiology, pathology, prevention, early detection, education, treatment and results. Proferred Papers were presented as Workshops instead of the classical reading, as in this way they could be discussed fully by the participants. 66 Workshops were held, this being the first time that free communications were presented in this way in a UICC Congress.

The Programme also included 22 "Meet the Experts", 7 Informal Meetings and more than a hundred films.

METHODOLOGY

The methodology used for the development of the Meeting and to make the scientific works profitable, had some original features that we would like to mention.

The methodology used in Lectures, Panels and Symposia was the usual one utilized in previous Congresses and functions satisfactorily. Lectures lasted one hour each. Panels were seven hours long divided into two sessions, one in the morning and one in the afternoon. They had a Chairman and two Vice-chairmen (one for each session). Symposia were three hours long. They had a Chairman, a Vice-chairman and a Secretary.

Of the 8164 registered members, many sent proferred papers of which over 2000 were presented. They were grouped in numbers of 20 or 25, according to the subject, and discussed in Workshops. The International Scientific Committee studied the abstracts of all the papers, and those which were finally approved were sent to the Chairman of the corresponding Workshop who, during the Workshop gave an introduction and commented on the more outstanding works. This was the first time such a method had been used in an UICC Cancer Congress.

"Meet the Experts" were two hours long, and facilitated the approach of young professionals to the most outstanding specialists. The congress was also the ideal place for an exchange of information between the specialists of different countries during the Informal Meetings. Also more than a hundred scientific films were shown.

The size of the task carried out in organising this Congress is reflected in some statistical data: More than 18,000 letters were sent to participants throughout the world; more than 2000 abstracts were published in the Proceedings of the Congress; more than 800 scientists were active participants of the various meetings.

There were 2246 papers presented at the Congress by 4620 authors from 80 countries.

The Programme lasted a total of 450 hours, and was divided into 170 scientific meetings where nearly all the subjects related to Oncology were discussed.

All the material gathered for the publication of these Proceedings has been taken from the original papers submitted by each author. The material has been arranged in 12 volumes, in various homogenous sections, which facilitates the reading of the most interesting individual chapters. Volume XII deals only with the abstracts of proffered papers submitted for Workshops and Special Meetings. The titles of each volume offer a clear view of the extended and multidisciplinary contents of this collection which we are sure will be frequently consulted in the scientific libraries.

We are grateful to the individual authors for their valuable collaboration as they have enabled the publication of these Proceedings, and we are sure Pergamon Press was a perfect choice as the Publisher due to its responsibility and efficiency.

Argentina
March 1979

Dr Abel Canónico
Dr Roberto Estevez
Dr Reinaldo Chacon
Dr Solomon Barg

General Editors

Introduction

This series of reports encompasses studies of breast, endometrial, cervical and ovarian carcinomata.

Epidemiological, prognostic factors and screening procedures are mentioned in connection with the tumour types, particularly for breast and endometrial cancer. Patient management with surgery, radiotherapy and chemotherapy is the subject of the majority of communications. Hormone receptor status of patients with breast malignancy is also mentioned.

N. THATCHER
March 1979

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Breast Cancer

High Risk Groups

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We have been engaged in prospective studies of a normal population of women living in the island of Guernsey in an attempt to identify risk factors that are important in the aetiology of breast cancer. In addition to eliciting information about reproductive history, previous breast disease, and family history by questionnaire, a variety of direct measurements of endocrine function have also been carried out.

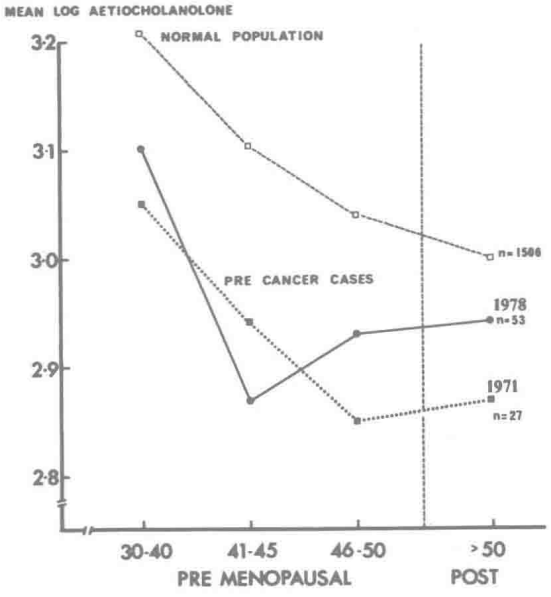

Fig. 1. Urinary excretion of aetiocholanolone (log µg/24hr) by normal women and by pre-cancer cases in Guernsey

The first Guernsey prospective study (1961-1967) involved the collection of 24-hour urine specimens from each of 5000 normal women aged more than 30 years. Since previous case-control findings had indicated that there was an abnormal urinary androgen/corticosteroid ratio in patients with breast cancer (Bulbrook and his colleagues, 1962), the amounts of these steroid hormone metabolites were determined in the normal population to see whether steroidal abnormalities preceded the diagnosis of breast cancer or whether they were merely a consequence of the disease.

By 1971, breast cancer had been found in 27 women (termed 'pre-cancer cases'). The mean excretion of androgen metabolites by these women was significantly subnormal (Bulbrook, Hayward and Spicer, 1971). A second statistical analysis was carried out in 1977, based on 48 cases: once again, it was shown that the mean excretion of aetiocholanolone by the pre-cancer cases was significantly less than that of the controls (Farewell, Bulbrook and Hayward, 1978). Current results are shown in Figure 1.

It will be noted that the abnormality in androgen excretion is mainly confined to pre-menopausal women.

Other significant determinants of enhanced risk in this Guernsey study were an early age at menarche, a late age at first child, previous breast disease, and a family history of breast cancer. All are weak factors and it is clear that they would be of little practical use for the precise identification of women at high risk (Table 1).

TABLE 1 The proportion of normal women and pre-cancer cases with unfavourable risk factors

High Risk Factor	Normal Women	Pre-cancer Cases
Less than 1mg Aetiocholanolone/24hr	27%	51%
Menarche before age 14 years	79%	96%
1st baby after 24 years	56%	78%
Previous breast disease	7%	17%
Family history	12%	31%

The next question was whether the above factors could be combined. A logistic-Weibull model was developed (Farewell, 1977) which led to the identification of five broad risk groups, shown in Table 2.

The calculated risk for a women with all factors unfavourable is about 1 in 4: in women with all factors favourable, the risk is 1 in 60. However, only a small proportion of the population fell within these extreme categories and once again, the results are not of such precision that practical advantage could be taken of them (for selection for intensive screening or other forms of intervention).

TABLE 2 Estimated probability of breast cancer for combinations of risk factors: factors used were family history, androgen excretion, age at menarche, age at first child

Number of factors unfavourable	Estimated probability of breast cancer
0	0.016
1	0.035
2	0.073
3	0.147
4	0.272

A second Guernsey trial had been started in 1968 in which blood was obtained from a further 5000 normal volunteers. The idea behind this experiment was that new analytical techniques made it possible to measure a detailed endocrine profile of plasma protein and steroidal hormones, including the precursors of the urinary metabolites which had already been shown to be related to risk of breast cancer. So far, 38 cases of breast cancer have occurred in this population. Endocrine assays have not been carried out yet in these cases since it is difficult to control variations in analytical results over long periods of time, and better precision is obtained if all samples are analysed simultaneously: some 50 pre-cancer cases will be required.

In the meanwhile, it so happened that many of the volunteers who had taken part in the first Guernsey trial (and for whom a calculated risk level was available) had also given blood in the second trial. It was possible, therefore, to ascribe a risk level to each of 765 blood samples.

The relation between endocrine function and risk is now being examined. Results obtained so far show that in post-menopausal women, neither plasma oestradiol nor progesterone vary with risk. In pre-menopausal women also, the plasma levels of oestradiol are not related to risk but there is a significant inverse relation between plasma progesterone levels in the luteal phase of the menstrual cycle and risk (Bulbrook and his colleagues, 1978). In addition, there is a poor but significant correlation between the amounts of aetiocholanolone in the urine (which was collected between 1961 and 1967) and the amounts of progesterone in the luteal phase of the cycle (in blood collected from the same women, between 1968 and 1975). This immediately raises the question whether the association between a subnormal excretion of androgen metabolites and risk is, in reality, an indirect measure of defective corpus luteum function, rather than a measure of a deficiency in the production of androgens. Secondly, the association between the two measurements of endocrine function, made 5 years apart, implies that the abnormality is relatively constant rather than sporadic. This view is strengthened by the finding that plasma androgen levels are also subnormal in the highest risk group, where urinary aetiocholanolone excretion is almost invariably subnormal (Dr. D.Y. Wang, personal communication).

The finding of a luteal phase dysfunction in high-risk groups affords confirmation for the Sherman-Korenman hypothesis (1974) that this factor is an important determinant of risk. In addition, Sitruk-Ware and co-workers (1977) showed that there was a subnormal plasma progesterone level in the luteal phase of women with benign breast disease and conversely, Kay (1977) reported that there was an inverse relationship between the progestagen content of steroidal contraceptives and the incidence of benign disease.

Plasma prolactin levels have been measured in some 2000 of the volunteers in the second Guernsey trial. The results indicate that there is a significant elevation of prolactin in the early hours of the evening with a distinct peak of the hormone preceding the large increase in levels found later at night. Preliminary results suggest that the early evening peak is higher in women at enhanced risk than in those with a lesser chance of developing the disease (Kwa and colleagues, 1976; Kwa and Wang, 1977; Kwa and colleagues, 1978; di Martino and colleagues, 1978).

It is not at all clear at present whether the early evening prolactin abnormality is related to corpus luteum deficiency in progesterone production or to the subnormal androgen levels. But there are, at last, enough experimental findings to make it possible to speculate about what may be the basic endocrinological features in the aetiology of human breast cancer. Thus, it could be postulated that the basic defects are an increased production of prolactin in the evening, at a time when particular target tissues are most responsive to this hormone; a related defect in progesterone production by the corpus luteum; and a deficiency in androgen production. If this were so, the fact that oestrogen production appears to be "normal" would assume a new significance in the face of diminished progesterone and androgen levels and enhanced prolactin secretion.

A third Guernsey experiment is now in progress in which both urine and blood samples are being collected: the results of this trial may enable us to establish whether the speculations outlined above are valid or not. In addition, mammograms are being obtained from each volunteer so that it can be determined whether any of the endocrine features so far discovered are related to the structural abnormalities reported by Wolfe (1977). Given a successful outcome to this experiment, it might then be possible to contemplate intensive screening of high risk groups or even attempt to reduce the incidence of breast cancer by manipulation of the endocrine environment.

I am indebted to my colleagues in the ventures described in this paper: J.L. Hayward, B.S. Thomas, D.Y. Wang, J.W. Moore, D. Tong, Rosemary Millis, C.C. Spicer and V.T. Farewell.

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