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Institute of Cancer Research
Royal Cancer Hospital of London

The Principles of Cancer Prevention

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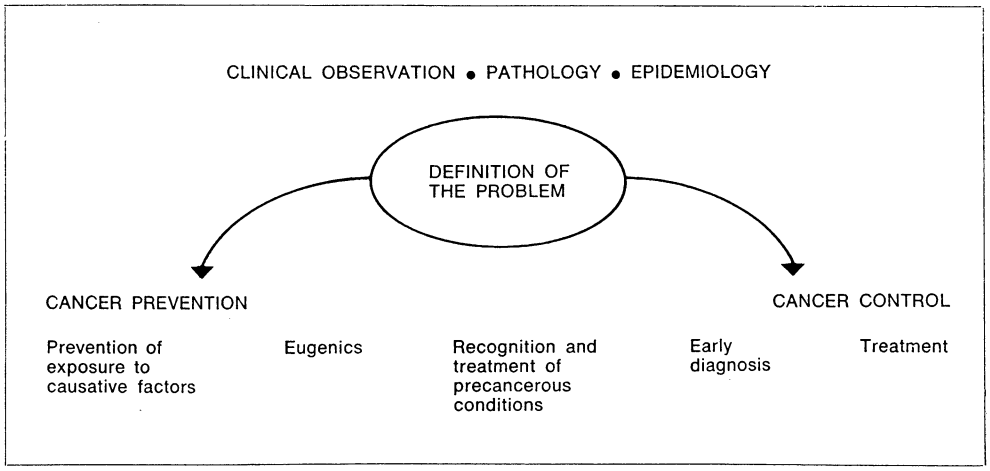
The author begins by defining the exact meaning of the term « cancer prevention », which does not *include early diagnosis, for example, and the meaning of the word « cancer », which refers not to a single disease but to a host of quite different diseases. He argues that there is a great deal of evidence to show that cancer is the product of environmental far more than of genetic factors and presents a number of exceedingly interesting data regarding the relations between cancer and age, the induction time, that is the interval between exposure to a carcinogen and the clinical onset of cancer, and the concept of « threshold dose » of carcinogens.*
Discussing the epidemiologic aspects of cancer prevention, the author explains that if statistical studies are to afford usable data, they must be designed on the principle of cohort analysis, and he goes on to discuss in detail the theoretical proportion of preventable. The study of cancer among migrants provides ammunition for the thesis that environmental factors are more important than genetic factors.
Coming to the theme of cancer prevention in the strict sense, the author divides the subject into four main blocks: the study of the causation of cancer by epidemiologic and experimental methods; the education of doctors, of industrial workers and of the general public; industrial and personal hygiene; and, lastly, the laws that govern or ought to govern industry, foodstuffs, pharmaceuticals and pollution generally, quoting actual examples of each of these aspects. The gravest gap in cancer prevention is the lack of adequate legislation and the reluctance of governments to take the initiative in this field.

The medical student is taught that disease is either genetic or environmental in origin. In reality, both genetic and environmental factors are often implicated in the genesis of a single disorder, but the proportions of their contributions vary widely. Cancer is like other diseases in these respects.
True cancer prevention, if it is not based on the practice of eugenics, must mean reducing or abolishing exposure to causative factors. Table I illustrates the distinction between cancer prevention and cancer control. Early diagnosis is not cancer prevention, although it may prevent death from the disease. The recognition of the precancerous nature of non-malignant lesions and their removal may also preclude the development of cancer, but successful cancer prevention would obviate the development even of the precancerous lesion.
Some of the aura of fear that surrounds even the word « cancer » stems from its being widely regarded as a causeless disease — a phenomenon that just happens. This concept is manifestly wrong, firstly because cancer is not a single disease, and secondly, because there is good evidence that exposure to particular environmental factors is of critical importance in the genesis of many forms of human cancer.

* English text of the Inaugural Lecture delivered on 28 November 1968, at the Oncological Centre of Genoa, under the auspices of the Italian Ministry of Health.

Table I - Distinction between cancer prevention and cancer control.



The nature of cancer

A modern concept of cancer

Cancer is to be regarded, not as a single disease, but as a group of diseases which differ widely among themselves (see table II).

The spectrum of types of cancer is at least as wide as that of types of infectious disease both in respect of manifestation and causation.

Rarely genetic factors appear solely to determine whether cancers arise, for example, von Recklinghausen's neurofibromatosis multiplex and some forms of acoustic neuroma.

More commonly, where there is information on causation, chemical factors or physical factors such as sun-light or X-irradiation, appear as the most important determinants, though in these cases it is often possible to show that susceptibility to cancer-induction by these agents is influenced by genetic constitution.

Mouse tumour viruses such as the Bittner milk virus and the Gross Passage A leukaemia virus are passed naturally from a mother to her progeny either through the placenta or through the milk after birth.

Their viral nature only became evident because it is possible to control the breeding of laboratory animals and to rule out genetic differences by systematic in-breeding through many generations.

In man these procedures cannot be followed. This may be the main reason why no human tumour virus has yet been discovered.

It is now known that some cancers induced experimentally in mice, following their exposure to X-irradiation or to a chemical agent, were primarily caused by a virus. In these experiments the role of the chemical was that of a co-factor or co-carcinogen.

It is possible that viruses capable of inducing cancer are as widely dispersed in man as they seem to be in mice, and that some cancers are due to the activation of such viruses by chemical agents or other means. Stress of the reticulo-endothelial and haematopoietic systems because of infection with falciform malaria may be the activating stimulus responsible for Burkitt's tumour, the true cause being a virus that is widely distributed in the areas where Burkitt's lymphoma is endemic (Burkitt, 1968).

Perusal of the epidemiological and experimental literature has led me to the view, which I hold strongly, that man is closely similar to other members of the Animal Kingdom in his response to carcinogenic agents. Studies on animals show that one

Table II - Modern concept of cancer

1. Comprises many different diseases
2. Due to a wide variety of causative factors: genetic, viral, physical or chemical
3. Multiple factors may be involved in genesis of one neoplasm: e.g., virus + chemical, chemical + chemical

type of cancer may be induced by a wide variety of agents and that multiple agents may contribute to the causation of a single cancer. It is highly likely that these observations apply equally to man.

Cancer in relation to age

It is tempting to regard cancer as a disorder associated with later life. With few exceptions (for example: brain, uterus, ovary and tongue) the risk of cancer developing in any organ of the body increases with age. On the other hand, no age group is immune to the possibility of developing cancer. Indeed, advances in the prevention and treatment of infectious diseases have left cancer, in its many forms, as the second commonest cause of death in early childhood. Accidents on the streets and in the home are still the most common cause. A proportion of the cancers of early childhood are now known to be due to exposure to X-irradiation *in utero.*

Some cases of cancer of the skin, lung or urinary tract which result from exposure to carcinogenic chemicals in industry arise relatively early in a man's working life. Men in their 20's or 30's may develop cancer of the skin of the scrotum if exposed to soot, coal tar or carcinogenic mineral oils. Cancer of the urinary bladder tends to arise 15-20 years after first exposure to dyestuff intermediates such as β-naph thylamine and benzidine though induction times of less than 5 years are recorded (Case et al, 1954). Some heavy cigarette smokers develop cancer of the bronchus before they are 40 years of age.

Induction time

In animal experiments the risk of cancer-development increases with dose. With increase of dose the average induction-time tends to approach a minimal, seemingly obligatory, period. When this point has been reached, further increase in dose is without effect on induction time. At the other end of the scale, however, reduction in exposure dose is associated with prolongation of the induction time, until, within the limits of a particular experiment, none of the exposed animals develop cancers before they die from other causes.

We have demonstrated these dose-response relationships in mice exposed just once, at birth, to a potent chemical carcinogen. The subcutaneous injection of less than one millionth part of a gram of the agent into one day-old mice increased the risk of their developing pulmonary tumours 50 weeks later. Increase in the dose given on the first day of life increased the chance of lung tumour development.

In both laboratory animals and man, it is evident that the risk of cancer development persists for a long time after all exposure to causative agents has ceased.

Studies on laboratory animals have led to the widely held view that the effects of carcinogens on tissues are irreversible. In other words, an increased risk of cancer development, resulting from exposure to a carcinogen, remains throughout life. In fact the evidence for this view is not complete, and it is possible that « repair » may lead to a gradual falling off in risk after exposure is stopped. In any case, wherever exposure to a carcinogen continues, so does the risk of cancer development.

Animal experiments indicate that genetic differences are associated with differences in susceptibility to the induction of cancer. These differences may be wide, but not so wide that the least susceptible animal can resist the effects of a potent carcinogen in high dosage. Differences in susceptibility undoubtedly exist between human beings, but at present there is no way of predicting an individual's susceptibility. It is, therefore, necessary to adjust exposure levels such that the most susceptible individuals are adequately protected. The requirements for such protection can be made on the basis of epidemiological information or by prediction from experimental studies on animals.

Fortunately, for reasons that are not fully understood, the time required for the induction of cancer in different species of animals varies with the normal life-span of the species. Thus, it takes at least a quarter of the life-span of man to induce bronchial carcinoma by the inhalation of tobacco smoke. It takes about the same time for the first skin tumours to appear in mice in response to the repeated application of tobacco smoke condensate.

Threshold exposure to carcinogens

There are no grounds for believing that exposure to any carcinogen at any level of exposure is truly safe. In animal experiments a risk of tumour-induction is seen to persist despite progressive reduction of dose if sufficient animals are studied for statistical comparison with untreated control animals. But since it is not possible to use animals in unlimited numbers, there is, for any biological system, a threshold dose of a carcinogen below which tumour-induction, for practical purposes, does not take place. It is reasonable to suppose that practical thresholds of the same kind apply to the response of man to carcinogens.

Some epidemiological aspects of cancer prevention

Competitive causes of death

From many points of view it is important to consider cancer as a one of several competing causes of death. Advances in microbiology culminating in the development of effective antibiotics and numerous immunization procedures have, during the past 60 or 70 years, dramatically changed the spectrum of causes of death. The risk of death from infectious diseases has been greatly reduced, the average age at death has risen, and more individuals are living to ages at which the risk of their developing one or other form of cancer is relatively high. During 1967, 20.3% of all deaths in England and Wales were recorded as being from neoplastic disease. In 1957, the figure was 18.2%. In the United States according to data collected by the National Office of Vital Statistics cancers accounted for 15.9% of all deaths in 1954 but only 3.4% of deaths in 1900.

Relative to other causes of illness and death, therefore, cancer has become, and is still becoming, progressively more important. By contrast the *risk* of dying from one of the many forms of cancer at any particular age is changing only slowly. But this overall view of the situation obscures important changes in risk in respect of particular forms of the disease. These changes are best defined by comparison of risk in relation to age and sex for cohorts of persons born during defined periods of time.

Cohort analysis

It is essential that anyone who is seriously concerned with epidemiological data in relation to the prevention of cancer bases his deductions on the assessment risk as determined by cohort analysis (Case, 1956). Figure 1, which relates to lung cancer in men in England and Wales, makes clear the distinction between *contemporary array* and *risk* at specified ages for *cohorts* of men born during stated periods. If only the contemporary array data were available, the fact that the risk of lung cancer is increasing in successive cohorts would be obscured.

In turn, the fact that the risk is increasing for successive cohorts during a period too short for marked genetic change, provides compelling evidence that causative factors of environmental origin are at work.

What proportion of cancers is theoretically preventable?

So far, we have been concerned with the definition of « cancer », making it clear that, from an aetiological point of view anyway, it should be regarded as a group of many different diseases, and we have been concerned with the relationship between exposure dose and induction time, and with the concept of *risk* in relation to type of cancer, age, sex and date of birth as the best measure of response of man to carcinogenic stimuli. The next task is to calculate the proportion of human cancers that are likely to be due to environmental causes.

My first approach to this was to study the present situation in England and Wales. Although in recent years there has been a welcome extension of the activities of Cancer Registries in Britain, the data available from such sources are not yet sufficiently reliable for the calculation of incidences of cancers of different types. It is necessary, therefore, to rely on cancer mortality figures as collected by the Registrar General.

In Figures 2 and 3, the total deaths from neoplastic diseases in men and women are represented by complete circles.

The proportions of deaths due to forms of cancer, which on the basis of present knowledge are mainly preventable (e.g. lung, skin, uterine cervix) or partly preventable (e.g. bladder, oral cavity), are shown as shaded segments. In men, because

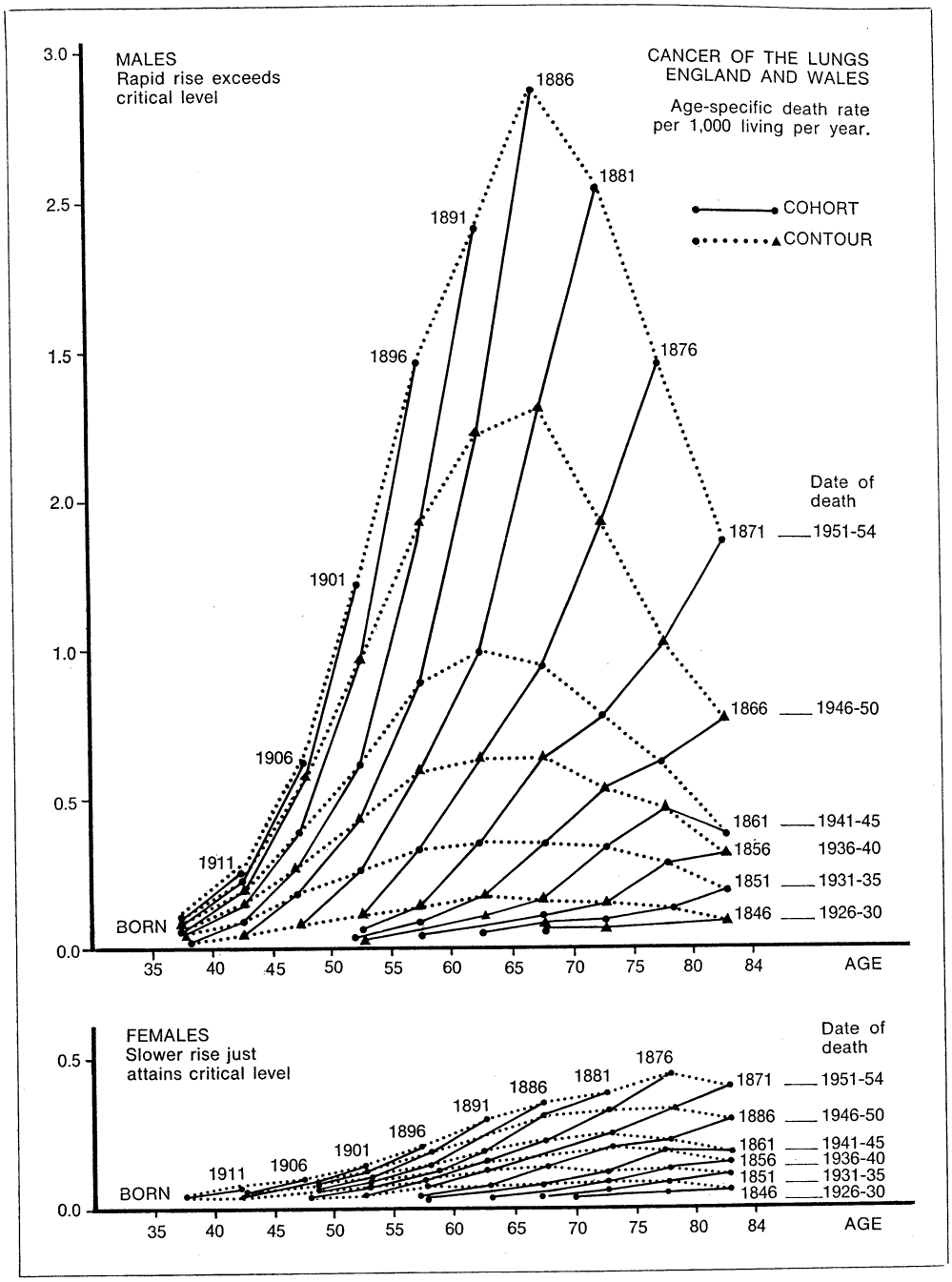


Fig. 1 - Environmental and cohort analysis of cancer mortality. Mortality data in quinary-five year groups distributed according to the years of birth (cohort analysis) and death (environmental analysis).

the present death rate from smoker's cancer has reached epidemic proportions, it transpires that over 40% of cancer deaths may be regarded as preventable. In women, the proportion is much smaller.

Both for men and women the application of knowledge with regard to the dangers from radiation (leukaemia), persistent chronic infection (e.g. of the gall bladder and penis) and other factors (Raven and Roe, 1967) is likely to reduce the number of deaths from cancer as mainly non-preventable on the basis of present knowledge, but the extent of the reduction that is possible is not easily predictable.

Another way of assessing the proportion of cancer attributable to exposure to environmental factors, is to compare death rates from cancers of different sites in various countries. Figure 4 shows that the sum of the lowest rates for different types

of cancer is, in both sexes, less than 20% of the sum of the highest rates. In other words, more than 80% of all cancers are probably of environmental origin and, therefore, potentially preventable. This encouraging figure is based on assumptions that may not be warranted. Differences in the methods of collection of data, and in their accuracy, between the 24 countries included in Segi and Kurihara's (1964) survey, which forms the basis of Figure 4 may have led to miscalculations. Also the bold assumption that none of the differences are genetic in origin may not be warranted.

One further assumption is implied, though not made, since Figure 4 is based on age-adjusted death rates. It is not necessarily true that the prevention of a large proportion of the cancers which at present cause deaths would be reflected in a comparable reduction in neoplastic disease as a competitive cause of death. Thus, a man who did not die of lung cancer when he was 50 might live to die from, say, lymphatic leukaemia when he is 70. Success of cancer-preventive measures may only be evident if measured as risk at specified ages.

Cancer in migrants

One way to distinguish between genetic and environmental factors in relation to cancer causation is to compare the incidence of cancer in people who migrate from one country to another. Such people tend, in the course of one or more generations, to renounce the way of life of their countries of origin and adopt the habits of the host country.

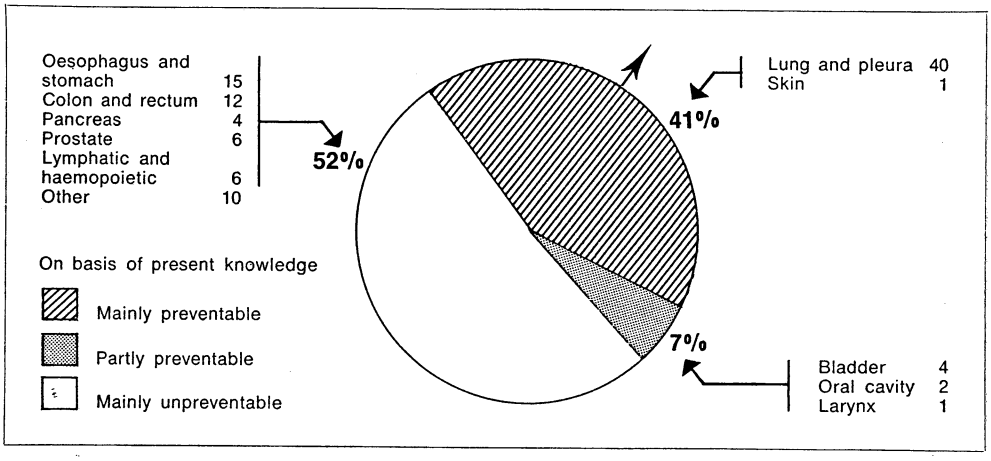


Fig. 2 - Preventable deaths due to cancer (England ans Wales, 1967): men.

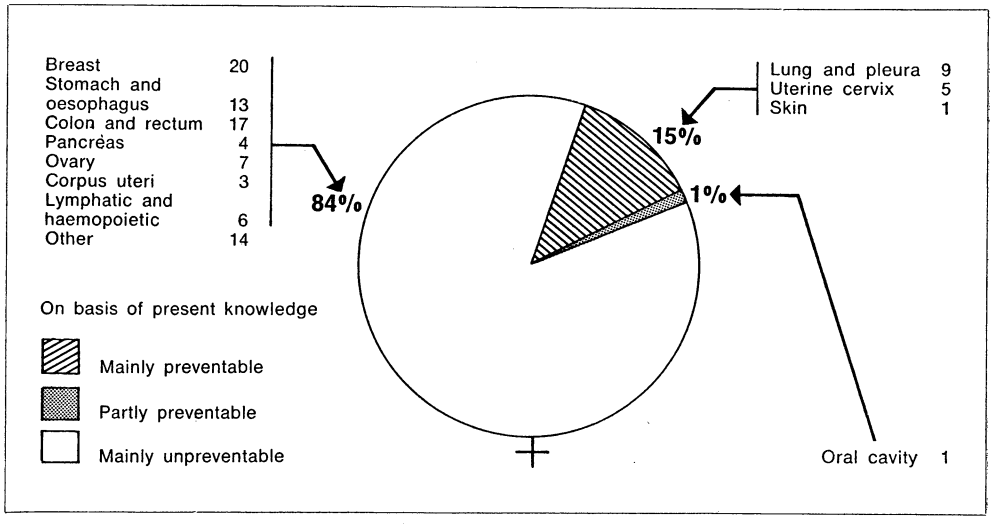


Fig. 3 - Preventable deaths due to cancer (England and Wales, 1967): women

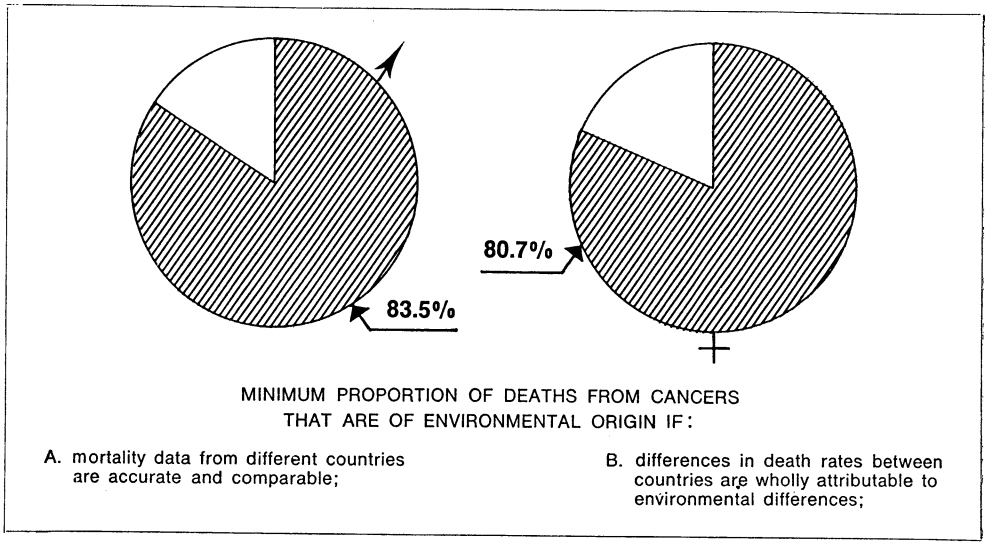


Fig. 4 - Calculations based on age-adjusted death rates for neoplastic diseases with a selected site (6/7th of all the cancer deaths) for 1960-61 in 24 countries (Segi, 1964).

Several studies of this kind have been reported, but perhaps the most crucial is that of Haenszel and Hillhouse (1959) on Japanese migrants to the United States and Hawaii, and on their descendants. The interpretation of cancer mortality rates for migrants themselves is complicated for three reasons. Firstly, their variable periods of exposure to the environment of their countries of origin may be critical. Secondly, they, more than their children, are likely to cling to eating and other habits followed since birth. Thirdly, people who choose to migrate may be temperamentally different from those who do not; this fact, or the insecurity they feel in the host country, may perhaps lead them to smoke or consume alcohol excessively. The same difficulties apply with much less force to the offspring of migrants.

Table III - Changes in Cancer Risk for Japanese Men who migrate to U.S.A.

Standardized mortality ratios (Japan = 100) for:	Japanese-born	Japanese-born Migrants to U.S.A.	U.S.A.-born Japanese	U.S.A. white
Stomach	100	72	38	17
Colon	100	374	288	489
Lung	100	306	166	316
Leukaemia	100	314	—	265

(From Haenszel and Hillhouse, 1959)

Table IV - Changes in Cancer Risk for Japanese Women who migrate to U.S.A.

Standardized mortality ratios (Japan = 100 for:	Japanese-born	Japanese-born Migrants to U.S.A.	U.S.A.-born Japanese	U.S.A. white
Stomach	100	55	48	18
Colon	100	218	219	483
Breast	100	166	136	591
Ovary	100	337	—	535
Cervix uteri	100	52	33	48

(From Haenszel and Hillhouse, 1959)

Except in the case of cancer of the breast, the calculations shown in Tables III and IV strongly suggest that the children of Japanese migrants to the United States, experience risks of dying from cancers of different sites, closely similar to those experienced by the white population of the host country.
It is reasonable to conclude that environmental rather than genetic factors are likely to be the chief determinants of the types of cancer listed. The results of this survey suggest that genetic factors may be more important in the case of breast cancer. However, other epidemiological studies indicate that environmental factors may also be of some importance.

Cancer prevention: Subdivision of the subject

In the light of a modern concept of cancer and of a definition of the scope of « Cancer Prevention », and because of the strong epidemiological evidence that environmental factors are important determinants of many forms of human cancer, it is reasonable to see how the subject of cancer prevention can be subdivided into its components parts (Table V).
Precise knowledge of causation is not a prerequisite to prevention. The important carcinogens in tobacco smoke have not been identified, and a wide variety of environmental factors, including irradiation, arsenic, nickel and chromium compounds air pollutants as well as tobacco smoke, are associated with an increased incidence of cancer of the lung. Despite this lack of knowledge, it cannot be doubted that the stopping of smoking alone would reduce the present incidence of lung cancer to an almost negligible level. The evidence for this comes partly from epidemiological and partly from experimental studies.

Research

The best evidence that a particular factor is important in the causation of cancer in man, must come from studies on man. But critical epidemiological studies are much more costly than well-designed tests on laboratory animals. The role of animal studies is threefold. Firstly, they may be used to « screen » environmental factors for carcinogenic activity. Secondly, they may be used to check theories or suspicions stemming from observations on man. Thirdly, they enable the study of mechanisms.
The relationship between man and his environment is immensely complex, so that even with the aid of an excellent computer service it is rarely possible to identify causative factors with certainty. For this and other reasons, epidemiological methods have, so far, only been successful in pointing to relatively potent carcinogens such as tobacco smoke or to industrial carcinogens to which only a few persons are

Table V - Different aspects of cancer prevention.

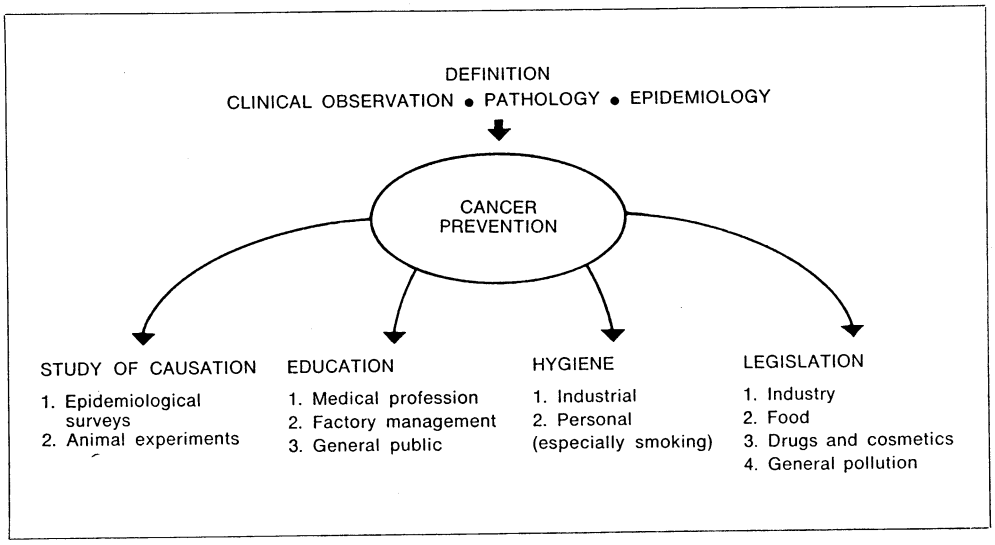


Table VI - Comparison of death rates from lung cancer in NZ-born whites and immigrants from UK

	Observed	Expected	Significance (X^2)
NZ-born	632	721.8	$p < 0.001$
Immigrants	369	279.2	
Immigrants under 30 on entry	187	231.9	$p < 0.001$
Immigrants over 30	168	123.2	

(After Eastcott: Lancet, 1956, i, 37)

exposed. If relatively weak carcinogens to which whole populations are exposed are to be identified, more detailed and longer-term studies will have to be made. Observations such as those of Eastcott (1956) and Stewart (1967) suggest that careful prospective studies of individuals and their environment from before birth until late in life may provide important information with regard to the causation of cancer. Eastcott (1956) reported that persons who migrated from Britain to New Zealand have a higher risk of developing lung cancer than native-born New Zealanders, despite similar genetic constitution and smoking habits. Furthermore, those who migrated after the age of 30 are at greater risk than those less than 30 at the time of migration (Table VI). Stewart (1967) showed that a proportion of cancers and leukaemias in young children are attributable to their exposure to ionizing radiation before birth. In most cases exposure was occasioned by the use of X-rays to measure the size and shape of the mother's pelvis.

In my opinion (Roe, 1966) the greatest danger in the interpretation of studies on laboratory animals is that they may sometimes lead those interested in the causation of human cancer in wrong directions. This is most likely to occur if there is a failure to appreciate that in a single test it is impossible to distinguish between a carcinogenic effect and a co-carcinogenic one, or if substances are tested unrealistically — for example, if an unabsorbable food constituent is regarded as carcinogenic because it gives rise to sarcomas at the site of its subcutaneous injection in rats.

Education

The more successful any measure of prevention is, the less interesting and topical it becomes. It is difficult to be excited about, or even thankful for, a cancer that has *not* appeared.

The concept of cancer as a largely preventable disease is not yet widely held. The first task of education in cancer prevention is to convince members of the Medical Profession that most cancers are, or might be preventable, and that « prevention », as an approach to the problem, is likely to be more successful than « treatment » or « control ». How many doctors when confronted with a case of cancer ask the question « What can I learn about the factors that caused the disease in this patient? » How many doctors collaborate willingly when they are asked to provide data in relation to epidemiological studies aimed at detecting causative factors? How many doctors instruct their patients to avoid known carcinogens such as tobacco smoke, asbestos dust, and mineral oils? A doctor may not himself be able or willing to give up the smoking habit, but one may question the integrity of a doctor who permits his habit to obscure from others the causal association between smoking and the risk of developing cancer of the lung.

Factory doctors have a specially important part to play in cancer prevention. First they should keep abreast of the latest knowledge of cancer causation. Secondly, in the light of their knowledge they should try to *anticipate* occupational cancer hazards and persuade factory managers that precautions are necessary. Thirdly, they should see that workers are adequately instructed with regard to the need for protection and use of protective clothing and other devices. There are, unfortunately, examples of the failure of factory doctors in all these functions. The danger of skin cancer from exposure to unrefined mineral oil should have been more than

evident in the light of the epidemic, particularly of scrotal cancer, in cotton spinners during the late 19th century and early 20th century. So serious was the epidemic in Britain that the use of unrefined oils for lubricating spindles was banned and the provision of facilities for biannual medical examination for skin lesions made compulsory. Nevertheless, the lesson learned in the Cotton Industry was not applied to the Engineering Industry, and the tragedy of scrotal cancer is once again becoming common in the Birmingham region of England. The men most frequently affected are tool-setters working on automatic machines in which unrefined mineral oils are used liberally for lubrication and cooling purposes.
Recently we reported that a sample of mineral oil taken from a batch in current use for the softening of jute caused invasive skin cancer in 25% of mice to which it was applied only 14 times (Roe et al, 1967).

Industrial hygiene

Unfortunately, it is not sufficient to warn workers about cancer hazards and to provide them with protective clothing and washing facilities. As long as protection is on a voluntary basis, some men will still be exposed to the hazard. Only a radical change in the industrial process, whereby the possibility of exposure to carcinogens is excluded, is likely to be really effective in preventing cancer. The difficulty stems from individual differences in personal hygiene standards, and from the fact that one man's carelessness or lack of skill may endanger many of his colleagues.
In the course of a recent visit to an engineering factory, I saw two men doing the same job. One wore protective clothing but was soaked in mineral oil and had oil on his face, hands and shoes. The other was immaculately clean as he sat in his white shirt and ordinary trousers. The latter was meticulously careful in the way he removed oil from surfaces into which he might come into contact. He was skilful and precise in each operation he performed. The other man was, from many points of view, « a dirty worker ». Devices designed to protect the dirty worker are liable unjustifiably to reduce the productivity of the clean worker.

Personal hygiene

As long ago as 1892 Henry Butlin compared the dirtiness of the average English chimney sweep and his heightened risk of developing cancer of the scrotum with the cleanliness of Swiss and German sweeps in whom scrotal cancer was rare.
However, the value of personal hygiene is not limited to occupational cancer hazards. It is well known that cancer of the oral cavity is closely associated with standards of oral hygiene. Cancers tend to arise at points of chronic irritation associated with dental malformation and decay. Tertiary syphilis, and severe periodontal disease predispose to oral cancer.
Cancer of the penis and uterine cervix are also closely associated with standards of personal hygiene. Chronic inflammation starting in the smegma under the foreskin of the uncircumcised penis is the usual starting point of cancer of this organ. Cancer of the uterine cervix is much more common in the wives of uncircumcised men than in the wives of circumcised men irrespective of race (Dunn, Buell, 1959). There is a 23-fold difference between the Jewish women and Puerto Rican women of New York in the incidence of cervical cancer (Haenszel, Hillhouse, 1959). Circumcision is probably no more than « compulsory personal hygiene ».
The risk of cancer of the cervix increases with the extent and range of a woman's sexual activities. The earlier in life that she first experiences sexual intercourse and the more men with whom she associates sexually, the greater her risk of developing cancer of the cervix (Elliott, 1967). It is not known at present whether the increased risk is due to poorer hygiene in a general sense, or to specific carcinogens in smegma or associated with micro-organisms transferred venereally. It is possible that cancer of the cervix will one day be regarded as mainly a venereal disease.
Another aspect of personal hygiene may well become an important subject in the future. The harmful effect of inhaling different types of dusts and fumes has only recently become a matter for serious study. At the same time the number and variety of aerosols to which man is exposed in the form of industrial and agricultural

sprays, paints, insecticides, cosmetics, and materials for domestic use, including foodstuffs, is increasing rapidly. Until data from animal experiments suggest that the inhalation of such aerosols carries no risk to health, the ordinary man would be well-advised to keep the level of his exposure to them to a minimum.

The role of legislation

a) *Industry.* Governments do only those things which they are forced to do, or which are easy to do. Their activities are sometimes influenced as much by political pressures as by scientific facts, and they are often inflexible in relation to the changing scene.

In Britain, legislation designed to protect workers in industry follows a very long time after the recognition of a cancer hazard, and even a long time after the cause-and-effect relationship is sufficiently established for compensation to be payable.

Because industry is competitive, employers are sometimes reluctant to introduce costly protective measures voluntarily. Smaller firms might go out of business if they did so when other employers did not. In these circumstances, reduction of cancer risk can only be achieved by firm legislative action.

b) *Food.* In the United States and Britain and most European countries the use of food additives is controlled. Before the use of a new additive is permitted, an expert committee consider its nature and the biological evidence for its safety as derived from animal tests. Because of this kind of scrutiny, it is unlikely thant any important new carcinogen could find its way into the human diet in these countries.

In animals, it is possible to induce cancer of almost any organ of the body by the oral administration of different carcinogens. However, the gastrointestinal tract and the liver are the organs most commonly affected if carcinogens are given by this route. It is, therefore, encouraging that the mortality rate from stomach cancer has been falling rapidly in the United States, and more slowly in Britain during the past 60 years. Moreover, the incidence of liver cancer, which has never been high, is not rising.

The control of the constituents of foodstuffs themselves, of traditional food additives, and of food contaminants is much less satisfactory. The present system of tests demanded by governments in respect of proposed new additives cannot possibly lead to any reduction in the existing incidence of any form of cancer. In recent years contamination of human food with two highly potent carcinogens has come to light accidentally rather than by the result of tests required by governments. I refer to *aflatoxin*, the product of a mould which may infect ground nuts and a wide variety of cereals stored under hot and humid conditions, and to *dimethylnitrosamine* that may be formed under certain conditions of heat by the reaction of nitrites with secondary or tertiary amines. Both nitrites and amines occur naturally in foodstuffs whilst nitrites are added to some meats, fishes and cheeses as a preservative. The use of nitrites provides the best safeguard man has against *botulism* — food poisoning due to a deadly toxin produced by *Clostridium botulinum*. But it was not botulism that killed mink and foxes on fur farms in Norway and England in 1961. The animals died because they were exceptionally sensitive to the acute toxic effects of dimethylnitrosamine formed when nitrite-preserved herrings were heated during processing to herring meal — a minor constituent of the diet of fur animals. Cancers of a wide variety of organs have been produced in various animal species with dimethylnitrosamine.

Man is the only animal who cooks his food; he is also the only animal that experiences a high mortality from cancer of the colon.

Could this be because nitrosamines are formed during cooking processes?

This type of problem deserves high priority, but at present Governments have no procedural means of dealing with it. Perhaps the discovery in a government-supported laboratory in Britain of a relatively high concentration of carcinogenic nitrosamines, in an alcoholic beverage consumed by Bantus who have an exceptionally high incidence of cancer of the oesophagus, heralds the day when priority is given to the search for potent carcinogens in traditional foodstuffs.

c) *Drugs*. There are welcome signs that the possibility of cancer induction by drugs is to be given more attention by governments and international bodies such as the International Cancer Union (U.I.C.C., 1967). The subject has been reviewed recently (Roe, 1966).

Concluding remarks

Much of the subject of cancer prevention lies in the future. Better definition of the human cancer burden, through higher autopsy rates, better pathology, better clinical records, and better death certification is a first requirement. Detailed and more extensive investigation of causation by epidemiological and experimental methods are the second requirement. But these efforts will be wasted unless accompanied by education of the workers and general public and by legislative measures designed to protect people from exposure to carcinogens. At present, much cancer that could be prevented is not prevented. Poor education and legislation is partly to blame, but the weaknesses of informed men are the greatest bar to rapid progress.

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