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Book Review

Prevention and Early Detection of Colorectal Cancer Editors: G.P. Young, P. and Rozen, B. Levin Publishers: W. B. Saunders, Philadelphia, U.S.A. (1996)

COLORECTAL CANCER is a preventable and curable disorder and it is, along with breast and lung cancer, one of the most common cancers in Western societies. In an ambitious attempt to integrate recent advances of biological, clinical and economic research, the editors have invited outstanding researchers and clinicians to contribute to the book.

The book has four sections. The first section explains the biological basis on which prevention of colorectal cancer should be based. Further chapters describe the pathology, including molecular biology of cancer development, addressing all stages from normal to invasive cancer cells. Those biological issues which might be amenable to manipulation and to identification prior to development of the invasive cancer cell are emphasised. The second section describes the various means available for manipulating biology of cancer development. In a separate chapter, newly emerging genetic information is integrated into clinical practice. The chapters on preventive measures based on lifestyle changes (e.g. diet) and administered agents (e.g. chemopreventive agents such as aspirin) are well balanced. The third section on "Management of Those at Risk for Colorectal Cancer" contains chapters which define the risk for colorectal cancer and describe disease states, some inherited, which dramatically influence risk. Other chapters deal with surveillance strategies for patients with colorectal adenomas or cancers, as well as the problem of cancer mortality in inflammatory bowel disease. The fourth section entitled "Community Approach to Prevention of Colorectal Cancer", describes the tools available for screening. In further chapters, the complex and controversial issue of prevention by early detection in those of undefined risk is discussed from various perspectives. A separate chapter is dedicated to the economical issues, discussing the cost-effectiveness of colorectal cancer screening in average-risk adults. Finally, a well-balanced overview on screening for colorectal cancer is provided.

This book represents a comprehensive approach to the issues involved in prevention ("primary prevention") and early detection ("secondary prevention") of colorectal cancer and its precursor states, such as adenoma. I congratulate both the editors and authors of this book since it provides an authoritative up-to-date analysis of the scientific information as well as practical advice based on critical review of the current state of knowledge. I am delighted to have this valuable book in my library and I highly recommend it to all clinicians dealing with gastrointestinal disease and those interested in preventive medicine and health economics.

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Letters

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Role of Radical Prostatectomy in Micrometastases Dissemination

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A MAJOR controversy is whether surgical manipulation in patients with prostate cancer causes cell dissemination, as seen in testicular germ cell neoplasm after orchidectomy, or

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whether it removes the source of micrometastases. In prostate cancer patients with elevated levels of prostate-specific antigen (PSA), who were subjected to treatment of the primary tumour, 60–80% experienced local relapse or metastatic disease [1]. This unfavourable behaviour could be due to cell dissemination by primary and/or distant tumour bulk or by surgical manipulation. Recent advances have allowed the development of a highly sensitive method for detecting occult haematogenous neoplastic cells both in malignant melanoma and prostate cancer. This method uses nested reverse transcriptase–polymerase chain reaction (RT–PCR) to assay for antigen-specific mRNAs [2, 3]. We examined the effects of surgical manipulation on haematogenous micrometastases dissemination in 30 prostate cancer patients with pT2 (organ-confined) and pT3 (locally advanced) disease as judged by histological analysis after prostatectomy. They had elevated levels of PSA (>20 ng/ml) but had not developed distant metastases at the time of diagnosis. An LNCaP cell line and female peripheral blood samples were used as positive and negative controls, respectively. Blood specimens were taken 24 h before and after surgical manipulation. A blood sample was also collected intra-operatively from the surgical field. Peripheral blood analysis was repeated three more times at 30 day intervals. Both blood and cell line samples were subjected to RNA extraction with guanidinium thiocyanate and phenol/chloroform method. The total RNA (750 ng) was reverse transcribed into cDNA and amplified by the nested-PCR method, using published sequence primers [3, 4]. The samples were run on tris-borate-EDTA 2% agarose gels containing ethidium bromide. The results were analysed by specific enzymatic cleavage with Dde I endonuclease and Southern blotting hybridisation using a PSA oligonucleotide probe. By this method, we found 5 patients (17%) who clearly had circulating prostate cells before radical prostatectomy, but not after surgical treatment (Figure 1). These blood specimens remained PSA mRNA negative in subsequent analyses. The PSA level for these subjects measured 30 days after surgical procedures was 0.1–0.3 ng/ml. In the other 25 patients (83%), we did not observe haematogenous metastases before or after the surgical manipulation. Intra-operative blood analysis from the surgical field showed only one positive patient. In contrast, in a study of 22 patients, Oefelein and associates [5] reported that in 91% of their samples, there was evidence of prostate cells in the intra-operative surgical field and haematogenous dissemination followed surgical manipulation. However, these results could possibly be due to illegitimate transcription corresponding to a basal transcription of any gene from any cell type. This phenomenon does happen when the RT–PCR is carried out under highly sensitive conditions. To avoid this problem, we used low quantities of mRNA, few PCR cycles and several negative controls. Therefore, our results may be more clinically relevant, since we demonstrated the presence of occult micrometastases in pT2–pT3 prostate cancer patients and have demonstrated the efficiency of a broad surgical excision for relieving circulating neoplastic cells. These encouraging findings may be helpful for understanding the importance of total prostatectomy with pelvic lymphadenectomy in removal of the metastases source and hence in the hindrance to lymphatic dissemination of prostate cancer. The negative results may leave the possibility that some tumour cells arrived at a favourable tissue that gave rise to quiescent neoplastic clone. The monthly screening of the same patients will allow us to determine the eventual relapse and, hence, intervene with an opportune treatment.

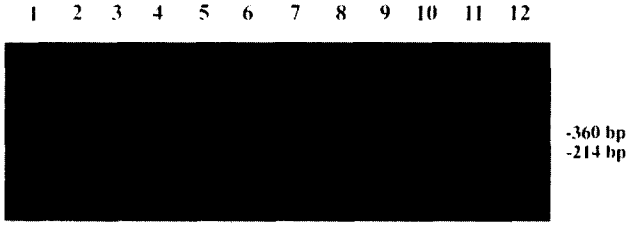

Figure 1. Detection of PSA mRNA in peripheral blood of prostate cancer patients. Lanes 1 and 12 = ΦX174/Hae-III DNA size marker; lanes 2, 4, 6 = different patients before the prostatectomy (the patient whose sample is in lane 6 was negative before surgical manipulation), and lanes 3, 5, 7 are, respectively, the same patients after prostatectomy (lane 7 shows the negative subject had DNA 360-bp product after surgery); lanes 8, 9 = positive controls (2 biopsies of prostate tissue); lanes 10, 11 = negative controls (2 healthy female subjects).

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