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Probability of Causation:  
Implications for Radiological Protection  
and Dose Limitation

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PROBABILITY OF CAUSATION:
IMPLICATIONS FOR RADIOLOGICAL PROTECTION
AND DOSE LIMITATION

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Preface

I must warn you from the outset—the subject of probability of causation of radiation-induced cancer is a boring one; there is no escape. It is an attempt to bring together biology, chemistry, physics and statistics to calculate a value in the form of a ratio expressed as a percentage. It involves the interactions of numerous cancer risk factors, and all are fraught with technical difficulties and uncertainties. It is a computational approach to a societal problem that should be resolved in the political arena by men and women of government and law. But, it must be examined, because at the present, we have no reasonable method to explain the complexity of the mechanism of radiation-induced cancer and the probability of injury to an individual exposed in the past to ionizing radiation, and because society does not know how to compensate such a person who may have been injured by radiation, and particularly low-level radiation.

In the coming hour, I should like to discuss five questions that concern probability of causation of radiation-induced cancer. First, what is it and how can we best define the concept? Second, what are the methods of estimation and cancer causation? Third, what are the uncertainties involved? Fourth, what are the strengths and limitation of the computational approach? And fifth, what are the implications for radiological protection and dose-limitation?

Introduction

Recently, there has been a great deal of interest in possible mechanisms for compensating cancer victims who have been exposed to a variety of carcinogenic agents, including ionizing radiation, either in the workplace or as a member of the general public. These have become increasingly important issues in legal cases (e.g., the case of Utah residents exposed to radioactive fallout during early atomic bomb tests), and efforts are in place in a number of countries to allocate acceptable judicial or administrative compensation through some method of determining attributable proportion of risk. Nevertheless, if an individual claims that his or her cancer was caused by exposure to some environmental factor, such as ionizing radiation, it is not possible for medical science to confirm or deny that claim; attribution of causality cannot be achieved. This is particularly cogent in radiation injury claims since, while there is certainty about the carcinogenic agent that is involved, what must be determined is the degree to which a radiation exposure sometime in the past may have contributed to the development of a cancer in an individual victim.

It is established that radiation acts to cause cancers in a largely random manner. In a situation in which a large number of people are exposed to large or moderate amounts of radiation, the numbers of specific cancers, e.g., breast cancer or leukemia, induced by that radiation can be estimated statistically. However, which individuals in the irradiated population will develop cancer cannot be predicted. Nor is it possible to determine whether a cancer that developed in an exposed individual was caused by radiation, since it is not possible to differentiate cancers induced by radiation from those that occur spontaneously in the population. Consequently, any method for adjudicating claims for radiation-related cancer will ultimately use arguments regarding the probabilities that the cancer in question was related to a specific prior dose of radiation or regarding the share of causation that the radiation should bear.

While a number of alternative administrative approaches has been suggested for dealing with radiation compensation claims, e.g., some similar to workmen’s compensation, some determined by adjudication, and some decided through the tort law system, a method is now proposed in the United States whereby a cancer victim whose cancer may or may not have been caused by a prior radiation exposure in question (e.g., inadvertent
exposure to radioactive fallout following nuclear weapons testing, occupational exposure in a uranium mine) would be entitled to partial compensation in proportion to the probability of causation of that cancer by radiation. Various schemes and computational approaches have been suggested in the United States, in Great Britain and in Canada, and the U.S. Congress charged the U.S. Department of Health and Human Services (National Institutes of Health) with developing radioepidemiological tables of probabilities of causation of radiation-induced cancer for different sexes, age groups, and cancer sites. The extent to which the assumptions and methods used for developing these tables provide a scientific basis for attributing causation is the subject of reports of the U.S. National Research Council, and of the U.S. National Council on Radiation Protection and Measurements and has now been the subject of a number of critiques during and since publication of the National Institutes of Health ad hoc Working Group Report.

Definition: Probability of Causation. During the past several years, over 4,000 claims have been filed against the United States government by individuals who allege cancer caused by exposure to ionizing radiation, due to fallout from atomic weapons tests during the 1950s, or as employees of uranium mines, nuclear power plants and national laboratories. Through the efforts of the U.S. Department of Labor, the National Council for Radiation Protection and Measurements and legislation by the U.S. Congress, a series of efforts have been undertaken in the United States to devise a method of compensation for such cancer victims based on radioepidemiological tables of probability of causation, or PC. The idea behind the radioepidemiologic tables is that it is possible to estimate the probability that a specific dose of radiation caused a specific cancer, given knowledge about the radiation, the type of cancer, and the various characteristics of the cancer victim. The probabilities being calculated must be based on a limited set of characteristics of the individual. It is necessary to have substantial data to make it possible to compute these estimates. Only those characteristics are used that place a person in a group about which cancer rates are known or can be estimated with and without exposure to radiation. The definition of these groups is only partly a scientific matter; social considerations such as ethnicity or occupation, also apply. Moreover, radiation may not be mutually exclusive of other possible causes of cancer.

The current probability of causation radioepidemiologic tables prepared by the National Institutes of Health Ad Hoc Working Group represent a complex computational approach that may be applied to a situation when a cancer is diagnosed in a person previously exposed to ionizing radiation, and to estimate the chance, or probability, that the prior radiation exposure was, in fact, the "cause" of that cancer. Studies indicate that it is possible to compute estimates of probability of causation for cancers that follow exposure to radiation. This is done by comparing two groups of people, exposed and not exposed. The estimates depend on the partition of the groups used for calculation and on the specific risk factors considered. The calculations provide an estimate of the share that might be assigned to the dose of radiation.

In its simplest form, the value of PC can be estimated as a ratio:

\[
P_C = \frac{\text{excess risk attributable to a particular radiation exposure}}{\text{total risk due to all causes}}
\]

The cancer risk may be defined as the expected increase over the spontaneous cancer incidence rate when a population is exposed to the radiation dose in question. In general, PC is a ratio where the numerator is the excess risk of cancer in a population which can be attributed to the radiation dose, and the denominator is the total cancer risk, i.e., the
Probability of Causation (PC) = \frac{RR}{RR + RN}

where RR is the cancer risk attributable to the radiation exposure; RN is the risk attributable to spontaneous causes (or normal baseline cancer incidence), and RR + RN is the total cancer risk, i.e., spontaneous or background risk plus the added risk due to radiation. This formula characterizes the increased cancer risk (or cancer incidence rate) due to exposure to a single factor, relative to the baseline incidence rate in the absence of added radiation.

The PC formula, in this form, does not attempt to assess the contribution of interactions among competing or interacting risk factors, but the formula can be extended to deal with multifactorial interactions. This can be done in order to consider effects of other carcinogenic agents, such as other sources of radiation or cigarette smoking, in the modified formulation:

\[
PCR = \frac{RR}{RR + RN + RO + RA}
\]

where PCR is the conditional probability that a radiation exposure was the cause of the excess risk of the cancer that has occurred; RR is the excess cancer risk attributable to that radiation exposure; RN is the risk due to natural causes; RO is the risk due to other radiation exposures (e.g., medical X-rays); and RA is the risk due to other carcinogenic agents in the environment (e.g., cigarette smoking).

Methods of Estimation and Cancer Induction

A number of assumptions form the basis of the calculations of PC. These deal primarily with mechanisms of causation, dose-incidence relationships, risk-projection models, data sources, technical difficulties and uncertainties.

Assumptions

Let us assume that in the United States a 32-year-old male develops leukemia 5 years after exposure to 0.01 Gy of gamma radiation. The probability of causation may be estimated from the spontaneous incidence rate of leukemia in males (for age 30-34, it is 28 x 10^-6 year^-1) obtained from the U.S. National Cancer Institute SEER Report, and the excess risk due to an additional 0.01 Gy of low-LET whole-body radiation (approximately 2 x 10^-6 year^-1) obtained from the 1980 NAS-BEIR III Report, so that PC = 2/(28 + 2) = 6.7%. In this example, if an individual who develops leukemia is selected at random from the exposed population, the "probability" that radiation caused his leukemia is 6.7%. This calculation assumes the reliability of baseline cancer incidence data and the risk coefficients for radiation as a cause of cancer, the application of appropriate risk-projection models, that no interaction occurs among sequential or interdependent causation factors, and that the PC derived is the characteristic of the individual with cancer. It is necessary to base PC calculations on several assumptions regarding latency intervals and their variation with time after irradiation, shapes of dose-response relationships, and time-response models. Several alternative statistical methods can be used, and in practice regression analyses of dose-response and time-response relationships can incorporate all the epidemiologic data.
simultaneously. Such factors as age-at-exposure and age-at-cancer diagnosis, radiation dose, etc., may be incorporated into the models as either continuous or categorical variables.

**Data Sources and Models**

In order to determine how much an individual’s cancer risk is increased by radiation, and what proportion of that individual’s total cancer risk that increase is represented, certain additional assumptions must be made concerning the epidemiological and radiobiological data. The probability that a cancer was caused by radiation depends on many factors, including estimates of the cancer induction rate per unit dose, the tissue dose, the type of radiation, the dose received, and its distribution in time. The total cancer risk includes the baseline cancer risk of that individual (i.e., cancer incidence rate) and any other cancer risk factors that characterize that particular individual (e.g., heavy cigarette smoker, benzene chemist, asbestos worker, etc.).

**Cancer Incidence Data.** For purposes of compensation, reliable baseline cancer incidence data are required for PC calculations. The possible causal relationship between the cancer and prior radiation exposure will invariably arise at the time of diagnosis, and this relationship will obtain also for cancers that do not cause death of the individual.

Cancer incidence data are usually more reliable than cancer mortality data especially in countries with comprehensive tumor registries and centralized health agencies. In the United States, for example, cancer incidence rates are available in the report of the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute. Age, sex, geography of residence, and race, as shown in the SEER data, are all important factors with respect to different cancers. Such data include the effects on spontaneous cancer rates of environmental risk factors that may have considerable influence on certain segments of the population (e.g., those exposed to radioactive fallout from weapons testing, occupational factors with respect to many cancers, including benzene-induced leukemia, and asbestos-induced lung cancers; and life-style factors, such as cigarette smoking-induced bronchial cancer).

**Cancer Risks from Radiation.** Cancer mortality risk coefficients, both for lifetime and on an annual basis, for populations exposed to ionizing radiation are currently available in the 1980 BEIR III Report and the UNSCEAR Report. The 1980 BEIR Report also provides cancer incidence risk coefficients for low-LET radiation based on the linear dose-response model, and linear-quadratic risk estimates for leukemia and mortality for cancers other than leukemia. The various reports of cancer risks from radiation have limitations, however, No one report is sufficiently comprehensive to provide reliable incidence risk coefficients, and all require constant revision and updating as new data become available. At present, it would appear best to rely primarily on the 1980 BEIR III risk coefficients; since that time new data on breast, thyroid and salivary gland cancers are available. Furthermore, it is now appropriate to omit lymphoma as a radiation-induced cancer, and avoid PC calculations for certain cancers following exposure at younger ages.

A large number of organ and tissue sites have demonstrated radiogenic potential, but not in all is there sufficient evidence of a statistical excess in carcinogenic risk above the natural incidence for estimation of probability of causation values. In general, these include primarily, leukemia (excluding chronic lymphocytic leukemia), bone cancer, thyroid cancer, breast cancer, lung cancer, stomach cancer, colon cancer, bladder cancer, liver cancer and salivary gland.

**Dose-Response Models.** For calculation of the carcinogenic effects of low-dose, low-LET radiation, the simplest dose-response models consistent with the epidemiological data may
be used. For leukemia and bone cancer, the data are consistent with a linear-quadratic model, and this provides the basis for the radioepidemiological tables for those cancers. Similarly, the linear-quadratic model has been used for all cancers except for thyroid and breast. For thyroid and breast, the data are consistent with a linear model, and the tables reflect this assumption. If a linear-quadratic model is used for extrapolation to low doses, no dose-rate correction is applied.

**Time-Response Models.** Assumptions must be made for the variation of carcinogenic risk with time after irradiation, that is, the number of cancers produced at any given time after irradiation in comparison with the number occurring in a similar population of the same age and sex not exposed to radiation. The risk coefficients provided in the 1980 BEIR-III Report are absolute risk estimates (based on an absolute-risk time-independent model) and measure the excess rate for all cancers or for specific cancer sites $\times 10^{-6}$ year$^{-1}$ $0.01$ Gy$^{-1}$ over a time interval of 20 to 30 years following exposure (for all cancers except leukemia and bone cancer). The 1980 BEIR Report also used a relative-risk time-projection model. For certain cancers, other absolute risk estimates depend on age at exposure, and all depend on sex. However, they do not appear to depend on time since exposure after a defined minimum latent interval. There are some epidemiological data, for example, from the Japanese experience, that appear to be consistent with a constant absolute-risk time-response model.

There is also support for a constant relative-risk time-response model; because it appears to fit the observations from most epidemiologic studies (particularly the Japanese atomic-bomb survivor breast and stomach cancer data available since the 1980 BEIR III Report) better than the absolute-risk model, except, perhaps, for leukemia and bone cancer. Modifications of both models are necessary to fit the data and, at present, there appears to be no scientific reason for the time-response of any radiation-induced cancer to fit either model precisely.

In their simplest formulations, both time-response models require the same data for estimation of probability of causation. For the constant absolute-risk time-response model,

$$PC = \frac{RR \times D}{RR \times D + RN}$$

where $RR$, again, is the absolute risk coefficient expressed as the excess cancer risk $\times 0.01$ Gy$^{-1}$; $RN$ is the baseline cancer rate at age of diagnosis, i.e., the risk due to natural causes, and $D$ is the radiation dose in Gy. For the constant relative-risk time-response model,

$$PC = \frac{RC \times D \times RN}{RC \times D \times RN + RN}$$

where $RC$ is the cancer risk coefficient expressed as the fractional increase per Gy in the spontaneous or baseline cancer incidence rate. In this formulation, the baseline cancer rates, $RN$, cancel out and

$$PC = \frac{RC \times D}{RC \times D + 1}$$
Here, once the minimal latent period has expired, the PC appears to be independent of the age of diagnosis of the cancer; if age remains a factor, its effect is masked.

High-LET Radiation. As yet, there appears to be insufficient epidemiologic data on cancer incidence in populations exposed to high-LET radiations such as neutrons and alpha particles and, therefore, no direct approach for calculating the PC values for high-LET radiation exposure. This is of particular concern for inhalation or ingestion of internal emitters, primarily, radon and its daughter products and, thus, for occupational exposure. This may be due to the fact that the radioepidemiologic studies are limited, and reliance may depend on indirect measures, such as application of quality factors, to low-LET radiation characteristics used for radiation protection guidance and conversion to specific quantities of dose, as in the case of alpha particle radiation dose received by uranium miners and estimated in working level months.

Multiple Causation and Interaction of Risk Factors

Cancer development is a complex, multistage process involving interactions between a number of endogenous and exogenous risk factors. Carcinogenesis involves several factors (including environmental factors and genetic susceptibilities) which may contribute in varying degrees to the occurrence and expression of the cancer. These factors may cause a person to develop cancer and interact in several ways, but very few of these interactions are known or understood. For example, a heavy cigarette smoker who is exposed to radiation and chemical carcinogens in the workplace may develop a lung cancer. Whether the lung cancer was caused wholly by one factor or by a combination or interaction of factors is, at the present time, not possible to determine. However, in certain limited situations, it may be possible to approach the problem of interaction of cancer risk factors for estimating probability of causation. This may be only possible for radiation carcinogenesis, provided that it is recognized that partitioning of risk factors in the population is limited at present, that is, by partitioning the population into categories based on very few factors, including age, sex, age at exposure to radiation, and smoking history.

There is very little known, about the interactive effects of ionizing radiation and other carcinogenic agents. The largest body of epidemiological data pertains to whether radiation and cigarette smoking are synergistic for lung cancer; data on other potential risk factors, e.g., asbestos, exposure to other carcinogens in the workplace, etc., are not available. Among miners who have had exposures to elevated levels of radon daughter products, the evidence is mixed; certain studies have shown a synergistic (or multiplicative) relationship between radiation and smoking, other studies have shown no interactive effects. Analysis of the Japanese atomic bomb survivors suggest an additive, nonsynergistic relationship.

Both additive and multiplicative models have been used by the NIH Committee to resolve the problem of interaction between cancer risk factors. It used a multiplicative constant-relative-risk model for all cancer types other than leukemia and bone cancer, and for all risk factors other than smoking and those forming the partition viz., sex, age and cancer site. Smoking was assumed to act additively with low-LET radiation, but multiplicatively with high-LET radiation.

For the two interaction models, the probability of causation method introduces a relative risk factor, $R_S$, appropriate to the level of a second risk factor, taking the general population as the basis for comparison. For the additive interaction model,
For the multiplicative interaction model, the PC is independent of the level of the second risk factor, whereas, for the additive model, application of the formula requires a knowledge of each RS, and the assumption that these relative risks are independent of age at the time of cancer diagnosis.

Uncertainties

In quantifying the attributable risk factors in the calculation of PC values, there are a number of significant sources of uncertainty associated with estimating each of the risk terms. The task of creating radioepidemiologic tables from available information is replete with technical difficulties and uncertainties. The data on radiation and cancer are too sparse by themselves to support any epidemiologic tables, and therefore assumptions must be made in order to carry out the calculations. Uncertainties in computing probability of causation arise not only from the available data used in calculations, but also from the assumptions and methods needed to convert basic epidemiologic and radiobiologic data into apportioned shares for radiation as a cause of cancer. Furthermore, even if an idealized set of PC values under given conditions could be computed (e.g., radioepidemiologic tables of probabilities of causation based on reliable radiation doses and dose rates, cancer incidence rates, radiation risk coefficients, time-response models, interaction models, etc.) rendering such values relatively free of uncertainties, the information required for application of such values to an individual cancer victim would still be highly uncertain. For example, reconstruction of the dose received in the past, the details of the radiation exposure, the precise cancer diagnosis, the cigarette smoking status, and the presence of other cancer risk factors are frequently poorly known.

Among the technical difficulties involved in developing radioepidemiologic tables, the most important are: methods used to analyze the available information on cancer in human populations exposed to radiation; methods to use information on radiation and cancer obtained in laboratory experiments with animals or cell cultures; extrapolating from high to low doses of radiation; determining the influence of age at exposure to radiation and time from exposure to diagnosis of the cancer; methods to treat risk factors for cancer other than irradiation; and sources of information on baseline cancer rates and radiation and related excess cancer to use.

As a result of these sources of uncertainty in the attributable risk terms for computation of PC values, the confidence interval surrounding the PC estimate could potentially be extremely broad, sufficient, some argue, to make it difficult and, in some cases, impossible, to draw reliable conclusions. What is currently lacking is a systematic approach to quantifying the nature and extent of these uncertainties, such as sites of cancer and cell types, source tables of cancer incidence, latent period, radiation dose and dose-rate effects, dose-response models, sampling errors in epidemiologic data, radiation risk coefficients, influence of age and sex, time-response models, other cancer risk factors and
interaction effects, transfer of risk coefficients from one population to another, etc. and their influence on the reliability of the computation of PC estimates.

The conceptual and statistical uncertainties involved in applying the PC methodology to the compensation of cancer cases where radiation may have been the basis for the position by some that the deficiencies in the approach preclude its use for public policy decision-making for compensation of individual claimants. There are several sources of uncertainty that enter into the PC calculation, and their combined impact, though difficult to quantify accurately, could be substantial. Three broad categories of uncertainty that deserve serious consideration are sampling variability in estimating human cancer incidence, inherent variability in the estimation of hazard rates for cancer at different dose levels, and the diversity, or nonhomogeneity of human populations, i.e., variability of hazard rates within the population due to the exogenous and endogenous factors.

We can identify and address a number of specific uncertainties; in general, the effect of their resolution on PC values can be predicted. These include the following.

(1) Dose to the individual. Its practical effect on PC calculations is highly variable especially if the individual did not wear a dosimeter or badge.

(2) Source tables on cancer incidence. In the United States, SEER tables may be used for all races and regions combined, but specific by age and sex; the data are limited to the period 1973-1981. Without proper adjustment for racial and geographic differences in cancer incidence rates, PC values may be high or low. In addition, not taking into account changes in cancer incidence over time may affect some PC values for the early onset of certain cancers.

(3) Influence of age at exposure. In many epidemiological studies, risk coefficients for younger age groups are not included; in addition, interpolation is required to obtain PC values for single years. This means fewer PC values are calculated for younger years, and PC estimates for exposure after 65 years of age are particularly uncertain.

(4) Sex differences. The few known sex differentials were used, notably breast and thyroid, but it is not known what practical effect resolution of uncertainty will have on the PC calculations.

(5) Cancer sites and cell types. There is some disagreement as regards the cancer sites to be included in the PC calculations; for example, lymphomas were excluded, and cancer of the liver, pancreas and salivary gland were included in the NIH PC tables. Some argue that exclusion of a site makes the PC approach inapplicable, whereas, inclusion of a site could provide wrong guidance for an administrative decision.

(6) Minimal latent period. At present, it appears appropriate to use a minimum latent period of 2 years for leukemia and bone cancer, and used a smoothing function for 5 to 10 years for solid cancers. This would result in fewer zero PC values within 10 years of exposure.

(7) Cancer risk coefficients. The best estimates available are the 1980 BEIR III linear risk coefficients for solid tumors adapted to the linear-quadratic model, except for breast and thyroid cancer, which are linear. Accordingly, the statistical uncertainties are carried forward into the PC calculations.
Dosimetry in the epidemiologic studies. These uncertainties are reflected in the 1980 BEIR III risk coefficients. However, revision of the atomic bomb dosimetry may increase many risk coefficients, perhaps by a factor of about 1.2 - 2.2 (as present knowledge broadly suggests) depending on a number of factors and may increase PC values somewhat less.

Dose-response function. The most prudent assumption is a linear-quadratic model for most cancer sites for low LET radiation exposure, and a linear model for thyroid and breast cancer. However, the true PC values may be greater or less, depending on the actual form of the Odose-response function.

Dose-rate. Fractionated or continuous radiation exposures occurring within a 24-hour period may be treated as single exposures; other exposures separated in time may be treated individually, not summed, and accumulated exposures over longer periods were treated as separate exposures occurring on different days.

Time-response model. The NIH Committee used a constant relative-risk time-response model for solid tumors (except for bone) and introduced a wave function for leukemia and bone cancer. For leukemia and bone cancer, the wave function appears to apply and any uncertainties relate to the precise form of the model. For solid cancer, the effect of the constant relative-risk model on PC calculations depends, in large measure, on the latent interval and whether it falls outside the period of observation. All current relative-risk models that use some variation over time might increase or decrease the particular PC estimates under consideration.

Other risk factors. The only adjustment that may be made for other competing risk factors (including life-style, diet, immunological status, etc.) at present is for smoking. In view of the fact that so little is known about competing and interacting risks and mutually exclusive causes, the effects on the PC calculations remain unknown and will depend on any interaction with radiation.

Given all these technical difficulties and uncertainties, any specific estimates of probabilities can be substantially uncertain, even if the characteristics of the cancer victims and their radiation exposures are well known. These uncertainties need to be acknowledged and taken into account if the PC tables are to be used for compensation decisions. Other methods for evaluating claims will also be subject to uncertainty, because they would have to take the information in the tables into account as well as other factors.

Strengths and Limitations of the Computational Approach. There are criticisms of the PC radioepidemiologic table that attempt to highlight issues concerned with administrative or policy decisions, rather than with the strengths of the scientific and statistical approach. In those matters impacting injury and compensation claims, these criticisms tend to single out the uncertainties and practical problems inherent in the PC methodology. Four important problems that require resolution have been raised. First, there are hundreds of suspected or known carcinogenic agents and risk data are available for only a few (e.g., radiation, smoking and certain hydrocarbons) causing an invariant formula approach to overestimate the importance of some factors such as ionizing radiation. Science cannot currently determine the exact cause of cancer, especially when a cancer victim has been exposed to a variety of carcinogenic agents. Second, emphasis on a formulation approach is dependent on accurate radiation dosimetry; reconstruction of the data on the dose of radiation to which a cancer victim may have been exposed sometime in the past can be extremely inaccurate, rendering formula computational results inaccurate. Third, in spite of considerable data available, cancer incidence data are still incomplete. The current computational approach does not take into account sufficiently such partitioning as racial,
geographical (regional), life-style, genetic and other differences in cancer incidence among individuals or groups of individuals. Fourth, the number of problems inherent in a formulation approach implies large uncertainties in the computed probabilities of causation, and this is particularly the case in the presence of joint or multiple causes.

What can emerge, from narrow application of the tables, therefore, is a policy judgment rather than a scientific estimate. Thus, it has been argued that if such formula results, based on arbitrary assignments of probabilities of responsibility to various risk factors, are applied to determine compensation eligibility, the chances of incorrectly granting or denying compensation to cancer victims whose PC values are close to the arbitrarily determined cutoff threshold can be very large. Furthermore, there is concern raised that radioepidemiological tables could be misused in court cases and administrative proceedings, and that the uncertainties underlying the PC values will be forgotten.

The current probability of causation methodology and related radioepidemiologic tables represent a departure from the conservative radiological risk assessment philosophy presently applied to radiation protection standards. This is particularly important in the use of best estimate, rather than upper bound, risk assessment approaches for application to probabilities of causation that may ultimately be applied to liability and injury compensation claims. The PC methodology is based on the best available population statistics (viz., general population, age- and sex-specific) and cancer incidence data, and provisions are made for competing and multiple causation risk factors, such as smoking and other nonradiation sources of risk, medical radiation, and risk relationships that are multiplicative in nature.

The present NIH, NCRP and National Academy of Sciences reports, however, have demonstrated that any calculation of probability ratios is necessarily complex, even for a single cause, such as ionizing radiation. But, in doing so, the procedures address methods for evaluating prospective risk that are more advanced than any previously available approach for quantifying risk impacting decision-making. It would appear that there may be some application of the method to the setting of radiation protection standards, as well as to retrospective estimates of cancer causation. At the present time, however, the current PC methodology does appear to incorporate a sufficient scientific basis that may be used as guidance to assist policy judgment, but not necessarily to replace it — for example, perhaps as a screening procedure, at least until such time that the method contains sufficient information for use in establishing liability and injury involved in compensation practices and procedures. The United States Veterans Administration has been considering potential application of the radioepidemiologic tables as a screening method in assessing compensation claims of veterans exposed to nuclear explosions during the 1950's.

It would appear that, while there may be some scientific hesitancy in accepting an effort to employ retrospective risk analysis, it is already being done on a practical basis, both in industry and in the courts. Thus, the present probability of causation methodology may be considered to be a step forward in helping to determine the scientific validity of causation in those cases of illness induced by an environmental carcinogen.

Implications for Medical Radiation

Once PC tables like those produced by the NIH committee exist, there may be little control over their further use. One such use could be compensation for cancer victims whose previous radiation exposure was medical for the treatment of a primary cancer or other condition. In considering the applicability of PC tables for such individuals, both scientific and societal issues must be addressed. The key scientific issue is whether the tables apply to cancers that followed radiation treatment. The current tables are based primarily on
individuals whose exposure was not elective and who were exposed when they were cancer-free. In contrast, patients who are intentionally irradiated for the treatment of an existing cancer are not typical of this population, and so for them the PC values from the NIH radioepidemiologic tables may be inappropriate. There is also the societal issue of whether physicians who irradiate patients as part of an accepted medical treatment should be held liable if these patients develop cancer as a result of the radiation.

Implications for Radiation Safety. The radioepidemiologic tables might have consequences for radiation safety and radiological protection regulations. In occupational settings, radiation exposure standards are set to minimize the number of future adverse health effects (cancer cases) among workers. However, because PC values are based on relative increases in baseline incidence rates of cancer, radiation workers who happen to develop cancer could have large probability of causation values. Thus, even though the worker may have had the standard protection agreed upon, and perhaps have been paid at higher rates because of the risk from exposure, it is not obvious that the worker could not use the PC tables as evidence of damage and ask for compensation. Therefore, the PC tables might have consequences for the amounts of money spent on safety in an industry, and conceivably lead to an increase or decrease in safety effort.

Other Considerations

Finally, the concept behind the probability of causation tables can be applied to substances other than radiation (e.g., chemical exposures). In many of these situations, the causal relationship between the exposure and cancer will not be as firmly established as with radiation and cancer. What rules should apply with respect to the appropriateness of PC tables for such toxic substances? These questions involve both scientific and societal considerations, and are unresolved.

Summary

1. Radiation-induced cancers have no unique characteristics in terms of tissue site or cell type; the current method to recognize an excess of cancer associated with radiation is by properly designed epidemiologic studies of exposed human populations. However, if an individual develops a cancer after being exposed to radiation, there is no known method to determine to what extent the radiation influenced the induction of that cancer. It is, nevertheless, possible to compute a "probability of causation" for cancers that occur after radiation exposure by comparing two otherwise similar groups of people, exposed and not exposed.

2. The probability of causation (PC) may be defined as the number of excess cancers in the exposed group divided by the total cancers. The quantities being computed are ratios and not probabilities in the usual sense. They are properties of the group to which a person belongs, and that property is then assigned to the person for some practical purpose, such as for compensation.

3. Mathematical formulation for PC computations applied in currently existing equations introduce a number of sources of uncertainty associated with estimating each of the attributable risk terms.

4. Technical difficulties and uncertainties arise from both the epidemiologic data used to compute the PC estimates and from the assumptions and methods required to convert the epidemiologic and radiobiologic data into PC values for radiation as a cause of cancer (e.g., dosimetry, baseline cancer incidence rates, age-, sex-, and race-specific radiation risk coefficients, interactions among risk factors, dose-
response and time-response models, etc.). As a result of these uncertainties, the confidence interval surrounding the PC estimates will be broad, making it difficult at times to draw useful conclusions. This has a bearing on the reliability and the usefulness of the PC formula as an administrative instrument for application to compensation claims.

5. However, our scientific knowledge is sufficient in many cases so that many PC estimates can be computed with some reasonable assurance for a limited number of known radiogenic cancers, particularly in the range of very low PC values where the calculation may show that, using even conservative estimates of dose and other risk factors, the chance is negligible that the radiation caused the cancer in question.

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