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Received November 6, 1980; accepted January 21, 1981.
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This article was commissioned as a report to the Office of Technology Assessment, U.S. Congress, to provide background material for their assessment of "Technologies for Determining Cancer Risks From the Environment" (OTA, 1981). It will be republished, by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback.

Acknowledgments

First and foremost, we wish to thank Mrs. Virginia Godwin for her assistance in preparing this report, and we are particularly indebted to Eugene Rogot, of the National Heart, Lung, and Blood Institute, for making available to us the data from the study of a quarter of a million U.S. veterans. Robert Fensterheim abstracted the cancer mortality data from 1953-78 from Government publications, and a tape of these data is available from R. Peto. The staff of the Populations Division of the Bureau of the Census provided corrected U.S. population estimates from 1950, Irene Stratton and Richard Gray analyzed the mortality data, and Cathy Harwood drew the figures. The Surveillance, Epidemiology, and End Results section of the Biometry Branch of the National Cancer Institute and the New York and Connecticut tumor registries kindly provided us with access to cancer incidence data. Finally, we wish to thank the dozens of known or anonymous scientists who, through us or through the Office of Technology Assessment, scrutinized and offered helpful criticism of previous versions of this report.

ABBREVIATIONS USED: ACS = American Cancer Society; AF2 = 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide; CPEAP = Committee on Prototype Explicit Analyses for Pesticides; DAB = p-dimethylaminoazobenzene; DES = diethylstilbestrol; DMBA = 7,12-dimethylbenz(a)anthracene; EPA = Environmental Protection Agency; GESAMP = Group of Experts on the Scientific Aspects of Marine Pollution; IARC = International Agency for Research on Cancer; ICD = International Classification of Diseases; NAS = National Academy of Sciences; NCI = National Cancer Institute; NIOSH = National Institute of Occupational Safety and Health; NIEHS = National Institute of Environmental Health Sciences; OSHA = Occupational Safety and Health Administration; PVC = polyvinyl chloride; SEER = Surveillance, Epidemiology, and End Results program of NCI; SNCS = Second National Cancer Survey; TNCS = Third National Cancer Survey; TSSC = Toxic Substances Strategy Committee; WHO = World Health Organization.
ABSTRACT—Evidence that the various common types of cancer are largely avoidable diseases is reviewed. Life-style and other environmental factors are divided into a dozen categories, and for each category the evidence relating those particular factors to cancer onset rates is summarized. Where possible, an estimate is made of the percentage of current U.S. cancer mortality that might have been caused or avoided by that category of factors. These estimates are based chiefly on evidence from epidemiology, as the available evidence from animal and other laboratory studies cannot provide reliable human risk assessments. By far the largest reliably known percentage is the 30% of current U.S. cancer deaths that are due to tobacco, although it is possible that some nutritional factor(s) may eventually be found to be of comparable importance. The percentage of U.S. cancer deaths that are due to tobacco is still increasing, and must be expected to continue to increase for some years yet due to the delayed effects of the adoption of cigarettes in earlier decades.

Trends in mortality and in onset rates for many separate types of cancer are studied in detail in appendixes to this paper. Biases in the available data on registration of new cases produce apparent trends in cancer incidence which are spurious. Biases also produce spurious trends in cancer death certification rates, especially among old people. In (and before) middle age, where the biases are smaller, there appear to be a few real increases and a few real decreases in mortality from some particular types of cancer, but there is no evidence of any generalized increase other than that due to tobacco. Moderate increases or decreases due to some new agent(s) or habit(s) might of course be overlooked in such large-scale analyses. But, such analyses do suggest that, apart from cancer of the respiratory tract, the types of cancer that are currently common are not peculiarly modern diseases and are likely to depend chiefly on some long-established factor(s). (A prospective study utilizing both questionnaires and stored blood and other biological materials might help elucidate these factors.)

The proportion of current U.S. cancer deaths attributed to occupational factors is provisionally estimated as 4% (lung cancer being the major contributor to this). This is far smaller than has recently been suggested by various U.S. Government agencies. The matter could be resolved directly by a “case-control” study of lung cancer two or three times larger than the recently completed U.S. National Bladder Cancer Study but similar to it in methodology and unit costs; there are also other reasons for such a study.

A fuller summary of conclusions and recommendations comprises the final section of this report.—JNCI 1981; 66:1191-1308.
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The percentage of today's fatal cancers that might, by suitable preventive measures, have been avoided is subject to some dispute. Indeed, the percentage avoidable by certain particular categories of preventive measure is subject to such vigorous dispute that the non-specialist (to whom the present review is addressed) may wonder whether research has yet discovered any solid facts at all about the avoidance of human cancer.

The truth seems to be that there is quite good evidence that cancer is largely an avoidable (although not necessarily a modern) disease, but, with some important exceptions, frustratingly poor evidence as to exactly what are the really important ways of avoiding a reasonable percentage of today's cancers. Perhaps because of this uncertainty, the number of different areas of current research into hypothetical ways of avoiding cancer is enormous. As a convenient framework in which to seek an overview of them all, we have divided the various hypothetical ways of increasing or decreasing cancer onset rates into a dozen groups, and for each such group we have attempted to review what is known about the percentage of current U.S. cancer deaths that might thereby be avoidable.

In some groups (e.g., smoking habits) the quantitative knowledge already available is quite reliable, whereas in others (e.g., dietary habits) it is not, and we have had to fall back on reviewing various current lines of research whose eventual outcome is still unknown. The "percentages" (of current cancer mortality thus avoidable) that we eventually cite for the separate groups are therefore not really comparable with each other. Some are fairly precisely known, whereas others are much less so. More importantly, some relate to quite specific preventive measures on which action would, at least in principle, be possible on present knowledge alone, whereas others relate to preventive measures (e.g., modification of dietary factors) where the changes that would be beneficial have not yet been reliably characterized. Moreover, even if two particular agents (e.g., asbestos and sunlight) happen to account for a similar percentage of all cancer deaths, that which is the more easily controlled is obviously of greater public health significance. Despite all these drawbacks, the "percentages" that we have attributed to each way or group of ways of avoiding cancer remain for us a useful summary of certain facts, and the estimation of those "percentages" remains a convenient way of structuring our review of the quantitative information that is already available or is emerging about the determinants of human cancer.

Our report consists of a review of the evidence that cancer is largely an avoidable disease, a review of recent upward or downward trends in the onset rates of various types of cancer, a review of our reasons for preferring an epidemiological rather than a laboratory-based approach to the quantitative attribution of human risk, and then a dozen separate sections, one on each of the possible ways or groups of ways of avoiding cancer. The final section then summarizes and brings together our principal conclusions. We have relegated most of our detailed discussions of trends and certain other matters to appendixes, for although these details might be of interest to the specialist, our principal aim has been to explain matters to interested non-specialists. Of course some isolated pockets of detail remain in the text, but we have used paragraph subheadings fairly liberally throughout in the hope that wherever any reader feels the amount of detail excessive a few pages can be skipped without losing the general sense of our argument.

Finally, following Russell (1946), a few words of apology and explanation are called for, chiefly addressed to the specialists on the various subjects we touch on. Most of these subjects, with the possible exception of tobacco, are better known to some others than to us. If reports covering a wide field are to be written at all it is inevitable, since we are not immortal, that those who write them should spend less time on any one part than can be spent by someone who concentrates on a single subject. Some, whose scholarly austerity is unbending, will conclude that reports covering a wide field should not be written at all, or, if written, should consist of chapters by a multitude of authors. There is, however, something lost when many authors cooperate. If any balance is to be achieved between the findings in laboratory experiments and the distribution of disease that actually occurs in the population as a whole, and if the major and minor causes of death are to be seen in proper perspective, then the various aspects should be synthesized in a consistent way, which would have increased in difficulty exponentially with the number of authors.
they lead people to smoke, drink, overeat, or enjoy some other harmful habit. In this respect it is perhaps relevant that studies of patients in mental hospitals provide no evidence of unexpected risks (Clemmesen and Hjalgrim-Jensen, 1977; Baldwin, 1979). Likewise, it might perhaps be that some form of immunological surveillance normally controls the development of certain types of cancer so that failure of such control would affect the onset rate of such cancers and that environmental factors affect the likelihood of such failure, but for the present this is all too speculative to quantify, as is the suggestion that some non-specific generalized effects of “aging” may be relevant.

6. SUMMARY AND CONCLUSIONS

Trends

Examination of the trends in American mortality from cancer over the last decade provides no reason to suppose that any major new hazards were introduced in the preceding decades, other than the well-recognized hazard of cigarette smoking, which has extended from men to women, and the cause (whatever it may be) of the increase in melanoma. Among people over 65 years of age there are increases in recorded mortality (especially among the very old) from brain tumors and from some other types of tumor which are not mainly due to smoking, but these apparent increases among the old may chiefly reflect progressive improvements in the accuracy with which the causes of death of old people are recorded (appendix C) due not only to better medical technology but also, in large part, to better medical care for the elderly. Among people under 65 years of age, most of the trends in recorded mortality are downward, those for adults under the age of 45 being particularly favorable, which bodes well for the future. Some decreases are due to improved treatment (for example, in the case of Hodgkin’s disease) while some are for unknown reasons (as in the case of cancer of the stomach) but cannot be accounted for by improvements in the outcome of treatment.

Trends in recorded incidence rates (in which both fatal and non-fatal cases of cancer are counted) are difficult to interpret because of the difficulty of allowing for the effects of more complete registration and of more screening. The latter is liable to create spurious increases due to the classification as cancer of borderline cases, some of which would never have presented as clinical cancer within the subject’s lifetime (as, for example, has probably happened in the case of cancer of the prostate or breast). These difficulties are substantial when we compare recorded cancer incidence rates now with those a quarter of a century ago in particular registries, and other difficulties of non-comparability appear to affect the comparison of the Second National Cancer Survey (1947–48) and Third National Cancer Survey (1969–71) with each other or particularly with the SEER program which has succeeded them. For a few of the less common types of cancer, large improvements in curability have occurred, and it is reasonable to hope that improvements will be demonstrated for breast cancer and perhaps for certain other common types of cancer as well. However, the apparent moderate improvements in 5-year relative survival rates over the past quarter of a century are, of course, themselves in part an artifact due to the same changes (in the completeness of case registration and in the nature of the lesions that are diagnosed) that have affected recorded incidence data. Consequently, as we are not convinced that changes in treatment have materially affected the outcome of most of the major types of potentially fatal cancer, it seems to us wiser for most types of cancer to estimate the real trends in disease onset rates chiefly from the recorded trends in mortality since 1950 among people under the age of 65. However, we look forward to the time when the SEER program will provide a sufficiently long and uniform series of data for trends in incidence to be assessed independently of mortality.

The fact that lung cancer rates in the United States, in comparison with those in other countries, are, if anything, somewhat lower than might be expected simply on the basis of the number of cigarettes Americans consume (appendix E) and the lack of any apparent overall upward trends in cancer other than those due to tobacco do not, of course, guarantee that apart from tobacco all is well. Indeed, although some thousands of Americans every year are now dying of asbestos-induced cancer, this public health disaster cannot be clearly seen in the national trends (except...
perhaps for the still rare asbestos-induced mesotheliomas), so an analysis of trends is clearly a crude tool. We have dwelt on it at length merely because so many people mistakenly believe most cancer onset rates to be rising rapidly and because that belief may in turn be a cause of mistaken priorities in cancer prevention.

Current Causes

The estimates of risk attributable to different classes of environmental agents that we made in section 5 are brought together in table 20. The sum of the estimates is less than 100% despite the fact that some agents interact with one another to produce the disease in the way described in section 4.4. When this happens, the removal of either factor may have almost as much effect as the removal of both so that a few avoidable cancers are counted twice. The sum would, however, have been a good deal more than 100% if it had been possible to characterize the unknown factors referred to in section 5.12. The firmest estimates in table 20 relate to the effects of tobacco, alcohol, and geophysical factors, while by far the largest estimates relate to tobacco and diet.

Similar but less detailed sets of estimates which have been made previously by Wynder and Gori (1977) and by Higginson and Muir (1979) are summarized in table 21. Both sets refer to cases rather than to deaths and hence attribute larger proportions to sunlight than does table 20, and Higginson and Muir refer to "lifestyle" rather than to diet, meaning by it, however, factors "such as lack of dietary fiber, excess fat and caloric intake, and possibly hormone carcinogenesis." Despite these differences, the patterns described in the three sets of estimates resemble one another reasonably closely, except that we have preferred not to try to force the total to add up to 100%.

Tobacco

Returning to our table 20, the only cause whose effects are both large and reliably known is tobacco, which has been accounted for about 120,000 cancer deaths in 1980, a figure that will probably account for between 130,000 and 140,000 U.S. cancer deaths in 1981. Although it appears inevitable that the percentage of U.S. cancer deaths due to tobacco will continue to rise for at least a few more years, reaching about 33% by the mid-1980's, non-prohibitive legislation (and the other sources of changes in public awareness discussed in section 5.1) may materially reduce national cigarette usage, while changes to lower tar cigarettes can materially reduce the risk per cigarette. Because of the likelihood of such changes cannot be foreseen, longer term prediction of the percentage of U.S. cancer deaths ascribable to tobacco is not reliable. These estimates of the effects of smoking are subject to some small uncertainty because there may be some misdiagnosis of lung cancers as other cancers and vice versa and also because of the need to generalize from the experience of samples of the non-smoking population (whose diet, occupation, and socioeconomic status may not be typical of the country as a whole) in order to estimate the small number (≈12,000) of lung cancers not due to tobacco which must be subtracted from the large number (≈100,000) of U.S. deaths attributed each year to cancer of the lung. Both qualifications are well recognized. Neither affects the validity of the conclusion that smoking is a cause of a large proportion of all cancer deaths, which is based on massive evidence from many sources. They do mean that it is impossible to be sure of the exact attributable risk. However, the current figure cannot be less than 25% or more than 40%. Cigarette smoking also causes many deaths from causes other than cancer, so there are unlikely to be any substantial hidden dangers in its avoidance. The most important area of uncertainty, which could be addressed by the large case-control study of lung cancer which we have recommended, concerns the relative effects of the various low-tar and other types of cigarette. If, as we suspect, the hazards of long-term use of low-tar cigarettes are smaller relative to high-tar cigarettes than is suggested by the report of the Surgeon General (1981), this might be of great public

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Table 21—Proportions of cancer cases attributed to various different factors by other authors

<table>
<thead>
<tr>
<th>Factor or class of factors</th>
<th>England, Birmingham region, based on Higginson and Muir (1979) Male</th>
<th>Female</th>
<th>United States, based on Wynder and Gori (1977)* Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>30</td>
<td>7</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>Tobacco/alcohol</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Diet</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Life-style</td>
<td>30</td>
<td>63</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Occupation</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Sunlight</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Ionizing radiations</td>
<td>1</td>
<td>1</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Exogenous hormones</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Congenital</td>
<td>2</td>
<td>2</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Unknown</td>
<td>15</td>
<td>11</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

* Deduced from histograms. Non-environmental factors equated with congenital and unknown.
health significance, yet reliable information remains elusive.

**Diet**

We have attributed the largest risk to dietary factors for reasons that are discussed in detail in section 5.3. It must be emphasized that the figure chosen is highly speculative and chiefly refers to dietary factors which are not yet reliably identified. Experimental findings and human observation alike provide many indications that dietary factors are of major importance in determining the risk of cancers of the gastrointestinal tract, some cancers of the female sex organs, and epithelial cancers in general, but there is as yet little decisive evidence on which firm conclusions can be based. From our review in section 5.3 of various current lines of research into dietary factors, it is probable that the most important would turn out to be not the ingestion of traces of powerful carcinogens or precarcinogens (although these should certainly be guarded against) but rather nutritional factors, ranging from gross aspects of diet to vitamins, trace elements, and other micronutrients which may either enhance or inhibit carcinogenesis. (If any minor components of diet do indeed materially reduce cancer risks, then their discovery might be of more immediate practical value than the discovery of harmful factors, for prescription may be more rapidly acceptable than proscription.) Several promising hypotheses have been developed sufficiently clearly for them to be tested in practice, and more definite evidence should be obtained within the next decade or two, especially if large, randomly controlled evaluations of certain of the more promising methods of intervention are undertaken. [Baird's (1979) plea that preventive measures be evaluated by scientific criteria as strict as those for laboratory science has our full support.]

**Other Factors**

None of the other factors in table 20 can approach the importance of tobacco or the probable importance of diet. One of the larger remaining percentages, however, relates to those aspects of sexual and reproductive behavior that affect the incidence of cancers of the breast, reproductive, and genital organs. The figure cited allows only for the known effects of sexual experience and the favorable effects of pregnancy on the incidence of cancer in women, but it is not impossible that some aspects of sexual behavior also affect the risk of cancer of the prostate and perhaps of the testis in men by, for example, infection or modification of hormonal secretion. For males, however, other determinants of hormonal status may be more important, and in the absence of clear leads the reasons for the variation in the incidence of specifically male cancers have been classed here as “unknown.” It cannot, of course, be expected that sexual behavior and reproduction will be much influenced by knowledge that they are likely to affect the incidence of cancer decades hence. When, however, we have more detailed knowledge of the ways in which the various diseases are produced, it may prove possible to diminish the risks by preventing infection, stimulating or inhibiting hormonal secretion, or modifying its effects.

The proportion of cancers that we have attributed to the specific hazards of occupation, pollution, the use of industrial products, medicines, and medical procedures are individually small. That does not, of course, imply that some of them are not of immense importance to sections of the population on whom the risks are concentrated, but it does mean that their control will have relatively little effect on the total incidence of cancer in the whole country. The uncertainties in our estimates have been emphasized, and a large case-control study of lung cancer could greatly reduce the uncertainty in the proportion of cancers currently ascribable to occupational factors in particular as well as perhaps identifying and therefore controlling more rapidly than might otherwise be the case some hitherto unrecognized occupational hazards. Once recognized, occupational hazards can usually be reduced or eliminated by immediately practicable means, which makes their identification particularly valuable. It is odd that despite the resources that are currently being devoted to laboratory tests of chemicals and regulation of occupational factors so little effort is being made to observe in a systematic way what is actually happening to the large numbers of people who might be at risk.

**Future Causes**

Our estimates of the small proportions of current cancer mortality due to occupation, pollution, etc., relate, of course, chiefly to those factors for which it has been possible to secure some direct evidence of an effect on humans. Many substances have begun to be used in recent years that are mutagenic to bacteria and carcinogenic in one or more species of laboratory animals. How far exposure to these substances will contribute to the production of cancer in humans in the future is a matter for speculation. On general biological principles, which we have discussed in section 4.2, it must be assumed that some (though not all) of these substances will involve a risk of cancer and, even though the doses to which humans are exposed are commonly minute in comparison with those used in laboratory experiments, this is not always the case and some harmful effects must be anticipated.

Cancer in humans is seldom produced until 10 or 20 years after exposure to the carcinogenic agent begins, and even then the risk may be extremely small in comparison with what it would be if exposure were to continue for several more decades. The human evidence that is currently available does not allow us to express any confident opinion about the extent of the harm that the introduction of these substances may or may not do in the future. The trends that are being recorded do not, however, suggest that the United States (or Britain; see Doll, 1979b) is beginning to experience an epidemic of cancer due to new factors.
Indeed, were it not for the effects of tobacco, total U.S. death rates would be decreasing substantially more rapidly than they already are, and we are more encouraged by the benefits that are already being demonstrated from the control of known causes of cancer and other disease than we are dismayed by the appearance of new ones.

The intelligent use of laboratory tests should provide a powerful means for the prevention of new hazards in the future. It will, however, be difficult to use them confidently until we have more exact knowledge of the mechanisms of human carcinogenesis and of the various different classes of factors which can accelerate or retard these mechanisms. Reliable quantitative prediction of human risks from animal or other tests is not yet practicable and may not become so for several years yet. However, the use of particular tests to establish approximate priorities for action on the few agents which by that test seem most dangerous (as discussed in section 4.2) may already be practicable, as should the establishment of a routine large-scale ongoing case-control study (presumably through the SEER program) on lung and perhaps some other type(s) of cancer. Such a study would provide objective data on new and old occupational hazards, on the relative effects of various supposedly less hazardous cigarettes, on "passive" smoking, and on trends in lung cancer among non-smokers.

Future Role of Epidemiology

The one trouble with any such studies is that the questions they answer are only those already posited. It may be no bad thing to answer these, but it should be obvious from our review of current lines of research (especially, perhaps, with respect to dietary factors) how far current cancer research may be from even knowing the right questions to ask. The present need, therefore, is for circumstances that will favor inquiry into all sorts of future questions without present knowledge of what these questions will be.

One useful recent development has been the establishment of a U.S. National Death Index, which greatly facilitates the task of the epidemiologist who wishes to ascertain the dates and causes of death of particular groups of people. Such a facility should be conveniently available to all bona fide medical research workers (both in clinical trials and in epidemiology), should not be dependent on financial support from each separate state, and, if possible, should be extended back to at least 1968 to allow assessment of the relevance of smoking, dietary, reproductive or, especially, occupational circumstances that have been recorded in earlier decades. Safeguards for citizens' privacy are understandably becoming increasingly stringent, but in any legislation or discussions of ethical matters special provision should be considered to exempt from restriction the legitimate needs of bona fide medical research workers for confidential access to causes of death (and medical records of non-fatal illnesses) of named individuals, and for confidential access to data on occupation, residence, and exposure to medical agents. (See, for example, the report of the Subcommittee on Oversight and Investigations, 1980.) Such facilities have long been in use in Britain and Scandinavia, and we know of no example of any serious abuse resulting from this provision of data for epidemiological purposes.

Another large step toward facilitating the quick epidemiological testing of novel hypotheses would be the establishment for public use by bona fide medical research workers of a "bank" of blood and perhaps other biological samples 46 (and open-ended questionnaires 77) from at least a few hundred thousand apparently healthy people whose names would be linked to the National Death Index. Small aliquots of the blood of people dead from one particular cause could then be sold off to research workers (together with aliquots of control samples) for quick case-control studies. The freedom of speculative epidemiologic inquiry that this facility could confer might well transform the epideiologic study of both neoplastic and non-neoplastic causes of death. Many such banks of specimens already exist, some of which are too small, some of which have been underexploited, and some of which have already been very fruitful in totally unexpected directions; however, no large bank of such samples is publicly available for use by all bona fide epidemiologists with the funds to buy small aliquots from it.

We have noted elsewhere (section 4.3) why a chiefly epidemiological approach is necessary for our present limited aim of a quantitative perspective. More generally, however, if we want to identify ways of preventing substantial proportions of cancer, then two main strategies are possible.

46 The ideal would be to obtain (and store, identified but not analyzed) a sample of blood taken from each subject on two occasions separated by perhaps 1 year, so that the within-person variability of any measured quantity can be estimated, for without this any null results of analyses might be difficult to interpret. Each of these samples should be stored in small subsamples that can be individually retrieved without disturbing the remainder of that sample. The number of biologically significant factors that can, with present or future technology, be estimated in stored blood is large. (It already includes smoking, many dietary factors, many medications, many latent or clinical diseases, and certain genetic factors, and may soon include several measures of DNA damage.) If practicable without undue extra cost, simultaneous storage of fecal samples might well be of great additional value.

77 A practicable scheme might be to ask each subject to self-complete an exhaustive questionnaire relating to their normal dietary, smoking and drinking habits, their present and past main occupations and places of residence, reproductive history, all long-term medications they are on or have been on, and a few specific extra questions, and then a 7-day dietary diary, the whole questionnaire to be posted back and microfiched (unsealed). As with the blood, so with the microfiches Small but unpredictable parts would be of great interest in future years to epidemiologists with novel hypotheses to test.
REFERENCES


BERENBLUM I, SHUBR P. The persistence of latent tumour cells induced in the mouse's skin by a single application of 9,10-dimethyl-1,2-benzanthracene. Br J Cancer 1949; 3:381-386.


BRIDWOOD K, DECOUPLE P, Fraumeni JF, et al. Estimates of the fraction of cancer in the United States related to occupational factors. (Bethesda, Md.: National Cancer Institute, National Institute of Environmental Health Sciences, and National Institute for Occupational Safety and Health, Sept. 1, 1978.) See section 3.6 for details of the context in which this manuscript was released.


CANTOR KP, HOYER R, MINNOW TJ, et al. Assimations of cancer...