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the Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today

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The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today

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Reprints are not available, as the article will be republished, by permission of the Editor in Chief of the JNCI, as an Oxford University Press paperback.

't Avoidable Risks of Cancer In the U.S. 1193 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). ft will be republished, by permission of the Editor in Chief of the J1``'CI, as an Oxford University Press paperback. Acknowledgments First and foremost, we wish to thank Mrs. Virginia Godwin for her assistance in prepa; ing this report, an& 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 1933-78 from Govern- ment publicatbons, 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 Grayy analyzed the mortality data, and Cathy Harwood drew the figures. The Surveillance, Epid'emiology; and End Results section of the Biometry Branch of the National Cancer Institute and the New York and Connecticut tumor registries kindliyy provided us with access to cancer incidence data. Finally, we wish to thank the d'ozens 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 osen: ACS=American Cancer Society; AF2=2-(2-furyl)-3-(5-nitro-2-ftiryl)acrylamide; CPEAP=Committee on Prototype Expliciu Analyses for Pesticides; DAB=p-dimethylaminoazo- benzene; DES=diethylstilbestrol: D14fBA=7,12-dimethylbenzfalanthracene; EPA=Environmental Protection Agency; GESAIN1P=Group of Experts on the Scientific Aspects of Marine Pollution; IARC=International Agency, for Research on Cancer; ICD=International Classification of Diseases; NAS=Natiunal Academy of! Sciences; NCI=National Cancer Institute; NIOSH=Na- tional Institute of Occupational' Safety and Health; N1EHS=National Institute of Environmental Health Sciences; OSHA=Occupational Safety, and Health Administration; PVC=polyvinyl chlo- ride; SEER=Surveillanee, Epidemiology,, and End Results program of NCI; SNCS=Second National Cancer Survey; TNC'.S='Phird National'Cancer Survey;,TSSC=Toxic Substances Strategy Committee; WPdO=1tiÂ•orld Health Organization. JKCI, ao: t,,,)tl\E 1981

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.

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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.

1194 Doll and Peto ABSTRACT-Evidence that the various common types of cancer are largely avoidable diseases is reviewed: Life-style and other environmentall factors are divided into a dozen categories, and for each category the evidence relating those particular factors to cancer onset rates is sum- marized. 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 im 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 alao 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 Ihere is no evidence of any generalizedincrease other than that due to tobacr.n- Moderate increases or decreases due to some new ag~ e) or habit(s) might of course be overlooked in such large-scale analyses. But~ such analyses do suggest that, aPart from cancer-f the respirat~v tract the types of cancer that are currently common are not ec di ses and are likel to depend chiefl on some long- established La_ctnLfs). (A prospec ive 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 occupatignal f~ctors is erovisionallv estimated as 496 (lung canrPr hpino thg m~ior rnn- tnibutor to this). This is far smaller than has recently been sugaested hy_ various U.S. Government agencies. The matter could be resolved directly by a"case-contro!" 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. J1c:1, tY)l.. tdi. Ntl. 1,, J1:1t.. 19M1

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.

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TABLE OF CONTENTS

1196 Doll and Peto PREFACE The percentage of today's fatal cancers that might, by suitable preventive measures, have been avoided is subject to some dispute. Indeed, the percentage avoid- able by certain particulttr categories of preventive measure is subject to such vigorous dispute that the non-specialist (to whom the present review is addressed) mav 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 noo necessarily a modern): disease; but, with some important exceptions, frustratingly poor evidence as to exactly what are the really important ways of avoiding ai 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 frame- ..ork in which to seek an overview of them all, we have divided the various hypothetical ways of increas- ing or decreasing, cancer onset rates into a dozen groups, an(L for each such group we have attempted' to review what is knouÂ•n about the percentage of! current U.S. cancer deaths that might thereby be avoidable. Its sonte groups (e.g., smoking habits) the quantita- tive 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 mor tality thus avoidabte)' that we eventually cite for the separate groups aree therefore not really comparabl'e with each other. Some are fairly precisely known, ~: hereas others are much less so. More importantly, some relate to quite specific preventive measures on which action would, at least in principleÂ„ be possible on present knowledge alone, whereas others relate to preventive measures (e.g., modification of dietary fac- tors) 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 draavbacks, the "Ixrcentages" 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 wav 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 hu- man 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 detail5 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 fairlyliberallythrough- out 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 ad- dressed 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 experi- ments and'e the distribution of disease that actually occurs in the population as a whole, and if the major an& minor causes of death are to be seen in proper perspective, then the various aspects should be synthe- sized in a consistent way,, which would have increased in difficulty exponentially with the number of authors. N ~ N ~ C.~ O ~ ~ ~ pc.t. Vc,t.. ,A. :vu i,. 1Vvt V#Ht

PREFACE

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.

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JNCI, VOL. 66, NO. 6, JUNE 1981

Avoidable Risks of Cancer In the U.S. 1197 1. DEFINITION OF AVOIDABILITY OF CANCER The various human cancers are diseases in whichi one of the many cells of which the human body is composed is altered in such a, way that it, inappropri- ately replicates itself again and again, producing mil- lions of similarly affected self-replicatingdescendant cells, some of which: may spread'~ to other parts of the body and eventually overwhelm it. t Some cancers are easily , curable, whereas others are almost always com- pletely incurable by the time they are diagnosed, depending largely on the organ of the body (lung, larynx, large intestine, etc.)' in which the first altered cell originated. The symptoms produced and the ap- proach to: treatment also vary with the site of': origin, so that it has been customary for doctors to regard tumorss originating from different organs as different diseases. Graduall)Â•, it has come to be realized that agents or habits -which greatly increase or decrease the likelihood of one particular type of cancer arising (in humans or experimental: animals) may have little effect on most other types of cancer, so that the preventiom of each type also must be considered separately. This realization reinforces the need to consider cancers of' different organs, as]hrgely independent diseases, just as we have to consider separately different infectious diseases such as sy,philis, smallpox, and tuberculosis. When we consider them separately, we see at once that although there are several dozen different organs from which tumors may arise, cancers of three organs,('lung, breast, and large intestine) are at present ofl outstanding importance as they currently account for half the U.S; cancer deaths (table 1). A substantial reductiom im any of these three cancers, particularly lung cancer, would materially reduce total U.S. cancer death rates, whereas such reductions in any other type of cancer would have relatively little effect. That the common fatal cancers occur in large part as a result of life-style and other environmental factors and are in principle preventable was recognized by anexpert committee of the WHO in 1964. The committee, which had been appointed to consider how existing knowledge could be applied to prevent cancer, began its report (WI+IO, 1964) by stating that: The potential scope of cancer preventiom is limited'by, the prolxonion of hurnan canc.ers in whiifi eatrinsiciactorsarc reÂ•sponsilile. These. lftrctorsl iirctude all emÂ•ironmeutal cao- cinuf; ens (whether identified or uot) as well' as 'fnodifving factuts' th:u fa.Â•our ncÂ•oplaciir of apparenthÂ• inuiitsic origin (e.g.Â• horntonal intbalanceÂ•s; dictarc drficiencies and nttÂ•ta- fiolic dcfects): The ratef;oricÂ•s of cancer that are thus influenetÂ•dÂ „ directly or indirectl,: by extriitsic f:utors in- clude ntany, tumours of thaÂ•- skin and ntouth, tlltÂ• rt:spiratory, t"Â•rumor" and "heol,lasm" fiave sinrilier nuÂ•anings. but strictlyy the xÂ•olef "tancer"' reÂ•latev only tci im tsrve .,olid turnors of czÂ•rtain tistiues. IlowesÂ•tÂ•r, runst Gual tunwrs, are "taturrs'' :tttell we shalll sornetimes ust+ this f:unili:rr Ienn llru.cly crv inr Iuali- fiodri srditl and rGlfustÂ• tutili};n,urt neolilirsrus plus somtÂ•times rten thr fattd benil;n tntnwts, as aÂ•eJl. TABLE I.-Nurnbers of death.4 certified as being due to earious types of tumor: United States. 1978 Type of tumor No. of deaths Percent of all deaths from tumors Cancer of the Lung"' 95,086 24 Large bowel (colomand 53.269 13 46 rectum) Breast' 34,609 9 Prostate 21,674 5 Pancreas 20 777 5 , 46 Stomach 14 452 4 29 other types or categories,b 128,705 32 each contributing less than 34'0 of deaths Other or unspecified tumors` 33.383 8 Total, all tumors 401,955 100 Â° The annual number of, lung cancer deaths is changing ' rapidly and will probably be =105.000 by 1981. If it is, cancers of the lung, breast, and'large intestine will account for just over half of all deaths from tumors where the site of~ origin of the tumor was specified on the death certificate (see footnote c). ' Including all ieukemias as one category. (A detaifed' break- down by sex and site is available in tables 17-19, pp. 1243-1244.) ` Comprising 4,963 deaths, attributed to tumors of benign or unspecified histol'ogy, and 28,420 deaths attributed to cancer for which the site of origin was not specified; at least half of the latter probably originated from the six commonest sites. gastrointestinal and urinary trac'ts, hormone dependent organs, (such as the breast, thyroid and uterus), haemato- ;i poietic and f}mphopoietic systems, which, collectively, account for more than three-quarters of huntan cancers- Itt tcould'& seemÂ• therefore, th:u the majorit.Â•, of human cancer is potentially preventible. Many individuals had already' expressed this belief previously, and the committee's report merely served~ to indicate that a consensus among most cancer research~ workers had been achieved. In the v.ears since that report was published, advances in knowledge have consolidated these opinions and few if any competent research workers now question its main conclusion. Individuals, indeed, have gone further and have sub- stituted' figures of' 80 or even 90% as the proportion of potentially preventable cancers in place of the 1964 committee's cautious estimate of "the majority." Unfortunately, the phrase "extrinsic factors" (or the phrase "environmental factors," which is often substi- tuted for it), has been misinterpreted by, many people to mean only "man-made chemicals," which was cer- tainly not the intent of the WHO committee. The committee included, in adclition to man-made or na- tural carcinogens, viral infections, nutritional defi- ciencies or excesses, reproductive activities, and a variety of other factors determined wholly or partly by per- sonal behavior. To avoid similar misunderstandings, we shall refer throughout this report to the percentages of cancers that "might be avoidable" in various ways, rather than to the percentages that'are due to various "extrinsic'" or "environrnentttl" factors, and have used theÂ• tt.rnt "avoidableÂ•" in our tille. We have had' in mind throuf;hout otr relxzrt thc avoidhnccr of cancer ottly, by .iNCI. 1'<ri.. twi! NU: 6, Jt'\}; 1981

1. DEFINITION OF AVOIDABILITY OF CANCER

The various human cancers are diseases in which one of the many cells of which the human body is composed is altered in such a way that it inappropriately replicates itself again and again, producing millions of similarly affected self-replicating descendant cells, some of which may spread to other parts of the body and eventually overwhelm it.[1] Some cancers are easily curable, whereas others are almost always completely incurable by the time they are diagnosed, depending largely on the organ of the body (lung, larynx, large intestine, etc.) in which the first altered cell originated. The symptoms produced and the approach to treatment also vary with the site of origin, so that it has been customary for doctors to regard tumors originating from different organs as different diseases. Gradually, it has come to be realized that agents or habits which greatly increase or decrease the likelihood of one particular type of cancer arising (in humans or experimental animals) may have little effect on most other types of cancer, so that the prevention of each type also must be considered separately. This realization reinforces the need to consider cancers of different organs as largely independent diseases, just as we have to consider separately different infectious diseases such as syphilis, smallpox, and tuberculosis. When we consider them separately, we see at once that although there are several dozen different organs from which tumors may arise, cancers of three organs (lung, breast, and large intestine) are at present of outstanding importance as they currently account for half the U.S. cancer deaths (table 1). A substantial reduction in any of these three cancers, particularly lung cancer, would materially reduce total U.S. cancer death rates, whereas such reductions in any other type of cancer would have relatively little effect.

That the common fatal cancers occur in large part as a result of life-style and other environmental factors and are in principle preventable was recognized by an expert committee of the WHO in 1964. The committee, which had been appointed to consider how existing knowledge could be applied to prevent cancer, began its report (WHO, 1964) by stating that:

> The potential scope of cancer prevention is limited by the proportion of human cancers in which extrinsic factors are responsible. These [factors] include all environmental carcinogens (whether identified or not) as well as 'modifying factors' that favour neoplasia of apparently intrinsic origin (e.g., hormonal imbalances, dietary deficiencies and metabolic defects). The categories of cancer that are thus influenced, directly or indirectly, by extrinsic factors include many tumours of the skin and mouth, the respiratory, gastrointestinal and urinary tracts, hormone dependent organs (such as the breast, thyroid and uterus), haematopoietic and lymphopoietic systems, which, collectively, account for more than three-quarters of human cancers. It would seem, therefore, that the majority of human cancer is potentially preventible.

TABLE 1.—*Numbers of deaths certified as being due to various types of tumor: United States, 1978*

Type of tumor	No. of deaths	Percent of all deaths from tumors	
Cancer of the			
Lung[a]	95,086	24	
Large bowel (colon and rectum)	53,269	13	46
Breast	34,609	9	
Prostate	21,674	5	
Pancreas	20,777	5	46
Stomach	14,452	4	
29 other types or categories,[b] each contributing less than 3% of deaths	128,705	32	
Other or unspecified tumors[c]	33,383	8	
Total, all tumors	401,955	100	

[a] The annual number of lung cancer deaths is changing rapidly and will probably be ≈105,000 by 1981. If it is, cancers of the lung, breast, and large intestine will account for just over half of all deaths from tumors where the site of origin of the tumor was specified on the death certificate (*see* footnote *c*).

[b] Including all leukemias as one category. (A detailed breakdown by sex and site is available in tables 17–19, pp. 1243–1244.)

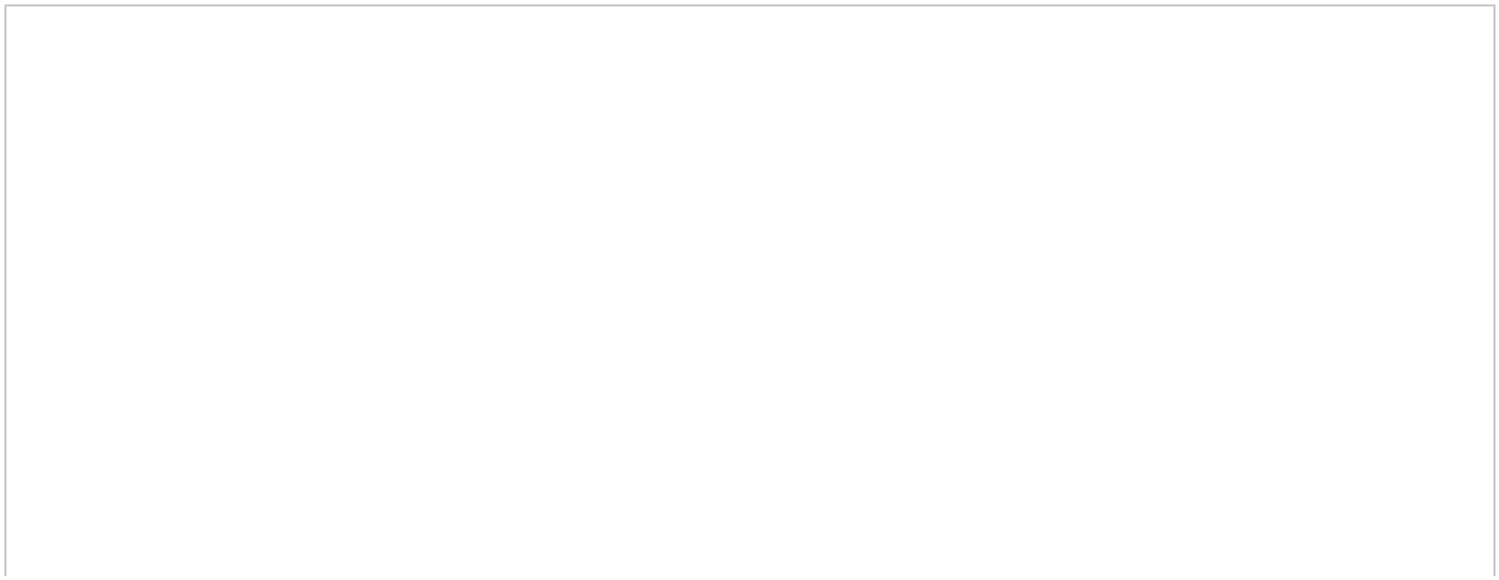
[c] Comprising 4,963 deaths attributed to tumors of benign or unspecified histology, and 28,420 deaths attributed to cancer for which the site of origin was not specified; at least half of the latter probably originated from the six commonest sites.

Many individuals had already expressed this belief previously, and the committee's report merely served to indicate that a consensus among most cancer research workers had been achieved. In the years since that report was published, advances in knowledge have consolidated these opinions and few if any competent research workers now question its main conclusion. Individuals, indeed, have gone further and have substituted figures of 80 or even 90% as the proportion of potentially preventable cancers in place of the 1964 committee's cautious estimate of "the majority."

Unfortunately, the phrase "extrinsic factors" (or the phrase "environmental factors," which is often substituted for it) has been misinterpreted by many people to mean only "man-made chemicals," which was certainly not the intent of the WHO committee. The committee included, in addition to man-made or natural carcinogens, viral infections, nutritional deficiencies or excesses, reproductive activities, and a variety of other factors determined wholly or partly by personal behavior. To avoid similar misunderstandings, we shall refer throughout this report to the percentages of cancers that "might be avoidable" in various ways, rather than to the percentages that are due to various "extrinsic" or "environmental" factors, and have used the term "avoidable" in our title. We have had in mind throughout our report the avoidance of cancer only by

[1] "Tumor" and "neoplasm" have similar meanings, but strictly the word "cancer" relates only to invasive solid tumors of certain tissues. However, most fatal tumors are "cancers" and we shall sometimes use this familiar term loosely to include both solid and diffuse malignant neoplasms plus sometimes even the fatal benign tumors as well.

1198 Doll and Peto means that might conceivably be socially acceptable,, either now or in some plausible social atmosphere in the reasonably near future. (F'otentially acceptable mea- sures might, for example, include a continuation of the current decrease in cigarette smoking or tar yields, which would reduce the risk of lung cancer, but would not include a first pregnancy for most females by 15 years of age, though this would reduce the risk of breast cancer.) Even with this restriction, however, two ambiguities remain in what is meant by the "avoid- ability" of cancer. First, by the year 2100 advances in basic research in biology may permit prevention of'cancer by means now utterly unforeseen. No useful estimate of the likelihood of such progress can be made, and we have therefore tried to restrict our attention chiefly to the a.Â•oi6bility of cancer by, means whose effects on cancer risks are already reasonably certaim or by means that might: well be devised over the next decade or two rather than in the indefinite future: For this we have not assumed that the mechanisms underlying such means are known or will be known in the near future, but chiefly that it should be possible to identify those things which different groups of people already doÂ„ or have done to them, that account for the marked d'ifferences in cancer risk between or within commu- nities and that this identification will in many in- stances lead to preventive strategies which are based either directlly or indirectly on the ways in which some people already live and are therefore reasonabliy prac- tical_ A second, more trivial', ambiguity in what we mean by the "ati~oidability'' of cancer arises simply because everybody is bound to die sooner or later. (If there are about two million births per year in the United States, there are in the long run also bound to be about two million deaths per year.), If exactly half the cancer deaths that now occur were somehow magically pre- vented and nothing else changed, those people who would have died of cancer might live on for a further 5,] 0; 20, or 30' more years (the average being 10 or 15 extra years), but they must eventuall), die of something and that something wottld for some of them be a.second cancer. Even so, we would still describe such a change as a halving of the cancer rate. To take an opposite example, if every cause of death other than cancer were suddtrnly abolislicÂ•d then of course everyone would eventually die of cancer, although it might be mis- leading to describe such a change in terms of'an increase in either the risk of cancer or the average age ar death from cancer, especially if one were interested. in the causes of cancÂ•er: The usual means of avoiding such absurdities is to avoid basing inferences on the percentage of people who "will eventually" die of cancer, on "crude" cancer rates, or on "the mean age at death front canccÂ•r." InstcÂ•ad, it is usual to restrict attention to "age-speÂ•cifir." or, "age-standardized" cancer rates (seP appcÂ•nclixcs A and fi): When we speak of the avoidktnce of a certttin perceÂ•uta};tÂ• of cancer, we there- fÂ„fe have in mind a rcÂ•ditctiou by that fx'rcentage in the ar;cr-stancLuciizcd rattÂ•s. (This ntay sound complicated, but it is merely the arithmetic equivalent of not advising people that the most reliable way of avoiding cancer is to commit suicide.) In summary, the aim of our report is to review the established evidence and current research relating to each of several different possible ways or groups of ways of avoiding cancer and to estimate the percentage reduction in today's age-standardized U.S. cancer death rates that they might confer, now or in the medium- term future. 2. EVIDENCE FOR THE AVOIDABILITY OF CANCER The evidence that much human cancer is avoidable can be summarized under four heads: differences in the incidence of cancer among different settled communities, differences between migrants from a community and those who remain behind, variations with time in the incidence of cancer within particular communities, and the actual identification; of many specific causes or preventive factors. Genetic factors and age also affect cancer onset rates, of course, but this does not affect the conclusion that much~ human cancer is avoidable. 2.1 Differences in Incidence Between Communities Evidence of differences in the incidence2 of particular types of cancer between different parts of the world has accumulated slowly over the past 50 years. At first the only quantitative data available referred to mortalitv'" rates in particular areas or, even more crudely, to the proportion of patients admitted to hospital suffering from different diseases. Such data were grosslyy affected by the age distribution of the population, the efficacy of treatment, and~ the frequency of other diseases. But even then data were sufficient to shou, that the inci- dence of some cancers among people of a given age in different parts of the world must vary by at least ten and possibly by a hundredfold. More recently, this evidence has been reinforced by the results of special surveys or by the establishment of registries in which records are consistently sought of all cases of cancer diagnosed in a defined poptilation~ over a long period. Registry data also need care in interpretation owing to trends with time, or differences between different parts of the world, in the provision of inedical services and in the extent to which they are used'.(especially by, old people, among whom a large proportion of fatal cancers may never be diagnosed at all). Reasonably reliable comparisons between different areas are ob- tained only if comparisons are limited to men and women in middle life (or earlier, for sonie specific types of cancer), when a sufficient number of cases can be anticipated for onset rates to be reliably estimated and yet efforts at diagnosis are still likely to be ' lkhffnitiort: 'rlitÂ• incidrncr (rattÂ•) drtxÂ•nd+ oW tht' total! nutnber of n('w (':IseY of caruer(txr y^(ar) : t.Â•hile ihtÂ• rrrortaG/yatsoc:Jled thr (ldÂ•ath rate;, ignurrs noudatai cstties. }.~ 1%Y;I, 1'c,t. Ui.,, NO. 6,)t!tit. 1l1RI.



means that might conceivably be socially acceptable, either now or in some plausible social atmosphere in the reasonably near future. (Potentially acceptable measures might, for example, include a continuation of the current decrease in cigarette smoking or tar yields, which would reduce the risk of lung cancer, but would not include a first pregnancy for most females by 15 years of age, though this would reduce the risk of breast cancer.) Even with this restriction, however, two ambiguities remain in what is meant by the "avoidability" of cancer.

First, by the year 2100 advances in basic research in biology may permit prevention of cancer by means now utterly unforeseen. No useful estimate of the likelihood of such progress can be made, and we have therefore tried to restrict our attention chiefly to the avoidability of cancer by means whose effects on cancer risks are already reasonably certain or by means that might well be devised over the next decade or two rather than in the indefinite future. For this we have not assumed that the mechanisms underlying such means are known or will be known in the near future, but chiefly that it should be possible to identify those things which different groups of people already do, or have done to them, that account for the marked differences in cancer risk between or within communities and that this identification will in many instances lead to preventive strategies which are based either directly or indirectly on the ways in which some people already live and are therefore reasonably practical.

A second, more trivial, ambiguity in what we mean by the "avoidability" of cancer arises simply because everybody is bound to die sooner or later. (If there are about two million births per year in the United States, there are in the long run also bound to be about two million deaths per year.) If exactly half the cancer deaths that now occur were somehow magically prevented and nothing else changed, those people who would have died of cancer might live on for a further 5, 10, 20, or 30 more years (the average being 10 or 15 extra years), but they must eventually die of something and that something would for some of them be a second cancer. Even so, we would still describe such a change as a *halving* of the cancer rate. To take an opposite example, if every cause of death other than cancer were suddenly abolished then of course everyone would eventually die of cancer, although it might be misleading to describe such a change in terms of an increase in either the risk of cancer or the average age at death from cancer, especially if one were interested in the causes of cancer. The usual means of avoiding such absurdities is to avoid basing inferences on the percentage of people who "will eventually" die of cancer, on "crude" cancer rates, or on "the mean age at death from cancer." Instead, it is usual to restrict attention to "age-specific" or "age-standardized" cancer rates (*see* appendixes A and B). When we speak of the avoidance of a certain percentage of cancer, we therefore have in mind a reduction by that percentage in the age-standardized rates. (This may sound complicated, but it is merely the arithmetic equivalent of not advising people that the most reliable way of avoiding cancer is to commit suicide.)

In summary, the aim of our report is to review the established evidence and current research relating to each of several different possible ways or groups of ways of avoiding cancer and to estimate the percentage reduction in today's age-standardized U.S. cancer death rates that they might confer, now or in the medium-term future.

2. EVIDENCE FOR THE AVOIDABILITY OF CANCER

The evidence that much human cancer is avoidable can be summarized under four heads: differences in the incidence of cancer among different settled communities, differences between migrants from a community and those who remain behind, variations with time in the incidence of cancer within particular communities, and the actual identification of many specific causes or preventive factors. Genetic factors and age also affect cancer onset rates, of course, but this does not affect the conclusion that much human cancer is avoidable.

2.1 Differences in Incidence Between Communities

Evidence of differences in the incidence[2] of particular types of cancer between different parts of the world has accumulated slowly over the past 50 years. At first the only quantitative data available referred to mortality[2] rates in particular areas or, even more crudely, to the proportion of patients admitted to hospital suffering from different diseases. Such data were grossly affected by the age distribution of the population, the efficacy of treatment, and the frequency of other diseases. But even then data were sufficient to show that the incidence of some cancers among people of a given age in different parts of the world must vary by at least ten and possibly by a hundredfold. More recently, this evidence has been reinforced by the results of special surveys or by the establishment of registries in which records are consistently sought of all cases of cancer diagnosed in a defined population over a long period. Registry data also need care in interpretation owing to trends with time, or differences between different parts of the world, in the provision of medical services and in the extent to which they are used (especially by old people, among whom a large proportion of fatal cancers may never be diagnosed at all). Reasonably reliable comparisons between different areas are obtained only if comparisons are limited to men and women in middle life (or earlier, for some specific types of cancer), when a sufficient number of cases can be anticipated for onset rates to be reliably estimated and yet efforts at diagnosis are still likely to be

[2] Definition: The *incidence* (rate) depends on the total number of new cases of cancer (per year), while the *mortality* (rate), also called the death rate, ignores non-fatal cases.

Avoidable Risks of Cancer In the U.S. 1199 thorough. The International Union Against Cancer (1i970) attdl IARC (1976) have recommended that, for the cancers of adult: life, attention be chiefly directed to the risks in the truncated age range of 35-64 years (and many artif'acts of interpretation of trends in U.S. cancer data might be avoided if this simple precaution were generally adopted). Table 2 shows for 119 common types of cancer their range of variation, among those cancer registries that have produc.ed data sufficiently reliabl'e to be published for the purposes of: international comparison by the IARC (11976)1 and the International Union Against Cancer (11966' and 1970). Types of cancer have been incl'uded if they are common enough somewhere to affect more than 1% of men (or women) by 75 years of age in the absence of other causes of d'eath, and ranges of variation are shown for standardized! incidence rates between 35 and 64 years of age.3 The range of variation (table 2) is never less than sixfold and is commonly much more. Some of this variation may beartifactual, due to different standards of medical service, case registration, and population enumeration, despite the care taken to exclude unreli- able tlata; but in many cases the true ranges will be ' The incidence of': mosn types of cancer increases with age soo rapidly that it may be misleading to compare disease onset ratess among people in one part of the world with those of'e people elsewhere if the proportions of people of different ages in the popu- lations being compared are not the same:,T)iis particular difficulty map be circumtiented by the use of'agr-standardized incidence rates tcee ;tpfjwndia A), andl the rates in~ table 2 are standardized as reccunnnendÂ•dbythe IARC (t9"r6)~. greater. First, large gaps remain in the cancer map of the world, and some extreme figures may have been overlooked because no accurate surveys have been practicable in, the least developed areas, these being just the areas that are likely to provide the biggest contrasts (both high and low) with Western society. Second, the rates cited in table 2 refer to cancers of whole organs, and in one particular organ such as the stomach, liver, or skin there may be many differenr; types of cells that are affecte& differently by different carcinogens or protective factors; for example, in the skin the few cancers arising from the cells that are responsible for the manufacture of the dark pigment melanin in blackss or in suntanned whites are called "melanomas," and differ greatly in etiology and prognosis from the many "non-melanoma skin cancers."' Third, various anatomic parts of one single organ such as the colon or skin may be affected differentlvy by different factors; for example, cancers of the skin have different principal' causes in the populations where they are common depending on whetherr they chiefly appear on the face, abdomen. forearm, or legs. Finall'y,, although cancers of the skin are so common in certain parts of the world that they ouniumber all other cancers, most are so easily cured that they engender little medical interest and are commonly not reported to; or in some cases sought by,, even some of the best cancer registries. For these reasons and because the extremes of variation in skin cancer incidence between~ different communities are affected by skin color as vvelil as by the means of avoidance which chiefly interest us, skin cancers ('other tham melanomas) are perhaps of less interest than any other type of cancer in table 2. TABLE 2:-Range, of incidence rates for common cancers ontong rnales (and for certain cancers among femalÂ¢s) Site of origin of cancer igh incidence area ex Cumulative incidence," % in high incidence area Ratio of highest rate to lowest rateb Low incidence area Skini(chiefly non-melanoma) Australia. Queensland a >20 >200 India, Bombay Esophagus Ih-an, northeast section a 20 300 Nigeria Lung and bronchus England! a, 11 35 Nigeria Stomach Japan a 11 25 Uganda Cervix uteri Colombia 4' 100 15 Israel: Jewish Prostate United States: blacks a 9 40 Japan Li Mozambi ue d 8 100~ En land ver Breast q Canada. British~ Columbia 4' 7 7 g Israel: non-Jewish N Colon United States, Connecticut: & 3 10~ Nigeria Corpus uteri United States, California 9 3 30 Japan Buccal cavity Bombay India a 2 25 Denmark ~ Rectum , Denmark & 2 20: Nigeria Bladder Unitecl' States, ConnecticuG & 2 6 Japan Ovary Denmark Y 2 6 Japan ~ Nasopharynx Singapore: Chinese a 2 40 England Pancreas New Zealand: Maori a 2 8' Bombay India Lar nx Brazil S3o Paulo a 2 10 . Ja an VI y Phar nx , Bombay India a 2 20 p Denmark C1t y Penis , ParLs of Uganda ; a, 1 300 Israel: Jewish w Â°' By aKe 75 yr, in the absence of other causes of death, ~" At ages :55-64 yr, st.-tntlardizeJ for age as in IAfiC (1976); At these ages, even the dat4L from cancer registries, in~poor countries are likely ur be reasonably reliable (although at older ages serious underre)K,rtinK may affect the data). JN(a. Vot.. t,t;. Â•- r,iU.E t9rst

thorough. The International Union Against Cancer (1970) and IARC (1976) have recommended that, for the cancers of adult life, attention be chiefly directed to the risks in the truncated age range of 35–64 years (and many artifacts of interpretation of trends in U.S. cancer data might be avoided if this simple precaution were generally adopted).

Table 2 shows for 19 common types of cancer their range of variation among those cancer registries that have produced data sufficiently reliable to be published for the purposes of international comparison by the IARC (1976) and the International Union Against Cancer (1966 and 1970). Types of cancer have been included if they are common enough somewhere to affect more than 1% of men (or women) by 75 years of age in the absence of other causes of death, and ranges of variation are shown for standardized incidence rates between 35 and 64 years of age.[3]

The range of variation (table 2) is never less than sixfold and is commonly much more. Some of this variation may be artifactual, due to different standards of medical service, case registration, and population enumeration, despite the care taken to exclude unreliable data; but in many cases the true ranges will be greater. First, large gaps remain in the cancer map of the world, and some extreme figures may have been overlooked because no accurate surveys have been practicable in the least developed areas, these being just the areas that are likely to provide the biggest contrasts (both high and low) with Western society. Second, the rates cited in table 2 refer to cancers of whole organs, and in one particular organ such as the stomach, liver, or skin there may be many different types of cells that are affected differently by different carcinogens or protective factors; for example, in the skin the few cancers arising from the cells that are responsible for the manufacture of the dark pigment melanin in blacks or in suntanned whites are called "melanomas," and differ greatly in etiology and prognosis from the many "non-melanoma skin cancers." Third, various anatomic parts of one single organ such as the colon or skin may be affected differently by different factors; for example, cancers of the skin have different principal causes in the populations where they are common depending on whether they chiefly appear on the face, abdomen, forearm, or legs. Finally, although cancers of the skin are so common in certain parts of the world that they outnumber all other cancers, most are so easily cured that they engender little medical interest and are commonly not reported to, or in some cases sought by, even some of the best cancer registries. For these reasons and because the extremes of variation in skin cancer incidence between different communities are affected by skin color as well as by the means of avoidance which chiefly interest us, skin cancers (other than melanomas) are perhaps of less interest than any other type of cancer in table 2.

[3] The incidence of most types of cancer increases with age so rapidly that it may be misleading to compare disease onset rates among people in one part of the world with those of people elsewhere if the proportions of people of different ages in the populations being compared are not the same. This particular difficulty may be circumvented by the use of age-standardized incidence rates (*see* appendix A), and the rates in table 2 are standardized as recommended by the IARC (1976).

TABLE 2.—*Range of incidence rates for common cancers among males (and for certain cancers among females)*

Site of origin of cancer	High incidence area	Sex	Cumulative incidence,[a] % in high incidence area	Ratio of highest rate to lowest rate[b]	Low incidence area
Skin (chiefly non-melanoma)	Australia, Queensland	♂	>20	>200	India, Bombay
Esophagus	Iran, northeast section	♂	20	300	Nigeria
Lung and bronchus	England	♂	11	35	Nigeria
Stomach	Japan	♂	11	25	Uganda
Cervix uteri	Colombia	♀	10	15	Israel: Jewish
Prostate	United States: blacks	♂	9	40	Japan
Liver	Mozambique	♂	8	100	England
Breast	Canada, British Columbia	♀	7	7	Israel: non-Jewish
Colon	United States, Connecticut	♂	3	10	Nigeria
Corpus uteri	United States, California	♀	3	30	Japan
Buccal cavity	India, Bombay	♂	2	25	Denmark
Rectum	Denmark	♂	2	20	Nigeria
Bladder	United States, Connecticut	♂	2	6	Japan
Ovary	Denmark	♀	2	6	Japan
Nasopharynx	Singapore: Chinese	♂	2	40	England
Pancreas	New Zealand: Maori	♂	2	8	India, Bombay
Larynx	Brazil, São Paulo	♂	2	10	Japan
Pharynx	India, Bombay	♂	2	20	Denmark
Penis	Parts of Uganda	♂	1	300	Israel: Jewish

[a] By age 75 yr, in the absence of other causes of death.
[b] At ages 35–64 yr, standardized for age as in IARC (1976). At these ages, even the data from cancer registries in poor countries are likely to be reasonably reliable (although at older ages serious underreporting may affect the data).

1200 Doll and Peto Variation in incidence is not, of course, limited to the types of cancer that are common enough some- where in the world! to have been included in table 2. For example, Burkitt's lymphoma: has nowhere been found in over 0.1% of the population, but even so is 100 times less common in North America than in the West Nile district of Uganda. Also; Kaposi's sarcoma, which is extremely rare in most of the world, is so common in parts of Central Africa that it accounted'for more than 10% of all tumors seen in the (mostly young): males in one hospital (Cook and Burkitt, 1971). Some few rather rare types of cancer, such as the nephroblastoma of childhood, may perhaps eventually be shown to occur with approximately the same frequency in all communities; but no common types of cancer will be found to do so. In the absence of other causes of death, cancer of: the breast would affect about 6 0 of Ui.S. women before the age of 75 years as against only 1% of non-Jewish Israeli women, and it is possible that an evem lower percentage would' be affected in certain other populations where reliable cancer regis- tries do not yet exist. With breast cancer as the only possible exception, for each type of cancer a popula- tion exists where the cumulative incidence by the age of 75 years is .vell under P%a: In other words, every type of cancer that is common in one district is rare somewhere else. Most of the figures in table 2 refer to the incidence of cancer in diff'erent communities defined by the area in which they live. Communities can, however, be defined in other ways and no matter how they are defined (whether by ethnic origin, religion, or economic status) similar or sometimes even greater differences will be found. Of particular interest are some of the differences that have been observed in the United States between members of different religious groups.Â° For example, in comparison with members of other religious groups living in: the same States, the tiiormons of Utah and the Seventh-day Adventists and Mormons of California experience low incidence rates for cancers of the respiratory, gastrointestinal, and genital systems. Of course, it is unlikely that any one single com- munity will by chance have the highest rates in the world for every single type of cancer, just as it is unlikely that any one single community will by chance have the lowest rates in the world for every single type of cancer. Consequently, when we consider total cancer rates, which are obtained by adding the rates for each separate type of cancer, in various communities we find less extreme variation (only threefold) between communities arotnul the world than was found for many separate single types of cancer. I-lowever, there is if, anything still more variation in these total cancer incidence rates than would have been expected if for ' G)r eÂ•x:tmplc; thc p:rtxÂ•rs Irom Ihe recrnt workshop on (:rnrrr and DInt-tality in Relil;irrus Gruups"i Lyon eti crl.. 19HQa; l.yun ct :rllÂ„ I'.lttOh;, f:n.uirnt, I!)N0; West et al.,, 1980; hhillips,ct al., IS/Hft; Martin ca ;rl.., 1980; 6King , :md Isw'kr, If1KU:r. each community the rates for the separate single types of cancer had been picked at random from the corre- sponding rates around the world for single types of cancer (Peto J: Unpublished calculations based on IARC, 1976). Consequently; the relative constancy of total cancer incidence rates around the world does not suggest that if one cancer is prevented another will tend to replace it;s it merely shows that if many things are added up, irregularities will tend to be averaged out. Apart from cancer of the skin, the risk of which is much greater for whites than for blacks (an& possibly also apart from the consistent lack among people of Chinese or Japanese descent of' certain lymphoprolifer- ative conditions) it does not seem likely that most of the large differences in cancer onset rates between communities could be chiefly due to genetic factors (see section 2.5), and such factors certainly cannot explain the differences observed'n on migration or with the passage oE time that are described in the following sections. 2.2 Changes in Incidence on Migration Evidence of a change in the incidence of cancer in a migrant group (from that in the homeland they have left toward that of their new country of residence) provides good evidence of the importance of life-style or other environmental factors in the production of the disease. That such changes have occurred and are occurring is beyond reasonable doubt, but strictly controlled quantitative evidence cornparing incidence rates in the three populations (original! country, mi- grant group, and new country) is hard to come by. Black Americans, for example, experience cancer inci- dence rates that are generally much more like those of white Americans than like those of the black popula- tion in West Africa from which they were originally drawn, as is indicated for selected sites6 in table 3. From the strict scientific point of view, this compari- son is unsatisfactory because the ancestors of black Americans would have come from many different parts of (chiefly West) Africa, some of which are likely to have cancer rates somewhat different from those ob- served in Nigeria. Nevertheless, the contrast is so great that there can be little doubt that new factors were ' The suggestion that environmental and life-style factors do not usuÂ•ally have much effect on whether or when an individual gets cancer, but merely affect the site at which a(hypotheticalty)' predestined cancer will appear, has recurred fronr titne to time for half a century ever since Cramer (1931) overlooketil the fact that the coefficient of variation of total cancer rates must of necessity be less than that of individual cancer rates. It is easily, disproved by noting that people exposed to hazards (cg., carcinogens in industry or cigarette smoke: Ikrlt, 1978) which affect sfxÂ•cific tyfxÂ•s of cancer do not have reduced risks of cancer of any other tylle. The cune is, of coursa, true arnaml; exfxrinrental anim: tls. ' We ornittcd data for (:utcer si(cs for whiCh the Ibadan rates nÂ•wmble the U_S. while rates (e.g., ese)(phagus and sturnach)- JN(a. 1't)t.. 1.6, 1;t, o. (t-t.F 1981

Variation in incidence is not, of course, limited to the types of cancer that are common enough somewhere in the world to have been included in table 2. For example, Burkitt's lymphoma has nowhere been found in over 0.1% of the population, but even so is 100 times less common in North America than in the West Nile district of Uganda. Also, Kaposi's sarcoma, which is extremely rare in most of the world, is so common in parts of Central Africa that it accounted for more than 10% of all tumors seen in the (mostly young) males in one hospital (Cook and Burkitt, 1971). Some few rather rare types of cancer, such as the nephroblastoma of childhood, may perhaps eventually be shown to occur with approximately the same frequency in all communities; but no common types of cancer will be found to do so. In the absence of other causes of death, cancer of the breast would affect about 6% of U.S. women before the age of 75 years as against only 1% of non-Jewish Israeli women, and it is possible that an even lower percentage would be affected in certain other populations where reliable cancer registries do not yet exist. With breast cancer as the only possible exception, for each type of cancer a population exists where the cumulative incidence by the age of 75 years is well under 1%. In other words, every type of cancer that is common in one district is rare somewhere else.

Most of the figures in table 2 refer to the incidence of cancer in different communities defined by the area in which they live. Communities can, however, be defined in other ways and no matter how they are defined (whether by ethnic origin, religion, or economic status) similar or sometimes even greater differences will be found. Of particular interest are some of the differences that have been observed in the United States between members of different religious groups.[4] For example, in comparison with members of other religious groups living in the same States, the Mormons of Utah and the Seventh-day Adventists and Mormons of California experience low incidence rates for cancers of the respiratory, gastrointestinal, and genital systems.

Of course, it is unlikely that any one single community will by chance have the highest rates in the world for every single type of cancer, just as it is unlikely that any one single community will by chance have the lowest rates in the world for every single type of cancer. Consequently, when we consider total cancer rates, which are obtained by adding the rates for each separate type of cancer, in various communities we find less extreme variation (only threefold) between communities around the world than was found for many separate single types of cancer. However, there is if anything still *more* variation in these total cancer incidence rates than would have been expected if for each community the rates for the separate single types of cancer had been picked at random from the corresponding rates around the world for single types of cancer (Peto J: Unpublished calculations based on IARC, 1976). Consequently, the relative constancy of total cancer incidence rates around the world does not suggest that if one cancer is prevented another will tend to replace it;[5] it merely shows that if many things are added up, irregularities will tend to be averaged out.

Apart from cancer of the skin, the risk of which is much greater for whites than for blacks (and possibly also apart from the consistent lack among people of Chinese or Japanese descent of certain lymphoproliferative conditions) it does not seem likely that most of the large differences in cancer onset rates between communities could be chiefly due to genetic factors (*see* section 2.5), and such factors certainly cannot explain the differences observed on migration or with the passage of time that are described in the following sections.

2.2 Changes in Incidence on Migration

Evidence of a change in the incidence of cancer in a migrant group (from that in the homeland they have left toward that of their new country of residence) provides good evidence of the importance of life-style or other environmental factors in the production of the disease. That such changes have occurred and are occurring is beyond reasonable doubt, but strictly controlled quantitative evidence comparing incidence rates in the three populations (original country, migrant group, and new country) is hard to come by. Black Americans, for example, experience cancer incidence rates that are generally much more like those of white Americans than like those of the black population in West Africa from which they were originally drawn, as is indicated for selected sites[6] in table 3. From the strict scientific point of view, this comparison is unsatisfactory because the ancestors of black Americans would have come from many different parts of (chiefly West) Africa, some of which are likely to have cancer rates somewhat different from those observed in Nigeria. Nevertheless, the contrast is so great that there can be little doubt that new factors were

[4] *See*, for example, the papers from the recent workshop on "Cancer and Mortality in Religious Groups": Lyon et al., 1980a; Lyon et al., 1980b; Enstrom, 1980; West et al., 1980; Phillips et al., 1980; Martin et al., 1980; King and Locke, 1980a.

[5] The suggestion that environmental and life-style factors do not usually have much effect on whether or when an individual gets cancer, but merely affect the site at which a (hypothetically) predestined cancer will appear, has recurred from time to time for half a century ever since Cramer (1934) overlooked the fact that the coefficient of variation of total cancer rates must of necessity be less than that of individual cancer rates. It is easily disproved by noting that people exposed to hazards (e.g., carcinogens in industry or cigarette smoke: Doll, 1978) which affect specific types of cancer do not have reduced risks of cancer of any other type. The same is, of course, true among experimental animals.

[6] We omitted data for cancer sites for which the Ibadan rates resemble the U.S. white rates (e.g., esophagus and stomach).

Avoidable Risks of Cancer In the U.S. 1201 TABLE 3, Comparison of cancer incidence ratesÂ° for Ibadan, Nigeria. and for two populations of blacks and whites in the United States Primary sitee of cancer Patients sex`' Annual incidence/milliom peopleÂ° Ibadan, United States' Nigeria, 1960-69 Blacks Whites Colon a 34 349 294 353 335 Rectum a 34 159 217 248 232 Liver 6 272 . 67 39 86 32 Pancreas a 55 200 126 250 122 Larynx a 37 236 141 149 141 Lung $ 27 1,546 983 1,517 979 Prostate a 134 724 318 577 232 Breast Q 337 1.268 1,828 1,105 1,472 Cervix uteri Q 559 507 249 631 302 Corpus uteri Q 42 235 695 208! 441 Lymphosarcoma' a 133 10! 4 at ages <15 yr 5 3 Â° From IARC (1976): 6 Ages 35-64 yr, standardized for age as in IARC (1976) j ` For brevity. wherever possible only the male rates have been presented, and sites for which the rates among U.S. whites resemble those in the country of origin of the nonÂ«white migrants have been omitted. Â° For each type of cancer, upper entry shows incidence in San Francisco Bay area, 1969r73; lower entry shows incidence in Detroit, 1969-71. ` Including Burkitt's lymphoma. The cited rates are the average of the age-specific rates at ages 0-4, 5-9 and 10-14 yr: introduced with migration. These, it would appear, are not chiefly the result of genetic dilution by inter- breeding, for at most major sites the differences between black and white Americans in defined areas seem largely independent of the degree of admixture of white-derived genes among the blacks in those areas (Petrakis, 1971). A similar comparison can be made between the Japanese and Caucasian residents in Hawaii and the Japanese in two particular prefectures of Japan (table 4): The close approximation of the rates in the two prefectures givcs some justification for believing that they may be typicat of the areas from which the Japanese migrants to Hawaii (or their ancestors); origi- nated, although the mii;rants will have come fronl other parts of Japan as wcÂ•Ill For every type of cancer except cancer of the lung, the rates for the migrants are more like those for the (:aucasian resider.ts than for those in Japan. Other groups for which data :uc available include Indians who went tr, :ultl' Scluth Africa (and Irlst their high risk ol devrli/I>ing oral c:In(err), liritolls .vho went to Fiji' (and acquired a high risk of' skin cancer),, and Central Europeans who went to North America and Australia. Data for some of these groups were reviewed in 1969, under the auspices of the Interna- tional Agency for Research on Cancer (Haenszel, 1970; Kmet, 1970), and recent data on cancer patterns in different ethnic groups within the United States were reviewed in 1980 under the auspices of the National Cancer Institute (Kolonel, 1980; King and Locke, 1!980b; Locke and King, 1980; Lanier et al., '1980). 2.3 Changes In Incidence Over Time Changes in the incidence of! particular types of cancer with the passage of time provide conclusive evidence that extrinsic factors affect those types of cancer. Such changes are, however, notoriously diffi- cult to estimate reliabliyÂ„ chiefly because it is difficult to compare the efficiency of case finding at different periods and partly because few incidence data have been collected for a sufficiently long time, so that we have to compare mortality rates, which record only fatal cases and thus may be influenced by changes in treatment. There are no uniform rules for deciding which of the manyy apparent changes in cancer inci- dence are real. Each set of incidence data and each~ type of cancer must be assessed', individually. It is relatively easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be diagnosed without complex investigations and its oc- TABLE 4. Comparison of cancer incidence ratesÂ°'in Japan and for Japanese and Caucasians in Hawaii Primar Annual incidence/million peopleb y site of Patients' sex` j Hawaii, 1968-72 cancer Japan Japanese Caucasians Esophagus 3' 150 46 75 112 Stomach a 1,331 397 217 1,291 Colon a 78 371 368 87 Rectum $ 95 297 204 90 Lung a 237 379 962 299 Prostate a 14 154 343 13 B reast 9 335 1.221 1,869 N ' 295 0 Cervix uteri Q 329 398 149 . 243 N Corpus uteri 9 32 407 714 ~ 20 ~ Ovary 9 51, 160 274 ~ 55 a From IARC (1976). w1 Â° Ages 35-64 yr. standardized for age as in IARC (1976).CA ` Male only, wherever possible; sites selected as in, table 3'~ Â° For each tvpe of, cancer, upper entry shows incidence in Miyagi prefecture, 1968-71: lower entryy shost s incidence in Osaka prefocture; 1970-71. J1(:1, \Â•Ul.. ta,, '.. ~, J1'tiE19M1

TABLE 3.—*Comparison of cancer incidence rates[a] for Ibadan, Nigeria, and for two populations of blacks and whites in the United States*

Primary site of cancer	Patients' sex[c]	Annual incidence/million people[b]		
		Ibadan, Nigeria, 1960–69	United States[d]	
			Blacks	Whites
Colon	♂	34	349	294
			353	335
Rectum	♂	34	159	217
			248	232
Liver	♂	272	67	39
			86	32
Pancreas	♂	55	200	126
			250	122
Larynx	♂	37	236	141
			149	141
Lung	♂	27	1,546	983
			1,517	979
Prostate	♂	134	724	318
			577	232
Breast	♀	337	1,268	1,828
			1,105	1,472
Cervix uteri	♀	559	507	249
			631	302
Corpus uteri	♀	42	235	695
			208	441
Lymphosarcoma[e] at ages <15 yr	♂	133	10	4
			5	3

[a] From IARC (1976).

went to Fiji (and acquired a high risk of skin cancer), and Central Europeans who went to North America and Australia. Data for some of these groups were reviewed in 1969, under the auspices of the International Agency for Research on Cancer (Haenszel, 1970; Kmet, 1970), and recent data on cancer patterns in different ethnic groups within the United States were reviewed in 1980 under the auspices of the National Cancer Institute (Kolonel, 1980; King and Locke, 1980b; Locke and King, 1980; Lanier et al., `1980).

2.3 Changes In Incidence Over Time

Changes in the incidence of particular types of cancer with the passage of time provide conclusive evidence that extrinsic factors affect those types of cancer. Such changes are, however, notoriously difficult to estimate reliably, chiefly because it is difficult to compare the efficiency of case finding at different periods and partly because few incidence data have been collected for a sufficiently long time, so that we have to compare mortality rates, which record only fatal cases and thus may be influenced by changes in treatment. There are no uniform rules for deciding which of the many apparent changes in cancer incidence are real. Each set of incidence data and each type of cancer must be assessed individually. It is relatively easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be

at ages <10 yr.

[a] From IARC (1976).
[b] Ages 35–64 yr, standardized for age as in IARC (1976).
[c] For brevity, wherever possible only the male rates have been presented, and sites for which the rates among U.S. whites resemble those in the country of origin of the non-white migrants have been omitted.
[d] For each type of cancer, upper entry shows incidence in San Francisco Bay area, 1969–73; lower entry shows incidence in Detroit, 1969–71.
[e] Including Burkitt's lymphoma. The cited rates are the average of the age-specific rates at ages 0–4, 5–9 and 10–14 yr.

introduced with migration. These, it would appear, are not chiefly the result of genetic dilution by interbreeding, for at most major sites the differences between black and white Americans in defined areas seem largely independent of the degree of admixture of white-derived genes among the blacks in those areas (Petrakis, 1971).

A similar comparison can be made between the Japanese and Caucasian residents in Hawaii and the Japanese in two particular prefectures of Japan (table 4). The close approximation of the rates in the two prefectures gives some justification for believing that they may be typical of the areas from which the Japanese migrants to Hawaii (or their ancestors) originated, although the migrants will have come from other parts of Japan as well. For every type of cancer except cancer of the lung, the rates for the migrants are more like those for the Caucasian residents than for those in Japan.

Other groups for which data are available include Indians who went to Fiji and South Africa (and lost their high risk of developing oral cancer), Britons who

easy to be sure about changes in the incidence of cancer of the esophagus, because the disease can be diagnosed without complex investigations and its oc-

TABLE 4.—*Comparison of cancer incidence rates[a] in Japan and for Japanese and Caucasians in Hawaii*

Primary site of cancer	Patients' sex[c]	Annual incidence/million people[b]		
		Japan[d]	Hawaii, 1968–72	
			Japanese	Caucasians
Esophagus	♂	150 112	46	75
Stomach	♂	1,331 1,291	397	217
Colon	♂	78 87	371	368
Rectum	♂	95 90	297	204
Lung	♂	237 299	379	962
Prostate	♂	14 13	154	343
Breast	♀	335 295	1,221	1,869
Cervix uteri	♀	329 398	149	243
Corpus uteri	♀	32 20	407	714
Ovary	♀	51 55	160	274

[a] From IARC (1976).
[b] Ages 35–64 yr, standardized for age as in IARC (1976).
[c] Male only, wherever possible; sites selected as in table 3.
[d] For each type of cancer, upper entry shows incidence in Miyagi prefecture, 1968–71; lower entry shows incidence in Osaka prefecture, 1970–71.

Document Navigation

View Range: 1 - 10 of 117

NEXT »

REDISPLAY