Pergamon

European Journal of Cancer Vol. 33, No. 3, pp. 329–330, 1997

Printed in Great Britain
0959-8049/97 $17.00 + 0.00

PII: S0959-8049(96)00509-6

Editorial

Prostate Cancer, Populations, Politicians and Power

D. Raghavan

Division of Solid Tumor Oncology, Carlton House, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, New York 14263, U.S.A.

IN 1996, more than 300 000 new cases of prostate cancer were reported in the United States, and around 40 000 deaths occurred from this disease. This represents a doubling of incidence in less than 5 years, compared with an increment of less than 30% in deaths over the same period. A similar 'epidemic', but perhaps on a lesser scale, appears to be evolving in the rest of Western society in association with the increasingly aggressive approach to screening for prostate cancer. However, we must be careful not to fall prey to the 'shell' game, identifying an apparently falling mortality rate as tantamount to progress when it may be that we are simply identifying a cohort of hitherto occult cancers that would never have led to cancer deaths if they had not been sought and diagnosed.

The public chronicling of cases of this neoplasm among prominent personalities, including politicians, business tycoons and entertainers, and the personal involvement of several of them in campaigns relating to funding of research and to the search for new strategies of treatment, has raised the public profile of this disease dramatically, and has disrupted the traditional approaches to the acquisition of support for medical research, while adding to the pressure on the medical profession to cure this disease as quickly as possible.

Several major issues have recently focused the attention of scientists and clinicians working in this area, and it is appropriate that in this and next month's issues (nos 3 and 4) of the *European Journal of Cancer* a section on Clinical Oncology Updates will be devoted to an assessment of some of the recent progress in prostate cancer. Part I, in this Issue (see pages 340–356), will cover epidemiology and prevention, and Part II, in Issue 4, will cover advances in clinical management. The demonstration of the utility of prostate specific antigen (PSA) as a marker of prostatic disease by Chu and colleagues at Roswell Park Cancer Institute, led to the emerging concepts and controversies regarding population screening for prostate cancer. PSA measurement and transrectal ultrasonography are used in an attempt to improve the sensitivity and specificity of digital rectal examination (see Kramer and associates (pages 348–353) and Lange (pages 354–356)). There has been a rapidly changing epidemiological database (reviewed by Mettlin (pages 340–347)), including the recent interest in fat intake as an aetiological factor for prostate cancer, as well as data suggesting associations with cigarette smoking and with vasectomy. The documentation of racial differences in incidence, stage at presentation and outcome of treatment, with African Americans having the highest incidence, but perhaps faring less well than their Caucasian counterparts, has also been of considerable interest. The identification of high-risk populations and the possibility that early hormonal blockage may act as prophylaxis against the development of prostate cancer in these high-risk groups is also under investigation.

Because of the disappointing cure rates for patients with advanced disease and the relative lack of progress in this domain of management, the greatest emphasis is now being placed on diagnosis and control of prostate cancer at an early stage. The conflict between the proponents of the outcomes movement (predicated on decision making based only on large databases) versus the supporters of traditional clinical decision making, has created the most intense debate, as summarised by the contrasting contributions of Drs Kramer and Lange. In the management of prostate cancer, the fundamental problem is to define what constitutes 'dangerous' prostate cancer. Unlike cancers of the breast and cervix, in which diagnosis at the earliest stage has been shown to contribute to improved survival, the discrepancy between the incidence figures at autopsy and data derived from the mortality and morbidity statistics in prostate cancer has caused substantial concern: it appears that there are two patterns of prostate cancer—one that is present incidentally in later life and appears not to cause death; and another that presents clinically during the life of the patient, and often causes morbidity and death. In this context, the ultimate object of screening is to identify asymptomatic patients with potentially dangerous prostate cancer at an early stage, in the hope that early therapeutic intervention will reduce the risk of cancer-related death. However, considerable controversy has surrounded the interpretation of the available clinical data, resulting in wide discrepancies in the public view on screening by responsible agencies, such as the American Cancer Society, American Urological

Received 12 Dec. 1996; accepted 16 Dec. 1996.

Association, National Institutes of Health and disparate cancer research and treatment organisations throughout the world.

The issue has been complicated by the divergence of views regarding the need for early intervention for asymptomatic, clinically localised prostate cancer at the time of diagnosis—thus, the proponents of a conservative approach of watchful expectancy (without radiotherapy or prostatectomy) also suggest that population screening is inappropriate or unnecessary for the majority of the population at risk, based on the high prevalence of occult prostate cancer found in the aged. By contrast, those who believe that early treatment for clinically localised disease contributes to improved outcomes cite this as the major reason for the promulgation of programmes of screening for prostate cancer, emphasising that screening identifies predominantly the 'dangerous' variant and not the occult tumour that is found in the elderly.

This issue can only be resolved with certainty by the completion of randomised clinical trials that test (i) the utility of screening (with morbidity and survival as the major indices of outcome); and (ii) the efficacy and safety of the conservative approach to early stage disease, as compared to radiotherapy or surgery. In the United States, the National Institutes of Health have developed a randomised trial of screening for prostate cancer, which will be of great importance. Whether this study succeeds will depend, in part, on the opposing evangelism of those who advocate screening without further investigation of its true role, and who may increase the level of public anxiety so that potential subjects will refuse to participate. In view of the potential costs of routine screening to patients (with respect to the morbidity of investigation and treatment) and to the community in fiscal terms, it would be most unfortunate for this to happen.

Whatever the outcome of the debate on the timing of treatment of prostate cancer, it is gratifying that important progress has been made in the treatment of early stage disease, with extensive documentation of the improvements in surgical technique and increased precision of delivery of radiotherapy, limiting the side-effects to normal tissues while enhancing the dosage to the cancerous tissues themselves (Zietman and Shipley (see Issue 4 next month)).

Although progress in the management of advanced disease has been slow, there is now an increasing precision in the assessment of new agents (Dawson (see Issue 4 next month)), and a more structured approach to the testing of new strategies of systemic therapy (Galbraith and associates and Raghavan and associates (see Issue 4 next month)) with the evolution of new hormonal manipulations (e.g. withdrawal of flutamide, new peripheral and adrenal blockers), novel compounds (such as suramin), and new applications of old cytotoxic agents (e.g. mitoxantrone, oral cyclophosphamide).

Research and treatment of prostate cancer has become something of a medical growth industry. With the proliferation of funds now becoming available as a result of political and social pressure, it is becoming increasingly important to ensure that logic and careful planning will dictate the strategy of our research efforts, and that rhetoric and the desire for quick progress should not lead to a disruption of carefully structured and meticulous scientific effort in favour of support for speculative high-risk, high-gain programmes—this latter strategy has not advanced medicine greatly in the past.