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Book Review

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Cancer Surveys—Volume 19/20: Trends in Cancer Incidence and Mortality

R. Doll, C.S. Muir and J.F. Fraumeni

THE REALISATION that the incidence of cancers that were at all common anywhere varied materially with place, social environment and time grew only slowly. By the end of the 19th century, it was clear that several different types of cancer could be produced by specific occupational exposures, but the large differences that were reported between the prevalence of cancer in developed and developing countries tended to be dismissed as being due to differences in age distribution, as artefacts of differential standards of diagnosis or perhaps to differences in genetic constitution. Gradually, attitudes changed, hastened in the U.K. by Percy Stocks' graphical demonstration in 1936 of the substantial variations in age-standardised mortality rates of the major cancers throughout the country [1]. By the 1950s, it came to be accepted that most of the differences reported between populations were not only real, but also provided potentially important clues to the aetiology of the disease.

The realisation that changes in incidence occurred over time came more slowly. Hoffman, actuary to the Prudential Assurance Company in the U.S.A. wrote in 1915 that "the evidence of cancer increase throughout the world is an incontrovertible statistical fact and absolutely conclusive" [2], but his opinion had little impact. Few reliable incidence data were available, and changes in incidence had to be inferred from hospital records, prevalence surveys and mortality statistics. The last were particularly valuable because of the large populations covered and the long periods for which, in some countries, they had been recorded. Changes in treatment had had little effect on mortality rates, but they were affected by changes in the provision of services and the standard of death certification, and clinicians and laboratory workers tended to dismiss the changes with time as diagnostic artefacts. Even the dramatic increase in mortality attributed to lung cancer, which began in the 1920s, for a long time failed to convince them that changes with time could also be as real and as important as the differences in geographical distribution.

By the mid 1960s, the difficulty in interpreting temporal trends in cancer mortality in populations under 75 years of age had been largely overcome in most of the developed countries, but just when mortality statistics had begun to prove their reliability as a reflection of cancer incidence, treatments began to be improved, in some cases dramatically, and the need for reliable incidence data became acute. Fortunately, this had been foreseen by a few epidemiologists and medical statisticians, and Harold Dorn [3] at the US National Cancer Institute, Johannes Clemmesen [4] in Denmark and Mitsuo Segi [5] in Japan had begun to attempt the collection of reliable incidence data on a large enough scale to enable moderate changes in the incidence of the less common cancers to be detected within 10 to 15 years—something that was essential if an early warning was to be obtained about the introduction of a major new hazard. The results were, however, dispersed in publications that were often difficult for the research worker outside the country of origin to obtain, and their value was greatly enhanced (enabling comparisons to be readily made between different communities) when the International Union Against Cancer, in 1966, produced the first volume of *Cancer Incidence in Five Continents* [6].

The interpretation of trends in incidence has, however, proved even more difficult than the interpretation of trends in mortality before the introduction of effective new treatments. For we have to consider not only the efficacy of registration, but also the effects of changing practice in the classification of lesions associated with different rates of fatality, and of the spread of screening to detect ever earlier stages of the disease. Such factors have had a major effect on the changes recorded in the incidence of many specific types of cancer: they are examined in this volume by Muir, Fraumeni and Doll, and an understanding of them provides an essential basis for the interpretation of the recorded changes in incidence.

The development of cancer incidence data, immensely valuable though they are, has not eliminated the need for mortality data. The trends in mortality continue to be of vital interest, partly as a check on the validity of the trends in incidence (an increase in the mortality from cancer of the thyroid, for example, justifying the belief that an increase in incidence is real and not just the result of intensive screening), and partly to help assess (in conjunction with trends in incidence) the effects of changing treatment. International mortality data have long been available for developed countries in the publications of the World Health Organization, but they were in too limited a form to be of maximum use. Thanks to Segi [5], the position was changed with the publication of his serial volumes on cancer mortality in 24 countries, and the detailed data that are needed, many of which are critically examined in this volume, can now be obtained from the International Agency for Research on Cancer on request.

Twenty-three chapters have been prepared by research workers with a special interest in individual types of cancer. The presentations are not all the same because authors were asked to describe what they themselves thought to be of greatest interest. They were, therefore, given only a few guidelines to ensure some degree of comparability between chapters, such as the use of the rounded off world population adopted by the International Agency for Research on Cancer as a standard for calculating age standardised rates and the suggested inclusion of data from Volume VI of *Cancer Incidence in Five Continents*, now produced jointly by the International Agency for Research on Cancer and the International Association of Cancer Registries [7], for at least one Nordic country, one west, one south and one east European country, one North American country and Japan, as well as data from their own country.

In total, the contributors provide incontrovertible evidence that temporal changes in incidence are the rule rather than the exception and that, although some of the changes in some countries are likely to be more artificial than real, there is overwhelming evidence that some cancers are becoming more

common and others less so. They also show that the changes are proceeding at different rates at different ages and in different countries, and sometimes even in different directions. Recognition that such changes are occurring provides evidence for those concerned with public health about the efficacy of their progammes for prevention, and clues for the research workers about where to look for environmental or behavioural causes that have yet to be detected.

The pioneering work of Dorn, Clemmesen and Segi has been acknowledged, and it is appropriate that the final chapter contains Aoki and Kurihara's appreciation of Segi's contribution. It records how Segi, with characteristic modesty, acknowledged his debt to the example of his predecessors. It is a debt that all who use cancer incidence data share, and it is hoped that the production of this volume may go some way to repay the share of those who have contributed to it.

1. Stocks P. *Distribution in England and Wales of Cancer of Various Organs*. 13th Annual Report of the British Empire Cancer Campaign, 1936, 240–280.
2. Hoffman FL. *The Mortality from Cancer Throughout the World*. New Jersey, Prudential Press, 1915.
3. Dorn HF. *Illness from Cancer in the United States*. Public Health Reports 59 35–48. 65–77. 97–115. Washington DC, US Department of Health, Education & Welfare, 1944.
4. Clemmesen J. The Danish Cancer Registry, under the National Anti-Cancer League. *Danish Med Bull* 1955, 2, 124.
5. Segi M. *Cancer Mortality for Selected Sites in 24 Countries* (1950–57). Sendai, Japan, Department of Public Halth, Tohoku University School of Medicine, 1960.
6. Doll R, Payne P, Waterhouse J. *Cancer Incidence in Five Continents: a Technical Report*. New York, Springer-Verlag, 1966.
7. Parkin DM, Muir CS, Whelan SI, Gao YT, Ferlay J, Powell J, eds. *Cancer Incidence in Five Continents*, Vol VI. IARC Scientific Publications No. 120. Lyon, International Agency for Research on Cancer, 1992.

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Letters

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Economic and Clinical Evaluation of Therapy of HIV-related Non-Hodgkin's Lymphoma with Chemotherapy and Granulocyte Colony-stimulating Factor (G-CSF)

U. Tirelli and E. Vaccher

TREATMENT OF HIV-related non-Hodgkin's lymphoma (NHL) with chemotherapy is associated with a substantial risk of side-effects, in particular bone marrow toxicity, that precludes therapy in the majority of patients [1, 2]. Granulocyte colony-stimulating factor (G-CSF) could partially overcome this side-effect [3], but the cost is high. However, G-CSF could theoretically reduce the overall cost of the treatment, with a decrease of required antibiotic therapy and days of hospitalisation.

This study reports the monoinstitutional experience of treatment of HIV-related NHL with chemotherapy and prophylactic G-CSF, in terms of the cost of the overall treatment, in addition to the evaluation of toxicity. A comparison of 37 consecutive patients who had received intensive chemotherapy regimens, 19 without G-CSF from July 1989 to June 1991, and 18 with G-CSF from July 1991 to September 1992, immediately after its availability, was carried out. G-CSF (5 μg/kg/day) was given subcutaneously 24 h after chemotherapy for 13 days in all cycles. The two groups of patients were comparable in terms of stage and regimens employed, i.e. the LNH84 regimen [4] and the CHOP-like regimen CHVmP/VCR-BLM [5] given for three to six cycles.

The mean cost of one day of hospitalisation at our division is approximately $450. For the cost evaluation, the following items have been considered: (1) daily cost of hospital stay ($263); (2) antibiotic prophylaxis against *Pneumocystis Carinii* pneumonia and antifungal prophylactic therapy (daily cost/patient $22); (3) antibiotic therapy administered during haematologic toxicity (parentheral cephalosporin plus aminoglicoside therapy, mean daily cost/patient $67); (4) supportive therapy including diagnostic procedures (mean daily cost/patient/toxic episode $90); (6) anti-retroviral therapy (daily cost/patient $8); (7) recombinant G-CSF (the actual cost of a 300 mg vial in Italy is $100).

Therapy and hospital cost did not change over the time period of the study.

At our centre the policy at that time was that patients with HIV-related NHL were hospitalised both for the administration of cycles of chemotherapy and when chemotherapy-related toxicity and HIV-related infections were observed. This approach was based on the high risk of severe complications associated with intensive chemotherapy in such patients with unfavourable NHL and severe immunodeficiency, and to the peculiar features of our HIV-positive population, i.e. the usual distant geographical area of residence, and logistic problems connected with the lifestyle of these patients who are often drug users. This policy did not change during the time of the study so that the two groups of patients were homogeneous for the cost evaluation.

G-CSF significantly reduced the duration of nadir to a mean of 8.4 days compared with 10.8 days in the control group ($P = 0.006$). Among patients with a CD4 count ≥ 200 mm^3, the nadir WBC was significantly higher in the G-CSF than in the control group (mean 1293 ± 143 versus 410 ± 285; $P = 0.009$). The event rates for febrile neutropenia and for culture confirmed infections were comparable among the two groups. The mean number of chemotherapy cycles for patients and the proportion of patients who receive full doses of chemotherapy were not significantly different in the two groups.

Correspondence to U. Tirelli.
The authors are at the Division of Medical Oncology and AIDS, Centro di Riferimento Oncologico, Via Pedemontana Occidentale, 33081 Aviano, Italy.
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