Secondary Prevention of Colorectal Cancer

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Secondary Prevention of Colorectal Cancer

An International Perspective

Volume Editors
P. Rozen, Tel Aviv
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Drug Dosage
The authors and the publisher have exerted every effort to ensure that drug selection
and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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Dedication: To Paul Sherlock, MD, 1928-1985

This book, the work of numerous collaborating experts in both hemispheres, chronicles a dramatic change in the world’s view of cancer of the colon, which has resulted from interrelated discoveries in the fields of epidemiology, experimental pathology, clinical research, and tumor biology. It is dedicated to one of the outstanding leaders of that international effort, the late Paul Sherlock.
The history of medicine has been greatly influenced by rare physicians who have broken out of traditional molds to create new working relationships between biomedical disciplines. When the resolve to do so is combined with a sound orientation to modern biology, high clinical skills, inherent qualities of diplomacy and leadership, and unfailing energy in their application, the impact of one person can be very large.
All these elements came together in the character and the professional accomplishments of Paul Sherlock. A broadly trained and brilliantly capable internist, he devoted 28 years of his life to the service of the Memorial-Sloan Kettering Cancer Center in New York City, in latter years as Chairman of its Department of Medicine. His interest in digestive diseases, his skills in endoscopy, and his collaboration with tumor biologists compelled his devoted and untiring efforts to improve the outcome of treatment of colorectal cancer through early detection and primary prevention. To this end, he aroused the membership of digestive disease societies to greater and better directed programs of research
and education; he long served as liaison between categorical agencies of
government and the private sector in the fields of internal medicine, digestive
disease, and cancer control; and he unswervingly pursued these
objectives as a convener of international conferences and as the first
Chairman of the National Digestive Diseases Advisory Board, chartered
by the Congress of the United States.

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In consequence of the work of the authors of this volume, and of the
many others who in the last decade have contributed to this field, colorectal
cancer has been transformed from an unspeakable visitation of uncontrollable
forces to a feasible objective for practical preventive medicine.
But Paul Sherlock was not to see the full fruition of these efforts. At
a time when recognition, responsibilities, and honors were converging
upon him as do iron filings upon a magnet, he fell ill with adenocarcinoma
of the bronchus and died in May, 1985, at the age of 56. His legacy is a
large one, will fall upon many hands, and will be long in unfolding. This
important volume by a global company of his friends and associates is a
worthy beginning.

Thomas P. Almy, MD,
Professor of Medicine and of
Community and Family Medicine, Emeritus
Dartmouth Medical School

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Preface

We are now at one of those rare points in medicine witnessing a series of exciting new developments in a relatively short period of time, bringing us to the threshold of important progress in a major disease. In the past decade we have gained insight into the familial and personal risk factors for colorectal cancer and have seen the introduction of potentially promising screening techniques such as the fecal occult blood test and fiberoptic sigmoidoscopy. This is in addition to colonoscopy, which allows an accurate diagnosis of colonic pathology, while colonoscopic polypectomy now provides the ability to remove almost all colonic adenomas without the need for major surgery. We also have a better understanding of oncologic precepts and new surgical techniques which allow more effective sphincter-saving operations.

We have learned about the nature of the transformation of the colonic mucosa into a premalignant mucosa once a single neoplastic lesion has developed and have obtained a much clearer understanding of the evolution of the adenoma into an adenocarcinoma of the colon. This, in turn, has led to a better understanding of the need for surveillance of synchronous and metachronous lesions. When one considers the history of medicine over the past several hundred years, these major developments, related to a single disease and its prevention occurring over a decade of time, are indeed dramatic.

Prevention can be considered in terms of primary or secondary prevention. Primary prevention includes the identification and eradication of environmental carcinogenic factors, and the concept of dietary intervention readily comes to mind. The secondary preventive approach is often a neglected one. It is the identification and eradication of premalignant lesions,
such as the adenoma, and the detection of early-stage cancer prior to the development of more advanced, disastrous, lethal disease. There has been a considerable focus of attention on the secondary prevention of colorectal cancer in the past few years. These approaches and studies initially dealt with the question of feasibility and at the present time certain studies are also addressing the question of the validity of this approach. The feasibility of these secondary preventive methods for colorectal cancer is related to the acceptance by patients of stool blood testing, the rate of positivity and predictive value of the stool blood test and the relative acceptability of flexible as opposed to rigid sigmoidoscopy. It also includes the risk to the patient of the diagnostic workup, the relative yield of colonoscopy and barium enema in the investigation of patients with abnormalities in their fecal occult blood tests or sigmoidoscopy, the risk and feasibility of removing colonic polyps by colonoscopy, the risk and technical aspects of modern surgical oncological techniques, and the acceptance by patients of follow-up surveillance. Many of the chapters in this book report on the feasibility of secondary preventive measures and include a number of data related to the various points mentioned above. Fecal occult blood test program results are reported from the United States, England, Italy, Germany, Austria, Hungary and other Eastern European countries, and Israel. Specific aspects of the fecal occult blood tests and of screening by sigmoidoscopy are discussed in detail in separate chapters, and the follow-up surveillance of patients after removing adenomas is reported from the US and England. The important issues of patient compliance are discussed in detail. Since cost-effectiveness is such a key issue in any approach involving large numbers of patients, the relative merits of physician-oriented and nurse-practitioner-oriented clinical screening approaches are discussed as well as the organization of such screening services on community and specialized clinic levels. A considerable segment of the book relates to the important questions of risk factors, with papers focussing on the personal risk factor of adenoma, ulcerative colitis, and the relevance of various types of family history, from the suggestive minimal family history to the striking family cancer syndrome. A considerable amount of data has now been generated directed to the question of the feasibility of secondary preventive approaches and it does indeed appear to be feasible in many respects. However, many obstacles need to be overcome and better studies are required regarding patient compliance, the legal aspects of identifying
persons at risk, physician awareness, and cost-effectiveness of the methodology used.

While the feasibility studies continue to generate important data and address that question, a second key question must be asked, ‘What is the validity of this approach?’ Many studies have reported a shift in stage to

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a higher proportion of more localized cancers in patients who have entered screening programs. However, it is well known that length bias and lead time bias may operate in a screening program to artificially increase the proportion of those early cases which, in the absence of a screening program, may have remained early when presenting with symptoms. The epidemiological basis and principles of screening are discussed, examining such questions when evaluating screening programs. The parameters that must be looked at, in addition to a shift in stage, are survival and mortality. A shift to an earlier stage and improved survival are key, early parameters of outcome that must be observed in order for the screening process to be deemed potentially valuable. However, stage and survival are subject to lead time and length bias and therefore a mortality reduction of the entire screened population must be demonstrated in order to validate the positive early-outcome parameters. Such mortality reduction data have as yet not been demonstrated convincingly for screening of colorectal cancer. It must be emphasized that such data are very difficult to obtain, requiring a high degree of cohort follow-up over a prolonged period of time. The reason that these data have not as yet been forthcoming is because ongoing programs have been initiated only in the past few years and will require more time to be evaluated in relation to this issue. Once again, it should be emphasized that these preventive approaches have been initiated only very recently for a disease which has a long natural history and therefore a considerable length of time is necessary for the final evaluation of these issues. We can expect that the mortality question will ultimately be reported by studies that are in progress in the United States and in Europe and their current status are discussed in this book.

While feasibility and validity studies are ongoing, two additional major benefits of the present programs are: to evaluate currently available tests, indicating their strengths and weaknesses and, even more importantly, to provide information on the critical issues of the screening process, its effectiveness, and how it relates to the natural history of the adenoma-adenocarcinoma sequence. Perhaps the greatest value of the screening programs is what we can learn about the natural history of the early stages of colorectal cancer and its precursor lesions. It is fully recognized
that currently available tests may not be those tests which will be utilized in the future for screening purposes. The specific tests that are at present available are reviewed in papers in this book, and there is a discussion of others that are under development or evaluation and may in the future replace or supplement the present tests. It is quite possible that immunological approaches, such as those utilizing monoclonal antibodies, may replace the current biochemical methodology of testing for fecal occult blood. Although efforts in the area of circulating markers have been disappointing, one day they may fulfill their long-expected promise and aid us in the identification of high-risk groups and the detection of neoplastic lesions. One could envision the possibility of a circulating marker being detected by a peripheral blood test followed by monoclonal antibody-linked imaging techniques for the identification and localization of the lesions, and then appropriate endoscopic or surgical intervention being applied. The treatment with immunologic techniques to localize and destroy the neoplastic lesion may be within the realm of reality in the future. In the meantime, as dealt with in this volume, there are promising developments of techniques which may allow us to recognize premalignant stages even within tissue appearing normal.

The question is often asked as to what should be done now, in the community, for the patient. While much exciting research continues into the etiology, natural history, prevention and treatment of this disease, several authoritative bodies, including the International Work Group for Control of Cancer, the American Cancer Society, and others have provided a reasonable approach. Patients should be encouraged to enter the health care system and symptomatic patients should be properly investigated. Risk factors should then be assessed, and patients divided into average and high-risk groups. The average-risk groups should have fecal occult blood testing and flexible sigmoidoscopy performed beginning somewhere between the ages of 40 and 50 years. Workup, including double-contrast barium enemas and, or colonoscopy should be planned for patients with positive tests, and then future surveillance should be recommended to search for metachronous lesions if neoplastic lesions have been uncovered. High-risk patients who have ulcerative colitis, adenomas or family histories need individual follow-up. Studies in the US, Italy, Israel and the UK are addressing these groups of high-risk patients and hopefully will provide guidelines in the near future. It is also quite clear, and as discussed in this book, that in addition to the basic labora-
tory research and trials that are going on now, we need greater efforts in
the area of patient education and physician awareness.
New developments will have a major impact only with greater inter-
national dialogue among people who are committed to a better under-
standing and a more effective control of colorectal cancer. Many national
and international organizations have devoted efforts to this end. The In-
ternational Workgroup on Colorectal Cancer developed in 1979, to which
many of the authors of this book have belonged, has made a major com-
mitment to the control of large bowel cancer. The World Health Orga-
nization has recognized the importance of control of this cancer on an
international basis, designating a WHO Collaborating Center for the Prevention

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of Colorectal Cancer at Memorial Sloan-Kettering Cancer Center.
The editors and many authors of this book, who have participated in
the international work group, will be actively involved in this new WHO
center. It is our hope that cooperation and exchange of data and thinking
on an international basis will aid us in our efforts. It is this principle that
governed the planning of this book which was meant to be, and is, an
international forum on the current status of secondary prevention of
colorectal cancer.
Finally, it was intended that this preface be written by Dr. Paul Sherlock.
His tragic and early demise has left many of us, including many of
the chapter authors in this book, without a friend, colleague and teacher.
We dedicate this book to his memory.

S. J. Winawer
P. Rozen
Editors