The Case for Cancer Prevention

People smoke. They drink. They mine uranium or work with asbestos. They get too many X-rays from their doctors. They eat food with carcinogenic additives or contaminants. Then they get cancer and they die. At present, neither screening for early cancer nor the most modern treatment can protect most of them.

Thus it is time to give serious attention to research on problems related to cancer prevention. Recent advances in both treatment and screening for early cancer have produced some outstanding results, but it would be a mistake to assume that future advances will necessarily be successful in eliminating cancer morbidity and mortality. We may well find that a substantial proportion of tumors will remain therapeutically intractable and that the large-scale detection of many kinds of cancer at early, curable stages will continue to be impossible or, at best, difficult and impractical.

PRESENT STATUS

By “cancer prevention” I mean actions taken to stop or reverse the initial development of malignant neoplasms that would at later stages threaten life or health. This definition includes, but is not limited to, the identification of high-risk persons and the reduction of their exposures, the identification and control of external hazards, and the use of measures to block or reverse the development of lesions among persons already exposed but in whom no cancer is (yet) detectable. Others have defined prevention in broader ways, sometimes qualified as “secondary prevention” or even “tertiary prevention.” These definitions are used to refer to programs for screening and treatment, as means for preventing some of the effects of cancer rather than preventing the cancer itself. Such activities are not included in my definition of prevention.

There seem to be no immediate opportunities for large-scale cancer prevention strategies that are not already well known, but there are serious barriers to the effective application of present knowledge. Thus, whereas needs for education, demonstration, and service programs in prevention are pressing, this editorial will focus on some aspects of research. A balanced program of research on cancer prevention must include studies on ways to develop and apply what is known about cancer causation as well as studies on causation per se. To some degree, this will involve research disciplines not commonly supported by organizations that fund traditional laboratory and clinical investigations.

A sharp distinction exists between an understanding of cancer causation—carcinogenesis—and an understanding of cancer prevention. These fields are closely related but they must be carefully differentiated and defined, and the road from one to the other is long. The difference is illuminated by a question: Do we know how to prevent most lung cancers? In a narrow sense perhaps we do—just persuade people to not smoke cigarettes. In a more important operational sense we may not, because 25 years of accumulating knowledge and effort have had only limited success in changing national patterns of tobacco use. To argue that we have not made the right kind of effort is no answer; we do not know, again in an operational sense, what are the right kinds of efforts and how such efforts should be designed, supported, and implemented.

In some important ways, research on cancer prevention now stands where research on cancer treatment stood 30 years ago. At that time there was widespread pessimism, even among medical investigators, that chemotherapy would ever be of much value or that the effectiveness of surgery and radiotherapy could be substantially enhanced. There was little research, little basic understanding of relevant tumor biology, little perception of the problems by the public or the medical professions, and little impetus to apply what was already known. Pessimism, apathy, and inertia were overcome by effective and dedicated leadership, massive infusions of money, and a few clear successes in treating certain previously untreatable cancers.

Cancer prevention has not received the same kind of leadership. Research in prevention (as distinct from research in carcinogenesis) has attracted little funding, and the few and limited successes in actual prevention of cancer seem not to have generated new interest and support. Further, by its very nature, prevention does not have the built-in constituency of supporters who believe that they (or their relatives or their friends) have benefited in a direct, important, and personal way from medical intervention in a condition that would otherwise have led to an early and unpleasant death. Nevertheless, disease prevention is now viewed with more favor than ever before, and this change will...
permit both research and service programs that could not have been undertaken in earlier years.

OTHER VIEWS

Recognition of cancer prevention as a legitimate scientific pursuit will not come easily, even (or especially) among clinicians dedicated to the clinical problems of cancer. Their views merit attention, though I believe that some of their conclusions are wrong.

For example, Martin (1) recently argued that: Even if a chemical is identified as a cause of cancer, will we be able to eliminate it from the environment? And will its elimination from industrial usage not likely result in its replacement by another carcinogen? . . . Similarly, for cancer, the major research effort must be directed toward the development of a therapeutic cure, since the goal of eliminating all cancer-inducing agents from the environment remains an obscure illusion.

In an editorial titled, “The Future of Cancer Control,” Frei and Frechette (2) concluded: It is our position that the most important next steps for the Cancer Control Program are to focus explicitly on the development of collaborative relations between community cancer-care systems and major cancer centers with investigational resources, as we are doing in New England, and to consider funding selected research projects that will support and facilitate the creation of true regional cancer-care systems.

The entire editorial discussed screening, treatment, and post-treatment care but included only one brief, oblique reference to prevention.

Djerassi (3), after noting that each year 20,000 Americans (out of some 700,000 with cancer) stand a chance of cure by chemotherapy, continues: But suddenly, in the midst of these momentous changes, we are told nothing has happened. Our revolution in therapy has passed unnoticed by some. Congressional leaders are demanding to know why ‘so little progress’ has been made in the seven years since passage of the National Cancer Act. Halberstam’s view (4) is that: All the people who prattle about how physicians should be ‘prevention-oriented’ would be sadly upset when, as it must to all men, illness finally settles upon them and the physicians they consult regret that they are ‘prevention-oriented’, but will try to stumble into a diagnosis. It is as dangerous to oversell the value of prevention now as it was to oversell curative medicine in the 1960’s, though, curiously enough, many of the same experts who did the latter are now pushing the former. And Israel (5) has written: No effort at prevention or detection will either eradicate cancer or make it curable . . . .

There will continue to be innumerable cases . . . . There is therefore an enormous need to discover better methods of treating tumors. Indeed, this is clearly the problem upon which we should concentrate our efforts. It would be an incomprehensible mistake to turn away from therapeutic research on the grounds that the progress we are making is slow.

Each of these views expresses an important truth. Cancer risks are widespread, diffuse, and likely to be difficult or impossible to control on an agent-by-agent basis. There is great momentum, generated by the research establishment as well as the traditional practice of medicine, toward more and better treatment rather than prevention. Past treatment successes do give us some reason to be optimistic about future, greater successes. Someone must provide medical care for persons who get the cancers that we do not or cannot prevent, both now and in the future. And prevention, alone, is no more likely to wipe out the threat of cancer than is screening, alone, or treatment, alone. Still I firmly disagree with any conclusion that cancer prevention will necessarily be so difficult, so incomplete, and so expensive that we should not look for promising opportunities.

CANCER SCREENING

The record of successes and failures in the screening and early detection of cancer is mixed and unclear, partly because there are few good data, demonstrably free of major biases, on changes in cancer morbidity and mortality that may be related to screening. The one generally accepted success is with cervical cytology, although even here some troublesome doubts remain because there has never been a clear-cut field demonstration that the Papanicolaou smear has led to reduced mortality from cervical cancer. In contrast, breast cancer screening, which is clearly of value for women past the age of 50, has been applied to younger women in the absence of any evidence of benefit; no value has been demonstrated in testing for occult blood in the stool or performing regular sigmoidoscopy to detect colon cancer; and several well designed clinical trials for the early diagnosis of lung cancer have not yet shown a reduction in mortality in the heavily screened groups.

Recent studies on screening for cancer of the urinary bladder provide several instructive lessons: High-risk groups can be identified (particularly workers in certain industries); easy and relatively inexpensive screening techniques are available; and a significant proportion of bladder cancers can be detected while they are still in situ and thus curable. However, long-term survival has not been improved by the screening because the only fully effective means of treatment is total cystectomy. This is drastic treatment indeed for noninvasive bladder neoplasms, many of which are likely never to progress to the point of invasion and metastasis. Total cystectomy carries an operative mortality as high as 10% even in good hands; it results in the complete loss of both urinary and sexual function;
and it is often followed by serious or lethal complications in the urinary tract. The limits to success in screening for cancer of the urinary bladder, as for some other forms of cancer, are not in the ability to detect the disease early but in the treatment that can be offered when cancer is found.

The total real cost of screening for any form of cancer may far exceed the cost of the screening procedure itself. For example, mammographic screening for breast cancer has led to increased radiation hazards, a marked increase in the number of biopsies and mastectomies for benign or in situ lesions that in themselves posed no serious long-term threat to life or health (though they may signal an increased risk for other, more serious lesions), and a considerable economic cost and personal distress associated with both false negative and false positive screening results. Similar problems exist in screening for occult blood in the stool. The high rate of false positives may lead to substantial morbidity and expense from the extra diagnostic procedures and follow-up required by each positive or doubtful test result.

In general, screening for early cancer has an important but currently limited role in reducing mortality. That role may grow over the coming years, but it is likely to grow slowly and in a limited and patchy way.

**CANCER TREATMENT**

After a clinically detectable cancer has developed, we are faced with the problems of treatment and its complications, post-treatment care, and rehabilitation. Advances in diagnostic evaluation, primary treatment, and rehabilitation have been numerous.

Unfortunately, however, overall cancer survival rates have not improved very much in recent years. Small improvements for persons 45 years of age and older and somewhat larger improvements for younger persons have been overshadowed by rising incidence rates, so that population-wide mortality is actually increasing. Much has been made of the fact that cancer survival has changed from one in five in the 1930's to one in three today. This is an improvement of about 13 percentage points (from 20% to 33%) over 40 years. The rate of improvement is now significantly slower than it was a decade or two ago, and except for Hodgkin's disease, leukemia, and perhaps cancer of the prostate gland, survival rates for persons at middle age and older seem to have reached a plateau.

An improvement of 13% is far from trivial, and it is particularly heartening that the greatest recent improvements have affected cancer in children and young adults. Nor is it trivial that we can help patients to survive longer, live more comfortably, and function better than they previously did. However, recent progress against the most common types of cancer has been slow, difficult, expensive, and not very striking. This progress has also led to its own problems, such as the induction of second cancers by drugs or radiation, the loss or impairment of important physical and metabolic functions, and enormous economic burdens.

Arguments that survival would immediately rise to 50% if people would just see their doctors earlier are also not very persuasive. The same could no doubt have been said 40 years ago, yet recent increases in public understanding of the symptoms and curability of cancer seem to have had little effect on overall survival rates. Despite the likelihood of continued small successes, I see no reason to believe that cancer mortality rates will be sharply reduced, at least for many years, by improved treatment.

**EVIDENCE THAT CANCER INCIDENCE CAN BE REDUCED**

There is widespread acceptance of estimates that 80-90% of all cancers in Western nations are caused by environmental factors. If one defines "environment" to include all factors that arise outside the human body, including elements of life-style such as smoking, diet, and alcohol consumption, these estimates are probably correct. There are two direct lines of evidence that controllable external factors are the major determinants of cancer risks. One line of evidence is temporal, the other is spatial.

The temporal evidence is based on careful long-term observations of cancer incidence and mortality in different parts of the world. When temporal changes in cancer incidence are observed and adequately verified, we must conclude that causative agents around us have also changed. Lung cancer has been increasing in part because of the increased use of tobacco. Leukemia has been increasing for reasons that are somewhat less certain. In Western nations, stomach cancer has declined sharply for unknown reasons, but the decline itself is sufficient evidence that environmental factors were important in the past. It is then reasonable to assume that environmental factors are still important in the cases which we continue to see and that they are still important in other populations that have not (yet) experienced a decline in incidence.

The spatial evidence that environmental factors are major determinants of cancer risks comes from studies of populations that have migrated. Thus we can compare cancer rates among various racial and ethnic groups in the United States, Canada, or elsewhere with rates in the geographic areas from which these groups or their ancestors came. We find, for example, that women of Japanese ancestry living in the United States have higher age-specific incidence rates for breast cancer than do women in Japan. Blacks in the United States have higher rates for prostate cancer and lower rates for liver cancer than blacks of similar ancestry living in Africa. Americans of Polish descent have less stomach cancer but more large bowel cancer than Polish nationals. Although migrants and nonmigrants may have genetic differences, it is hard to escape the conclusion that environmental differences, broadly interpreted, are responsible for many of the differing rates of cancer from country to country.

Of course, this does not mean that we know just which environmental factors are at fault or, even if we did know, that the environment could and should be
In many cases, the notions of the environment as the all-pervasive offender and of the individual as the unsuspecting or helpless victim must be modified to include an element of personal responsibility in cancer cause and prevention. Effective prevention will require a well-designed combination of individual protective action; generalized disease prevention (clean workplace, clean living environment, clean air, clean water); Government regulations and policies on taxes, farm production, health insurance, and workmen's compensation; and countless other activities. However, none of these factors is likely to have much impact on a broad scale without better knowledge of how to use them effectively.

To develop the kinds of knowledge needed for effective cancer prevention will require research on more than carcinogenesis, especially in fields not traditionally supported by any of the large cancer-oriented organizations. These fields include behavioral sciences, education, economics, sociology, law, and perhaps even the political process. It seems likely that substantial progress in understanding cancer prevention, as distinct from knowledge of cancer causation, will depend on increased research support to these fields. Of course, the work supported must be encouraged, developed, selected, conducted, and reported with the same attention to the rigors of the scientific method as work now supported in the so-called "hard sciences."

The distinction between research on causation and research on prevention is not the same as the distinction between basic and applied research. Understanding of cancer prevention may well require fundamental theoretical studies of, for example, processes in the modification of behavior that would be of value to people who want to quit smoking. Each discipline important in cancer prevention will probably need substantial support for a spectrum of activities from basic research to demonstration and service programs. Certainly, some research monies should be directed toward very pragmatic problems of doing something as soon as possible with what we already know, or may learn, about prevention.

OTHER EFFECTS OF CANCER PREVENTION

Many steps useful in cancer prevention will have other beneficial effects and might be justified on medical, social, or economic grounds that have nothing to do with cancer. The relationship of cigarette smoking to a variety of cardiovascular and respiratory diseases is well known. Ionizing radiation, even in low doses, is mutagenic, and it may have other harmful effects. Clean air, clean water, and clean places of work are not only desirable for reasons related to health, but they also have a strong esthetic appeal. Thus cancer prevention should be considered in the broader context of a comprehensive program of disease prevention and health maintenance.

Cancer prevention on a large scale will require, and can be used to promote, desirable changes in the health
care system of the nation from one based primarily on complaint-response to one based more on health maintenance. Our present system for cancer, as for most other health problems, is largely characterized by individual recognition of some problem followed by a personal decision to consult a physician or other practitioner, who then responds as best he or she can. This is a good system for some types of problems, such as accidental injury or minor infections. It is not a good enough system for cancer or for health problems in general. In addition to present health services we need systematic attention to the circumstances of life such as pollutants in our air and water and to our habits of daily living. We need periodic surveillance of individuals for conditions of abnormal or potentially abnormal risk as well as problems already present, and we need prompt investigation and treatment of significant, though perhaps asymptomatic, abnormalities. This approach to cancer prevention could well serve as a model or prototype for new initiatives throughout our entire health care system.

Major efforts to change dietary and smoking habits, encourage healthful exercise, and otherwise alter life-styles are being widely recommended. It is perhaps curious that many of the most effective advocates for changes in life-style have no formal medical training, and some have no scientific background at all. This had led to an unfortunate polarization that may not disappear by itself: Leaders in the well-recognized health disciplines may become more and more reluctant to participate in activities that have, by default, been left more and more to persons with other orientations. This could lead to unproductive feuding. What we need, rather, is a cooperative interchange among persons whose interests are primarily focused on prevention, screening, or treatment as we try to come to an optimum balance in emphasis, whether in research or in applications. The alternative may be a dual system of health activities in which the medical component of our present system is at odds with a newly developed professional group dedicated to prevention.

Therapists, screeners, and etiologists share a hope for some major breakthrough—a universal cure, a universal and specific test for early cancer, or a universal preventive such as vaccination against cancer. Imaginative research along these lines should be encouraged and supported, but breakthroughs cannot be produced on demand. The bulk of research support should continue to go to the case-by-case, site-by-site, step-by-step, trial-and-error development of stepwise advances that will lead to incremental improvements wherever we can make them. So far, cancer prevention has been largely excluded from this process.

REFERENCES
(3) DJERASSI I: Cancer cure: No longer a chimera. Medical World News, August 21, 1978, p 71