
INTRODUCTION

Overview, and Some Practical Implications of This Work

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- **Part 1. Practical Implications of Hypotheses One and Two**

During the 1990s, approximately 23% of the U.S. deaths have been caused by Cancer, and 22% by Ischemic Heart Disease (also called Coronary Heart Disease, and Coronary Artery Disease).

Would anyone NOT welcome a simple, safe, and painless way either to postpone many cases of such diseases or to prevent many cases from occurring at all? The findings in this book, combined with already-published wisdom from some mainstream radiologists and radiologic physicists, identify such a way --- with certainty for Cancer, and with great likelihood for Ischemic Heart Disease (IHD).

The word "practical" is featured above, because prevention of these two diseases has always been our chief reason for investigating their causes. The evidence assembled and analyzed in this monograph identifies medical radiation as a very important cause of both diseases. The work is organized around two hypotheses.

1a. Statement of Hypothesis-1 (Cancer) and Hypothesis-2 (IHD)

- Hypothesis-1 is this: Medical radiation is a highly important cause (probably the principal cause) of cancer mortality in the United States during the Twentieth Century. (Hypothesis-1 is about causation, so it is silent about radiation-therapy used after a Cancer has been diagnosed.)

We are well aware of a belief that medical radiation causes only a very low percentage of cancer mortality. That belief rests on a few estimates whose input-data are highly unreliable and sometimes inherently irrelevant, for the reasons presented in Chapters 1, 2, and 67 (Part 5). By contrast, the evidence in this book strongly supports Hypothesis-1. We are confident --- for the reasons listed in Chapter 1 --- that our findings are far more credible, scientifically, than the low estimates. Also we are confident, for reasons stated in Part 5, that our findings do not conflict with estimates that more than half of the cancer rate is a result of smoking and poor diet.

- Hypothesis-2 is this: Medical radiation, received even at very low and moderate doses, is an important cause of Ischemic Heart Disease (IHD); the probable mechanism is radiation-induction of mutations in the coronary arteries, resulting in dysfunctional clones (mini-tumors) of smooth muscle cells. (Here at the outset, we can prevent some confusion about Hypothesis-2 by stating that (a) it was discovered decades ago that medical radiation at very high doses can damage the heart and its vessels, and that (b) the kinds of damage reported from very high-dose radiation seldom resemble the lesions of Ischemic Heart Disease --- details in Appendix J.)

Chapter 45 presents a Unified Model of Atherogenesis and Acute IHD Events which is consistent with the evidence in this book, is consistent with the findings (first by Earl Benditt in 1973) of monoclonal cells in atherosclerotic plaques, is consistent with well-established knowledge about atherogenic lipoproteins and other non-xray causes of fatal IHD, and is consistent with recent findings about the weaker connection than expected between degree of arterial stenosis and the fatal rupturing of specific atherosclerotic plaques.

1b. What Constitutes "Medical Radiation"?

Because not all readers will "arrive" here from the same fields, or with the same backgrounds, or with English as the native language, this book defines various terms and concepts in the fields of

radiation, Cancer, Ischemic Heart Disease, and dose-response analysis. Definitions can be located with the combined Index and Glossary.

By medical radiation, Hypotheses One and Two mean primarily but not exclusively xrays (including fluoroscopy and CT scans).

There is no doubt that medical radiation can both be a cause of Cancer and also be used to treat Cancer. Cancerous activities are done by living cells, whose cancerous behavior can result from radiation-induced mutations of numerous types --- types which do not kill or sterilize the cells. When radiation is used for treatment of Cancer, it is used in very high doses which do enough damage to kill or sterilize cells. Clearly, dead or non-dividing cells cannot behave like cancer cells.

1c. Practical Implications of Hypotheses One and Two

The validity of Hypotheses One and Two is a question with major implications for future health, in the USA and elsewhere. Validity means that medical professionals and other humans have, already at hand, an opportunity which is guaranteed to achieve large reductions in FUTURE mortality-rates from Cancer and which is very likely to achieve similar reductions in Ischemic Heart Disease, in countries where medical radiation is widely in use.

Knowledgeable "mainstream" experts in radiology and radiologic physics have shown that xray dosage, from nontherapeutic diagnostic and interventional radiology in current medicine, could readily be cut by a factor of two or more (Chapter 1, Box 3) --- while still obtaining all the benefits of such radiology and without eliminating a single procedure (specifics in Chapters 1 and 2). Example: While radiographers have reduced the xray dose per mammographic examination by more than 10-fold, use of mammography has risen dramatically. The result of dose-reduction has certainly not been less mammography --- but rather, less-risky mammography.

Beyond diagnostic radiology, there is extensive and growing use of xray fluoroscopy, nondiagnostically, during placement of catheters and during surgical procedures. There is no doubt that dosage could be reduced many-fold during such procedures (Chapter 1, Box 3; Chapter 2, Part 3).

● Part 2. Differing Origins of the Two Hypotheses

How we happened to arrive at Hypothesis-1 is related in Chapter 2, Part 9. It deserves emphasis that Hypothesis-1 is not "Medical radiation can induce Cancer." Induction of Cancer in humans by ionizing radiation, including xrays, was proven long ago (Chapter 2, Part 4). The proof is so solid that it is accepted even by industries and professions which irradiate people.

Hypothesis-1 is that MEDICAL radiation causes a very LARGE part of the nation's cancer problem. This book was undertaken in order to test, modify, or discard Hypothesis-1. In the process, the work also provides a bonus: Some of the most powerful evidence ever assembled CONFIRMING that ionizing radiation is a potent cause of virtually all types of human cancer.

By contrast, ionizing radiation was NOT a proven cause of Ischemic Heart Disease when Hypothesis-2 came into existence. Hypothesis-2 "fell out of the data" which we assembled in order to test Hypothesis-1. This book presents the first powerful evidence that ionizing radiation IS a cause of Ischemic Heart Disease --- a very important cause.

● Part 3. Some Rather Dazzling Results to Examine

In approximately 50 years of biomedical research, we have rarely seen support for an hypothesis (Hypothesis-1), and indication for a new hypothesis (Hypothesis-2), "fall out of data" so strongly as they do in this monograph. Such events have to be taken seriously by objective analysts.

Even though the evidence is uncomplicated and the logic is straightforward, this book is long because we have the unusual policy of showing the steps which connect the raw data with the conclusions. For readers who want to know only the "bottom line," we provide an Abstract and Executive Summary (Chapter 1).

● Part 4. Why Our Findings Do Not Challenge the Importance of Other Causes of Cancer and IHD

Both Cancer and Ischemic Heart Disease are well established as multi-cause diseases. There is convincing evidence that several different causes increase the death-rate from Cancer, and likewise, that several different causes increase the death-rate from IHD. Moreover, it is safe to say that multiple causes generally (perhaps always) contribute to a SINGLE CASE of fatal IHD, and to a SINGLE CASE of fatal Cancer. The case would not occur when it does, without co-action by multiple causes.

The concept of NECESSARY co-actors is an old one. For instance, in the famous 1964 "Surgeon General's Report" on cigarette smoking as a cause of Lung Cancer, the authors wrote (p.31): "It is recognized that often the co-existence of several factors is required for the occurrence of a disease, and that one of the factors may play a dominant role; that is, without it, the other factors (such as genetic susceptibility) seldom lead to the occurrence of the disease."

The assumption, of more than one cause per case of Cancer, arises from various lines of evidence. For example, the rate of Breast Cancer is higher in women who inherit one mutated copy of a "Breast Cancer Gene" than in women without that inheritance, but that inheritance certainly does not guarantee the development of Breast Cancer in every breast-cell --- even though every breast-cell contains the mutation. One or more additional causes are necessary in order to turn even one of those breast-cells into a Cancer.

The concept, that more than ONE cause is necessary to produce a case of Cancer, is embraced by the widely accepted initiator-promoter model of Cancer. In that model, inherited or acquired carcinogenic mutations require help from a "promoter" --- for example, a hormone or infectious agent. The concept of mutually dependent co-actors is also inherent in the widely accepted multi-mutation multi-step models of carcinogenesis --- i.e., Cancer "is typically a multi-step process resulting from an accumulation of as many as 10 genetic changes in a single cell" (p.471 in Understanding Genetics: A Molecular Approach, Norman V. Rothwell; Wiley-Liss Publishers, 1993).

By definition, absence of a NECESSARY co-actor prevents the result. When two or more co-actors each have a required role, in producing a particular case of disease, then the absence of any ONE of them will prevent the case. We would regard such co-actors as equally important.

Thus, neither Hypothesis-1 nor Hypothesis-2 challenges the very important roles, already established, for various nonradiation causes of Cancer and IHD. When we propose that medical radiation is a highly important cause of Cancer and IHD mortality, we mean that in the ABSENCE of medical radiation, many or most of the cases would not have occurred when they did. While medical radiation has not been the ONLY factor contributing to such cases, we mean that it has been a NECESSARY co-actor in such cases. Discussion of co-action continues in Chapter 6, Part 6.

● Part 5. How to Reconcile High Fractional Causations by Xrays, Smoking, Diet

Fractional Causation refers to the fraction of the cancer mortality rate which would be absent (prevented) in the absence of a specified carcinogen --- which is medical radiation, in this monograph. Therefore, Fractional Causation is the fraction or percentage of the cancer mortality rate attributable to medical radiation --- or caused by medical radiation, in ordinary parlance.

A related term, widely in use, is "radiation-induced Cancer." The term is a brief and convenient way to refer to cancer cases which would have been absent in the absence of exposure to ionizing radiation. It does not mean that radiation is necessarily the ONLY cause contributing to cases of radiation-induced Cancer. Similarly, when people refer to "occupationally-induced Cancer," they do not mean that occupation is the ONLY cause contributing to such cases. They refer to cases which would have been absent in the absence of occupational exposure to carcinogens.

An Illustration of 100 Cancer Cases Resulting from Co-Action

Suppose that the evidence in this book indicates that Fractional Causation by medical radiation, of the national cancer death-rate, is 90% in a certain decade. Because of co-action, such a finding would NOT leave only 10% for all other causes combined --- as we will illustrate here with some hypothetical values. We will limit our illustration to only four carcinogens: Xrays, smoking,

poor diet, and particular inherited mutations. For brevity, we exclude other workplace, at-home, and environmental carcinogens. Then, we arbitrarily specify that the total cancer death-rate per year is 100 cases per 100,000 population and that these 100 cases are the result of co-action as follows. Our First List (illustrative):

- 40 cases by co-action of xrays + smoking + poor diet.
- 25 cases by co-action of xrays + poor diet + inherited mutations.
- 25 cases by co-action of xrays + smoking + inherited mutations.
- 10 cases by co-action of smoking + poor diet + inherited mutations.

The meaning of the first row, above, is that xrays, smoking, and poor diet each make a NECESSARY contribution to each case of Cancer in the first row. In the absence of any ONE of the necessary co-actors, the 40 cases in the first row could not occur. That is the meaning of "necessary." The meaning is similar for all four rows of hypothetical values.

A Second List, also adding up to 100 cases, would have very different implications if it were: 90 cases caused by xrays acting ALONE, 4 cases caused by a dietary factor acting alone, 3 cases caused by smoking acting alone, and 3 cases caused by an inherited mutation acting alone. In both lists, the sum of cases = 100 cases, but every case in the First List is the result of more than one cause per case, whereas every case in the Second List is the result of only one cause per case (no co-action in the Second List).

The Illustrative Fractional Causations by Xrays, Diet, Smoking, and Inherited Mutations

Out of the mixture of cases in the First List, we will explore how many cases could be prevented if we could remove just ONE cause, while the other causes remain as they were. Xrays are a required co-actor in (40 + 25 + 25), or 90 cases per 100 total cases. Because absence of a required co-actor prevents the result, 90% of the cancer death-rate would be absent, in the absence of exposure to medical radiation. Fractional Causation = 90% by medical radiation.

Next, we put radiation back into the mixture, and we remove just "poor diet." In our supposition, it is a required co-actor in (40 + 25 + 10), or 75 cases per 100 total cases. Because absence of a required co-actor prevents the result, 75% of the cancer death-rate would be absent, in the absence of poor diet in this illustration. Fractional Causation = 75% by poor diet. In our hypothetical illustration, Fractional Causation = 75% by smoking and 60% by inherited mutations. It is obvious that a HIGH Fractional Causation by xrays does not require a LOW Fractional Causation by any other cause of Cancer.

Because Fractional Causation means the fraction or percentage of the death-rate which would be absent (prevented) by the absence of a specified co-actor, ADDITION of the separate Fractional Causations produces nonsense (a total greater than 100%). Such addition would be equivalent to counting the same cases of absent Cancer more than once.

Our warning against adding Fractional Causations applies to a statement in the 1999 report of the National Research Council's sixth Committee on the Biological Effects of Ionizing Radiation (the BEIR-6 Report, from the National Academy Press, 1999). The BEIR-6 Committee, referring to evidence of co-action between smoking and exposure to radon (and radon's decay-products), states that "Some lung-cancer cases reflect the joint effect of the two agents and are in principle preventable by removing either agent" (BEIR-6, p.33). Although Fractional Causation of such cases is 100% by radon and 100% by smoking, addition of the two Fractional Causations would clearly count each prevented case twice.

Implications of Co-Action for Progress in Preventing Cancer and IHD

When more than one cause is REQUIRED per case of Cancer or Ischemic Heart Disease, it means that reducing exposure to a single necessary carcinogen or atherogen reduces the impact of all its partners. If one can identify a single agent which is a necessary co-actor in a high fraction of cases of Cancer and Ischemic Heart Disease, one can make real progress in preventing these diseases by reducing exposure to that cause. The evidence uncovered in this book strongly indicates that medical radiation is such an agent.

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