Changing Concepts Concerning Cancer

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THE UNITED STATES has manifested an unswerving dedication to the solution of the cancer problem. The National Cancer Institute Act of 1937 is a concrete demonstration of the conviction that the problem of cancer can and will be solved by scientific research.

One manifestation of progress in cancer research is that our concepts regarding cancer have not remained static. A whole series of changed and changing ideas and approaches has occurred during the past few years.

This, of course, is not surprising. All of medicine shares in the technological revolution of our times. Discoveries and opportunities are upon us at a rate that exceeds available resources of men, space, and time to exploit them. Cancer research certainly is not an exception.

I have selected a few concepts concerning cancer that seem to me to reflect the main streams of progress. I shall deal with them under three general headings: (*a*) some biological aspects, (*b*) some clinical aspects, and (*c*) some social aspects of cancer.

Some Biological Aspects

Cancer is not an entity, but a great class of diseases with distinct etiologies, pathogenetic stages, and, probably, distinct intracellular and subcellular mechanisms and reactions.

The distinct identity of different neoplastic reactions is well illustrated by two experimental tumor models in the mouse, the interstitial testicular tumor induced with estrogens and the adenomatous pulmonary tumor induced with urethan.

Figure 1 presents Howard Andervont's data (*1*) on the appearance of interstitial testicular tumors in BALB/c mice implanted subcutaneously with 5 mg. pellets containing 20 percent diethylstilbestrol in cholesterol. Each line represents a group of 50 to 75 animals. When the pellet is retained continuously testicular tumors appear in practically all mice, starting in about 7 months (line A). If the pellet is removed after 8 weeks, no gross tumors develop, although many testes have identifiable effects of estrogen months later (line B). When the pellet is removed after 8 weeks and reimplanted 24 weeks later, the reaction proceeds as indicated by line C. The appearance of tumors is parallel to the response to continuous stimulation, but is delayed by 24 weeks, the period during which estrogen was withdrawn. For this neoplasm, 8 weeks of estrogenic stimulus is insufficient. If the stimulus is withdrawn, the reaction neither progresses nor regresses, but stops at that stage, to resume without interruption upon the reintroduction of the stimulus.

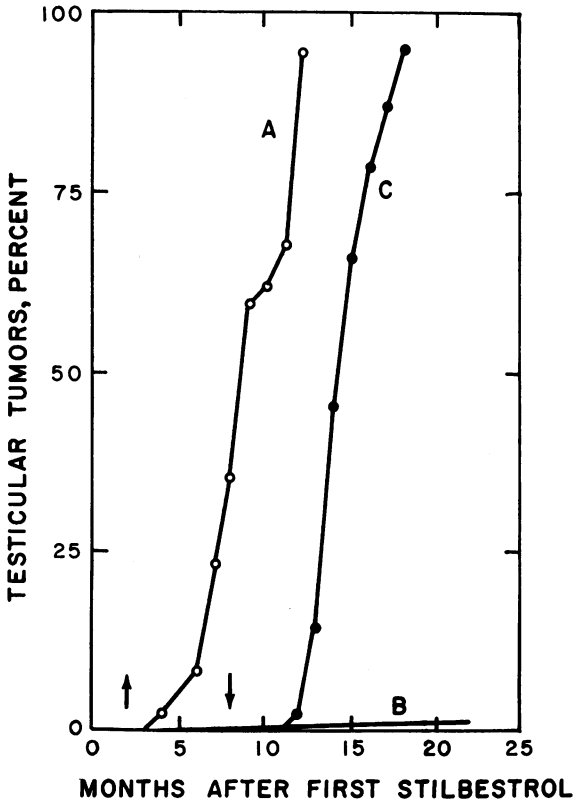
Figure 2 records the induction of multiple pulmonary tumors in strain A mice that received a single intraperitoneal injection of urethan, 1 mg. per gram of body weight (*2*). All mice had grossly visible multiple tumors within 3 months. Microscopically tumors are identifiable by the end of 3 weeks and all appear to have been induced by the end of 6 weeks. Urethan is degraded and excreted by the animal within a few hours. Analysis of the data indicates that this neoplastic reaction is induced and completed by a single brief exposure to a carcinogen.

Dr. Shimkin, associate director for field studies, National Cancer Institute, Public Health Service, *presented this paper at the Fourth National Cancer Conference, Minneapolis, Minn., September 13, 1960. The paper will be included in the forthcoming proceedings of the conference.*

The growth patterns of these two tumor entities are also quite distinct. The interstitial cell tumors, on the withdrawal of estrogen, may progress, regress, or remain stationary; in animals having tumors of both testes, the two tumors may behave in a diametrically opposite fashion. The growth of pulmonary tumors, on the other hand, appears to proceed regularly and is described by a progressive decrease in rate, probably because the cells toward the center of this organoid neoplasm divide at a lower rate than those toward the periphery. Both interstitial cell and pulmonary tumors can be transplanted and both develop occasional metastases, but these features also demonstrate biological differences.

It is difficult not to conclude that even if all neoplasms were eventually shown to be the effect of intracellular virus activation, different viruses are involved in the two processes. Or, if all tumors eventually were to be described in terms of desoxyribosenucleotide alteration, different changes are produced through different biochemical reactions.

Figure 1. Induction of interstitial testicular tumors in BALB/c mice implanted subcutaneously with 20 percent diethylstilbestrol-cholesterol pellets: A, continuous presence of pellet; B, pellet removed after 8 weeks; C, pellet removed after 8 weeks and reimplanted 24 weeks later



An important new concept of cancer is that many neoplasms are the end result of a long series of progressive changes and stages rather than being the effect of single mutation-like alterations endowing cells with immutable new characteristics. We owe this contribution primarily to the work of Berenblum on skin cancer, and of Furth, Gardner, and others on endocrine gland tumors. As with any other generalization regarding cancer, there are both exceptions to and modifications of this concept. The pulmonary tumor of the mouse may represent an example of a single-event induction.

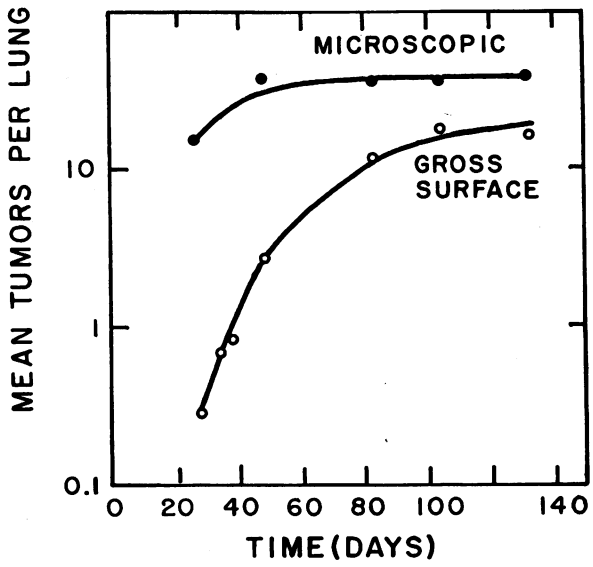
Closely related to the concepts of tumor progression and of environmental dependence is the question of whether neoplasms arise from single altered cells, or whether a population of cells has to be affected. It appears probable that here also no generalization can be made, and that examples of both mechanisms may exist.

Plasma cell tumors of the mouse exhibit specific individual electrophoretic patterns rather than the wide variety of patterns observed among plasma cells. This finding is interpreted by Potter and Fahey (*3*) as evidence that each tumor arises from a single plasma cell. In contrast, skin carcinomas evoked by ultraviolet radiation appear to involve the recurrent selective stimulation of a large population of cells (*4*).

Cancer can be defined as a disease of the cell that is transferred to the descendants of the cell (*5*). Yet in metazoan organisms a single cell is almost an abstraction, biologically meaningless without the interrelationship of the whole organism. A single cell that acquires the undefined characteristics of cancer is not the disease we call cancer until many cell generations later and until an interaction has taken place with the organismal environment.

One of the healthy developments in cancer research has been the increasing interest in the study of host-tumor relationships: changes that

Figure 2. Induction of multiple pulmonary adenomatous tumors in strain A mice injected once intraperitoneally with 1 mg. urethran per gram of body weight, as seen on the surface and as detected by microscopy of serial sections



tumors produce in the host and, perhaps, changes that have to occur in the host before a neoplasm can develop, grow, and metastasize.

There is an impressive list of biochemical alterations in animals and in man afflicted with a wide variety of neoplasms. The late Jesse Greenstein's observations on the decrease in catalase in the presence of tumors (*6*) falls into this category, and lactic dehydrogenase is one of the later claimants of our interest (*7*). Unfortunately, all these changes take place when the tumor process is advanced, and thus they preclude implications of tumor specificity or of diagnostic utility.

One limiting factor in these investigations may be simply the dilution effect of even a million neoplastic cells in a population of 10^{13} cells that comprise an adult human body, especially when the observations are made on tissue fluids or their end products. For this reason, investigations that bring the tumor-interphase-host area into closer focus are of great potential. The late Glenn Algire (*8*) attempted to achieve this with implanted transparent windows and diffusion chambers. The fate of hematopoietic cells implanted subcutaneously in diffusion chambers, as reported by Shelton (*9*) and by Petrakis (*10*) represent recent contributions of interest.

An interesting series of problems has resulted from the rediscovery that tumor cells can be found in the blood of a small but significant proportion of patients with cancer (*11*). The presence of tumor cells in the blood is not necessarily indicative of metastasis, just as the recovery of tumor cells in the operative field does not indicate that a local recurrence is inevitable (*12*). This is a forceful demonstration of the systemic factors of resistance that must exist in some patients against some neoplasms, factors that it will be fruitful to define. Also, it is excellent evidence that cancer cells and the diseases we call cancer are not the same thing.

The most active and promising recent trend in cancer research is the exploration of the viral etiology of tumors. Wendell Stanley's lucid plea at the 1956 National Cancer Conference (*13*) that for research purposes it be assumed that most, if not all, kinds of cancer, including cancer in man, are due to viruses, came at an appropriate time and fell on receptive ears. With typical American vigor, we have programed this approach on a national scale and have pledged support by seven-figure financial commitments over many years. Exciting findings are being made in this field of research at a rapid pace (*14*).

I should like to suggest that a Nobel prize for Peyton Rous is overdue. We should also honor that doughty small group who kept on working when viruses were not allowed in many a cancer research institution: Richard Shope, J. J. Beard, Ludwig Gross, Ray Bryan, and Sarah Stewart in this country, Gye in England, and Zilber in Russia.

This praise should not be interpreted as total agreement with the concept of the viral etiology of tumors. The data for such a position are still very incomplete. Even with most well-defined animal tumor viruses, the tumor may represent a relatively late, uncommon event, perhaps rarer than the development of paralysis after exposure to poliomyelitis virus. Tumor virus may be no more equivalent to neoplastic disease than is an individual tumor cell. Also, to some traditionalists, the intrusion of a virus into some carcinogenic responses to chemi-

cals and physical agents seems somewhat akin to the addition of x to both sides of an equation.

The only value in this argument is to maintain a balance between the investments being made in virus research and in the studies of chemical and physical carcinogens, especially the complex carcinogenic environments that are being revealed and clarified by epidemiologic research (*15*).

The epidemiologic method has two primary uses in cancer: the first is to define and to measure the occurrence and distribution of cancer in populations; the second is to test hypotheses of causation through studies on the interrelationships of various characteristics to cancer. The occupational scrotal cancer, known since 1775, was the forerunner of an impressive list of neoplasms attributable to environmental exposure to carcinogens. Such carcinogens are not limited to exotic industries, but exist in the air we breath, the water we drink, the food we eat, and some habits we cherish.

After a long period of relative quiescence, we are seeing a resurgence of epidemiologic studies on cancer. In this our British colleagues, Bradford Hill, Percy Stocks, and the late Ernest Kennaway have had preeminent roles.

Epizoology, the systematic study of the occurrence of neoplasms in animals, deserves much more attention than it is receiving at present. Almost 100 million cattle and other stock animals are slaughtered in this country every year. A steady rise of leukemia in cattle has become a problem of importance in Europe (*16*). Neoplastic diseases, particularly leukosis, cause one-third of the mortality among pullets and hens (*17*). Recently the northwestern fisheries became aware of a marked increase in the occurrence of hepatoma among older rainbow trout (*18*), a finding previously reported from northern Italy (*19*). Dogs and cats, domestic animals of closest proximity to man, develop many neoplasms. But our knowledge of neoplastic diseases among such animals is limited to anecdotal descriptions of sporadic cases. Unless we assume that man and his animal relatives inhabit unrelated universes, it is high time to begin the examination of the neoplastic interrelationships that must exist between different species and the environments they share. The name for this approach is ecology, which encompasses epidemiology, endemiology, and epizoology. The basic material for its studies is a defined population in a defined geographic environment; the basic methods are long-term observations and statistical analysis. In heart disease, Framingham, Mass., and in sociology, "Middletown," are the early prototypes; in cancer, Hagerstown in Maryland (*20*), Alameda County in California, and Erie County in New York may become as well known as some of our renowned laboratories and clinics.

It is my conviction that the development of the ecology of cancer to full stature should form the next large programmatic support area in cancer research.

Some Clinical Aspects

An important development in cancer research during the past few years has been the increasingly fuller participation of clinical investigations, so that now these represent more equal partnerships with the laboratory sciences. One of the many yields of this reorientation of approaches is that less is heard about the sterile semantic distinctions between fundamental and applied research. For indeed, investigations on man can be as fundamental as investigations on fruit flies; and from another viewpoint, all research on cancer is applied research by definition.

The rise of clinical investigations is attributable to several factors, not the least important being the financial support that now allows these expensive studies. However, the predominant reason is the acceptance by clinicians of rigorous scientific methods to a degree that was almost unthinkable only a decade ago (*21*). The statistical methods developed by Fisher, Gaddum, and others which converted agricultural and pharmacological research from a trial-and-error collection of impressions to exact experimental sciences now also form the requirements for clinical studies. We have learned of the need for unequivocal definitions and criteria and for meticulous experimental design; of the requirement of randomized controls and of the innumerable sources of bias that can be avoided by double-blind techniques; of the placebo effect, to which the investigator

is as liable as the subject; of the economy and safety contributed by sequential procedures; and of the biometrician who questions our plans, makes impossible demands, and finally doubts our interpretation of the results (*22*).

In these new frontiers of science, cancer research has played a significant part, especially in the field of experimental chemotherapy of cancer. This search has now been organized into a national commitment and an international effort of a scope and complexity for which it is difficult to find a parallel in the biomedical sciences (*23*). Among the many pioneers and leaders in the endeavor, the names of Sidney Farber, Alexander Haddow, Charles Huggins, and the late Cornelius Rhoads tower above the rest.

It should be emphasized that the national cancer chemotherapy program has in no way replaced or reduced other approaches in cancer research; in many instances, it has nurtured and supported them. Also, placing the chemotherapy program in the clinical section of this paper merely recognizes its direct clinical aim, which is but the last phase of investigations that have their roots in chemistry and pharmacology.

The number of chemicals and crude products that have been tested on mice and other animals bearing transplanted tumors now approaches 100,000, and over 100 materials have received clinical attention. The collected progress reports from the 150 collaborating institutions engaged in this aspect of the program have been published recently (*24*). It is sufficient merely to mention that at least 20 chemical agents already have gained a place in the clinical management of cancer, and in specific types of disseminated neoplastic disease some of these agents produce complete remissions that are maintained for many months. These effects are real but incomplete. Truly effective agents for the treatment of cancer are not to be found among the drugs now available, but await discovery in the future.

An interesting modification of the drug-testing program was the exploration of the use of chemotherapeutic agents as adjuvants to surgical resection performed with curative intent in gastric, rectal, and pulmonary cancer (*25*). The results are negative insofar as demonstrating any value of the specific chemotherapeutic addition to the specific neoplastic diseases is concerned. But the yield for the future is far from negative. The studies demonstrated how well a large group of clinicians can work together on problems beyond the capacities of any one investigator. It was demonstrated that potentially hazardous experimental procedures can be undertaken ethically on man, without compromising with scientific criteria. And it was demonstrated that the disciplined group requirements of such studies are entirely compatible with the individualistic private medicine that America espouses.

Another collaborative national effort to pool data for the evaluation of the results of treatment is the End Results Evaluation Program (*26*), which began at the 1956 National Cancer Conference. Because of this program we now have more reliable information on what happens to cancer patients.

While for the eventual future we are accentuating efforts in chemotherapy, we have to use and to improve the methods we have at hand, surgery and radiation. But even the most universally accepted procedures require periodic reexamination, because only in the treatment of skin cancer do we have any right to be satisfied with our results. Biometrically designed, controlled clinical trials are not limited to the testing of new drugs. Their application to many accepted forms of surgical and radiological treatment of cancer is long overdue.

A case in point is the radical mastectomy. The removal of the breast en bloc with the pectoral muscles and the axillary contents was devised 70 years ago. In almost all surgical centers in the United States, it is the only accepted procedure for cancer of the breast. A decade ago, some heretics began to publish their lack of conviction regarding the assumed benefits of this operation. Park and Lees (*27*), by deductive logic, and McWhirter (*28*), by canny Scottish empiricism, described their doubts in persuasive papers that could not be ignored. The emotional reaction that was aroused was not followed by a calm appraisal and recourse to scientific inquiry.

The table is a compilation of 5-year survival figures gathered by Deaton (*29*), to which has been added a series recently reported by Smith

and Meyer (*30*). These crude data allow no conclusion that simple mastectomy, with or without radiation, is or is not superior, inferior, or equal to the classical radical dissection. Unbiased data for acceptable evaluation simply do not exist. But the figures do suggest that such an evaluation would be useful. If the simple mastectomy yields all the benefits to be expected from the more hazardous, more deforming, and more crippling radical operation, or if the additional trauma of radiation does not improve the outcome, what medical, economic, or ethical justification is there to continue our traditional policies?

Two years ago the National Advisory Cancer Council recommended a rigidly controlled clinical trial of the radical mastectomy compared with the simple mastectomy, plus radiation and other ancillary procedures. The recommendation has not been accepted by our surgical organizations, and without such sponsorship a national study is impossible, if only for medicolegal reasons.

Breast cancer is the most common single neoplastic entity in the United States; more than 50,000 new cases are diagnosed annually, and of these more than 25,000 would be considered operable. But a small fraction of cases diagnosed during one year would be sufficient to mount a clinical trial that would allow us to replace clinical impressions with solid facts.

We are emerging from a period during which supraradical operations were being applied to a variety of neoplastic diseases. The acceptance of clinical chemotherapy is a manifestation of the disappointments of these heroic measures. It is now timely to reexamine not only the radical mastectomy for breast cancer, but also the pneumonectomy for lung cancer, the en bloc skin and lymph node excisions for melanoma, prophylactic neck dissections, and many other cherished techniques. It is time to recognize that without the test of a designed clinical trial the old dictum, "the smaller the cancer the larger the operation," may be an exercise in circular thinking.

There are also neoplastic diseases in which our usual therapeutic attack may not be sufficiently aggressive. The results in Hodgkin's disease reported by Vera Peters (*31*), for example, deserve wider study, and indicate that small doses of irradiation and alkylating agents are as contraindicated for clinically localized Hodgkin's disease as they would be for any other clinically localized cancer. Bloedorn's observations on radical preoperative radiation in lung cancer (*32*) also deserve further study.

Five-year survival rate for patients with breast cancer following radical and simple mastectomy

Type of mastectomy	Series of patients	Number receiving operation	Percent surviving
Radical	11	3, 279	54
Simple	7	905	59

SOURCE: Deaton (*32*) and Smith and Meyer (*33*).

Some Social Aspects

Laboratory research on cancer is sterile unless eventually some of its results can be applied to man. Clinical research also has not been fully developed until its fruits are applied to the whole population. In turn, these applications generate problems that need to be brought back to the laboratories and clinics. Furthermore, problems of public health, sociology, and economics are as relevant to some aspects of cancer as the chromosomal structure of neoplastic cells, and are equally demanding of the use of the scientific method.

Cancer research has made a number of advances for which the dramatic word "breakthrough" is entirely appropriate. But a breakthrough is only potential unless it is exploited. There are two such areas in which significant results in the control of cancer could be achieved if our knowledge were more fully utilized.

The first breakthrough is in vaginal cytology. It is now over two decades since Papanicolaou placed in our hands a method of detecting cancer of the uterine cervix at the preinvasive stage, when it is entirely curable. The importance of cytology is not as a diagnostic aid but as a detection method, by means of which preinvasive cancer is discovered well in advance of clinical symptoms or signs. Its full potential is reached only if it is used as a screening method on large populations.

Figure 3. Frequency of intraepithelial and invasive carcinoma of the uterine cervix in two successive screenings: combined data from Memphis, Madison, and San Diego

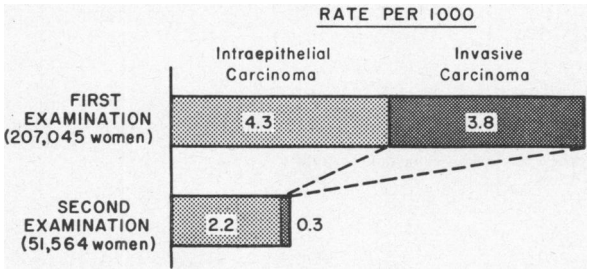


Figure 3 shows what happened in three populations, Memphis, Madison, and San Diego, where 200,000 women were examined (*33*). The preinvasive lesion was found in 4.3 women per 1,000, and in 3.8 women per 1,000 an invasive cancer was found, usually symptomless and unsuspected. When a portion of these women were reexamined 1 to 2 years later, the frequency of the preinvasive lesion was reduced by half, to 2.2 per 1,000; these presumably are new lesions that arose during the period between examinations. The important finding, however, was that invasive cancer dropped to 0.3 per 1,000 or to one-tenth of the frequency at the first examination. The inference is inescapable that a substantial proportion of the mortality from cervical cancer could be eliminated if the cytological test were available and were performed annually on all women, and if appropriate therapy were instituted. This neoplastic entity now accounts for some 10,000 deaths per year.

But how many women actually undergo this examination regularly? What logistic planning is going on to create the necessary facilities? What public health education is being organized to teach women that a cytology test is as important as a permanent? The size of the problem of screening 30 to 50 million slides per year indicates that mechanical means of analysis, such as the cytoanalyzer, must be developed, and that self-obtained smears (*34*) that could be sent through the mails must be accepted as a collection method supplemental to specimens obtained in doctors' offices.

No cytoanalyzers will be made until there is a demand for them, and communitywide cancer cytology centers will not become universal until physicians take an active lead. The experience in San Diego (*35*) demonstrates that this can be done with the control and management being retained by private physicians. Once again we have evidence that public health and preventive medicine are entirely compatible with private medical practice, but the "block and don't tackle" tactic as an answer to medical and public health problems is compatible with neither.

The findings in cervical cancer have a more general implication, as a demonstration that curable cancer is symptomless cancer. The experience of the University of Minnesota Cancer Detection Center with 9,000 persons examined since 1948, as recently reported by Sullivan (*36*), forcibly reiterates the lessons Elise l'Esperance tried to teach us years ago. An increasing number of industries have accepted the fact that periodic examinations of their executives are a good investment. It is just as good an investment for everyone else. Again, the logistics of the situation simply are not met by the wishful slogan, "Every doctor's office a detection center." Physicians must meet the need, through voluntary action at the community level.

The second unexploited breakthrough in cancer research is the establishment of the fact that tobacco smoking causes a significant proportion of malignant neoplasms of the lung, larynx, and oral cavity.

Figure 4 presents data of the classic Hammond and Horn (*37*) study on the relationship of smoking to mortality among 180,000 men. It is taken from a recent paper by Joseph Berkson (*38*) that forms a part of a valuable Mayo Clinic symposium on the effects of tobacco smoking in man. His interpretations of the findings, however, are somewhat at a variance with mine. The many statistical investigations, all coming to the conclusion that smoking and lung cancer are associated, the extensive laboratory experiments that establish the presence in tobacco smoke of at least 10 chemicals with carcinogenic activity in animals, the careful pathological observations of human material, and the pathophysiological studies on the effect of tobacco smoke on the bronchial epithe-

lium have been thoroughly reviewed and analyzed by many national and international committees (*39*).

It all adds up to this: If tobacco smoking, at least in the form of cigarettes, were terminated, the annual mortality from lung cancer could be reduced by more than 60 percent, a saving of at least 20,000 lives in the United States alone.

Tobacco is considered neither a food nor a drug, and it appears to be immune from all regulations except taxation. Therefore, apparently more can be done to protect the population from rat goiterogens in berries and from hepatomas in fish, where the dangers for man are at most theoretical, than from a product with demonstrably deleterious effects for man. Accepting the theory that it is a constitutional right to choose one's poison, does this right extend to children?

Figure 5, taken from a recent analysis by Lombard and Snegireff (*40*), shows that the earlier smoking is begun, the higher the eventual prevalence of lung cancer. The facts recorded here cannot be ignored.

The problem is immense, with social and economic ramifications that require the judicious consideration of many elements of society in addition to the medical profession. But first it requires that physicians and scientists concerned with health recognize that smoking is a serious public health problem. Our convictions are known by our actions: not smoking in public and before youngsters and prohibiting smoking in hospitals and clinics, including doctors' lounges, may be powerful medicine.

Figure 4. Age-adjusted death rates for various disease groups in relation to amount of smoking

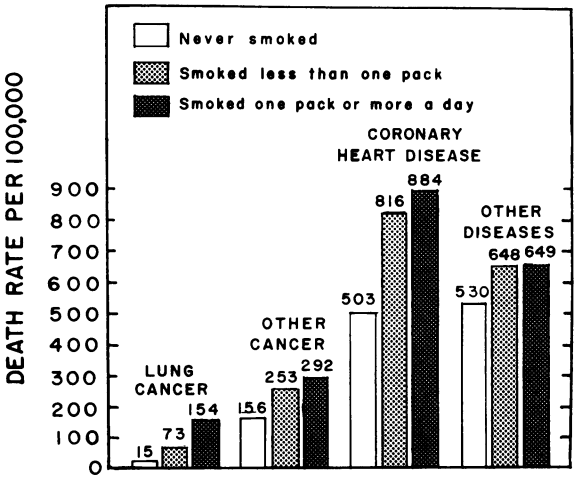
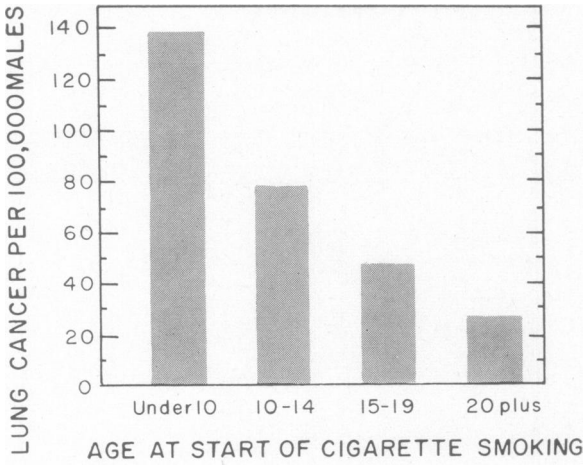


Figure 5. Prevalence of lung cancer per 100,000 males in relation to age at which cigarette smoking was started



Last, but certainly not least, mention should be made of the change in the attitude of physicians toward patients with cancer that is beyond surgical or radiological intervention. During the preantibiotic days, clinicians who made detailed daily notes on patients with subacute bacterial endocarditis or tuberculous meningitis, then rapidly and universally fatal, had little interest in patients with recurrent neoplastic disease. Now the course of patients with progressive cancer is of increasing clinical interest. This is of definite benefit to both the patient and the physicians. It is also an effective preventive to the despairing recourse to charlatanism.

The social and economic problems of cancer patients, however, have remained much the same. Two-thirds of all patients diagnosed as having cancer die of or with their disease, after long, expensive treatments that debilitate the purses and the hearts of their families. The lingering death of a cancer patient at home leaves unhealing psychological wounds. The topic of terminal care is important but unglamorous and requires more attention than it receives.

One approach that would help to alleviate the inevitable problem of the care of patients with

terminal cancer is the greater use of such patients in research. Perhaps this would also hasten the fulfillment of the promise made by that time-tested prophet H. G. Wells (*41*) in 1927: "The disease of cancer will be banished from life by calm, unhurrying, persistent men and women, working with every shiver of feeling controlled and suppressed, in hospitals and laboratories, and the motive that will conquer cancer will not be pity nor horror; it will be curiosity to know how and why."

Our present concepts concerning cancer must remain fluid, susceptible to responsive modification on the basis of new information. Cancer research has no place for fixed concepts, for vested interests, for orthodoxy. But we can stand firm on this: cancer is a solvable problem, within the capabilities of human intelligence using a human thought and action process we call scientific research.

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Hospitals for Indians

A new 38-bed hospital at Keams Canyon, Ariz., and a 50-bed hospital at Kotzebue, Alaska, have recently been completed as part of the Public Health Service's Indian health program.

The Keams Canyon hospital replaces an outmoded facility on the Hopi Reservation and will serve patients from both the Hopi and Navajo tribes. The Kotzebue hospital, which replaces a 15-bed nonfireproof unit built in 1930 and a 24-bed quonset hut, will serve more than 7,500 Alaska natives, mostly Eskimos.

In South Dakota, the Rosebud and Pine Ridge hospitals serving the Sioux have been modernized and enlarged.

Since 1955, when the Public Health Service was given responsibility for the program, 5 new hospitals and 15 field health centers have been constructed, and 10 hospitals have been modernized and enlarged.

Preventive, curative, and rehabilitative services are provided by the 52 Indian hospitals, 22 health centers, 18 school health centers, and several hundred health stations on the reservations. In 1960, admissions to the Indian hospitals totaled 56,900, and 900,000 outpatient visits were made to all Indian facilities.